National Clinical Guideline Centre

Final

Major trauma: assessment and initial management

Major trauma: assessment and management of major trauma

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Appendices G-I

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Appendix G: Clinical evidence tables

G.1 Assessment and management of chest trauma

G.1.1 Pre-hospital chest imaging

Table 1: Press 2014[74]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Press 2014[74]	Prospective	293	Adult patients (>18 years) mainly blunt trauma (88.4%) with a mean ISS of 16 (SD 11). 34 HEMS providers volunteered for the study and 33 completed training	HEMS providers performing eFAST if time allowed during transfer after stabilisation. eFAST – portable ultrasound machines with phased-array cardiac probes were used for helicopter imaging (M-Turbo and P-21x	Predetermined order of modalities to determine the presence of injury once in hospital: CT (72.3%), operative/procedural findings, chest radiography (26%), and clinical evaluation during hospital stay (1.7%). Final attending	Unclear	**eFAST versus later CT, chest radiography and clinical evaluation for pneumothorax**		Grant support and funding sources received from Sonosite, Inc.	No information provided on blinding, time between eFAST and reference standard procedures and a range of reference standards employed.
							TP	8		
							FP	2		
							FN	35		
							TN	444		
							Sensitivity	0.19		
							Specificity	1.00		
							Positive predictive	0.80		
							Negative predictive	0.93		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			including a 1 day didactic and hands-on course, six weekly internet-based training modules, proctored scanning sessions in the ED, pocket flashcards, a review session and pre-, post- and remedial training for those that needed it.	transducer; Sonosite). Right lung and left lung views were performed. HEMS – a hospital based, accredited, critical care, air medical service operating within a 50-mile radius of a large urban medical centre.	radiologists reads were used for imaging reports. Receiving teams were blinded to HEMS eFAST, unless providers felt it essential to share critical information. CT imaging was performed at the discretion of the ED physician and trauma service, but trauma patients requiring hospital transport frequently received chest radiography and pan-CT (head, cervical spine, chest, abdomen and pelvis).		**eFAST versus later CT, chest radiography and clinical evaluation for pneumothorax requiring intervention (thoracostomy or thoracotomy)**			
							TP	9		
							FP	1		
							FN	10		
							TN	469		
							Sensitivity	0.47		
							Specificity	1.00		
							Positive predictive	0.90		
							Negative predictive	0.98		

G.2 Imaging assessment of chest trauma

Table 2: Abbasi 2013[1]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Abbasi 2013[1]	Prospective	146	Convenience sample of adults aged ≥16, admitted to ED with thoracic trauma. Exclusion: tension pneumothorax, subcutaneous emphysema, presence of 'sucking wounds' and haemodynamically unstable. 12.3% women; mean age 37 (14) years [range 16-92 years]; 82.2% had multiple traumas	Chest US, done on a Honda 2000 or Sonosite machine with 7.5MHz linear probes. Pneumothorax was considered present if there was no lung sliding AND no comet tail artefacts. This was carried out by four emergency physicians who had undergone a formal course in FAST exam and performed about 100 FAST exams each. They had received no prior training in thoracic US and undertook a 2 hour training course in utilising a 2 step diagnostic algorithm to diagnose	CT, examined by 2 radiologists blinded to US findings	Unclear but appears to be immediate	**US versus CT for pneumothorax**		No conflicts of interest	Adequately blinded
							TP	32		
							FN	5		
							FP	0		
							TN	109		
							Sensitivity	0.864 (0.704-0.949)		
							Specificity	1 (0.957-1)		
							Positive predictive	1 (0.866-1)		
							Negative predictive	0.956(0.895-0.983)		
							CXR versus CT for pneumothorax			
							TP	18		
							FN	19		
							FP	0		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
				pneumothorax with US. No blinding needed as US was always before CT. OR CXR in supine			TN	109		
							Sensitivity	0.486 (0.322-0.653)		
							Specificity	1 (0.957-1)		
							Negative predictive	100 (0.781-1))		
							Positive predictive	0.851 (0.895-0.983)		

Table 3: Abdulrahman 2015[2]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Abdulrahman 2015[2]	Single-blinded prospective observational study. Conducted in the setting of level 1 trauma centre in	305 adults in a trauma centre in Qatar	Adults with a median age of 34 (18-75) **Inclusion:** All adults admitted with blunt chest trauma (BCT) who underwent resuscitation and required further CT chest evaluation	1) EFAST, performed by eight trauma surgeons after hands on training prior to initiation of study that were blinded to results of CXR. 2) Chest radiograph (CXR) images reviewed by consultant trauma radiologist who was blinded to the	Chest CT scan images reviewed by consultant trauma radiologist who was blinded to the results of EFAST and clinical examination.	Timing not stated explicitly but following EFAST, all patients underwent CXR and chest CT	**EFAST/CT for predicting Pneumothorax**	95% CI included in brackets	None stated	The clinician performing EFAST and reporting CXR were both blinded. Immediately after documenting the EFAST and the clinical examination, the case report
							TP	32		
							FN	43		
							FP	10		
							TN	525		
							sensitivity	0.427 (0.313-0.546)		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
	Qatar		according to the ATLS guidelines. **Exclusion:** Patients in whom chest tube was inserted before CT chest examination, patients with penetrating chest trauma as well as cases with incomplete or inaccurate data were excluded from the study	results of EFAST and clinical examination.		scan	specificity	0.981(0.966-0.991)		form (CRF) was kept in a closed envelope to ensure blinding from the results of the CXR and the CT scan. No clear timings between the tests described, however following EFAST, all patients underwent CXR and chest CT scan
							+ve predictive value	0.762(0.606-0.87		
							-ve predictive value	0.924(0.89-0.945		
							CXR/CT for predicting Pneumothorax	95% CI included in brackets		
							TP	8		
							FN	67		
							FP	6		
							TN	529		
							sensitivity	0.107 (0.047-0.19)		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
							specificity	0.989 (0.977-0.996)		
							+ve predictive value	0.571(0.289-0.822		
							-ve predictive value	0.887 (0.86-0.91)		

Table 4: Alkadhi 2005[3]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Alkadhi 2005[3]	Unclear	60	26/60 were women; age 48 (17-67) years; Trauma patients with traffic accidents (29/60), falls (17/60), domestic (9/60) and occupational (5/60) accidents.	Bedside Chest X-ray in supine with ceiling mounted x ray (Siemens Mobilett XT) set up in the emergency room. Ideally done with the patient inspiring. Unclear whom the operator was.	Multidetector row CT. 16 channel MDCT scanner (Sensation 16, Siemens). Ideally done with the patient inspiring with arms raised. The gold standard diagnosis used the MDCT	Within 1 hour	**Chest X-ray versus MDCT for pneumothorax**		There is a reference to support from two non-commercial bodies, but also one called' Computer aided'. Unclear if this is a	Insufficient information to extract raw data. Blinding unclear
							Sensitivity	0.6		
							Specificity	1.0		
							Positive predictive	1.0		
							Negative predictive	0.91		
							Chest X-ray versus MDCT for haemothorax/			

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
					results interpreted by an experienced radiologist as well as all other images, including clinical data.		**pleural effusion**		commercial body.	
							Sensitivity	0.7		
							Specificity	0.87		
							Positive predictive	0.77		
							Negative predictive	0.9		

Table 5: Barrios 2010[5]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Barrios 2010[5]	Retrospective	374	Patients with trauma at a level 1 trauma centre. Inclusion: received CXR, thoracic CT and abdominal CT scan. 73% male; mean age 34 years; 91% blunt trauma; 98% survival rate.	Chest X-ray. Interpreted by an attending radiologist.	Thoracic/abdominal CT scan. Interpreted by an attending radiologist.	Not clear	**CXR versus CT for pneumothorax**		Not reported	No blinding reported. No useful raw data provided. Only sensitivities able to be extracted.
							Sensitivity	0.44		
							CXR versus CT for pulmonary contusions			
							Sensitivity	0.44		
							CXR versus CT for haemothorax			
							Sensitivity	0.29		
							CXR versus CT for aortic injury			
							Sensitivity	0		

Table 6: Biquet 1996[7]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Biquet 1996[7]	Unclear-probably retrospective	28	Consecutive patients (1987-1993) who were haemodynamically stable or rapidly stabilised after resuscitation; 21/28 men; age 19-75 years with a mean of 43 years; all had sustained blunt trauma after rapid deceleration (28 in MVA and 1 in fall). 7 intubated at admission. All had a suspicious X-ray – thoracic mediastinal index >0.3)	CT with a Somatrom DRH (Siemens) – a frontal digitised radiograph of the thorax was obtained. A contrast agent was also given. 8-mm thick slices obtained at 1 com intervals. CT images viewed by a staff chest and vascular radiologist.	Arterial digital subtraction arteriography and/or surgery findings or MRI or later clinical findings. Person examining the arteriograms not described.	Not described	**CT versus arteriography /surgery for thoracic aortic rupture**		None reported.	No blinding reported. Raw data, and diagnostic data needed to be extrapolated from the paper as not clearly reported.
							TP	12		
							FN	1		
							FP	0		
							TN	15		
							Sensitivity	0.92		
							Specificity	1		
							Positive predictive	1		
							Negative predictive	0.9375		

Table 7: <Insert Table Title here>

Table 8: Blaivas 2005[8]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Blaivas 2005[8]	Prospective single blinded study.	176. no exclusions	76% female. 12 patients had chest tube inserted after US/CXR but before CT. Inclusion criteria: blunt trauma patients aged>17; Received all 3 types of scan. Chest tubes were not an exclusion criterion. Exclusion: examination could not be completed with the 3 devices for any reason.	Focussed assessment with sonography for trauma (US) using Sonosite 180+ with a 4-2MHz transducer. Protocol views consisted of 4 locations of each hemithorax to assess for the presence of a sliding lung sign. Power Doppler was used to enhance diagnostic accuracy. This was carried out by 5 experienced and trained physicians. They were blinded to X-ray and CT findings, as well as any relevant clinical findings. AND Portable supine chest X-ray,	CT, using multigated scanner, with 5 mm slices. Radiologist blinded to US results	CXR immediately after US, but timing of CT unclear.	**US versus CT for pneumothorax**	With 95% CIs in brackets			Blinding between US and CT but not clear if there was blinding between CXR and CT. Timing of reference standard unclear.
							TP	52		
							FN	1		
							FP	1		
							TN	122		
							Sensitivity	0.981 (0.899 - 0.999)		
							Specificity	0.992 (0.956 - 0.999)		
							Positive predictive	0.981 (0.893 - 0.999)		
							Negative predictive	0.992 (0.956 - 0.999)		
							X-ray versus CT for pneumothorax	With 95% CIs in brackets		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
				interpreted by a radiologist blinded to US results			TP	40		
							FN	13		
							FP	0		
							TN	123		
							Sensitivity	0.755 (0.617 - 0.862)		
							Specificity	1 (0.971 -1)		
							Positive predictive	1 (0.912 -1)		
							Negative predictive	0.904 (0.842 - 0.948)		

Table 9: Blasinska-Przerwa 2013[9]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Blasinska-Przerwa 2013[9]	Retrospective	30	Inclusion: patients with chest trauma; haemostatic stability; both MDCT and CXR	CXR – no details of operators, device or procedures.	Multidetector CT (MDCT), using a 16-MDCT scanner. Non-ionic iodine contrast	48 hours maximum	**CXR versus MDCT for pneumothorax**		None reported. No conflicts of interest	No blinding reported.
							Sensitivity	0.579		
							Specificity	1.00		
							CXR versus			

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			data Exclusion; urgent surgical intervention.		medium was used for all. Assessed in pulmonary, mediastinal and bone windows in 3 planes. Detection of several injuries were sought. No details of operators.		**MDCT for haemothorax**			
							Sensitivity	0.583		
							Specificity	1.0		
							CXR versus MDCT for lung contusion			
							Sensitivity	0.727		
							Specificity	1.0		

Table 10: Brook 2009[13]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Brook 2009[13]	Prospective	169 (thus 338 lung fields)	Age range 6 months - 88 years (mean 31 years; as no age sub-grouping this sample should be taken as an adult sample). Inclusion: consecutive patients with	Extended FAST performed by 5 residents in radiology with at least 6 months of dedicated US training, plus 2 attending radiologists. All were given prior training on detection of pneumothoraces on US, including	Chest CT was performed with an MX 8000 IDT or MX 8000 multislice helical system after administration of non-ionic iodinated contrast medium. 3mm slices	2 hours between all	**US versus CT for pneumothorax**		Not reported	The inclusion criterion was people scanned with all 3 devices 'when clinically indicated' (rather than because they were being
							TP	20		
							FN	23		
							FP	3		
							TN	292		
							Sensitivity	0.465 (0.325 -0.61)		
							Specificity	0.99 (0.971 -		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			trauma treated at the trauma room in the emergency department who underwent chest X-ray, eFAST and chest CT when clinically indicated within 2 hours of admission. Exclusion: patients with known pneumothoraces or previous chest tube insertion.	lectures and practical sessions. Diagnosis was made in real-time. The scanning was carried out with an SSD-1400 system (Aloka) with 3.5MHz transducer, with the focus level to the pleura. The scans were performed at 2 sites on each lung field – 2nd-4th intercostal spaces at the midclavicular line and 6th -8th spaces in the midaxillary line. Absence of comet tail artefacts and pleural sliding were diagnostic. Unclear if performed in supine. OR	obtained. Unclear if supine.			0.997)		included in a diagnostic accuracy study). These may therefore be a special set of people, perhaps those with inconclusive US/CXR findings. This would tend to reduce sensitivity. EFAST performed blind from chest X-ray and CT. Unclear if X-ray and CT blinded. Included children – with no sub-grouping, although
							Positive predictive	0.869 (0.679 - 0.955)		
							Negative predictive	0.926 (0.893 - 0.951)		
							X-ray versus CT for pneumothorax			
							TP	7		
							FN	36		
							FP	0		
							TN	295		
							Sensitivity	0.163 (0.081 - 0.298)		
							Specificity	1 (0.987 -1)		
							Positive predictive	1 (0.646 -1)		
							Negative predictive	0.893 (0.856 - 0.922)		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
				Chest X-ray in supine , with Mobilette Plus Portable radiography system (Siemens).			Note: When sub-grouping by pneumothorax size, the sensitivity improved with larger (and more clinically relevant pneumothoraces). For moderate pneumothoraces, sensitivity was 100% for eFAST and 56% for CXR.			diagnostic accuracy likely to differ across ages.

Table 11: Bruckner 2006[15]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Bruckner 2006[15]	Retrospective	856 had CXR and gold standard; 206 had CT and gold standard.	Patients with widened mediastinum on CXR or suspicious mechanism of injury.	CT, using either a General Electric single-slice spiral CT scanner, or a high-speed multislice scanner (Somatom Sensation 16 slice). Contrast material was used. 3-5mm thickness of images. The review was	Aortogram – common femoral artery cannulated and after injection of non-ionic contrast, the images were examined in AP, left anterior oblique and steep right anterior oblique-right	Unclear	**CT versus gold standard for aortic injury using DIRECT SIGNS**		Not reported	No mention of blinding Use of index tests to contribute to gold standard diagnosis will have artificially increased accuracy.
							TP	19		
							FN	1		
							FP	112		
							TN	74		
							Sensitivity	0.95		
							Specificity	0.4		
							Positive predictive	0.15		
							Negative	0.99		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
				carried out by the most senior radiologist and surgeon. Direct signs of aortic injury were: vessel lumen-filling defects, contour abnormality, false aneurysm or extravasation of contrast. These were only sought in the proximal ascending aorta. OR CXR	lateral projections. To reach the final gold standard diagnosis, the CXR and/or CXR were also used.		predictive			
							CXR versus gold standard for aortic injury			
							TP	28		
							FN	3		
							FP	511		
							TN	314		
							Sensitivity	0.9		
							Specificity	0.38		
							Positive predictive	0.05		
							Negative predictive	0.99		

Table 12: Chardoli 2013[17]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Chardoli 2013[17]	Prospective	200	Haemodynamically stable patients of at	Chest X-ray in PA view (0.02 mSv) or lateral	Chest CT done without contrast using	No reported	**CXR versus CT for haemothorax**		Not reported	No blinding reported

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			least 16 years with blunt chest trauma. Exclusion: pregnancy, haemodynamically unstable patients. 84% male; All had thoracic wall tenderness and only one had respiratory distress in physical examination	view (0.04 mSv)	Toshiba Asteion dual detector device		Sensitivity **CXR versus CT for pulmonary contusion** Sensitivity **CXR versus CT for pneumothorax** Sensitivity	0.2* 0 0		*only raw data given was that 3 had a positive CXR and 14 had a positive CT scan. Because we don't know how many of the 3 positive X-ray findings were false positives, we cannot use this to determine sensitivity. It is assumed the authors of the paper had information on the number of false positives at hand to calculate the

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
										sensitivity as 0.2

Table 13: Cook 2001[18]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Cook 2001[18]	Retrospective	188	Consecutive patients with blunt trauma, with suspected aortic laceration undergoing portable chest radiography and aortography/ CT/ emergent thoracotomy.	Portable Chest X-ray. Radiographs given a binary rating on 15 different criteria by a single fellowship-trained thoracic radiologist who was unaware of the patient's final diagnosis. These 15 criteria were: mediastinum >8 cm; M:C ratio >0.25; opacified AP window; irregular aortic knob; blurred aortic contour; nasogastric tube deviation; trachea shifted to R; pulmonary contusion; wide	Aortography/ CT/emergent thoracotomy. No details of examiner expertise given	Unclear	**MEDIASTINUM >8 cm X-ray sign versus aortograms for aortic injury**		Not reported	Blinding of X-ray examiner but unclear if gold standard reading was blinded.
							TP	9		
							FN	1		
							FP	126		
							TN	54		
							Sensitivity	0.9 (0.67-1)		
							Specificity	0.3 (0.24-0.37)		
							Positive predictive	0.066		
							Negative predictive	0.982		
							M:C ratio>0.25 X-ray sign versus aortograms for			

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
				left paraspinal line; left apical cap; any other rib fracture; thoracic spinal fracture; depressed left main bronchus; first rib fracture; clavicle fracture. Only the signs in the top 5 for sensitivity are given in the outcomes column, along with two sets of combinations of some of these signs. This is for brevity and also because the sensitivities of other signs were so low as to be diagnostically irrelevant.			**aortic injury**			
							TP	9		
							FN	1		
							FP	157		
							TN	10		
							Sensitivity	0.9 (0.67-1)		
							Specificity	0.06 (0.03-0.1)		
							Positive predictive	0.054		
							Negative predictive	0.909		
							Opacified AP window X-ray sign versus aortograms for aortic injury			
							TP	9		
							FN	1		
							FP	82		
							TN	85		
							Sensitivity	0.9(0.67-1)		
							Specificity	0.51(0.43-0.58)		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
							Positive predictive	0.099		
							Negative predictive	0.988		
							Irregular aortic knob X-ray sign versus aortograms for aortic injury			
							TP	8		
							FN	2		
							FP	34		
							TN	73		
							Sensitivity	0.8 (0.33-1)		
							Specificity	0.68 (0.58-0.77)		
							Positive predictive	0.190		
							Negative predictive	0.973		
							Blurred aortic contour X-ray sign versus aortograms for aortic injury			
							TP	7		
							FN	3		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
							FP	82		
							TN	92		
							Sensitivity	0.7(0.38-1)		
							Specificity	0.53(0.46-0.61)		
							Positive predictive	0.078		
							Negative predictive	0.968		
							Combined X-ray sign (either mediastinal width>0.8 OR wide paraspinal line) versus aortograms for aortic injury			
							Sensitivity	1		
							Specificity	0.28		
							Combined X-ray sign (either mediastinal width>0.8 OR MC ratio >0.25 OR opacified aortopulmonary window)			

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
							versus aortograms for aortic injury			
							Sensitivity	1.0		
							Specificity	0.05		
							Combined X-ray sign (either mediastinal width>0.8 OR MC ratio >0.25) versus aortograms for aortic injury			
							Sensitivity	0.9		
							Specificity	0.06		

Table 14: Donmez 2012[26]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Donmez 2012[26]	Prospective	68 (each had both hemithoraces examined so the effective number was 138)	31 trauma patients with unilateral and 2 with bilateral pneumothoraces. Inclusion: Patients with multiple trauma	Thoracic US done with a NEMIO scanner and a 5 MHz linear probe in supine done by one of 2 radiologists. Pleural surfaces were scanned at	Chest CT. Expert not defined. Mediastinal, bine and parenchymal settings used.	CXR within 3 hours of US. Time between CT and other two not reported	**US versus CT for pneumothorax**		Not reported	US/CT blinding carried out (but only reported in abstract). US/CXR blinding carried out.
							TP	32		
							FN	3		
							FP	3		
							TN	98		
							Sensitivity	0.914		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			undergoing thoracic US, Chest X-rays and chest CT Exclusion: insertion of a chest tube prior to US	the midaxillary line from the 4th -8th intercostal spaces and at midclavicular line from 2nd-5th intercostal spaces. The absence of both comet tail artefacts and lung sliding were needed for a diagnosis. OR Supine chest X-ray by a different radiologist. Etched diaphragm sign, etched mediastinum sign, deep sulcus sign, visible visceral pleura and hyperlucent hemithorax sign were sought.		.	Specificity	0.97		Poor reporting of methodology – for example, never explained that CT was the reference test.
						Positive predictive	0.914		
						Negative predictive	0.97		
						X-ray versus CT for pneumothorax			
						TP	24		
						FN	5		
						FP	11		
						TN	96		
						Sensitivity	0.827		
						Specificity	0.897		
						Positive predictive	0.685		
						Negative predictive	0.95		

Table 15: Durham 1994[27]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Durham 1994[27]	prospective	155	Patients with suspected blunt aortic injury who had both index and reference tests. Suspicion of aortic injury based on mechanism of injury (as in sudden deceleration or direct impact, falls greater than 20 feet, pedestrian collisions with vehicles at >20mph) and/or CXR findings (that is, mediastinal widening) and clinical signs (that is, precordial systolic murmur). Exclusion: patients requiring resuscitation Majority had a MVA (129), MCA	CT done on a GE 9800 scanner or (n=2) GE Hi-Lite Advantage helical scanner or 9n=3) a Siemens Somatron Dynamic scanner. Contrast material was used. Each scan reviewed retrospectively by 4 attending radiologists unaware of patient's clinical course and angiographic findings and those of the other radiologists. These were all experienced in the interpretation of chest CT in trauma. A scan was considered diagnostic for aortic injury if any of the following were present:	Biplane thoracic aortography with contrast material injected. Unclear expertise of examiners.	Approximately 2 hours	**CT versus aortograms for aortic injury radiologist 1**				Blinding of radiologists doing CT, but unclear if aortogram interpretations were blinded?
							TP	8		
							FN	0		
							FP	83		
							TN	59		
							Sensitivity	1		
							Specificity	0.42		
							Positive predictive	0.09		
							Negative predictive	1		
							CT versus aortograms for aortic injury radiologist 2			
							TP	7		
							FN	1		
							FP	41		
							TN	101		
							Sensitivity	0.88		
							Specificity	0.71		
							Positive predictive	0.26		
							Negative predictive	0.73		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			(15), motor-pedestrian accident (4) or fall (4).	ascending/descending aorta size discrepancy; false lumen; thickening of aortic wall; irregularity of aortic wall; intraluminal lucency; periaortic hematoma; dilatation of the aorta at the L subclavian artery; focal hematoma not adjacent to the aorta; diffuse mediastinal hematoma; aortic diameter >5 cm.			**CT versus aortograms for aortic injury radiologist 3**			
							TP	7		
							FN	1		
							FP	105		
							TN	37		
							Sensitivity	0.88		
							Specificity	0.26		
							Positive predictive	0.6		
							Negative predictive	0.97		
							CT versus aortograms for aortic injury radiologist 4			
							TP	5		
							FN	3		
							FP	38		
							TN	104		
							Sensitivity	0.63		
							Specificity	0.73		
							Positive predictive	0.12		
							Negative predictive	0.97		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
							CT versus aortograms for aortic injury average across the 4 radiologists			
							Sensitivity	0.85		
							Specificity	0.53		
							Positive predictive	0.11		
							Negative predictive	0.98		

Table 16: Dyer 1999[30]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Dyer 1999[30]	Probably prospective	382	Patients with blunt chest trauma and possible aortic injury at two Level I trauma centres, that were examined with CT first and then aortography.	CT performed with conventional GE9800 scanners (GE Medical Systems) or helical CT HiSpeed Advantage (GE Medical Systems) scanners. Ionic or non-ionic contrasts were injected IV. The interpretation of scans was always confirmed by an	Aortography performed using a standard intra-arterial digital subtraction technique. Contrast material injected and images obtained in the right	Not reported	**CT versus aortography for aortic injury**		None reported	No blinding reported.
							TP	10		
							FN	0		
							FP	15		
							TN	357		
							Sensitivity	1.0 (0.69-1)		
							Specificity	0.96 (0.93-		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
				attending radiologist (initial after-hours interpretation was done by a resident trained in CT for aortic injury). CT scans were regarded as diagnostic if any of the following were present: change in aortic calibre, intraluminal irregularity, and abnormal contours of the aorta or great vessels. are considered direct signs.	anterior oblique and left anterior oblique projections. Not described who did the interpretation.			0.98)		
							Positive predictive	0.4(0.21-0.61)		
							Negative predictive	1(0.99-1)		

Table 17: Fishman 1999[32]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Fishman 1999[32]	Retrospective	40	Patients at a 1600 bed level I trauma centre referred with a	Helical CT done on a HiSpeed Advantage GE Medical Systems scanner, with 5mm	Unclearly reported. Appears to be aortograph	Not clear	**CT versus gold standard for aortic injury using sign of MEDIASTINAL**		Not reported	Blinding unclear

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			clinical indication of blunt chest trauma undergoing chest CT.	slices. Mediastinal hematoma, periaortic hematoma and direct signs of aortic injury were sought. The examiner was an attending emergency radiologist, emergency radiology fellow or senior radiology resident	y for most, operative findings and autopsy		**HEMATOMA for observer 1**			
							TP	17		
							FN	0		
							FP	12		
							TN	16		
							Sensitivity	1.000		
							Specificity	0.571		
							Positive predictive	0.586		
							Negative predictive	1.000		
							CT versus gold standard for aortic injury using sign of MEDIASTINAL HEMATOMA for observer 2			
							TP	16		
							FN	1		
							FP	12		
							TN	16		
							Sensitivity	0.941		
							Specificity	0.571		
							Positive predictive	0.571		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
							Negative predictive	0.941		
							CT versus gold standard for aortic injury using sign of MEDIASTINAL HEMATOMA for observer 3			
							TP	13		
							FN	3		
							FP	7		
							TN	21		
							Sensitivity	0.813		
							Specificity	0.750		
							Positive predictive	0.650		
							Negative predictive	0.875		
							CT versus gold standard for aortic injury using sign of PERIAORTIC HEMATOMA for observer 1			
							TP	16		
							FN	1		
							FP	3		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
							TN	25		
							Sensitivity	0.941		
							Specificity	0.893		
							Positive predictive	0.842		
							Negative predictive	0.962		
							CT versus gold standard for aortic injury using sign of PERIAORTIC HEMATOMA for observer 2			
							TP	15		
							FN	2		
							FP	3		
							TN	25		
							Sensitivity	0.882		
							Specificity	0.893		
							Positive predictive	0.833		
							Negative predictive	0.926		
							CT versus gold standard for aortic injury using sign of			

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
							PERIAORTIC HEMATOMA for observer 3			
							TP	11		
							FN	5		
							FP	4		
							TN	24		
							Sensitivity	0.688		
							Specificity	0.857		
							Positive predictive	0.733		
							Negative predictive	0.828		
							CT versus gold standard for aortic injury using DIRECT SIGNS for observer 1			
							TP	17		
							FN	0		
							FP	0		
							TN	28		
							Sensitivity	1.000		
							Specificity	1.000		
							Positive predictive	1.000		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
							Negative predictive	1.000		
							CT versus gold standard for aortic injury using DIRECT SIGNS for observer 2			
							TP	17		
							FN	0		
							FP	0		
							TN	28		
							Sensitivity	1.000		
							Specificity	1.000		
							Positive predictive	1.000		
							Negative predictive	1.000		
							CT versus gold standard for aortic injury using DIRECT SIGNS for observer 3			
							TP	14		
							FN	2		
							FP	0		
							TN	28		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
							Sensitivity	0.875		
							Specificity	1.000		
							Positive predictive	1.000		
							Negative predictive	0.933		

Table 18: Gavant 1995[38]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Gavant 1995[38]	Prospective	127	Patients experiencing non-trivial blunt chest trauma. 68% male; mean age 40 (range 14-89) years. 30% of all were stable.	CT done with a HI Speed Advantage helical scanner (GE Medical system) with a contrast agent. Scans were done by certified technologists and supervised by radiology residents, fellows and staff, and interpreted by experienced board-certified radiologists blinded to findings at surgery	Surgical or clinical outcome	Not reported	**CT versus gold standard for aortic injury**		Not reported	Blinding of surgery and aortography findings from CT examiners. Very poor reporting of results.
							Sensitivity	1		
							Specificity	0.817		
							Positive predictive	0.474		
							Negative predictive	1		
							TP	18		
							FN	0		
							FP	20		
							TN	89		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
				(aortography also tested but outside the scope of this review).						

Table 19: Holmes 2001B

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Holmes et al. prevalence and importance of pneumothoraces visualised on abdominal computed tomographic scan in children with blunt trauma. The journal of trauma, infection and critical care 2001; 50: 516-520	Prospective	538	Children aged <16 undergoing abdominal CT scan for the evaluation of possible intra-abdominal injury and plain chest radiography.	AP Chest X-rays in supine during maximal inspiration if possible. No mention of blinding from CT results. Expertise of the examiner interpreting the CXRs not stated, but a random selection were subjected to quality control review by a blinded faculty radiologist (not the one doing the CT scans)	Abdominal CT scanning done with a Toshiba-900 CT scanner or a helical CTi. CTs were interpreted by a faculty radiologist blinded to CXR findings.	Unclear	**CXR versus abdominal CT for pneumothorax**			Abdominal CTs would pick up pneumothoraces as well, but possible that apical ones would be missed? This could thus possibly exaggerate sensitivity of CXR. Although known that 518 had no CT findings, no information on how
							TP	9		
							FN	11		
							Sensitivity	0.45		
							FP+TN	518		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
										many of these were false positives and how many were true negatives – hence no specificity, or positive /negative predictive findings were calculable

Table 20: Hyacinthe 2012[47]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Hyacinthe 2012[47]	Prospective	119	82% male; age 39 (22-51) years; GCS 14(7-15); ISS 17(9-29); 95% of trauma due to RTA, falls or sports; 5/119 had penetrating	Thoracic US given with Envisor C (Philips) and abdominal 5-2 MHz probe by one of 3 trained operators, each with at least 50 thoracic US experiences and	Thoracic CT scans in supine with Somatom Sensation 16 (Siemens). Independent radiologist	90 minutes maximum	**US versus CT for pneumothorax**		None received.	Blinding carried out for both index tests. TNs and FPs not given in paper but extracted from other
							TP	28		
							FN	25		
							FP	9		
							TN	175		
							Sensitivity	0.53		
							Specificity	0.95		
							Positive	0.53		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			thoracic trauma; admitted to ED within 2.5 hours of trauma; 9 later died; 17 required thoracic decompressio n using chest tubes. Inclusion: patients attending an emergency department who had indication for a thoracic CT scan within 6 hours of their original trauma; US had to be given within 90 minutes of the CT. Exclusion: None specified.	blinded to CXR. Not blinded to CT, but CT was always done after US. Pneumothorax, haemothorax and lung contusion were sought. The upper, middle and lower parts of the anterior and lateral regions of the 2 chest walls were sequentially examined with the patient in supine. Absence of lung sliding, A lines and lung point were diagnostic of pneumothorax. Lung contusion was suggested by 1) irregularly shaped image with hypoechoic blurred lesions with no change during respiration, or hyperechoic punctiform images, 2) multiple B lines.	interpreted results blinded from index test results. Also, in patients with a chest tube, gold standard diagnosis of pneumoth orax or haemothor ax was made if bubbles or blood were seen to emerge.		predictive			data given (that is, total scans, true diagnoses, FNs, sensitivity and specificity). this allowed positive and negative predictive values to be calculated.
							Negative predictive	0.95		
							US versus CT for haemothorax			
							TP	13		
							FN	22		
							FP	8		
							TN	194		
							Sensitivity	0.37		
							Specificity	0.96		
							Positive predictive	0.37		
							Negative predictive	0.96		
							US versus CT for lung contusion			
							TP	90		
							FN	57		
							FP	18		
							TN	71		
							Sensitivity	0.61		
							Specificity	0.80		
							Positive predictive	0.61		
							Negative predictive	0.80		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
				Haemothorax was defined by the sinusoid sign. The operator recorded diagnoses on a probability scale of 0-3. Scores of 2 and 3(suspicion and 'sure') were taken as a definitive diagnosis. OR Chest X-ray in supine, along with clinical examination by a 'physician'. This is not included in this review as the combination assessment is not on the protocol.						

Table 21: McLean 1991[58]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
McLean	Retrospecti	17	All patients	Chest CT (no more	Aortography	Not	**CT versus**		Not	No blinding

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
1991[58]	ve		undergoing aortography to evaluate the aorta for traumatic aortic rupture. All had CT and aortography. Mean age 34.9 (18.4) years, 64.8% male; MVA 88.2%, fall 11.8%.	details given)	(no more details given)	reported	**aortography for aortic injury**		reported	reported. Incorrect diagnostic accuracy results calculated (but raw data has been used for recalculation).
							TP	3		
							FN	2		
							FP	2		
							TN	10		
							Sensitivity	0.600		
							Specificity	0.833		
							Positive predictive	0.600		
							Negative predictive	0.833		

Table 22: Miller 1989[59]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Miller 1989[59]	Prospective	104	Patients with blunt trauma with a mechanism of injury consistent with a major force transmission sufficient to cause aortic	Chest CT with a Philips Tomoscan 60 TX machine, with contrast medium injected. Scan was from the sternal notch to below the carina, with 10mm slices. The scan was considered	Angiography, done by a transfemoral approach using the Seldinger technique. No mention of examiner used.	Described as 'little delay'	**CT versus angiography for aortic injury**		Not reported	No blinding reported The paper reported findings with 3 CT results – positive, equivocal and negative.
							TP	6		
							FN	5		
							FP	31		
							TN	62		
							Sensitivity	0.545		
							Specificity	0.667		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			injury AND an X-ray sign suggestive of arterial injury (for example, mediastinum > 8 cm; blurring or loss of the aorticopulmonary window) AND stable enough to have CT imaging. 131/153 were men; Mean age 41 (range 16-88) years. Mean ISS was 21	positive if it showed a false aneurysm, lucency within the aortic wall, irregularity of the aortic lumen, periaortic or intramural aortic hematoma or dissection. No mention of the examiner's expertise			Positive predictive	0.162		The equivocal CT findings have been converted into positive findings for the purposes of this review (on the basis that clinically this would almost certainly be the approach given the catastrophic consequences of a false negative).
							Negative predictive	0.925		

Table 23: Mirvis 1998[60]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Mirvis 1998[60]	Prospective	1104	All blunt trauma patients with	Contrast-enhanced spiral thoracic computed	Aortography, surgery or clinical status	Not reported	**CT versus aortograms for aortic injury**		None reported	Blinding not reported

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			abnormal mediastinal contours on admission chest radiographs, who had CEST-CT.	tomography (CEST-CT) using a Siemens Somatrom Plus 4 scanner. Scanning was from the thoracic inlet to the upper abdomen. Diagnostic findings were any one of: pseudoaneurysm formation, intimal flaps, other aortic contour abnormalities, intraluminal thrombus and pseudocoarctation. Expertise of examiners not reported	at discharge		TP	25		
							FN	0		
							FP	3		
							TN	1076		
							Sensitivity	1		
							Specificity	0.997		
							Positive predictive	0.89		
							Negative predictive	1		

Table 24: Nandipati 2011[64]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Nandipati 2011[64]	Prospective	204	25.5% female; Age: 43.0 (19.5) years; of 21 with	EFAST examination carried out by senior resident (level V) or	CT scan. No details of operators or blinding.	Not reported	**FAST versus CT for pneumothorax**		None. No conflicts of interest	Blinding unclear
							TP	20		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			pneumothorax, 12 due to blunt trauma. Most blunt trauma was due to MVC (53.8%), falls (24.4%), and assault (15.4%). Patients at a community based level 1 trauma centre, with polytrauma, blunt and penetrating trauma to the chest or thoracoabdominal area. Exclusion: chest tube placement without sonogram or CXR; abdominal or extremity	attending on trauma team, familiar with the principles of the FAST exam, who had attended a formal US course. These sonographers had additional instruction (with video demonstration) on the principles of thoracic US , and were instructed on the absence of comet tail artefacts and sliding pleura as diagnostic criteria for pneumothorax. The portable US device was a 7.5MHz linear probe. Patients were in supine and an examination of anterior thorax was performed with the probe			FN	1		
							FP	1		
							TN	182		
							Sensitivity	0.95		
							Specificity	0.99		
							Positive predictive	0.95		
							Negative predictive	0.99		
							X-ray versus CT for pneumothorax			
							TP	15		
							FN	4		
							FP	1		
							TN	184		
							Sensitivity	0.79		
							Specificity	0.99		
							Positive predictive	0.94		
							Negative predictive	0.98		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			injuries.	placed in the second intercostal space in the midclavicular line. Bilateral US images were obtained and compared, and absence of both lung sliding and comet tail artefact were diagnostic. OR Chest X-ray. No details of operators or blinding.						

Table 25: Ng 2006[68]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Ng 2006[68]	Unclear, but likely to be prospective (as blinding occurred).	53	39/53 men; mean age 35 (range 14-65) years. Patients with significant	Helical CT scan of thorax (HCTT) using HiSpeed Advantage scanner (General Electric Medical system). Scanned with 5mm	Surgical findings if the patient underwent surgery, or on aortography	Not reported	**CT versus arteriography/ surgery for aortic injury**		None reported	Consensus on findings between 2 CT examiners may not mimic
							TP	22		
							FN	0		
							FP	3		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			injury mechanism suggesting deceleration injury and chest radiographic findings of possible mediastinal hematoma. Even if there were no suspicious X-ray findings, clinical suspicion was also an inclusion criterion.	cuts from thoracic inlet to upper abdomen. Iodine based contrast bolus injected. Direct signs of aortic injury were an intimal flap, an irregular aortic contour, a luminal thrombus and periaortic contrast material extravasation. Any ONE of these was regarded as diagnostic. Examined by 2 experienced radiologists, blinded to reference test results, but aware of trauma history. They came to a consensus decision	results if no surgery.		TN	28		clinical practice – so external validity may be reduced. Blinding to reference test results.
							Sensitivity	1.0		
							Specificity	0.903		
							Positive predictive	0.88		
							Negative predictive	1.0		

Table 26: Parker 2001[71]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Parker 2001[71]	prospective	142	Patients with blunt trauma and potential thoracic trauma on X-ray; needed to have bot CT and aortography.	CT scanning on the PQ 6000 (Picker international), with contrast medium injected. Direct diagnostic signs were pseudoaneurysm, intimal flap, pseudocoarctation, dissection and contrast material extravasation. CT exams monitored by one of 4 staff radiologists trained in either thoracic imaging or trauma radiology. Reviewing of images was done immediately by at least 2 of these radiologists. No blinding required as CT always before aortography	Aortography, using right and left anterior oblique projections. Later in the study, rotational aortographic techniques were used. Interpreted by trained and experienced interventional radiologists blinded to Ct results	Aortography was always immediately after CT	**CT versus aortography for aortic injury**		None reported	Blinding rigorous The gold standard was poorly described.
							TP	7		
							FN	0		
							FP	14		
							TN	121		
							Sensitivity	1.0		
							Specificity	0.896		
							Positive predictive	0.333		
							Negative predictive	1.0		

Table 27: Raptopoulos 1992[75]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Raptopoulos 1992[75]	Unclear	127	Patients with decelerating blunt injury to the trunk, most commonly due to a MVC or falls. All had an abnormal chest X-ray and all had Chest CT scans.	Chest CT done with CT/T 9800 scanners or CT/T 9800 Quick scanners (both GE Medical Systems) and contrast material. Diagnostic features were an intraluminal flap and mediastinal bleeding.	Aortography (n=111) or clinical judgement in terms of the absence of later (4 months) complications relating to aortic injury (n=16)	Not clear	**CT versus aortograms for aortic injury**		Not reported	No blinding reported
							TP	8		
							FN	0		
							FP	31		
							TN	88		
							Sensitivity	1		
							Specificity	0.693		
							Positive predictive	0.205		
							Negative predictive	1		

Table 28: Rocco 2008[77]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Rocco 2008[77]	Prospective	15	Trauma patients admitted to the intensive care unit at a level I emergency and trauma hospital with	Lung US evaluation using an Aloka SSD 1700 and a convex 9 cm probe. Pulmonary contusion was defined as a moderately hypoechoic	Chest CT scan. Done using the 16 Multidetector CT scanner. No mention of blinding to US/CXR. Expertise of	Maximum of 1 hour	**US versus CT for lung contusion***		None reported	*Based on 180 lung areas in 15 patients. Raw data not provided in paper. No reporting
							Sensitivity	0.89 (0.8-0.95)		
							Specificity	0.89 (0.82-0.95)		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			acute respiratory failure. Inclusion: whole body CT scan confirming thoracic trauma; age ≥18 years. Exclusion: 2nd scan at 48 hours regarded as 'futile'. Age 42 (14) years; 67% male; GCS 7 (3); ISS 38(34-45)	blurred lesion with indistinct margins whose dimensions remained unchanged during the inspiration phase. Internal hyperechoic punctiform images, representing air bronchograms, could be present as multiple vertical hyperechogenic lines arising from a perpendicular to the pleural surface (A lines) representing the involvement of the interstitial space. No mention of blinding to CT findings. Expertise of scanning personnel not reported. OR Chest X-ray, using	scanning personnel not reported.		**CXR versus CT for lung contusion***			of blinding.
							Sensitivity	0.39 (0.28-0.51)		
							Specificity	0.89 (0.82-0.95)		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
				a portable radiograph (Siemens Mobilett II). CXR read by radiologists blinded to CT findings.						

Table 29: Rowan 2002[78]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Rowan 2002[78]	Prospective	27	25 male; mean age 42 (17-83) years. The 27 patients were those who needed to have CT for clinical reasons, such as discordant US/clinical findings, spinal column injury, aortic disruption. Thus these may be a special group.	Thoracic US performed by staff radiologist or radiology resident, trained in US pneumothorax detection. 128XP (Acuson) unit used with a 7 MHz linear probe in supine. Bilateral pleural interfaces were examined at the second to the fourth intercostal spaces anteriorly and at the 6th-8th	CT, performed with a CT scanning unit (CT HighSpeed advantage (GE medical systems) with IV ioversol injection. 3 mm slices. Mediastinal and lung windows presented. Carried out by US-blinded staff radiologists	US within 30 minutes after CXR but no details on interval between CT and US/CT	**US versus CT for pneumothorax**		None reported	US performed blind from chest X-ray and CT. Unclear if X-ray and CT blinded.
							TP	11		
							FN	0		
							FP	1		
							TN	15		
							Sensitivity	1 (0.74-1)		
							Specificity	0.94 (0.72-0.99)		
							Positive predictive	0.92 (0.65-0.99)		
							Negative predictive	19 (0.8-1)		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			Inclusion: patients sustaining blunt thoracic trauma undergoing US, CXR and CT scanning; chest imaging warranted on opinion of the attending emergency physician or trauma surgeon; criteria for trauma team activation. Exclusion: patients treated with tube thoracostomy prior to scanning.	spaces in the midaxillary line. Absence of lung sliding and the comet tail artefact were diagnostic. Diagnosis made in real-time. OR Chest X-ray in supine. Visualisation of visceral pleural separated from the chest wall with loss of lung markings laterally, demonstration of a deep sulcus sign, crisp definition of the diaphragm, and demonstration of a continuous diaphragm sign. Carried out by US-blinded staff radiologists			**X-ray versus CT for pneumothorax**			
							TP	4		
							FN	7		
							FP	0		
							TN	16		
							Sensitivity	0.36 (0.15-0.65)		
							Specificity	1 (0.81-1)		
							Positive predictive	1 (0.51-1)		
							Negative predictive	0.7 (0.49-0.84)		

Table 30: Scaglione 2001[80]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Scaglione 2001[80]	Retrospective	1419	Patients with major blunt trauma	Helical CT scans from lung apices to aortic hiatus of diaphragm, after IV injection of non-ionic contrast media; 5-mm thick sections. Intimal flap, pseudoaneurysm, lumen abnormality, contour irregularity and extravasation of contrast material were the direct signs and viewed as diagnostic.	Thoracotomy for those with an 'abnormal' chest CT scan (n=77 [either the diagnostic direct signs]). See index test information or indirect signs of mediastinal haemorrhage (not regarded as diagnostic). For those with no 'CT abnormalities' (n=1342) thoracotomy was not carried out and the gold standard was 8 month clinical and radiographic follow up.	Unclear	**CT versus thoracotomy for thoracic aortic injury**		None reported	No blinding reported. Incorrect diagnostic accuracy values reported in the paper (for example, they calculate sensitivity from TP/TP + FP, which is really a positive predictive value. The raw data reported in the text has been used to construct correct results.
							TP	21		
							FN	0		
							FP	2		
							TN	1396		
							Sensitivity	1.0		
							Specificity	0.964		
							Positive predictive	0.91		
							Negative predictive	1.0		

Table 31: Soldati 2006[86]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Soldati 2006[86]	Retrospective for 109 and prospective for remaining 12.	88	Consecutive patients with isolated blunt chest trauma or polytrauma with chest involvement and an injury severity score of >15. Exclusion: any pneumothorax or subcutaneous emphysema adequate to compromise the examination for lung contusion.	US performed by one examiner. Expertise not described but was a study author with MD so likely to be high level. Done with Toshiba model 220 SSA with convex 3.5 MHz probe; or Esaote Megas convex multi-frequency 3.5-5MHz probe; or Hitachi model H21 convex multi-frequency 2-5 MHz probe. Lung contusion was diagnosed in the presence of alveolar interstitial syndrome, defined as the presence of multiple B lines or by the presence of a peripheral parenchymal lesion, defined as the presence of c	Chest CT scanning was done with a multislice 4-detector scanner of a helical device with a single detector. Expertise or blinding of examiners not reported.	Within 60 minutes	**US versus CT for lung contusion**		No commercial funding; funding from a public health body	
							TP	35		
							FN	2		
							FP	2		
							TN	49		
							Sensitivity	0.946		
							Specificity	0.961		
							Positive predictive	0.946		
							Negative predictive	0.961		
							CXR versus CT for lung contusion			
							TP	10		
							FN	27		
							FP	0		
							TN	51		
							Sensitivity	0.270		
							Specificity	1.000		
							Positive predictive	1.000		
							Negative predictive	0.654		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
				lines, confluent consolidations, or the presence of parenchymal disruption with localised pleural effusion. OR Chest X-ray in supine, done immediately after the US.						

Table 32: Soldati 2008[85]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Soldati 2008[85]	Unclear	109	Consecutive patients admitted to an emergency department for chest trauma or major trauma. Mean age 41.4 (20.5) years; 62.9% were men; 65 chest trauma and 44 multiple trauma.	Lung US within 1 hour of admission. Carried out by emergency physicians with at least 1 year experience of chest US. Blinded to CT and CXR. Echograph model SSA 250 (Toshiba) with a 5.2 MHz	Spiral CT scanning with 5mm collimations. Details of operator not given.	Within 1 hour	**US versus CT for pneumothorax**		None reported	Blinding between US and CT but not clear if achieved between X-ray and CT. Raw data calculated from other
							TP	23		
							FN	2		
							FP	1		
							TN	191		
							Sensitivity	0.92		
							Specificity	0.995		
							Positive	0.958		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			Inclusion: aged >18 years with blunt chest or multiple trauma. Exclusion: need for chest decompression for tension pneumothorax; mechanical ventilation; haemodynamic instability; subcutaneous emphysema; chest wall injuries precluding US.	convex probe. Scanning was through longitudinal, anterior and lateral scanning along the anatomic lines of the thorax. Absence of pleural sliding and comet tail artefacts or the presence of lung points in each intercostal space and accentuation of image reinforcements due to air reverberation were regarded as diagnostic. OR			predictive			data in paper.
							Negative predictive	0.990		
							Chest X-ray versus CT for pneumothorax			
							TP	13		
							FN	12		
							FP	0		
							TN	192		
							Sensitivity	0.52		
							Specificity	1		
							Positive predictive	1		
							Negative predictive	0.942		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
				Supine chest X-ray by a radiologist who was not necessarily the same as the CT operator. Absence of lung parenchyma and dishomogeneous appearance of diaphragm, incongruence of the plural line or the deep sulcus sign were diagnostic.						

Table 33: Soult 2015[87]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Soult 2015[87]	Retrospective	345	Consecutive patients presenting at the emergency department of a level 1 trauma centre	Chest eFAST performed by a Chief Resident or attending staff. Chest X-ray in supine.	CT	Not reported	**eFAST versus gold standard for tension pneumothorax**		Not reported	Blinding not clear
							TP	27		
							FN	2		
							FP	41		
							TN	275		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
							Sensitivity	0.40		
							Specificity	0.99		
							Positive predictive	0.93		
							Negative predictive	0.87		
							CXR versus gold standard for tension pneumothorax			
							TP	16		
							FN	0		
							FP	52		
							TN	277		
							Sensitivity	0.24		
							Specificity	1		
							Positive predictive	1		
							Negative predictive	0.84		

Table 34: Tomiak 1993[88]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Tomiak 1993[88]	Retrospective	18	14/18 male; Age range 6-85 years; half were men aged 27-54	CT scan done on a Siemens DR3 scanner or GE 9800 (in	Aortograms performed using biplane cut film	Unclear	**Ct versus arteriograms for aortic rupture**		None reported	No blinding reported (or likely as this was a

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			years. For 83% the mechanism of injury was a motor vehicle accident. Consecutive (years 1984-1991) cases of patients presenting to the emergency department with suspected aortic injury from blunt chest trauma that were evaluated by both CT and aortography.	one case only an Imatron fast-scanner was used). Contrast enhancement with a 50ml bolus infusion of Conray-60.No mention of expertise of the examiners, but they were described as 'attending radiologists'.	techniques, with more recent studies supplemented by digital arteriography. Done by 'attending radiologist'.		TP	0		retrospectiv e review). Raw data, and diagnostic data needed to be extrapolated from the paper as not clearly reported.
							FN	3		
							FP	6		
							TN	9		
							Sensitivity	0		
							Specificity	0.6		
							Positive predictive	0		
							Negative predictive	0.75		

Table 35: Varin 2009[91]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Varin 2009[91]	Retrospective	299	Consecutive patients with penetrating torso injuries (either stab wounds or	Chest X-ray in supine. No details of examiners or diagnostic indicators	CT or surgery within 2 hours after arrival. Evaluated by residents of radiology,	Maximum of 2 hours	**CXR versus gold standard for pneumothorax**		Not reported	Blinding not clear
							TP	56		
							FN	22		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			gunshot wounds) presenting at the emergency department of a level 1 trauma centre		surgery and emergency medicine.		FP	2		
							TN	219		
							Sensitivity	0.71		
							Specificity	0.99		
							Positive predictive	0.97		
							Negative predictive	0.91		
							CXR versus gold standard for haemothorax			
							TP	49		
							FN	29		
							FP	0		
							TN	220		
							Sensitivity	0.63		
							Specificity	1		
							Positive predictive	1		
							Negative predictive	0.88		

Table 36: Zhang 2006[95]

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Zhang 2006[95]	Prospective	135 – 31 from	Mean age 45 (15) years; Blunt	US in supine performed by	CT with 16 slice spiral CT	Interval between	**US versus CT for**	95% CI includ	None	Double blinding of

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
	study	resuscitation room and 104 from the emergency ICU.	trauma was traffic accident (61.5%), falls (20.7%), crush injuries (9.6%), and others (8.2%). 83 had mechanical ventilation. Average injury severity score was 29.1(12.4). APACH II score 19.9(11.6). Inclusion: Patients with major trauma in either the resuscitation room or emergency intensive care unit Exclusion: subcutaneous emphysema and/or cardiac arrest after probable tension	3 emergency department clinicians with experience and attendance on a 28 hour course. Device used was the portable SSD-900 (Aloka) with a 3.5 MHz convex probe (or occasionally 7.5 MHz linear probe). The anterior, lateral and posterior thoraces were examined for 1) pleural line, 2) lung sliding and 3) comet tail artefacts OR Portable CXR with a AD125P-	scanner (Volume Zoom, Siemens). Interpreted by independent radiologists (expertise unstated) unaware of US findings. If chest drain was present this was used as a definitive guide instead from the observation of air bubbles.	US scans and CXR or CT was always less than 3 hours, either before or after.	**pneumothorax**	ed	received	CT/CXR from US operators Blinding between CT and CXR was unclear
							TP	25		
							FN	4		
							FP	3		
							TN	103		
							Sensitivity	0.862 (0.737 - 0.988)		
							Specificity	0.972 (0.94-1)		
							Positive predictive	0.893 (0.778 -1)		
							Negative predictive	0.963 (0.927 - 0.999)		
							X-ray versus CT for pneumothorax			
							TP	8		
							FN	21		
							FP	0		
							TN	106		
							Sensitivity	0.276 (0.113 -		

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			pneumothorax	MUXH scanner in supine. Interpreted by independent radiologists (expertise unstated).				0.439)		
							Specificity	1 (1-1)		
							Positive predictive	1 (1-1)		
							Negative predictive	0.835 (0.77-0.899)		

G.3 Assessment and management of haemorrhage

G.3.1 Pelvic binders

Table 37: Fu 2013

Study	Fu 2013[34]
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=585)
Countries and setting	Conducted in Taiwan; Setting: Level 1 trauma centre
Line of therapy	Adjunctive to current care
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Stratified then randomised: stratifies by stable or unstable pelvic fracture (NRS)
Inclusion criteria	Patients with pelvic fractures referred to the participating hospital within 24 hours (of injury/admission?)

Study	Fu 2013[34]
Exclusion criteria	Patients who had received invasive treatment before transfer (for example, surgery, interventional radiology), patients with other concomitant haemorrhage requiring emergent surgery
Recruitment/selection of patients	Consecutive patients referred to the centre between May 2008 and September 2012 meeting inclusion criteria.
Age, gender and ethnicity	Age - Mean (SD): 40.4 years (28.6). Gender (M:F): 91:44. Ethnicity: not reported
Further population details	1. Degree/Presence of shock at baseline: Not applicable / Not stated / Unclear (Overall).
Indirectness of population	No indirectness
Interventions	(n=153) Intervention 1: Pelvic Binder. Non-invasive pelvic circumferential compression device (PCCD), including pelvic binder and wrapping sheets. Duration Unclear. Concurrent medication/care: Not described (n=432) Intervention 2: No binder. No pre-transfer application of a non-invasive pelvic circumferential compression device (PCCD).. Duration Unclear. Concurrent medication/care: Not described
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PELVIC BINDER versus NO BINDER Protocol outcome 1: Mortality at 1 month - Actual outcome: Mortality at unclear; Group 1: 0/153, Group 2: 4/432; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: Volume of blood products used at Define - Actual outcome: Mean blood transfusion in patients with unstable pelvic fractures at unclear; Group 1: mean 398.4 ml (SD 417.6); n=91, Group 2: mean 1954.5 ml (SD 249); n=44; Risk of bias: High; Indirectness of outcome: Serious indirectness - Actual outcome: Mean blood transfusion in patients with stable pelvic fractures at unclear; Group 1: mean 120.2 ml (SD 178.5); n=62, Group 2: mean 231.8 ml (SD 206.2); n=388; Risk of bias: High; Indirectness of outcome: Serious indirectness	
Protocol outcomes not reported by the study	Quality of life at Define; Mortality at 12 months; Adverse effects at Define; Pain at Define; Mortality at 24 hours

Table 38: Ghaemmaghami 2007

Study	Ghaemmaghami 2007[40]
Study type	Retrospective cohort study

Number of studies (number of participants)	1 (n=237)
Countries and setting	Conducted in USA; Setting: Level 1 trauma centre
Line of therapy	1st line
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall: No age data provided
Subgroup analysis within study	Not applicable
Inclusion criteria	Unstable fracture pattern defined as anteroposterior compression (APC) grade 2 or 3, lateral compression grade 2 or 3, or vertical shear, fracture in patients older than 55 years or age or fracture with presenting systolic blood pressure <90 mmHg
Exclusion criteria	none reported
Recruitment/selection of patients	Intervention group recruited from November 2003 to June 2006, historic control recruited from January 2002 to October 2003
Age, gender and ethnicity	Age - Other: Not reported. Gender (M:F): Define. Ethnicity: Not reported
Further population details	1. Degree/Presence of shock at baseline: In shock on application of binder (Authors state that 100% of patients receiving EMC and 92% of patients not receiving EMC were hypotensive on arrival to the ED).
Indirectness of population	Serious indirectness: In-hospital population of confirmed unstable pelvic fractures
Interventions	(n=118) Intervention 1: Pelvic Binder. 18 inch wide circumferential woven cloth binder with string pulley . Duration unclear. Concurrent medication/care: not reported (n=118) Intervention 2: No binder. No standardised use of pelvic binders for patients with pelvic fractures. "Occasional" use of a sheet wrap around the pelvis.. Duration unclear. Concurrent medication/care: Not reported
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PELVIC BINDER versus NO BINDER

Protocol outcome 1: Mortality at 1 month
- Actual outcome: Mortality at before hospital discharge; OR .90 (95%CI 0.3 to 2.5) (p-value .835); Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Volume of blood products used at Define - Actual outcome: Need for massive transfusion (>6 units of packed red blood cells) at within 24 hours; OR 1.40 (95%CI 0.58 to 3.3) (p-value .446); Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at Define; Mortality at 12 months; Adverse effects at Define; Pain at Define; Mortality at 24 hours

G.3.2 Haemostatic agents

Table 39: Boffard 2005-1[10]

Study	**Boffard 2005-1[10]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	2 (n=301)
Countries and setting	
Line of therapy	1st line
Duration of study	Intervention + follow-up: 48 hours
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients 16 years or over and younger than 65 years. Guy shot wound to the head, GCS <8 unless in the presence of normal CT, base deficit >15 mEq/litre or severe acidosis with Ph <7, transfusion of 8 units or more of RBCs before arrival at the trauma centre, and injury sustained > or equal to 12 hours before randomisation
Exclusion criteria	Cardiac arrest prehospital or in ER
Age, gender and ethnicity	Age - Mean (SD): Placebo 35 (13) rFVIIa 33 (13). Gender (M:F): 70% male. Ethnicity: not stated
Further population details	1. Age:
Extra comments	Placebo: ISS 32 (12) GCS < or equal to 8 11% 9-12 24% 13-15 65%, SBP 111 (27) mmHg rFVIIa ISS 33 (13), GCS < or equal to 8 16% 9-12 16% 13-15 68%, SBP 102 (24)

Indirectness of population	No indirectness
Interventions	(n=69) Intervention 1: Recombinant activated factor vii. 200 (given immediately after transfusion of eighth units of RBCs) , 100 (1 hour after initial dose) and 100ug/kg (3 hours after initial dose). Duration 48 hours. Concurrent medication/care: Transfusion of 8 units of more of RBCs within 4 hours of admission (inclusion criteria) (n=74) Intervention 2: Standard care. Dose as for intervention. Duration 30 days. Concurrent medication/care: None mentioned
Funding	Equipment/drugs provided by industry (Novodisk)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RECOMBINANT ACTIVATED FACTOR VII versus STANDARD CARE Protocol outcome 1: Mortality at 30 days - Actual outcome: Mortality at 30 days; Group 1: 17/69, Group 2: 22/74; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: Thrombotic events - Actual outcome: Thromboembolic AEs at 30 days; Group 1: 2/69, Group 2: 3/74; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 3: RBC use at Define - Actual outcome: RBC transfusion at 48 hours; Other: 2.0 (0.0 to 4.6) p=0.07; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality at 24 hours; Mortality at 1 year; Quality of life at Define; Venous-thromboembolism at Define; MI/Stroke at Define; Over-transfusion related morbidity/infection at Define; Pulmonary embolism at Define; Over transfusion related morbidity at Define; Sepsis at Define; Plasma use at Define; Cryoprecipitate use at Define; Psychological well-being at Define; Time to definitive control of haemorrhage at Define; Platelet use at Define; Length of stay at Define

Table 40: Boffard 2005-2[10]

Study	**Boffard 2005-2[10]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=143)

Countries and setting	
Line of therapy	1st line
Duration of study	Follow-up (post intervention): 30 days
Method of assessment of guideline condition	--
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Define
Exclusion criteria	Define
Age, gender and ethnicity	Age - --: . Gender (M:F): Define. Ethnicity:
Further population details	1. Age:
Indirectness of population	--
Interventions	(n=70) Intervention 1: Recombinant activated factor vii. 200 micrograms/kg plus two subsequent 100 micrograms/kg doses. Duration 30 days. Concurrent medication/care: None mentioned (n=64) Intervention 2: Standard care. Placebo as for intervention. Duration 30 days. Concurrent medication/care: None mentioned
Funding	Equipment/drugs provided by industry (Novo Nordisk)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RECOMBINANT ACTIVATED FACTOR VII versus STANDARD CARE

Protocol outcome 1: Mortality at 30 days
- Actual outcome: Mortality at 30 days; Group 1: 17/70, Group 2: 18/64; Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 2: Thrombotic events at Define
- Actual outcome: Thromboembolic AEs at 30 days; Group 1: 4/70, Group 2: 3/64; Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 3: RBC use at Define - Actual outcome: Total RBC transfusions at 48 hours; Other: 0.2 (90%CI -0.9 to 2.4) p=0.24; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality at 24 hours; Mortality at 1 year; Quality of life at Define; Venous-thromboembolism at Define; MI/Stroke at Define; Over-transfusion related morbidity/infection at Define; Pulmonary embolism at Define; Over transfusion related morbidity at Define; Sepsis at Define; Plasma use at Define; Cryoprecipitate use at Define; Psychological well-being at Define; Time to definitive control of haemorrhage at Define; Platelet use at Define; Length of stay at Define

Table 41: Hauser 2010-1[44] (Dutton 2011[29])

Study (subsidiary papers)	**Control trial: Hauser 2010-1[44] (Dutton 2011[29])**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=560)
Countries and setting	
Line of therapy	First-line
Duration of study	Follow-up (post intervention): 90 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Aged 18-70 years. Continuing torso and/or proximal lower extremity bleeding after receiving 4 units of RBCs despite standardised haemostatic interventions.
Exclusion criteria	Patients who were moribund, had severe brain injury or were injured > 12 hours before randomisation or > 4 hours before hospital arrival
Age, gender and ethnicity	Age - Mean (SD): rFVIIa 39.2 (14.3) years control 39.9 (14.2) years. Gender (M:F): 73% male. Ethnicity: Blunt (approximately 80% white) Penetrating (37-63% white)
Further population details	1. Age:
Extra comments	rFVIIa: ISS 32.8 (11.3), GCS 13.0 (11.3), SBP mmHg 100.9 (27.17), base deficit 6.10 (3.04), total RBC before dose 5.61

	(1.46). Control ISS 32.8 (11.5), GCS 13.2 (2.9), SBP mmHg 96.6 (26.29), Base deficit 8.66 (4.13), total RBC 5.61 (1.46)
Indirectness of population	No indirectness
Interventions	(n=226) Intervention 1: Recombinant activated factor vii. 200 micrograms/kg initially, 100 micrograms/kg at 1 hour and 3 hours). Duration Treatment (3 hours) and 90 days (follow-up). Concurrent medication/care: Patients had received 4 units of RBCs but had not received the 8th (inclusion criteria) (n=255) Intervention 2: Standard care. 200 micrograms/kg, 100 micrograms/kg and 100 micrograms/kg initially, 1 hour and 3 hours. Duration 3 hours (treatment) and 90 days (follow-up). Concurrent medication/care: Patients received 4 units of RBC but not the 8th (inclusion criteria)
Funding	Equipment/drugs provided by industry (Novo Nordisk)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RECOMBINANT ACTIVATED FACTOR VII versus STANDARD CARE

Protocol outcome 1: Mortality at 30 days
- Actual outcome: Mortality - dichotomous at 30 d; Group 1: 24/218, Group 2: 26/242; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Venous-thromboembolism at Define
- Actual outcome: Venous TEs at 90 days; Group 1: 29/224, Group 2: 24/250; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 3: Thrombotic events at Define
- Actual outcome: Thrombotic AEs at 90 days; Group 1: 36/224, Group 2: 33/250; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 4: MI/Stroke at Define
- Actual outcome: Cerebral infarct at 90 d; Group 1: 5/270, Group 2: 5/290; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 5: Sepsis at Define
- Actual outcome: Sepsis at 90 d; Group 1: 33/224, Group 2: 45/250; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 6: RBC use at Define
- Actual outcome: RBC at 48 hours; Group 1: mean 7.8 (SD 10.6); n=221, Group 2: mean 9.1 (SD 11.3); n=247; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 7: Plasma use at Define - Actual outcome: FFP at 48 hours; Group 1: mean 5.3 (SD 6.7); n=221, Group 2: mean 8 (SD 10.1); n=247; Risk of bias: ; Indirectness of outcome: No indirectness Protocol outcome 8: Cryoprecipitate use at Define - Actual outcome: Cryoprecipitate at 48 hours; Group 1: mean 0.9 (SD 3.3); n=221, Group 2: mean 1.4 (SD 4.5); n=247; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 9: Platelet use at Define - Actual outcome: Platelets at 48 hours; Group 1: mean 3.7 (SD 8.6); n=221, Group 2: mean 3.9 (SD 7.8); n=247; Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality at 24 hours; Mortality at 1 year; Quality of life at Define; Over-transfusion related morbidity/infection at Define; Pulmonary embolism at Define; Over transfusion related morbidity at Define; Psychological well-being at Define; Time to definitive control of haemorrhage at Define; Length of stay at Define

Table 42: Shakur 2012[82]

Study	**CRASH-2 trial: Shakur 2012[82]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=20,211)
Countries and setting	
Line of therapy	1st line
Duration of study	Intervention + follow-up: Four weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not stratified but pre-specified: Estimated time since injury, systolic BP, GCS, type of injury
Inclusion criteria	Adult patients with significant haemorrhage (SBP <90 mmHg or heart rate >110 beats per minute) or who were considered at risk of significant haemorrhage and who were within 8 hours of injury
Exclusion criteria	Define

Age, gender and ethnicity	Age - Mean (SD): TXA 34.6 (14.1) control 34.5 (14.4). Gender (M:F): TXA 83.6% male Control 84%. Ethnicity: Not stated
Further population details	1. Age: Not applicable/Not stated/Unclear
Extra comments	TXA time since injury 2.8 (2.2), blunt 67.5%, < 75 15.5%, 76-89 16%, GCS severe (3-8) 17.8%, moderate (9-12) 13.4%, mild (13-15) 68.7% Control time since injury 2.9 (2.6), blunt 67.7%, SBP < 75 15.9%, 76-89 16.8% > 90 67.1%, GCS severe 18.2% moderate 13.4% mild 68.3%
Indirectness of population	No indirectness
Interventions	(n=10096) Intervention 1: Tranexamic acid. Loading dose of 1 g over 10 minutes followed by iv infusion of 1 g over 8 hours. Duration 8 hours. Concurrent medication/care: None stated (n=10115) Intervention 2: Standard care. Placebo dosing as for intervention. Duration 8 hours. Concurrent medication/care: None stated
Funding	Academic or government funding (Pfizer funded the drugs. Main funding NIHR HTA programme)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANEXAMIC ACID versus STANDARD CARE

Protocol outcome 1: Mortality at 30 days
- Actual outcome: Mortality at 28 days; Group 1: 1463/10060, Group 2: 1613/10067; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Thrombotic events at Define
- Actual outcome: Deep vein thrombosis at 28 days; Group 1: 40/10060, Group 2: 41/10067; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 3: MI/Stroke at Define
- Actual outcome: MI/Stroke at 28 days; Group 1: 92/10060, Group 2: 121/10067; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 4: Pulmonary embolism at Define
- Actual outcome: Pulmonary embolism at 28 days; Group 1: 72/10060, Group 2: 71/10067; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 5: RBC use at Define
- Actual outcome: Blood products transfused at 28 days; Group 1: 5067/10060, Group 2: 5160/10067; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcomes not reported by the study	Mortality at 24 hours; Mortality at 1 year; Quality of life at Define; Venous-thromboembolism at Define; Over-transfusion related morbidity/infection at Define; Over transfusion related morbidity at Define; Sepsis at Define; Plasma use at Define; Cryoprecipitate use at Define; Psychological well-being at Define; Time to definitive control of haemorrhage at Define; Platelet use at Define; Length of stay at Define

G.3.3 Haemorrhage shock prediction/risk tools

Table 43: Brockamp 2012[12]

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
Brockamp T, Nienaber U, Mutschler M, Wafaisade A, Peiniger S, Lefering R et al. Predicting on-going hemorrhage and transfusion requirement after severe trauma: a validation of six scoring systems	Retrospective observational cohort (validation)	n=5147 complete datasets (9% of the complete data set) Mean age 45.7 (SD 19.3) years, mean ISS 24.3 (13.2). 95% had sustained blunt trauma	Patients entered on the TraumaRegister DGU, Germany. Patients aged 18 years or over, where the amount of packed red blood cells was known. Only patients who survived until ICU were considered, to avoid bias from early deaths prior to administration of any blood product or massive transfusion Patients who had received haemostatic agents such as fibrinogen, prothrombin	Prince of Wales/Rainer score Heart rate ≥120 bpm, systolic blood pressure ≤90 mmHg, Glasgow Coma Scale ≤8, displaced pelvic fracture, CT scan or FAST positive for fluid, base deficit >5 mmol/litre, heart rate >105 bpm, INR >1.5, haemoglobin ≤7 g/dl, and haemoglobin 7.1 to 10.0 g/dl Threshold ≥ 2.5 Vandromme score Blood lactate ≥5 mmol/litre, heart rate >105 bpm, INR 1.5, haemoglobin ≤11 g/dl and systolic blood pressure <110 mmHg Threshold ≥1.5 ABC Penetrating mechanism,	Number of cases receiving massive transfusion	289/5147	Unfunded study Only 9% of total data included
					Rainer		
					Sensitivity	80.6%	
					Specificity	77.7%	
					Positive predictive value	17.7%	
					Negative predictive value	98.5%	
					AUC (95%CI)	0.860 (0.839 to 0.881)	
					TP	234	
					FP	1069	
					FN	55	
					TN	3789	

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
and algorithms on the TraumaRegister DGU(R). Critical Care (London, England). 2012; 16(4):R129. (Guideline Ref ID BROCKAMP2012)			complex concentrate, recombinant activated factor VII or any antifibrinolytics with potential influence on the amount of administered packed red blood cells were excluded from the study.	systolic blood pressure ≤90 mmHg on ER arrival, heart rate ≥120 bpm on ER arrival and positive FAST examination Threshold ≥ 0.5 Schreiber score (derived from military) Haemoglobin, INR and penetrating mechanism of injury Threshold ≥ 0.5 Larson score (derived from military) Heart rate, systolic blood pressure, haemoglobin and base deficit. Threshold ≥ 1.5 Reference test ≥ 10 units packed red blood cells between arrival to the emergency room and the intensive care unit.			
					Vandromme		
					Sensitivity	78.9%	
					Specificity	76.2%	
					Positive predictive value	16.5%	
					Negative predictive value	98.4%	
					AUC (95%CI)	0.840 (0.817 to 0.863)	
					TP	228	
					FP	1166	
					FN	61	
					TN	3692	
					Larson		
					Sensitivity	70.9%	
					Specificity	80.4%	
					Positive predictive value	17.4%	
					Negative predictive value	97.9%	
					AUC (95%CI)	0.823 (0.800 to 0.847)	

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
					TP	205	
					FP	972	
					FN	84	
					TN	3887	
					Schreiber		
					Sensitivity	85.8%	
					Specificity	61.7%	
					Positive predictive value	11.8%	
					Negative predictive value	98.7%	
					AUC (95%CI)	0.800 (0.773 to 0.828)	
					TP	249	
					FP	1846	
					FN	41	
					TN	3012	
					ABC		
					Sensitivity	76.1%	
					Specificity	70.3%	
					Positive predictive value	13.2%	
					Negative predictive value	98.0%	
					AUC (95%CI)	0.763 (0.732 to 0.794)	

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
					TP FP FN TN	220 1443 69 3415	

Table 44: Cancio 2008[16]

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
Cancio LC, Wade CE, West SA, Holcomb JB. Prediction of mortality and of the need for massive transfusion in casualties arriving at combat support	Retrospective validation cohort	n=692 n=536 complete data	US combat casualties. The majority of cases were contributed by the US Army CSH at Ibn Sina Hospital, Baghdad, Iraq	Revised Trauma Score GCS SBP Respir Coded value 13-15 >89 10-29 4 9-12 76-89 >29 3 6-8 50-75 6-9 2 4-5 1-49 1-5 1 3 0 0 0 $RTS=0.9368*GCS_{code}+ 0.7326*SBP_{code} + 0.2908*RR_{code}$ Modified Field Triage Score GCS_{total} 8= 0 >8 =1 SBP <100 mmHg = 0	RTS AUC (95%CI) Sensitivity Specificity Modified FTS AUC (95%CI)	 0.638 (0.590 to 0.686) 0.618 (0.569 to 0.666)	High rate of missing data Combat casualties No funding reported

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
hospitals in Iraq. Journal of Trauma. 2008; 64(2 Suppl):S51 -S56. (Guideline Ref ID CANCIO2008)				>100 = 1 Reference standard Ten units of packed red blood cell transfusion within 24 hours			

Table 45: Cotton 2010[20]

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
Cotton BA, Dossett LA, Haut ER, Shafi S, Nunez TC, Au BK et al. Multicenter validation of a simplified score to	Retrospective observational cohort (validation)	Validation sample 1 n=513 Validation sample 2 n=372 Validation sample 3 n=133 Country: USA	Adult trauma patients who were admitted between July 2006 and June 2007 who were transported directly from the scene and who received at least one unit of blood during the stay	ABC score cut of ≥2 Reference standard: Massive transfusion defined as 10 units or more of red blood cells in the first 24 hours	Validation 1 Number of cases of massive transfusion Sensitivity Specificity TP FP FN TN	72/513 82.7 87.6 60 55 12 386	

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
predict massive transfusion in trauma. Journal of Trauma. 2010; 69 Suppl 1:S33-S39. (Guideline Ref ID COTTON2010)					Validation 2 Number of cases of massive transfusion Sensitivity Specificity TP FP FN TN	56/372 75.6 86.0 42 44 14 272	
					Validation 3 Number of cases of massive transfusion Sensitivity Specificity TP FP FN TN	19/133 89.0 67.3 17 37 2 77	

Table 46: Krumrei 2012[51]

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
Krumrei NJ, Park MS, Cotton BA, Zielinski MD. Comparison of massive blood transfusion predictive models in the rural setting. Journal of Trauma and Acute Care Surgery. 2012; 72(1):211-215. (Guideline Ref ID KRUMREI2012)	Retrospective observational cohort (validation)	n=373	Patients treated at a single American College of Surgeons-certified level 1 trauma center January 2008 to December 2009	TASH score Seven independent variables: systolic blood pressure, haemoglobin concentration, FAST, complex long bone and/or pelvic fractures, HR, base excess and gender. The variables are weighted using a total of 16 different scores, for a score range of 0 to 28. The probability of MT is calculated using the exponential equation: P = 1[1 + e^(4.9 – (0.3*[TASH]))] McLaughlin Score Four variables (HR >105, SBP <110 mmHg, pH <7.25, and haematocrit <32%) with each component identified as a yes or no. If all four variables were present, an 80% chance of MT existed. The final predictive equation was as follows: Log (p[1-p]) = 1.576 + (0.825*SBP) + (0.826*HR) + (1.044*Hct) + (0.462*pH) ABC score	Number of cases of massive transfusion TASH score (threshold 80% probability of MT) Sensitivity Specificity TP FP FN TN	38/373 2.6% 99.7% 10 1 28 (37 specified in paper but figure is not compatible with sensitivity/ specificity data) 334	No funding reported
					McLaughlin Sensitivity Specificity TP	 15.8% 98% 6	

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
				Uses four data points (penetrating mechanism, SBP < 90 mmHg, HR > 120 and positive FAST) with a range of scores 0-4. A score of 2 or greater is predictive of MT requirement. Reference standard: Massive transfusion defined as 10 units or more of red blood cells in the first 24 hours	FP FN TN	6 32 328	
					ABC Sensitivity Specificity TP FP FN TN	 89% 85% 33 49 4 285	

Table 47: McLaughlin 2008[57]

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
McLaughlin DF, Niles SE, Salinas J, Perkins JG, Cox ED, Wade CE et al. A predictive model for	Retrospective observational study (validation)	n=396 Country: USA (database)	Patients entered on the Joint Theater Trauma Registry (JTTR) maintained at the United States Army Institute of Surgical Research. Exclusion: If they were not transfused at least one	Index test: Heart rate >105 bpm, Systolic blood pressure <110 mmHg, pH <7.25, haematocrit <32% Equation: log (p/[1-p]) = 1.576 + (0.825 x SBP) + (0.826 x HE) + (1.044 x Hct) + (0.462 x pH), where the variables have the	Sensitivity Specificity Positive predictive value Negative predictive value AUC	59.4% 77.4% 66.4% 71.7% 0.747%	Military population 2 x 2 could not be calculated No funding reported

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
massive transfusion in combat casualty patients. Journal of Trauma. 2008; 64(2 Suppl):S57-S63. (Guideline Ref ID MCLAUGHLIN2008)			unit of blood in the first 24 hours after presentation to hospital. Treatment at another medical facility before transfer to the combat support hospital, younger than 18 years, or designation as a security internee	value of 0 or 1 based on whether or not the value is classed as predictive Reference standard: Need for massive transfusion (≥10 units of blood in the initial 24 hours after admission).	TP FP FN TN		

Table 48: Mitra 2012[62]

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
	Retrospective observational cohort (validation)	n=4254 registry patients n=1234 included Country: Australia	Patients entered on the Alfred Trauma Registry. Collects data on all major trauma patients (defined as ISS >15), patients who died post-trauma and trauma patients admitted for more than 72 hour post-trauma.	Prince Wales Hospital (PWH) Cut off ≥6 The variables included systolic blood pressure, Glasgow Coma score, heart rate, displaced pelvic fracture, a positive FAST or CT, base deficit or haemoglobin ABC score Four variables: penetrating mechanism, systolic blood pressure, heart rate and	No of cases receiving massive transfusion PWH Sensitivity Specificity Positive predictive value Negative predictive value	195/1234 36.92 (34.23 to 39.62) 97.11 (96.18 to 98.05) 70.59 (68.05 to 73.13) 89.13 (87.40 to	High rate of missing data

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
				positive FAST Cut-off 2 TASH Blood pressure, gender, haemoglobin, FAST, pulse, base excess and extremity or pelvic fractures. Weighted score Cut-off 18 points Reference standard: Massive transfusion defined as the administration of ≥5 units of packed red blood cells in the first 4 hours since presentation to the emergency department.	AUC TP FP FN TN TASH Sensitivity Specificity Positive predictive value Negative predictive value AUC TP FP FN TN	90.87) 0.8419 72 27 123 912 25.13 (22.71 to 27.55) 99.81 (99.56 to 100) 96.08 (95.00 to 97.16) 87.66 (85.82 to 89.49) 0.7822 49 146 2 937	

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
					ABC Sensitivity Specificity Positive predictive value Negative predictive value AUC TP FP FN TN	 45.64 (42.86 to 48.42) 94.23 (92.92 to 95.43) 59.73 (57.00 to 62.47) 90.23 (88.57 to 91.89) 0.8986 89 54 106 885	

Table 49: Nunez 2009[69]

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
Nunez TC, Voskresensky IV, Dossett LA, Shinall R, Dutton WD, Cotton BA. Early prediction of massive	Retrospective validation cohort	n=596	Trauma Registry of the American College of Surgeons	Index test TASH score Blood pressure, gender, haemoglobin, FAST, pulse, base excess and extremity or pelvic fractures. P = 1/[1+_exp(4.9 – 0.3 X TASH) McLaughlin Score	No of cases of massive transfusion TASH AUC Sensitivity Specificity Area under curve (95%CI)	76/596 0.842	No funding reported

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
transfusion in trauma: simple as ABC (assessment of blood consumption)? Journal of Trauma. 2009; 66(2):346-352. (Guideline Ref ID NUNEZ2009)				HR >105 bpm, systolic blood pressure <110 mmHg, pH <7.25, and haemocrit < 32% Log (p/[1 – p) = 1.576 + (0.825 x SBP) + (0.826 x HR) + (1.044 x Hct) + (0.462 x pH) ABC score The data is not reported as the paper describes the derivation of this scoring system Reference standard Ten units of packed red blood cell transfusion within 24 hours	TP FP FN TN		
					McLaughlin AUC Sensitivity Specificity	0.767	

Table 50: Poon 2012[73]

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
Poon KM, Lui CT, Tsui KL. Comparison of the accuracy of local and international	Retrospective observational cohort (validation)	n=1030	Patients entered on the Tuen Mun Hospital Trauma Registry from 1st January 2005 to 31st December 2010. Patients aged over 12 years,with an ISS of ≥ 9 were included. Patients who were dead on arrival, had known chronic renal failure or	Trauma-Associated Severe Haemorrhage (TASH) score. The TASH scoring system utilised seven independent variables to predict the need for a massive transfusion. The weighted variables include systolic blood pressure, gender, haemoglobin, presence on intra-abdominal fluid, heart	No. of cases receiving massive transfusion Rainers TP FP FN	27/1003 9 18 18	No funding reported Majority of patients Chinese

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
prediction models for massive transfusion in major trauma patients. Hong Kong Journal of Emergency Medicine. 2012; 19(3):189-197. (Guideline Ref ID POON2012)			anaemia (with haemoglobin <7 g/dL), or who were transfused < 10 units of blood but died within 24 hours were excluded	rate, base excess, and extremity or pelvic fracture. Possible range of scores would be from 0 to 28, using 16 as a cut-off for binary prediction model of massive transfusion Assessment of Blood Consumption (ABC) score The ABC scores consisted of four dichotomous physical examination components. The presence of any one component would contribute one point to the total score, for a possible range of scores from zero to four. The parameters included presence of penetrating mechanism, systolic blood pressure of 90 mmHg or less in the emergency department (ED), heart rate of 120 beat per minute or greater in ED and positive FAST. ABS score of 2 or greater would be used as the cut-off point for predicting massive transfusion. Rainer's Score This prediction rule was built with weighing of seven independent variables to	TN Sensitivity Specificity AUC ABC TP FP FN TN Sensitivity Specificity AUC TASH TP FP FN TN Sensitivity Specificity AUC	985 33.3 (15.6 to 51.1) 98.2 (97.4 to 99.0) 96.5 (95.4 to 97.6) 9 32 18 971 33.3 (15.6 to 51.1) 96.8 (95.6 to 97.9) 95.1 (93.7 to 96.4) 7 8 20 995 25.9 (9.4 to 42.5) 99.2 (98.7 to 99.8) 97.3 (96.3 to 98.3)	

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
				identify patients who would require massive transfusion. These included the systolic blood pressure, GCS, heart rate, displaced pelvic fracture, positive FAST or CT scan, base deficits and haemoglobin. Rainer's score was a 10-point score using 6 as the cut-off point for predicting massive transfusion. Reference standard Patient either receiving a transfusion equivalent to the patient's blood volume or ≥ 10 units of packed blood cells in 24 hours			

Table 51: Vandromme 2011[90]

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
Vandromme MJ, Griffin RL, McGwin GJ, Weinberg JA, Rue LW, Kerby JD. Prospective	Retrospective observational cohort (validation)	n=208	Patients admitted to the University of Alabama at Birmingham trauma service January 2005 to December 2008. Validation cohort	Haemoglobin ≤11 g/dl, systolic blood pressure <110 mmHg, international normalised ratio >1.5, blood lactate ≥5 mmol/litre, heart rate >105 bpm	Sensitivity Specificity PPV NPV TP FP	61.3 96.0 15.6 99.5	No funding reported Additional information:

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
identification of patients at risk for massive transfusion: an imprecise endeavor. American Surgeon. 2011; 77(2):155-161. (Guideline Ref ID VANDROME2011)			admitted January 2007 to December 2008	Reference test 10 units or more of packed red blood cells within 24 hours of admission	FN TN		
					Sensitivity Specificity		

G.3.4 Intraosseous (IO)/intravenous (IV) access

Table 52: Leidel 2012[52]

Study (subsidiary papers)	Leidel 2012[52] (Leidel 2009[53])
Study type	Within-subject cohort
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in Germany; Setting: Emergency department of Level I Trauma Centre
Line of therapy	1st line
Duration of study	Follow up (post intervention): 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis

Stratum	Overall
Subgroup analysis within study	Stratified then randomised
Inclusion criteria	Severely injured or critically ill patients (physiological criteria not documented) with unsuccessful peripheral IV access 3 times for a maximum of 2 minutes.
Exclusion criteria	Age under 18, pregnancy, prisoners
Recruitment/selection of patients	Consecutive suitable patients between November 2007 and May 2009
Age, gender and ethnicity	Age - Mean (SD): 48 (21) years. Gender (M:F): 27:13. Ethnicity:
Further population details	
Indirectness of population	Serious indirectness: Proportion of trauma patients not clear
Interventions	(n=40) Intervention 1: Intraosseous - Humeral. Device delivered either by EZ-IO system or BIG (bone injection gun). Duration 1 day. Concurrent medication/care: Not specified Further details: 1. Delivery device: (n=40) Intervention 2: Intravenous - Central venous. Central venous catheterisation of either internal jugular or subclavian vein. Duration Unclear. Concurrent medication/care: No details given Further details: 1. Delivery device:
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HUMERAL versus CENTRAL VENOUS

Protocol outcome 1: Adverse Effects - multiple failure at Define
- Actual outcome: Failure of first attempt at 1 day; Group 1: 6/40, Group 2: 16/40; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Time to establish access at Define
- Actual outcome: Procedure time at 1 day; Group 1: mean 2 minutes (SD 3.1268); n=40, Group 2: mean 8.5 minutes (SD 14.0706); n=40; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcomes not reported by the study	Quality of life at Define; Hospitalisation at Define; Mortality at 24 hours; Mortality at 1 month; Mortality at 6 months; Adverse Effects - pain at Define; Adverse Effects - thrombosis at Define; Adverse Effects - infection at Define; Adverse Effects - compartment syndrome at Define; Adverse Effects - fracture at Define; Patient reported outcomes (psychological wellbeing) at Define; Length of stay at Define

G.3.5 Volume resuscitation

Table 53: Bickell 1994[6]

Study	Bickell 1994[6]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=598)
Countries and setting	Conducted in USA; Setting: Level 1 trauma centre in Urban city
Duration of study	Intervention + follow up: 37 Months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Penetrating trauma: Pre-hospital; Penetrating Injury; Adults
Subgroup analysis within study	Not applicable
Inclusion criteria	Age >16 with gunshot or stab wounds to the torso who had a systolic blood pressure of >90 mm Hg, including patients with no measurable blood pressure, at the time of the initial on-scene assessment by the paramedic.
Exclusion criteria	Pregnant women were not enrolled. Those with a revised trauma score of zero at the scene of the injury, those with fatal gunshots to the head, and patients with minor injuries not requiring operative intervention.
Age, gender and ethnicity	Age - Mean (SD): 31 (10.5). Gender (M:F): 9:1. Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	(n=289) Intervention 1: Fluid Resuscitation - Permissive hypotension. IV Fluid resuscitation was delayed until operative procedure. Duration: Until admission at A&E. Concurrent medication/care: Treated with standard paramedic protocol including endotracheal intubation assisted ventilation with oxygen when appropriate, rapid transport to the emergency centre, an insertion of two or more 14 gauge catheters in the upper extremities for rapid infusion of isotonic crystalloid enroute to hospital. Blood products were administered as required by standard clinical procedure. Hypotension defined as <90 mm Hg. (n=309) Intervention 2: Fluid Resuscitation - Resuscitation with normotension as the aim. Immediate fluid

Study	Bickell 1994[6]
	resuscitation on the scene by paramedic. Duration: Until admission at A&E. Concurrent medication/care: Treated with standard paramedic protocol including endotracheal intubation assisted ventilation with oxygen when appropriate, rapid transport to the emergency centre, an insertion of two or more 14 gauge catheters in the upper extremities for rapid infusion of isotonic crystalloid enroute to hospital. Blood products were administered as required by standard clinical procedure. Hypotension defined as <90 mm Hg.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERMISSIVE HYPOTENSION versus RESUSCITATION WITH NORMOTENSION AS THE AIM Protocol outcome 1: Mortality at 30 Days - Actual outcome: Death; Group 1: 86/289, Group 2: 116/309; Risk of bias: Low; Indirectness of outcome: Some indirectness: Time to follow up not 30 days. Protocol outcome 2: Multi-organ failure - Actual outcome: >1 complication; Group 1: 55/238, Group 2: 69/227; Risk of bias: Low; Indirectness of outcome: No indirectness Protocol outcome 3: Days in ICU - Actual outcome: Days in ICU ; Group 1: mean 7 (SD 11); n=238, Group 2: mean 8 (SD 16); n=227; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality at 24 hours; Mortality at 12 Months; Quality of life; Neurological outcome; Blood product use; Time to definitive haemorrhage control; Patient reported outcomes - Pain; Patient reported outcome - psychological outcome; Patient reported outcomes - Return to normal activity.

Table 54: Dutton 2002[28]

Study	Dutton 2002[28]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=110)
Countries and setting	Conducted in USA; Setting: Level One Trauma Centre
Line of therapy	1st line
Duration of study	Intervention + follow up: 20 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis

Study	Dutton 2002[28]
Stratum	Age - Adults (18 and over): Adult; Hospital; Penetrating and Blunt
Subgroup analysis within study	Not applicable
Inclusion criteria	Presented directly from the scene of traumatic injury with evidence of on-going haemorrhage, and an SBP<90 mm Hg recorded at least once within the first hour of injury.
Exclusion criteria	Pregnant, central nervous system injury impairing consciousness or motor function, older than 55, or previous history of coronary artery disease of diabetes.
Age, gender and ethnicity	Age - Mean (SD): 30.9 (11.73). Gender (M:F): 4:1. Ethnicity: Not reported
Indirectness of population	Serious indirectness: Population is made up of Penetrating and Blunt Injury
Interventions	(n=55) Intervention 1: Fluid Resuscitation - Permissive hypotension. Fluid administration titrated to 70 mm Hg. Duration: Until Discharge. Concurrent medication/care: Blood pressure below the target level was treated with administration of crystalloid or blood products, as appropriate to elevate the SBP to the target level while maintaining a hematocrit of at least 25%. (n=55) Intervention 2: Fluid Resuscitation - Resuscitation with normotension as the aim. Fluid administration titrated to 100 mm Hg. Duration: Until Discharge. Concurrent medication/care: Blood pressure below the target level was treated with administration of crystalloid or blood products, as appropriate to elevate the SBP to the target level while maintaining a hematocrit of at least 25%.
Funding	Academic or government funding (Pangborn Grant at the university of Maryland)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: PERMISSIVE HYPOTENSION versus RESUSCITATION WITH NORMOTENSION AS THE AIM

Protocol outcome 1: Mortality at 24 hours
- Actual outcome: Death at Until discharge; Group 1: 3/55, Group 2: 2/55; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at 30 Days
- Actual outcome: Death at Until discharge; Group 1: 4/55, Group 2: 4/55; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 3: Time to definitive haemorrhage control
- Actual outcome: Time to definite control of haemorrhage at Until discharge; Group 1: mean 2.57 (SD 1.46); n=52, Group 2: mean 2.97 (SD 1.75); n=53; Risk of bias: High; Indirectness of outcome: No indirectness

Study	Dutton 2002[28]
Protocol outcomes not reported by the study	Mortality at 12 Months; Quality of life; Neurological outcome; Length of stay - (ICU); Blood product use; Multi-organ failure; Patient reported outcomes - Pain; Patient reported outcome - psychological outcome; Patient reported outcomes - Return to normal activity .

G.3.6 Fluid replacement

Table 55: Holcomb 2015[45]

Study	PROPPR trial: Holcomb 2015[45]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=680)
Countries and setting	Conducted in USA
Line of therapy	1st line
Duration of study	Intervention + follow up: 30 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Children and adults 15 yrs and over
Subgroup analysis within study	Not applicable
Inclusion criteria	At least 1 unit of any blood product component transfused prior to hospital arrival or within 1 of admission and prediction by an American Assessment of Blood Consumption score of 2 or more or by physician judgement of the need for a massive transfusion (10 or more units of RBCS within 24 hrs).
Exclusion criteria	Indirect transfers, required thoracotomy prior to randomised blood products
Age, gender and ethnicity	Age - Median (range): 34.5 to 34. Gender (M:F): 77.8 to 82.7% male. Ethnicity: 62.1 to 65.5% white
Further population details	1. Adults: 15-65 2. Children: Not applicable / Not stated / Unclear 3. Hypertension: Not applicable / Not stated / Unclear 4. TBI: Not applicable / Not stated / Unclear
Extra comments	Patients meeting the highest level of activation at 1 of 12 participating level 1 trauma centres. Estimated age 15 yrs or over.

Indirectness of population	No indirectness
Interventions	(n=338) Intervention 1: Blood product ratio - High ratio. Plasma. platelet and red bllod cell 1:1:1. Duration As clinically indicated. Concurrent medication/care: Not reported (n=342) Intervention 2: Blood product ratio - Low ratio. Plasma. platelet and red blood cells 1:1:2. Duration As clinically indicated. Concurrent medication/care: Not reported
Funding	Academic or government funding (US National Heart Lung and Blood Institute and US Dept of Defense)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HIGH RATIO versus LOW RATIO

Protocol outcome 1: Mortality at 24 hrs
- Actual outcome: Mortality at 24 hrs; Group 1: 43/338, Group 2: 58/342; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Mortality at 30 days
- Actual outcome: Mortality at 30 days; Group 1: 75/338, Group 2: 89/342; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 3: Quality of life at Define
- Actual outcome: ICU free days at Not applicable; Risk of bias: Low; Indirectness of outcome: No indirectness
- Actual outcome: Glasgow Outcome Scale - Extended at At discharge?; Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 4: AE - Transfusion associated circulatory overload at Define
- Actual outcome: Transfusion-associated circulatory overload at 30 days; Group 1: 1/338, Group 2: 0/342; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 5: AE - Previously uncategorised complications of transfusion at Define
- Actual outcome: Transfusion-related metabolic complication at 30 days; Group 1: 53/338, Group 2: 59/342; Risk of bias: Low; Indirectness of outcome: No indirectness
- Actual outcome: Transfusion-related metabolic complication at 30 days; Risk of bias: ; Indirectness of outcome: No indirectness

Protocol outcome 6: Return to normal activities at Define
- Actual outcome: Discharged home at 30 days; Group 1: 118/338, Group 2: 105/342; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 7: Time to definitive control of haemorrhage at Define
- Actual outcome: Achieved haemostasis at 30 days; Group 1: 291/338, Group 2: 267/342; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcomes not reported by the study	Mortality at 12 months; Length of intensive care stay at Define; AE - Acute transfusion reaction at Define; AE - Haemolytic transfusion reaction – acute at Define; AE - Haemolytic transfusion reaction – delayed at Define; AE - Post transfusion purpura at Define; AE - Transfusion associated dyspnoea at Define; AE - Transfusion related acute lung injury at Define; AE - Transfusion associated graft versus host disease at Define; AE Transfusion transmitted infections at Define; Psychological wellbeing at Define

Table 56: Neal 2012[67]

Study	**Neal 2012[67]**
Study type	Prospective cohort study
Number of studies (number of participants)	1 (n=452)
Countries and setting	Conducted in USA
Line of therapy	First-line
Duration of study	Intervention + follow-up: In-hospital
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Blunt mechanism of injury, systolic hypertension or elevated base deficit, blood transfusion requirements in first 12 hours and any region exclusive of the brain with an abbreviated injury score of greater than or equal to 2.
Exclusion criteria	Patients <16 years and >90 years. Cervical spinal cord injury
Age, gender and ethnicity	Age - Range: 17-89. Gender (M:F): 70% male. Ethnicity: Not reported
Further population details	1. Adults: Not applicable/Not stated/Unclear 2. Children: Not applicable/Not stated/Unclear 3. Hypertension: Not applicable/Not stated/Unclear 4. TBI: Not applicable/Not stated/Unclear
Extra comments	Patients who received 10 units or more of PRBC in the first 24 hours.
Indirectness of population	No indirectness
Interventions	(n=114) Intervention 1: Crystalloid: RBC - Highest. Greater than or equal to 1.5:1. Duration In hospital. Concurrent

	medication/care: Not stated (n=111) Intervention 2: Crystalloid: RBC - High. Greater than or equal to 1:1 and < 1.5:1. Duration In hospital. Concurrent medication/care: Not stated (n=113) Intervention 3: Crystalloid: RBC - Medium. Greater than or equal to 1:5:1 and < 1.1. Duration In hospital. Concurrent medication/care: Not stated (n=114) Intervention 4: Crystalloid: RBC - Low. < 0.5:1. Duration In hospital. Concurrent medication/care: Not stated
Funding	Academic or government funding (NIH)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HIGHEST versus LOW Protocol outcome 1: Mortality at 30 days - Actual outcome: Mortality at In hospital; OR 0.9 (95%CI 0.58 to 1.45); Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: AE - Previously uncategorised complications of transfusion at Define - Actual outcome: Multiple organ failure at In hospital; OR 1.7 (95%CI 1.2 to 2.6); Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 3: AE – Transfusion-related acute lung injury at Define - Actual outcome: Acute respiratory distress syndrome at In hospital; OR 2.2 (95%CI 1.5 to 3.1); Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 4: AE Transfusion transmitted infections at Define - Actual outcome: Nosocomial infection at In hospital; OR 1.3 (95%CI 0.68 to 2.5); Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality at 24 hours; Mortality at 12 months; Quality of life at Define; Length of intensive care stay at Define; AE - Acute transfusion reaction at Define; AE - Haemolytic transfusion reaction – acute at Define; AE - Haemolytic transfusion reaction – delayed at Define; AE - Post transfusion purpura at Define; AE - Transfusion associated circulatory overload at Define; AE - Transfusion associated dyspnoea at Define; AE - Transfusion associated graft versus host disease at Define; Return to normal activities at Define; Psychological wellbeing at Define; Time to definitive control of haemorrhage at Define

G.4 Control of haemorrhage in hospital

G.4.1 Haemorrhage protocols

Table 57: [65]

Study (subsidiary papers)	**TRFL study trial: Nascimento 2013[65] (Nascimento 2011[66])**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=78)
Countries and setting	Conducted in Canada; Setting: Level 1 trauma centre, Toronto.
Line of therapy	First-line
Duration of study	Intervention + follow up: 28 day follow-up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall: Aged 16-90 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with traumatic injuries, aged 16-90 years, bleeding and expected to require massive transfusion (anticipated to need either 4 units of RBC within next 2 hours or great than or equal to10 units of RBC in 24 hours, or required uncrossmatched RBC), and had systolic blood pressure of less than or equal to 90 mmHg.
Exclusion criteria	Arrived at A&E more than 6 hours after injury, received more than 2 units of RBC before arrival, had a severe brain injury (as indicated by GCS <3, need of immediate neurosurgery, focal signs for example, anisocoria, CT evidence of intracranial bleeding, had a catastrophic brain injury [for example, transcranial gunshot wound, open skull fracture with exposure of brain matter, or expert medical opinion based on clinical presentation or CT]), had shock unrelated to haemorrhage (that is, cardiogenic, septic, neurogenic or obstructive [cardiac tamponade, tension pneumothorax or massive pulmonary emboli]), had an underlying hereditary or acquired coagulopathy, or were moribund.
Recruitment/selection of patients	Consecutive patients requiring transfusion and meeting inclusion criteria were invited to participate in the study.
Age, gender and ethnicity	Age - Median (IQR): Fixed-ratio = 41 (23-58); Lab testing = 34 (25-40). Gender (M:F): 47:22. Ethnicity: Not stated
Indirectness of population	No indirectness

Interventions	(n=40) Intervention 1: Major haemorrhage protocol - Empiric/transfusion. Fixed ratio (1:1:1) RBC, frozen plasma and platelet transfusion protocol. As plasma thawed on demand, these were often transfused later. Each set = 4 units of frozen plasma, 4 units of RBC, and 1 pool of platelets derived from the buffy coat (4 donor units). Duration maximum 12-hours (median 5 hours). Concurrent medication/care: Treatment as usual: Urgent operation/angioembolisation (n=22), decompressive craniectomy (n=2), administration of crystalloid (median = 4900 ml; IQR = 3000-7150), colloid (median = 0ml; IQR = 0-0), cryoprecipitate (median = 0 units; IQR = 0-0), tranexamic acid (n=5) Comments: Stated that laboratory testing was performed at the discretion of the attending physician. So lab-guided treatment may have occurred in some patients. (n=38) Intervention 2: Major haemorrhage protocol - Targeted (laboratory-guided/point-of-care guided). Blood tests (including complete blood count, international normalised ratio, partial thromboplastin time, and fibrinogen) conducted at least every 2 hours to guide transfusion. Transfusion of RBCs if haemoglobin level fewer than or equal to 70 g/litre, frozen plasma transfused in doses of 3-4 to maintain international normalised ratio of < 1.8, transfusion of platelets given to patient 4 units at a time if platelets dropped to <50 x 10^9/litre. Duration maximum 12 hours (median 5 hours). Concurrent medication/care: Treatment as usual: Urgent operation/angioembolisation (n=21), decompressive craniectomy (n=2), administration of crystalloid (median = 6050 ml; IQR = 4000-8781), colloid (median = 0 ml; IQR = 0-625), cryoprecipitate (median = 0 units; IQR = 0-10), tranexamic acid (n=6)
Funding	Academic or government funding (Canadian forces health services; defence research and development Canada; the national blood foundation, American association of blood banks)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: FIXED RATIO versus LABORATORY-GUIDED

Protocol outcome 1: Mortality at 30 days
- Actual outcome: Mortality (all causes) at 28 days; Group 1: 11/37, Group 2: 3/32; Risk of bias: Low; Indirectness of outcome: No indirectness
- Actual outcome: Mortality (exsanguination) at 28 days; Group 1: 8/37, Group 2: 3/32; Risk of bias: Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Blood product use
- Actual outcome: Median RBC units per patient during protocol; Risk of bias: Low; Indirectness of outcome:
- Actual outcome: Median frozen plasma units per patient during protocol; Risk of bias: Low; Indirectness of outcome:
- Actual outcome: Median platelet units per patient during protocol; Risk of bias: Low; Indirectness of outcome:
- Actual outcome: Median cryoprecipitate units per patient during protocol; Risk of bias: Low; Indirectness of outcome:

Protocol outcome 3: Thromboembolism

- Actual outcome: Incidence of deep vein thrombosis within 28 days; Group 1: 3/37, Group 2: 0/32; Risk of bias: Low; Indirectness of outcome: Protocol outcome 4: Blood product waste - Actual outcome: Plasma wasted during protocol; Group 1: 86/390, Group 2: 30/289 ; Risk of bias: Low; Indirectness of outcome:	
Protocol outcomes not reported by the study	Mortality at 24 hours; Mortality at 12 months; Health related quality of life; Length of intensive care stay; Over-transfusion related morbidity; Transfusion reactions; Infections; Patient reported outcomes

G.4.2 Haemorrhage imaging

Table 58: Brooks 2002[14]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Statistical measures and 2x2 tables				Comments
Brooks 2002[14]	**Study type:** Prospective cohort **Setting:** Accident and emergency department of a large teaching hospital **Country:** UK **Recruitment:** All patients	n=50 Final n=47 adults (3 excluded: gross surgical emphysema prevented adequate imaging) **Inclusion criteria:** Adult patients with multiple or suspected blunt abdominal injury. **Exclusion criteria:** Patients with sustained penetrating injury and those in extremis	**Male: Female** NR **Mean age:** NR **Other characteristics:** Mechanism of injury: MVC (20) MBC (13) Fall (7) Pedestrian v. vehicle (4) Assault (3) Other (3) ISS:	**Index test** FAST (Sonosite 180 handheld ultrasound) – standard 4 view technique (perisplenic, perihepatic, pericardial, pelvis). **Reference standard** Investigation of choice for attending surgeon/accident and emergency physician – 4 slice MDCT, diagnostic peritoneal lavage, laparoscopy, laparotomy or clinical observation. Time between index test and reference standard		Ref std +	Ref std -	Total	**Source of funding:** Support from the Drummond Foundation. **Limitations:** A range of reference standards used. For the 5 positives: 3 laparotomies, 2 of which followed from CT, 1 DPL and 1 post-mortem (cardiac arrest in the ED with massive HI so resuscitation abandoned) For the 42 negatives: 20 CT and 22 clinical
					Index test +	5	0	5	
					Index test -	0	42	42	
					Total	5	42	47	
					Sensitivity		100		
					Specificity		100		
					PPV		100		
					NPV		100		
					PLR		-		
					NLR		0.00		
					AUC		NR		

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Statistical measures and 2x2 tables		Comments
	triaged to resuscitation room from 1 June 2001 for a six-month period.	(where US would have led to a delay in definitive treatment).	Mean 13 Range 1-75	FAST @ circulation phase of primary survey or early in secondary survey. Time of reference standard is unclear. **Target condition** Haemoperitoneum			observations. Blinding: Unclear whether the two doctors performing FAST could also be the attending physician/A&E consultant deciding on follow-up care. <u>Additional data:</u> Two doctors performing index test were trained in FAST.

Table 59: Fox 2011[33]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Statistical measures and 2x2 tables				Comments
Fox 2011[33]	**Study type:** Prospective cohort **Setting:** Tertiary care Level 1 trauma centre emergency	n=431 Final n=357 children (74 excluded: no consent signatures, no confirmatory studies, wrong mechanism of injury) **Inclusion criteria:** Children (0-17 years)	**Male: Female** 230:127 **Age range:** 0-2: 34 2-6: 88 7-12: 79 13-17: 156 **Other**	**Index test** FAST (B+H Hawk 2102, Sonosite Titan or Sonosite Maxx) **Reference standard** 16 slice multi-detector CT or surgery.		Ref std +	Ref std -	Total	**Source of funding:** Second author supported by Alpha Omega Alpha Carolyn Kuckein research grant. **Limitations:** Although both CT and surgery used as RS,
					Index test +	12	13	25	
					Index test -	11	321	332	
					Total	23	334	357	
					Sensitivity Specificity		52 96		

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Statistical measures and 2x2 tables		Comments
	department **Country:** USA **Recruitment:** Paediatric blunt abdominal trauma requiring trauma team activation between 2004-2007.	with a blunt mechanism – falls, MVC, automobile v. pedestrian, non-accidental blunt trauma, and battery. **Exclusion criteria:** Injuries not considered as blunt abdominal trauma.	**characteristics:** Mechanism of injury: Automobile v. pedestrian/ cyclist 144 MVC 125 Fall 52 Blunt other (sports, animal, object) 24 Battery 7 Unknown 5 ISS: IQR (4-12)	Time between index test and reference standard: FAST on arrival and CT of the abdomen and pelvis within 30 minutes, or underwent laparotomy. **Target condition** Clinically important intraperitoneal free fluid (haemoperitoneum): • FAST – any FF in hepatorenal, splenorenal, suprapubic windows. • CT – moderate or more (for example, trivial, trace or small were not considered clinically important).	PPV NPV PLR NLR	48 97 13.4 0.50	only one patient received surgery, all others were CT. **Additional data:** Experienced physicians performed and interpreted FAST (all with at least 300 ultrasound exams).
					AUC	NR	

Table 60: Gaarder 2009[35]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Statistical measures and 2x2 tables				Comments
Gaarder 2009[35]	**Study type:** Prospective cohort **Setting:** Major European	n=110 Final n=104 (6 excluded for incomplete charts) **Inclusion criteria:** Potentially unstable	**Male: Female** 69:35 **Mean age (SD):** 31 (17) **Other characteristics:**	**Index test** FAST (LogiqbookXP) – standard four view (right and left upper quadrants, pelvis, and pericardium). **Reference standard**		Ref std +	Ref std -	Total	**Source of funding:** NR **Limitations:** Range of reference standards including: CT (67), DPL (7), laparotomy (11) and observation (19). True negative could be
					Index test +	16	3	19	
					Index test -	10	75	85	
					Total	26	78	104	

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Statistical measures and 2x2 tables		Comments
	trauma centre. **Country:** Norway **Recruitment:** All patients initiating trauma team activation between May 2005 to June 2006.	patients defined by initial systolic BP ≤90 mmHg, pulse rate ≥120 or base deficit ≥8. **Exclusion criteria:** Incomplete radiologic or patient chart information.	Mechanism of Injury: Blunt 90% (MVA, fall, other) Penetrating 10% Mean ISS 24	4 slice Helical CT, DPL or laparotomy. Time between index test and reference standard: Adjunct to primary survey (performed within 5-10 minutes of ED arrival. **Target condition** Haemoperitoneum.	Sensitivity Specificity	62 96	uneventful recovery with no further investigations = no confirmatory imaging or surgical investigation. Mixed population including 10% penetrating injury not stratified, and including children not stratified. Population restricted to only unstable patients. May be a mixed population, unclear what proportion of patients are children or young adults. **Additional data:** All FAST performed by trauma team radiologist. True positive defined as more than minimal fluid confirmed by CT or laparotomy.
					PPV NPV PLR NLR	84 88 16 0.40	
					AUC	NR	

Table 61: Hsu 2007[46]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Statistical measures and 2x2 tables	Comments

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Statistical measures and 2x2 tables				Comments
Hsu 2007[46]	**Study type:** Prospective cohort **Setting:** Tertiary referral teaching hospital designated as a Major Trauma Service. **Country:** Australia **Recruitment:** Between Sept 1999 and Dec 2004 and trauma patient that came through the emergency department.	n=463 Final n=410 (53 excluded due to lack of corresponding gold-standard investigation). **Inclusion criteria:** Potential blunt truncal injuries. **Exclusion criteria:** No results confirmed by CT or laparotomy.	**Male: Female** 291:119 **Mean age (SD):** 37.1 (23) 5 patients <16 years	**Index test** FAST (B-K Medical Panther) – standard four views (Morrison's pouch, splenorenal recess, pelvis and pericardial area. **Reference standard** 4 slice MDCT or laparotomy Time between index test and reference standard: Unclear. **Target condition** Intra-abdominal free fluid.		Ref std +	Ref std -	Total	**Source of funding:** NR **Limitations:** Mixed population (1% children). Unclear when index test and reference standard were performed. **Additional data:** FAST performed by Emergency Medicine Consultants (7), Emergency Medicine Registrars (8) or Surgical Registrars (2), all of whom had completed ultrasound training course. Trace free fluid, predominately in the pelvis, was the main findings on CT scans of false negative FAST examinations (largely clinically insignificant).
					Index test +	78	8	86	
					Index test -	22	302	324	
					Total	100	310	410	
					Sensitivity		78		
					Specificity		97		
					PPV		91		
					NPV		93		
					PLR		30.2		
					NLR		0.23		
					AUC		NR		

Table 62: Patel 1999[72]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Statistical measures and 2x2 tables				Comments
Patel 1999[72]	**Study type:** Retrospective cohort **Setting:** Level 1 trauma centre **Country:** USA **Recruitment:** Identified by querying the paediatric trauma registry for all children with blunt torso trauma from May 1995 to August 1997.	n=94 children **Inclusion criteria:** Paediatric blunt torso trauma. **Exclusion criteria:** NR	**Male: Female** 44:50 **Mean age (SD):** 11.3 (4.0) **Other characteristics:** Mechanism of injury: MVC 42 Vehicle versus pedestrian 25 Vehicle versus bike 15 Fall 5 Terrain vehicle 3 Motorcycles 1 Assault 1 Other 2 Mean ISS (SD) 21 (15.5)	**Index test** FAST – (pericardial space, subhepatic space (Morrison's pouch), splenorenal recess, and retrovesical space. **Reference standard** Operative intervention. MDCT at attending surgeon's discretion. Time between index test and reference standard: FAST performed during initial resuscitation phase. Unclear time between this at CT/laparotomy. **Target condition** Free intraperitoneal fluid.		Ref std +	Ref std -	Total	**Source of funding:** NR **Limitations:** Range of reference standards used including: laparotomy (3) CT (19), non-operative management (72). **Additional data:** FAST performed by senior in-house radiology resident. Median time of 10.5 minutes (mean 14 minutes) after arrival.
					Index test +	5	0	5	
					Index test -	8	81	89	
					Total	13	81	94	
					Sensitivity		38		
					Specificity		100		
					PPV		100		
					NPV		91		
					PLR		-		
					NLR		0.61		
					AUC		NR		

Table 63: Verbeek 2014[92]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Statistical measures and 2x2 tables	Comments
Verbeek 2014[92]	**Study type:** Retrospective cohort **Setting:** Level 1 trauma centre **Country:** Netherlands **Recruitment:** Identified by querying the hospital's prospective trauma database and ICD9 database from Jan 2004 to Dec 2009.	n=120 adults **Inclusion criteria:** High energy major pelvic fracture, involving disruption of the pelvic ring in at least 2 places. **Exclusion criteria:** Isolated pelvic fractures; transfer patients; patients dead on arrival	**Male: Female** 90:30 **Median age (IQR): 37 (28-53)** **Other characteristics:** Mechanism of injury: MVC 23% Mean ISS (SD) 26 (14)	**Index test** FAST – performed by trauma team radiologist, who was trained in its use. Aloka prosound SSD 3500Plus used. Considered positive if hemiperitoneum detected in any of the3 abdominal regions. **Reference standard** Multislice CT scanning. Read by two senior radiology residents, blinded to prior FAST. Laparotomy findings were also used to contribute to the gold standard diagnosis. Time between index test and reference standard: FAST performed during initial resuscitation phase. Unclear time between this at CT/laparotomy. **Target condition** hemiperitoneum.	ALL hemoperitoneums Ref std + / Ref std - / Total Index test +: 27 / 5 / 32 Index test -: 15 / 73 / 88 Total: 42 / 78 / 120 Sensitivity 0.64 Specificity 0.94 PPV 0.84 NPV 0.83 Moderate and large hemoperitoneums only Ref std + / Ref std - / Total Index test +: 18 / 5 / 23 Index test -: 3 / 73 / 76 Total: 21 / 78 / 99 Sensitivity 0.86 Specificity 0.94 PPV 0.78 NPV 0.96	**Source of funding:** NR **Limitations:** No reported time between tests, but highly likely there was no confoundingly long interval. **Additional data:** None

G.4.3 Whole-body computed tomography (CT)

Table 64: Yeguiauan 2012[94]

Study	Yeguiayan 2012[94]
Study type	Prospective cohort study
Number of studies (number of participants)	(n=1696)
Countries and setting	Conducted in France; Setting: ICU's and emergency departments from 14 university hospital in France.
Line of therapy	1st line
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients over the age of 18 with a severe blunt trauma requiring admission to the ICU within 72 hours of injury, or in the case of death.
Exclusion criteria	Patients with penetrating trauma, deaths before implementation of any trauma saving technique,
Age, gender and ethnicity	Age - Other: Stratified by age. Gender (M:F): 3:1. Ethnicity: Not reported
Further population details	
Indirectness of population	No indirectness
Interventions	(n=1696) Intervention 1: Full-body CT - vertex to pelvis. Defined by the trauma team.. Duration Not reported. Concurrent medication/care: Not applicable Further details: 1. Timing of full-body CT: Not applicable / Not stated / Unclear (n=254) Intervention 2: Selective imaging - Including x-ray and/or USS and/or focused CT. Selective CT to body area,. Duration Not reported. Concurrent medication/care: Not reported. Further details: 1. Timing of full-body CT: Not applicable / Not stated / Unclear
Funding	Academic or government funding (French Military of Health)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INCLUDING X-RAY AND/OR USS AND/OR FOCUSED CT versus VERTEX TO PELVIS	

Study	Yeguiayan 2012[94]
Protocol outcome 1: Mortality at 1 month - Actual outcome: Mortality at 30 Days; Risk of bias: High; Indirectness of outcome: Serious indirectness. GIV analysis for OR – 0.68 (0.45-1.04)	
Protocol outcomes not reported by the study	Quality of life; Mortality at 24 hours; Mortality at 6 months; Length of ICU stay; Blood products used; Patient reported outcomes (psychological wellbeing); Time to surgery; Long-term radiation risk; Delayed diagnosis/missed injury; Time to definitive haemorrhage control

G.4.4 Interventional radiology

Table 65: Azizzadeh 2013[4]

Study	Azizzadeh 2013[4]
Study type	Prospective cohort study
Number of studies (number of participants)	1 (n=106)
Countries and setting	Conducted in USA
Line of therapy	First-line
Duration of study	Intervention and follow-up: In-hospital
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	None stated
Exclusion criteria	None stated
Age, gender and ethnicity	Age - Mean (SD): 36.4. Gender (M:F): 74:106 male. Ethnicity: Not reported
Further population details	1. Severity of haemorrhage: Overall/mixed 2. Source of haemorrhage: Thoracic
Extra comments	Patients with blunt traumatic aortic injuries. Trauma registry 2002-2010

Indirectness of population	Very serious indirectness: Grade 2 intramural hematoma, grade 3 aortic pseudoaneurysm and grade 4 free rupture. Only the grade 4 patients went for immediate repair but the results of these are not reported separately
Interventions	(n=56) Intervention 1: Definitive surgery. Aortic clamping was performed to the left of the subclavian artery. The aorta was opened longitudinally and the tear inspected. An approximate sized woven Dacron tube graft was anastomosed to the proximal aorta. The distal anastomosis was performed and the graft was flushed. Duration Not relevant. Concurrent medication/care: Not stated Further details: 1. Time to IR: Not applicable / Not stated / Unclear (n=50) Intervention 2: Interventional radiology - Stent grafts. n=33 TAG (W L gore and Associates). n=18 Talent (Medtronic). All but two patients received a single device. Duration Not relevant. Concurrent medication/care: Not stated Further details: 1. Time to IR: Not applicable / Not stated / Unclear
Funding	Academic or government funding (National Institutes of Health Clinical and Translational Science Award Grant)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DEFINITIVE STENT GRAFTS versus SURGERY Protocol outcome 1: Mortality at 1 month - Actual outcome: Presence of complication including in-hospital death at In-hospital; OR 0.33 (95%CI 0.11 to 0.97) (p=0.45); Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: Length of intensive care stay at Define - Actual outcome: Length of ICU stay at ICU stay; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality at 24 hours; Mortality at 12 months; Health related quality of life at Define; Failure rate or re-intervention rate at Define; AE - ischaemic damage at Define; AE - necrosis at Define; AE - renal failure at Define; Time to definitive control of haemorrhage at Define; Blood product use at Define; Pain/discomfort at Define; Return to normal activities at Define; Psychological wellbeing at Define

Table 66: Demetriades 2008[25]

Study	**Demetriades 2008[25]**

Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=193)
Countries and setting	Conducted in USA
Line of therapy	1st line
Duration of study	Intervention + follow up: In hospital
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (18+years)
Subgroup analysis within study	Not applicable
Inclusion criteria	None stated
Exclusion criteria	None stated
Age, gender and ethnicity	Age - Mean (SD): 40.2 (18.7). Gender (M:F): 75.6% male. Ethnicity: Not stated
Further population details	1. Severity of haemorrhage: Overall/mixed 2. Source of haemorrhage: Thoracic
Extra comments	American Association for the Surgery of Trauma multicentre (18 centres). Patients with blunt traumatic thoracic aortic injuries
Indirectness of population	Very serious indirectness: 20.5% have an initial tear, 58.4% aneurysm and 25.4% dissection. The mean time to intervention is 54.6 hrs
Interventions	(n=125) Intervention 1: Interventional radiology - Stent grafts. Gore N=89. Cook N=17. Duration Time to procedure 48.1 hrs. Concurrent medication/care: None stated Further details: 1. Time to IR:

	(n=68) Intervention 2: Definitive surgery. Open repair. Duration Time to repair 67.6 (SD 136.0) hours. Concurrent medication/care: Not stated Further details: 1. Time to IR: Overall/mixed
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: STENT GRAFTS versus DEFINITIVE SURGERY Protocol outcome 1: Mortality at 1 month - Actual outcome: Mortality at In hospital; OR 8.42 (95%CI 2.76 to 25.69); Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: Failure rate or re-intervention rate at Define - Actual outcome: Systemic complications at In hospital; OR 1.41 (95%CI 0.75 to 2.34); Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 3: Blood product use at Define - Actual outcome: Blood products transfused units at In hospital; MD 4.98 (95%CI 0.14 to 9.82); Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 4: Length of intensive care stay at Define - Actual outcome: ICU length of stay days at Not applicable; MD 1.28 (95%CI -2.41 to 4.98); Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Hospital length of stay days at Not applicable; MD 4.77 (95%CI -5.33 to 14.86); Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality at 24 hours; Mortality at 12 months; Health related quality of life at Define; AE - ischaemic damage at Define; AE - necrosis at Define; AE - renal failure at Define; Time to definitive control of haemorrhage at Define; Pain/discomfort at Define; Return to normal activities at Define; Psychological wellbeing at Define

Table 67: Katsura 2013[50]

Study	**Katsura 2013[50]**
Study type	Retrospective cohort study

Number of studies (number of participants)	1 (n=317)
Countries and setting	Conducted in Japan
Line of therapy	First-line
Duration of study	Intervention and follow-up: In hospital
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Blunt trauma, pelvic fracture and hemoperitoneum (positive FAST)
Exclusion criteria	Severe head injury (AIS greater than or equal to 5) and those who underwent an initial therapeutic intervention (for example, craniotomy)
Age, gender and ethnicity	Age - Mean (SD): 48.8 (22.5). Gender (M:F): 58% male. Ethnicity: Japanese
Further population details	1. Severity of haemorrhage: 2. Source of haemorrhage:
Extra comments	Japan Trauma Bank 2003 to 2010
Indirectness of population	--
Interventions	(n=123) Intervention 1: Definitive surgery. Laparotomy. Duration Not relevant. Concurrent medication/care: None stated Further details: 1. Time to IR: (n=194) Intervention 2: Interventional radiology - Embolization. Transcatheter arterial embolisation. Duration Not relevant. Concurrent medication/care: None stated Further details: 1. Time to IR:
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DEFINITIVE SURGERY versus EMBOLIZATION	

Protocol outcome 1: Mortality at 24 hours - Actual outcome: Mortality (regression) at In hospital; OR 1.20 (95%CI 0.61 to 2.39); Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Mortality (propensity score) at In hospital; OR 1.13 (95%CI 0.63 to 2.01); Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality at 1 month; Mortality at 12 months; Health related quality of life at Define; Failure rate or re-intervention rate at Define; AE - ischaemic damage at Define; AE - necrosis at Define; AE - renal failure at Define; Time to definitive control of haemorrhage at Define; Blood product use at Define; Length of intensive care stay at Define; Pain/discomfort at Define; Return to normal activities at Define; Psychological wellbeing at Define

G.5 Monitoring

G.5.1 Coagulation testing

Table 68: Cotte 2013[19]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables	Comments

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
Cotte J, D'Aanda E, Chauvin V, Kaiser E, Meaudre E. Point-of-Care Coagulation Testing for Trauma Patients in a Military Setting: A Prospective Study. Journal of Special Operations Medicine. 2013; 13(4):59-62.	**Study type:** Prospective cohort study **Setting:** French military hospital **Country:** Afghanistan **Recruitment:** All trauma patients from October 2011 to January 2012	n=40 (69 measurements) **Inclusion criteria:** • Trauma patients **Exclusion criteria:** • Pre-existing non-traumatic coagulopathy • Technical issues that made it impossible to obtain and treat blood samples	**Male: Female** 95%:5% **Median (range)** • Age: 22.5 (6-70) • ISS: 13.7 (1-41) • 16 civilians • 70% penetrating injuries	Samples drawn for all tests at the same time **Index test** Point of care PT Quick value using CoaguChek XS. A Quick value of >60% was considered a positive test. This was chosen from the ROC as it represents the author's belief of the best cut-off between sensitivity specificity Index test performed by a hospital anaesthesiologist **Reference standard** Laboratory PT Quick value **Target condition** Laboratory PT Quick value >50%	Sensitivity Specificity	77.1% 94.1%	**Source of funding:** None detailed

Table 69: Davenport 2011[22]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables	Comments

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
Davenport R, Manson J, De'Ath H, Platton S, Coates A, Allard S et al. Functional definition and characterization of acute traumatic coagulopathy. Critical Care Medicine. 2011; 39(12):2652-2658.	**Study type:** Prospective cohort study **Setting:** Single centre. Level 1 trauma centre **Country:** UK **Recruitment:** January 2007 – June 2009	n=300 **Inclusion criteria:** • Adult trauma patients (>15 years) who met local criteria for full trauma team activation **Exclusion criteria:** • Arrival at emergency department (ED) more than 2 hours after injury • Administration of more than 2000ml if IV fluid prior to ED arrival • Transfer from another hospital • Burns covering more than 5% of total body area • Patient declined to give consent • Patient taking anticoagulant medications • Patient had	**Male: Female** 82%:18% **Median (IQR)** • age: 33 (23-48) • ISS: 12 (4-25) • Time from injury to blood sampling: 86 (69-112) **Number of patients (%)** • ISS >15: 126 (42) • Penetrating injury: 62 (21) • Any PRBC: 68 (23) • PRBC >10: 11 (4) • FFP: 46 (15)	Samples drawn for all tests at the same time **Index test** Point of care PT using CoaguChek XS. ATC was considered present in patients with PTr >1.2. No detail of who performed index test. **Reference standard** Laboratory PT **Target condition** Acute traumatic coagulopathy (ATC) was defined as a laboratory PTr >1.2.	False negative rate False positive rate Detection rate	29% 23% 77%	**Source of funding:** Supported by the National Institute for Health Research. Pentapharm GmbH (Munich, Germany) provided ROTEM reagent and equipment on an unrestricted basis.

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
		moderate or severe liver disease or a known bleeding diathesis					

Table 70: David 2012[23]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
David JS, Levrat A, Inaba K, Macabeo C, Rugeri L, Fontaine O et al. Utility of a point-of-care device for rapid determination of prothrombin time in trauma patients: a preliminary study. Journal of Trauma and Acute	**Study type:** Prospective cohort study **Setting:** Trauma resuscitation unit. **Country:** France **Recruitment:** Non-consecutive trauma patients. December 2007 - May 2009.	n=48 (50 samples) **Inclusion criteria:** • Trauma patients **Exclusion criteria:** • People on VKA	**Male: Female** 67%:33% **Mean age (95% CI):** 45 (39-50) **Number of patients (%)** • Blunt trauma: 44 (92%) **Median (IQR)** • ISS: 18 (9-32)	Samples drawn for all tests at the same time **Index test** INRatio Monitoring System. INR >1.5 considered a positive result. (Study also reported post-hoc sensitivity and specificity for positives >1.3 and >1.4 INR) No detail of who performed index test. **Reference standard** Standard INR laboratory coagulation assay. **Target condition** Need for transfusion. This was defined as a laboratory result of INR >1.5	Sensitivity Specificity PPV NPV AUC (95% CI)	50 (21-79) 100 (91-100) 100 86 0.946 (0.845-0.982)	**Source of funding:** Institutional funding from Hospices Civils de Lyon **Limitations:** Non-consecutive patients **Additional data:**
					Post-hoc analysis >1.4 INR Sensitivity Specificity PPV NPV >1.3 INR Sensitivity	 83 (52 to 98) 89 (75 to 97) 71 94 92 (62 to 100)	

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
Care Surgery. 2012; 72(3):703-707.					Specificity PPV NPV	79 (63 to 90) 0.58 0.97	

Table 71: Hagemo 2015[43]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
Hagemo JS, Christiaans SC, Stanworth SJ, Brohi K, Johansson PI, Goslings JC et al. Detection of acute traumatic coagulopathy and massive transfusion requirements by means of rotational	**Study type:** Prospective cohort study **Setting:** Four major trauma centres in 3 countries: UK, Denmark, Norway **Recruitment:** Non-consecutive trauma patients. January 2007 – November 2011.	n=808 **Inclusion criteria:** • Adults requiring full trauma team activation **Exclusion criteria:** • Received more than 2000mL of fluid before arrival in ED • Arrived in ED more than 2 hours after injury • Pregnancy • Liver failure • Bleeding disorders • Taking oral anticoagulant medication other than acetyl salicylic	**Male: Female** 77%:23% **Median (IQR):** Age: 38 (28) ISS: 16 (20) Blunt trauma: 82% Massive transfusion: 49 (6%) patients Acute traumatic coagulopathy: 89 (11%) patients	Samples drawn for all tests at the same time – within 20 minutes of arrival in hospital **Index test** ROTEM Delta Test performed by dedicated study personnel **Reference standard** • Future blood product use for massive transfusion • Conventional coagulation tests **Target condition** • Massive transfusion (MT): defined as 10 or more units of PRBC within 24 hours • Acute traumatic coagulopathy (INR>1.2 through laboratory PT)	**Massive transfusion** Clotting time (CT) Pre-set cut-off Detection rate False positive rate PPV NPV EXTEM CA5 Pre-set cut-off Detection rate False positive rate PPV NPV Alpha angle Pre-set cut-off Detection rate False positive rate	 >94 seconds 0.289 0.088 0.165 0.955 ≤35mm 0.455 0.161 0.144 0.963 <65 degrees 0.372 0.122	**Source of funding:** Support from TEM International in the form of reagents and leasing of devices at reduced prices **Limitations:** Non-consecutive patients

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
thromboelastometry: an international prospective validation study. Critical Care. 2015; 19(1):823.		acid			PPV	0.151	
					NPV	0.960	
					Massive transfusion		
					EXTEM CA5		
					Optimised cut-off	≤40mm	
					Detection rate	0.727 (0.57-0.85)	
					False positive rate	0.313 (0.28–0.35)	
					PPV	0.122	
					NPV	0.977	
					FIBTEM CA5		
					Optimised cut-off	≤9mm	
					Detection rate	0.775 (0.62-0.89)	
					False positive rate	0.328 (0.29-0.36)	
					PPV	0.114	
					NPV	0.982	
					Acute traumatic Coagulopathy		
					EXTEM CA5		
					Optimised cut-off	≤37mm	
					Detection rate	0.663 (0.55-0.76)	
					False positive rate	0.188 (0.16-0.22)	
					PPV	0.299	
					NPV	0.952	
					FIBTEM CA5		
					Optimised cut-off	≤8mm	

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
					Detection rate	0.675 (0.56-0.78)	
					False positive rate	0.207 (0.18-0.24)	
					PPV	0.269	
					NPV	0.956	

Table 72: Jeger 2012[48]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
Jeger V, Willi S, Liu T, Yeh DD, de Moya M, Zimmermann H et al. The Rapid TEG alpha-Angle may be a sensitive predictor of transfusion in moderately injured blunt trauma patients. TheScientificWorldJo	**Study type:** Prospective cohort study **Setting:** Level 1 trauma centre **Country:** Switzerland **Recruitment:** Trauma patients from November 2009 – May 2010	n=76 **Inclusion criteria:** • > 16 years old • Suspected multiple injuries • Physician with TEG experience available **Exclusion criteria:** • None detailed	**Male: Female** 55:21 **Mean (SD):** • Age: 49 (21) • ISS: 18 (10) • Lactate (mmol/litre): 2.3 (1.8) • Hct (%): 36.5 (6.8) • Base deficit (mEq/L): -2.7 (3.3) **Number (%):** • Blunt trauma: 63 (83)	Samples drawn for all tests at the same time **Index test** • Kaolin TEG • Rapid TEG Cut-off values selected by optimising sensitivity and specificity using ROC Run in resuscitation bay Physicians blinded to results. **Reference standard** Need for transfusion within 24 hours **Target condition** Need for transfusion. Defined by future transfusion within 24 hours	Rapid K Cut-off Sensitivity Specificity PPV NPV AUC Kaolin K Cut-off Sensitivity Specificity PPV NPV AUC Rapid α-angle Cut-off Sensitivity Specificity PPV	 >1.8 minutes 68% 78% 61% 83% 79% >1.7 minutes 68% 59% 46% 78% 67% <74.7 degrees 84% 57% 49%	**Source of funding:** • Supported by AACC Critical and POC Testing Research Grant 2009. • TEG reagents and consumables provided by Haemonetics Corporation **Limitations:** Non-consecutive patients **Additional data:**

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
urnal. 2012; 2012:821794.					NPV	88%	
					AUC	77%	
					Kaolin α-angle		
					Cut-off	<58.5 degrees	
					Sensitivity	72%	
					Specificity	61%	
					PPV	47%	
					NPV	82%	
					AUC	66%	
					Rapid MA		
					Cut-off	<59.6 mm	
					Sensitivity	68%	
					Specificity	80%	
					PPV	63%	
					NPV	83%	
					AUC	75%	
					Kaolin MA		
					Cut-off	<58.4 degrees	
					Sensitivity	56%	
					Specificity	88%	
					PPV	70%	
					NPV	80%	
					AUC	70%	
					Rapid TMA		
					Cut-off	>17.3 minutes	

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
					Sensitivity	76%	
					Specificity	57%	
					PPV	46%	
					NPV	83%	
					AUC	69%	
					Kaolin TMA		
					Cut-off	>24.7 minutes	
					Sensitivity	64%	
					Specificity	63%	
					PPV	46%	
					NPV	78%	
					AUC	58%	
					Rapid G		
					Cut-off	<7374 d/sc	
					Sensitivity	68%	
					Specificity	78%	
					PPV	61%	
					NPV	83%	
					AUC	73%	
					Kaolin G		
					Cut-off	<7073 d/sc	
					Sensitivity	56%	
					Specificity	88%	
					PPV	70%	
					NPV	80%	
					AUC	70%	

Table 73: Levrat 2008[55]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
Levrat A, Gros A, Rugeri L, Inaba K, Floccard B, Negrier C et al. Evaluation of rotation thrombelastography for the diagnosis of hyperfibrinolysis in trauma patients. British Journal of Anaesthesia. 2008; 100(6):792-797.	**Study type:** Prospective cohort study **Setting:** Trauma resuscitation unit **Country:** France **Recruitment:** All trauma patients admitted between July 4th and October 30th 2004.	n=23 **Inclusion criteria:** • Trauma patient **Exclusion criteria:** • Oral anticoagulant treatment [from Rugeri 2007]	**Male: Female** 78%:22% **Median (IQR):** • Age: 25 (21-47) • ISS: 38 (24-75) • 87% blunt trauma	Samples drawn for all tests at the same time **Index test** ROTEM coagulation analyser. • The positive test thresholds chosen for each parameter were ideal values taken from the ROC • Δ parameter = (parameters_APTEM – parameter_EXTEM)/ parameter_EXTEM) × 100 No detail of who performed index test. **Reference standard** ELT **Target condition** Hyperfibrinolysis: defined as ELT <90 minutes	Value (95% CI) CA_{10} Threshold Sensitivity Specificity AUC CA_{15} Threshold Sensitivity Specificity AUC MCF Threshold Sensitivity Specificity AUC CLI_{30} Threshold Sensitivity Specificity AUC CLI_{60} Threshold Sensitivity Specificity AUC ΔMCF Threshold	 ≤10 1 (0.81-1) 1 (0.48-1) 1 (0.85-1) ≤12 1 (0.81-1) 1 (0.48-1) 1 (0.85-1) ≤18 1 (0.81-1) 1 (0.48-1) 1 (0.85-1) ≤71 1 (0.75-1) 0.75 (0.2-0.96) 0.87 (0.61-0.98) ≤1 1 (0.63-1) 1 (0.4-1) 1 (0.4-1) >7	**Source of funding:** Institutional funding

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
					Sensitivity	1 (0.81-1)	
					Specificity	0.8 (0.29-0.97)	
					AUC	0.92 (0.72-0.99)	
					ΔCA_{15} Threshold	>4	
					Sensitivity	1 (0.81-1)	
					Specificity	0.6 (0.15-0.94)	
					AUC	0.87 (0.66-0.97)	
					ΔCLI_{30} Threshold	>2	
					Sensitivity	1 (0.71-1)	
					Specificity	0.75 (0.2-0.96)	
					AUC	0.75 (0.47-0.93)	
					ΔCLI_{60} Threshold	>43	
					Sensitivity	1 (0.63-1)	
					Specificity	1 (0.4-1)	
					AUC	1 (0.73-1)	

Table 74: Mitra 2012[61]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables				Comments
Mitra B, O'Reilly G,	**Study type:**	n=72	**Male: Female**	Samples drawn for all tests at the same time		Ref std +	Ref std -	Total	**Source of funding:**

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables				Comments
Collecutt M, Cameron PA, Phillips L, Davis A. Prospective comparison of point-of-care international normalised ratio measurement versus plasma international normalised ratio for acute traumatic coagulopathy. EMA - Emergency Medicine Australasia. 2012; 24(4):363-368.	Prospective cohort study **Setting:** Major trauma centre **Country:** Australia **Recruitment:** Trauma patients admitted in 2010	**Inclusion criteria:** • Met trauma call-out criteria • COAST score ≥3 **Exclusion criteria:** • None detailed	54:18 **Mean age:** 41.6 (18.7) Penetrating trauma: 10 (13.9%)	**Index test** CoaguChek XS **Reference standard** Laboratory INR (using STAR Evolution). In resuscitation bay **Target condition** Acute traumatic coagulopathy Defined as INR >1.5 or aPTT >60 seconds from reference standard	Index test +	24	4	28	CoaguChek XS machine donated by Roche Australia. Test strips for the system were funded by the Transfusion Outcomes Research Collaborative.
					Index test -	14	30	44	
					Total	38	34	72	

Table 75: Rugeri 2007[79]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
Rugeri L, Levrat A, David JS, Delecroix E, Floccard B, Gros A et al. Diagnosis of early coagulation abnormalities in trauma patients by rotation thrombelastography. Journal of Thrombosis and Haemostasis. 2007; 5(2):289-295.	**Study type:** Prospective cohort study **Setting:** Trauma centre **Country:** France **Recruitment:** All patients admitted to trauma centre between July and October 2004	n=88 **Inclusion criteria:** • Trauma patient **Exclusion criteria:** • Oral anticoagulant treatment	**Male: Female** 68:20 **Mean (SD):** • age: 34 (16) • ISS: 22 Median INR on admission was 1.3	Samples drawn for all tests at the same time **Index test** ROTEM Thresholds chosen as ideal values from ROC No detail of who performed index test. **Reference standard** MDA II: for PT, INR, APTT Fibriquick: for fibrinogen SE-9500: for platelets and haemoglobin **Target condition** Need for transfusion It is defined as any of the following: • PT >1.5 of control value • APTT > 1.5 of control value • Platelet count < 50×10^9 L^{-1} • Fibrinogen < 1 g/litre	CA_{15}-EXTEM Cut-off Sensitivity Specificity PPV NPV AUC CFT-INTEM Cut-off Sensitivity Specificity PPV NPV AUC CA_{10}-FIBTEM Cut-off Sensitivity Specificity PPV NPV AUC CA_{15}-INTEM Cut-off	Value (95% CI) versus PT 32 mm 87 (72-87) 100 (99-100) 100 (83-100) 99 (98-99) 0.98 versus APTT 112 seconds 100 (84-100) 74 (73-74) 23 (19-23) 100 (98-100) 0.94 vs fibrinogen 5 mm 91 (72-93) 85 (84-86) 55 (45-60) 99 (97-100) 0.96 versus platelets 46 mm	**Source of funding:** Support from BIODIS

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
					Sensitivity Specificity PPV NPV AUC	100 (71-100) 83 (82-83) 17 (12-17) 100 (98-100) 0.92	

Table 76: Woolley 2013[93]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
Woolley T, Midwinter M, Spencer P, Watts S, Doran C, Kirkman E. Utility of interim ROTEM-« values of clot strength, A5 and A10, in predicting final assessment of coagulation status in severely	**Study type:** Prospective cohort study **Setting:** UK military field hospital **Country:** Afghanistan **Recruitment:** Trauma patients who were admitted between 21st May 2009 and 3rd July 2009	n=48 (108 samples) 30 (40 samples) received both tests **Inclusion criteria:** • Met criteria for full trauma team activation **Exclusion criteria:** • None detailed	**Male: Female** 100%:0% **Median (IQR)** • Plt (10^9/l): 142 (107-213) • Fib (g/dl): 2.9 (2.3-3.7) • NISS: 34 (17-43) • Age: 24 (21-26)	Samples drawn for all tests at the same time **Index test** ROTEM Coagulopathy defined as EXTEM MCF <40 mm. Undertaken by designated OR staff. **Reference standard** Standard laboratory PT **Target condition** Coagulopathy. Defined as lab test PT >1.5 normal values (which corresponds to PT >18 seconds).	TP TN FP FN Sensitivity Specificity	6 17 9 8	**Source of funding:** Funded by the UK Ministry of Defence **Limitations:** 18 (38%) included patients did not receive index test or gold standard **Additional data:**

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard and target condition	Statistical measures and 2x2 tables		Comments
injured battle patients. Injury. 2013; 44(5):593-599.							

G.6 Warming

Table 77: Gentilello 1997[39]

Study	Gentilello 1997[39]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=47)
Countries and setting	Conducted in USA
Line of therapy	First-line
Duration of study	2 Years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (18 and over)
Inclusion criteria	Patients of 18 years or older admitted to the intensive care unit (ICU) after injury if a pulmonary artery catheter was required to guide initial resuscitation and the initial core temperature reading was <34.5 Celsius.
Exclusion criteria	Patients with an injury that precluded access to the femoral artery or with an non-survivable brain injury.
Age, gender and ethnicity	Age - Mean (SD): 46.55 years. Gender (M:F): 1:1. Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	(n=29) Intervention 1: Combination of above - Combination. Continuous arteriovenous rewarming (CAVR). Percutaneous cannulation of the femoral artery with a specially designed 8.5-French catheter. Blood was heated extracorpeally to 36oC before infused again. Duration of study. Concurrent medication/care: Simultaneous administration of warm intravenous fluids (Sims Level 1 Technologies, Rockland, Ma), airway re-warming (Concha Therm II; Hudson Respiratory Care, Inc, Temecula, CA), a convective air blanket (Augustine Medical, Eden Prairie, MN)

Study	Gentilello 1997[39]
	and aluminzed Therma Drape Hat (OR Concepts, Dallas, TX) (n=28) Intervention 2: Combination of above - Combination. Simultaneous administration of warm intravenous fluids (Sims Level 1 Technologies, Rockland, Ma), airway re-warming (Concha Therm II; Hudson Respiratory Care, Inc., Temecula, CA), a convective air blanket (Augustine Medical, Eden Prairie, MN) and aluminised Therma Drape Hat (OR Concepts, Dallas, TX). Duration of study. Concurrent medication/care: Not reported
Funding	Industry and Government; Supported by a grant from Sims Level 1 Technologies Inc., Rockland, Maryland, USA and CDC Grant #R40-CCR-00-2750
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINATION versus COMBINATION Protocol outcome 1: Mortality at 24 hours - Actual outcome for Adults (18 and over): Mortality at 24 Hours; Group 1: 4/29, Group 2: 12/28; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life; Length of intensive care stay; Adverse effects: Skin burns, hyperthermia, infection; Neurological outcome; Patient reported outcome: Pain/discomfort, return to normal activities, psychological wellbeing

G.7 Pain

G.7.1 Pain management

Table 78: Bounes 2010 [11]

Study	Bounes 2010[11]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=108)
Countries and setting	Conducted in France; Setting: All inclusions were performed in the out-of-hospital Emergency Service of Toulouse University Hospital (Purpan Hospital, Toulouse, France), located in an urban area but also covering suburban and rural areas (1,156,000 inhabitants, 6,300 km^2 [2,400 square miles]). France has a sophisticated and modern system of out-of-hospital emergency care. It is 2 tiered, with basic life support ambulances staffed by emergency medical

Study	Bounes 2010[11]
	technicians or firemen and physician-staffed ambulances. These mobile ICUs consist of a physician (usually an experienced emergency physician or anaesthesiologist), a nurse, and an emergency medical technician, and only those ambulances enrolled subjects and carried out the study.
Line of therapy	First-line
Duration of study	Intervention + follow-up: 8 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults 18 years or over
Inclusion criteria	Patients were eligible for inclusion if aged 18 years or older, with acute severe pain (defined as a numeric rating scale score of 6/10 or higher) caused by trauma.
Exclusion criteria	The exclusion criteria were known morphine, sufentanil, acetaminophen, or ketoprofen allergies; patient-reported history of chronic respiratory, renal, or hepatic failure; inability to understand or communicate; altered consciousness or judgment because of alcohol or sedative drugs; previous use of analgesic medication within 6 hours; life-threatening situations; uncontrolled epilepsy; treatment with monoamine oxidase inhibitor; pregnancy or breastfeeding; drug addiction; and inclusion in another clinical trial.
Recruitment/selection of patients	A standard statement that briefly explained the nature of the study was read to eligible patients, and if they (or any family members present) did not refuse participation, they were enrolled.
Age, gender and ethnicity	Age - Mean (range): 45.5 years (29-65 years). Gender (M: F): 3:1. Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	(n=54) Intervention 1: Intravenous Opiates - Morphine. Intravenous 0.15 mg/kg morphine followed by 0.075 mg/kg every 3 minutes until pain relief defined as a numeric rating scale score of equal to or less than 3/10. Duration 15 minutes. Concurrent medication/care: Each 20-ml syringe contained 1.5 mg/ml morphine. The first volume administered was 1 ml per 10 kg (0.15 mg/kg morphine) followed by 0.5 ml per 10 kg (0.075 mg/kg morphine) every3 minutes until pain relief. At the first injection, patients also received 1 g acetaminophen and 100 mg ketoprofen, both in a 15-minute intravenous infusion. Further details: 1. Dose: (n=54) Intervention 2: Intravenous Opiates - Fentanyl. Duration 15 minutes. Concurrent medication/care: Each 20-ml syringe contained either 1.5 micrograms/ml sufentanil. The first volume administered was 1 ml per 10 kg (0.15 micrograms/kg sufentanil) followed by 0.5 ml per 10 kg (0.075ug/kg sufentanil) every 3 minutes until pain relief. At the first injection, patients also received 1 g acetaminophen and 100 mg ketoprofen, both in a 15-minute intravenous infusion. Further details: 1. Dose:

Study	Bounes 2010[11]
Funding	Academic or government funding (Toulouse University Hospital)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MORPHINE versus SUFENTANIL Protocol outcome 1: Pain levels - Actual outcome for Adults 18 years or over: % Patients achieving pain remission at 15 minutes; Group 1: 38/54, Group 2: 40/54; Risk of bias: High; Indirectness of outcome: Serious indirectness. Protocol outcome 2: Adverse effects (Nausea, Respiratory depression, hallucinations) - Actual outcome for Adults 18 years or over: Incidence of Nausea at 15 minutes; Group 1: 0/54, Group 2: 3/54; Risk of bias: Low; Indirectness of outcome: No indirectness. - Actual outcome for Adults 18 years or over: Supplementary O_2 required due to SpO2 lower than 90% at 15 minutes; Group 1: 2/54, Group 2: 1/54; Risk of bias: Low; Indirectness of outcome: No indirectness. Protocol outcome 3: Level of consciousness - Actual outcome: Sedation level on 4 point Sedation scale at 15 minutes; Group 1: 2/54, Group 2: 5/54; Risk of bias: High; Indirectness of outcome: Serious Indirectness.	
Protocol outcomes not reported by the study	Health-related quality of life; Patient reporting outcomes (psychological wellbeing)

Table 79: Craig 2012 [21]

Study	Craig 2012[21]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=55)
Countries and setting	Conducted in United Kingdom; Setting: Emergency department of NHS Hospital with 60,000 patients per annum.
Line of therapy	First-line
Duration of study	Intervention time: 10 month
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults 18 years or over
Inclusion criteria	Isolated limb trauma, Moderate to severe pain, with initial verbal pain score of 7 or more, Age >15 and <66 years,

Study	Craig 2012[21]
	Estimated weight >50 kg.
Exclusion criteria	Chest pain, Glasgow Coma Scale <15, Allergy to morphine or paracetamol, Known liver disease, or patient clinically jaundiced, Major trauma, Known pregnancy, Breast feeding, Patients requiring an immediate limb-saving procedure, Patients in extreme distress, Communication difficulties (foreign language, prior confusion)preventing informed consent or cooperation with pain scoring.
Recruitment/selection of patients	Patients were required to provide informed consent.
Age, gender and ethnicity	Age - Mean (range): 36.5 years (16-62 years). Gender (M: F): 1:1. Ethnicity: Not reported
Indirectness of population	Serious indirectness: Major trauma patients excluded but definition meets other inclusion criteria.
Interventions	(n=28) Intervention 1: Intravenous Opiates - Morphine. 10 mg of morphine sulphate. Duration 15 minutes. Concurrent medication/care: After the initial infusion the patient's pain relief was judged to be inadequate, intravenous morphine titrated to effect was used as 'rescue analgesia'. If the patient complained of nausea, intravenous metoclopramide was offered as an antiemetic to those older than 21 years. If the patient was discharged following the study they were advised to take no more than 3 g of paracetamol in the next 24 h. If admitted, an inpatient drug chart was written so that no more than 3 g of paracetamol could be administered over the next 24 h. If the patient was discharged following the study they were advised to take no more than 3 g of paracetamol in the next 24 h. If admitted, an inpatient drug chart was written so that no more than 3 g of paracetamol could be administered over the next 24 h. If the patient was discharged following the study they were advised to take no more than 3 g of paracetamol in the next 24 h. If admitted, an inpatient drug chart was written so that no more than 3 g of paracetamol could be administered over the next 24 h. If the patient was discharged following the study they were advised to take no more than 3 g of paracetamol in the next 24 h. If admitted, an inpatient drug chart was written so that no more than 3 g of paracetamol could be administered over the next 24 hours. (n=27) Intervention 2: Intravenous Paracetamol - Acetaminophen. 1g of intravenous paracetamol. Duration 15 minutes. Concurrent medication/care: After the initial infusion the patient's pain relief was judged to be inadequate, intravenous morphine titrated to effect was used as 'rescue analgesia'. If the patient complained of nausea, intravenous metoclopramide was offered as an antiemetic to those older than 21 years. If the patient was discharged following the study they were advised to take no more than 3 g of paracetamol in the next 24 h. If admitted, an inpatient drug chart was written so that no more than 3 g of paracetamol could be administered over the next 24 h. If the patient was discharged following the study they were advised to take no more than 3 g of paracetamol in the next 24 h. If admitted, an inpatient drug chart was written so that no more than 3 g of paracetamol could be administered over the next 24 h. If the patient was discharged following the study they were advised to take no more than 3 g of paracetamol in the next 24 h. If admitted, an inpatient drug chart was written so that no more than 3 g of

Study	Craig 2012[21]
	paracetamol could be administered over the next 24 h. If the patient was discharged following the study they were advised to take no more than 3 g of paracetamol in the next 24 h. If admitted, an inpatient drug chart was written so that no more than 3 g of paracetamol could be administered over the next 24 h. Further details: 1.
Funding	Academic or government funding (College of Emergency Medicine)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MORPHINE versus ACETOMINOPHEN Protocol outcome 1: Pain levels - Actual outcome for Adults 18 years or over: Change in Pain at 15 minutes; Group 1: mean (SD) 61.6 (19.8); n=27, Group 2: mean (SD) 69.9 (17.8); n=28; Visual analogue scale 0-100 Top=High is poor outcome; Risk of bias: High; Indirectness of outcome: No indirectness. - Actual outcome for Adults 18 years or over: Change in Pain at 30 minutes; Group 1: mean (SD) 55.0 (29.7); n=27, Group 2: mean (SD) 63.5 (22.3); n=28; Visual analogue scale 0-100 Top=High is poor outcome; Risk of bias: High; Indirectness of outcome: No indirectness. - Actual outcome for Adults 18 years or over: Change in Pain at 30 minutes; Group 1: mean (SD) 44.0 (22.6); n=27, Group 2: mean (SD) 52.9 (27.4); n=28; Visual analogue scale 0-100 Top=High is poor outcome; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: Adverse effects (Nausea, Respiratory depression, hallucinations) - Actual outcome for Adults 18 years or over: Incidence of Adverse Effects at 60 minutes; Group 1: 8/27, Group 2: 2/28; Risk of bias: High; Indirectness of outcome: Serious indirectness. Protocol outcome 3: Patient reporting outcomes (psychological wellbeing) - Actual outcome for Adults 18 years or over: Patients Satisfaction at 60 minutes; Group 1: 14/26, Group 2: 9/25; Risk of bias: High; Indirectness of outcome: No indirectness.	
	Health-related quality of life; Level of consciousness

Table 80: Farsi 2013 [31]

Study	Farsi 2013[31]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=200)

Countries and setting	Conducted in Iran; Setting: The study was conducted in the ED of an academic large trauma center.
Line of therapy	First-line
Duration of study	2 Years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults 18 years or over
Inclusion criteria	Patients over 20 years of age presenting to the ED with pain following acute limb trauma of less than three days' duration, and considered by the ED attending professors to require opioid analgesia, were suitable for inclusion.
Exclusion criteria	Exclusion criteria were: requirement of rescue analgesia, death of patients in less than one hour, referral of patients to the operating room in less than one hour, multiple trauma patients for whom the ED attending professor ordered naloxone or more opioids, unwillingness to provide informed consent or to receive a second dose of analgesic, serious life-threatening complications such as respiratory depression after the first dose injection, previous adverse reaction to morphine, cognition problems, or disoriented patients who were unable to cooperate.
Recruitment/selection of patients	Patients had to be able to supply written consent prior to involvement.
Age, gender and ethnicity	Age - Other: Group 1, 32.8 years (30.4-35.2 years); Group 2, 33.1 years (30.3-35.9years). Gender (M: F): 4:1. Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	(n=100) Intervention 1: Intravenous Opiates - Morphine. 0.15 mg/kg of morphine. Duration 60 minutes. Concurrent medication/care: All participants received an initial dose of morphine sulfate at 0.10 mg/kg. Reassessment of pain was performed at 30 minutes from baseline, followed immediately by intravenous administration of morphine at 0.05 mg/kg. (n=100) Intervention 2: Intravenous Opiates - Morphine. 0.10 mg/kg Morphine. Duration 60 minutes. Concurrent medication/care: All participants received an initial dose of morphine sulfate at 0.10 mg/kg. Reassessment of pain was performed at 30 minutes from baseline, followed immediately by intravenous administration of colourless placebo.
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MORPHINE versus MORPHINE

Protocol outcome 1: Pain levels
- Actual outcome for Adults 18 years or over: Between group difference in mean before after change in pain score at 30 minutes; Group 1: mean 5.2 (SD 2.6); n=100,

Group 2: mean 5.69 (SD 2.5); n=100; Visual Analogue Scale 0-10 Top=High is poor outcome; Risk of bias: Low; Indirectness of outcome: No indirectness. Protocol outcome 2: Adverse effects (Nausea, Respiratory depression, hallucinations) - Actual outcome for Adults 18 years or over: Incidence of Nausea at Not specified; Group 1: 8/100, Group 2: 10/100; Risk of bias: High; Indirectness of outcome: No indirectness. - Actual outcome for Adults 18 years or over: Incidence of Respiratory Depression at Not specified; Group 1: 0/100, Group 2: 0/100; Risk of bias: Low; Indirectness of outcome: No indirectness. - Actual outcome for Adults 18 years or over: Decreased level of consciousness at Not specified; Group 1: 4/100, Group 2: 5/100; Risk of bias: Low; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Health-related quality of life; Level of consciousness; Patient reporting outcomes (psychological wellbeing)

Table 81: Galinski 2007 [37]

Study	**Galinski 2007[37]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=73)
Countries and setting	Conducted in France; Setting: Five emergency departments using mobile intensive care units.
Line of therapy	First-line
Duration of study	Intervention and follow-up: 2 Years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults 18 years or over
Inclusion criteria	Patients were eligible for inclusion if they presented a trauma with a severe acute pain defined as a visual analogue scale (VAS) score of at least 60/100; were aged between 18 and 70 years; and were without acute respiratory, hemodynamic, or neurologic compromise (respiratory distress signs, systolic blood pressure V90 mmHg, Glasgow Coma Score greater or equal to 15).
Exclusion criteria	Exclusion criteria included the presence of a psychiatric history; chronic respiratory, renal, or hepatic failure; known ketamine sensitivity; known opioid allergies; treatment of chronic pain or treatment with opioids; incapacity to understand the VAS; pregnancy; or indication for local or regional analgesia. Patients who had already received an opioid analgesic (either by self-administration or by another attending physician) were also excluded.
Recruitment/selection of patients	All patients provided written informed consent
Age, gender and ethnicity	Age - Other: Presented separately for groups Group 1, 35 years (13 years); Group 2, 40 years (14 years). Ethnicity: Not

Study	Galinski 2007[37]
	reported
Indirectness of population	No indirectness
Interventions	(n=35) Intervention 1: Intravenous Opiates - Morphine. 0.2 ml/kg of placebo was given over 10 minutes with 0.1 mg/kg of morphine, followed by additional doses of 3 mg every 5 minutes until pain relief was obtained as defined by a VAS score not exceeding 30/100. Duration 30 minutes. Concurrent medication/care: Initial morphine dose administrated against pain score. (n=38) Intervention 2: Intravenous Ketamine - Ketamine. The dilution of ketamine was 1 mg/Ml. The first volume administered was 0.2 ml d kg^{-1} (0.2 mg d kg^{-1}) of ketamine (Ketamine; Panpharma, France). 3 mg of morphine was allowed every 5 minutes until pain relief was obtained as defined by a VAS score not exceeding 30/100.Duration 30 minutes. Concurrent medication/care: Initial morphine dose administrated against pain score.
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MORPHINE versus KETAMINE Protocol outcome 1: Pain levels - Actual outcome for Adults 18 years or over: Final pain score at 30 minutes; Group 1: mean (95% CI) 39.5 (32.4-46.6) ; n=32, Group 2: mean (95% CI) 34.1 (25.5-42.6); n=33; Risk of bias: High; Indirectness of outcome: No indirectness. Protocol outcome 2: Adverse effects (Nausea, Respiratory depression, hallucinations) - Actual outcome for Adults 18 years or over: Presence of Nausea at 30 minutes; Group 1: 4/32, Group 2: 8/33; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome for Adults 18 years or over: Ramsey Score (Greater than or equal to 3) at 30 minutes; Group 1: 2/32, Group 2: 7/33; Risk of bias: High; Indirectness of outcome: No indirectness. Protocol outcome 3: Patient reporting outcomes (psychological wellbeing) - Actual outcome for Adults 18 years or over: Patient satisfaction at 30 minutes; Group 1: 22/32, Group 2: 18/33; Risk of bias: Very high; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Health-related quality of life; Level of consciousness.

Table 82: Gurnani 1996 [42]

Study	Gurnani 1996[42]

Study	Gurnani 1996[42]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=40)
Countries and setting	Conducted in India; Setting: Accident and Emergency Departments
Line of therapy	First-line
Duration of study	Unclear
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis
Stratum	Adults 18 years or over
Inclusion criteria	Patients suffering from acute musculoskeletal trauma not requiring immediate corrective surgical intervention.
Exclusion criteria	Patients in severe shock or those suffering from hypertension, hepatic, renal, cardiac, or debilitating diseases
Recruitment/selection of patients	Consecutive patients were randomised following informed consent.
Age, gender and ethnicity	Age - Mean (SD): 32.1 years (0.5 years). Gender (M: F): 2:1. Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Intravenous Opiates - Morphine. Initial administration of 0.1 mg/kg morphine followed by further doses of 0.1 mg/kg diluted in physiological saline every 4 hours. Duration Every 4 hours. Concurrent medication/care: Inadequate analgesia (Pain score above 5) were administered top does of 3mg morphine on demand. (n=20) Intervention 2: Intravenous Ketamine - Ketamine. Initial bolus of 0.25 mg/kg of ketamine administered, followed by a constant infusion of 0.1 mg/kg/hour. Duration Every 4 hours. Concurrent medication/care: Inadequate analgesia (Pain score above 5) were administered top does of 3mg morphine on demand.
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MORPHINE versus KETAMINE

Protocol outcome 1: Pain levels
- Actual outcome for Adults 18 years or over: Change in Pain score at 1 hour; Risk of bias: Very high; Indirectness of outcome: Only provides information provided graphical information. Full results are not reported.

Protocol outcome 2: Adverse effects (Nausea, Respiratory depression, hallucinations)
- Actual outcome for Adults 18 years or over: Incidence of nausea at 24 hours; Group 1: 7/20, Group 2: 0/20; Risk of bias: High; Indirectness of outcome: No

Study	Gurnani 1996[42]
indirectness. - Actual outcome: Incidence of Hallucinations at 24 hours; Group 1: 0/20, Group 2: 2/20; Risk of bias: High; Indirectness of outcome: Serious indirectness.	
Protocol outcomes not reported by the study	Health-related quality of life; Level of consciousness; Patient reporting outcomes (psychological wellbeing).

Table 83: Jennings 2012A [49]

Study	Jennings 2012A[49]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=135)
Countries and setting	Conducted in Australia; Setting: The study was undertaken in 6 regional and 4 metropolitan sites in Victoria, Australia,. The state of Victoria is serviced by a single out-of-hospital provider, Ambulance Victoria, which services 5 rural regions and a metropolitan region. The metropolitan region provides an emergency medical response to Melbourne (population 3.9 million people15; area 9,000 km^2). The rural regions provide care to the remainder of the state (population 1.4 million people15; area 218,416 km^2). Emergency medical services (EMS) respond to approximately 450,000 calls each year.
Line of therapy	First-line
Duration of study	Intervention and follow-up: 30 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults 18 years or over
Inclusion criteria	Patients were eligible for enrolment if they were assessed by the attending paramedics as having all of the following: were aged 18 years or older, conscious (Glasgow Coma Scale [GCS] score_15), reporting traumatic pain with a verbal numeric rating scale pain score greater than or equal to 5 after a total dose of intravenous morphine of 5 mg (and methoxyflurane according to clinician judgment if clinically indicated), and speaking and able to rate their pain with the verbal numeric rating scale
Exclusion criteria	Patients were excluded if any of the following applied: known allergy to ketamine or morphine, pregnant or lactating, current ischemic chest pain or acute pulmonary edema, severe hypertension (systolic blood pressure _180 mmHg) and evidence of a head injury, a history of loss of consciousness or GCS score less than 15, inability to obtain venous access, and presumed intoxication with alcohol or illicit substances.
Recruitment/selection of patients	The requirement for informed consent was waived in accordance with Australian government regulations. All patients were contacted within 8 weeks to be provided with further information about the study and to gain informed consent to access their medical record.

Study	Jennings 2012A[49]
Age, gender and ethnicity	Age - Median (range): 43 years (26-66 years). Gender (M:F): 3:2. Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	(n=65) Intervention 1: Intravenous Opiates - Morphine. Morphine 10 mg was diluted in 9 ml of normal saline solution, resulting in 1 mg/ml of solution. The dosing schedule for morphine was an initial bolus of up to 5 mg (up to5 ml), followed by 5-minute increments of 1 to 5 mg (1 to 5ml). Paramedics used their clinical judgment on dosing according to patient age and body size. Morphine continued to be administered according to this schedule until the patient became pain free, there was a serious adverse event (for example, profound hypotension, unconsciousness, respiratory depression requiring ventilatory support), or the patient arrived at the receiving emergency department (ED).. Duration Until patient arrived at ED. Concurrent medication/care: After initial dose of 5mg (IV) morphine. Further details: 1. Dose: Not applicable/Not stated/Unclear (n=70) Intervention 2: Intravenous Ketamine - Ketamine. Ketamine 200 mg was diluted in 18 ml of normal saline solution, resulting in 10 mg/ml of solution. The dosing schedule for ketamine was an initial bolus of 10 or 20 mg (1 or 2 ml), followed by increments of 10 mg (1 ml) every 3 minutes. Paramedics used their clinical judgment on dosing according to patient age and body size. Ketamine continued to be administered according to this schedule until the patient became pain free, there was a serious adverse event (for example, profound hypotension, unconsciousness, respiratory depression requiring ventilatory support), or the patient arrived at the receiving emergency department (ED). Duration Until patient arrived at ED. Concurrent medication/care: After initial dose of 5 mg (IV) morphine. Further details: 1. Dose:
Funding	Academic or government funding (Transport Accident Commission (TAC) Health Research Fellowship)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MORPHINE versus KETAMINE

Protocol outcome 1: Pain levels
- Actual outcome for Adults 18 years or over: Change in verbal pain score; Group 1: mean 3.2 (SD 3.29.1); n=65, Group 2: mean 5.6 (SD 2.56); n=70; Verbal numeric rating score 0-10 Top=High is poor outcome; Risk of bias: High; Indirectness of outcome: Very serious indirectness

Protocol outcome 2: Health-related quality of life
- Actual outcome for Adults 18 years or over: Physical Component Summary SF36 at One Month; Group 1: mean 47.9 (SD 10.9); n=50, Group 2: mean 49 (SD 11.1); n=47; SF36 0-100 Top=High is good outcome; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome for Adults 18 years or over: Mental Component Summary SF36 at One Month; Group 1: mean 50 (SD 13.2); n=50, Group 2: mean 50 (SD 12); n=47; Risk of bias: High; Indirectness of outcome: No indirectness

Study	Jennings 2012A[49]
Protocol outcome 3: Adverse effects (Nausea, Respiratory depression, hallucinations) - Actual outcome for Adults 18 years or over: Incidence of Nausea at discharge; Group 1: 6/65, Group 2: 3/70; Risk of bias: Low; Indirectness of outcome: No indirectness - Actual outcome for Adults 18 years or over: Loss of consciousness (GCS score equal to or less than 13) at discharge; Group 1: 1/65, Group 2: 3/70; Risk of bias: Low; Indirectness of outcome: No indirectness - Actual outcome: Hallucinations (characteristic of Emergence Phenomenon at discharge; Group 1: 0/65, Group 2: 4/70 Risk of bias: Low; Indirectness of outcome: Serious indirectness	
Protocol outcomes not reported by the study	Level of consciousness; Patient reporting outcomes (psychological wellbeing)

Table 84: Smith 2012 [84]

Study	Smith 2012[84]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=214)
Countries and setting	Conducted in USA; Setting: Prehospital: Patients transported by helicopter for evaluation of traumatic injuries. Each team consists of a critical care nurse and a flight physician. Physicians are a combination of board-certified emergency physicians, senior emergency medicine residents, and some surgeons/anaesthesiologists with critical care and advanced life support training.
Line of therapy	First-line
Duration of study	Intervention and follow-up: Not specficied
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults 18 years or over
Inclusion criteria	Patients were enrolled if they reported pain and could communicate to the medical crew their pain severity on a numeric pain scale (NPS).
Exclusion criteria	Patients were excluded if they reported an allergy to morphine or fentanyl, or if they were hypotensive before receiving the first dose of the study drug (systolic blood pressure <100 mmHg). They were also excluded if they were in custody or known to be pregnant.
Age, gender and ethnicity	Age - Mean (SD): 38 years (13 years). Gender (M: F): 3:1. Ethnicity: Not stated
Indirectness of population	No indirectness

Study	Smith 2012[84]
Interventions	(n=104) Intervention 1: Intravenous Opiates - Morphine. Each millilitre contained either 4 mg of morphine. Patients who reported any pain score other than zero were then given the study drug in a 1-ml intravenous bolus. Patients were then reassessed every 5 minute (normal flight protocol, with automated monitor and clinical evaluation) during transport with a complete set of vital signs (including pulse oximetry) and another numeric pain score. During each reassessment, a 1-ml bolus of the study drug was given for any pain score >0. Duration Not reported. Concurrent medication/care: Not reported Further details: 1. Dose: Low Dose (0.05 ml/kg). (n=100) Intervention 2: Intravenous Opiates - Fentanyl. Each millilitre contained either 50 micrograms of fentanyl. Patients who reported any pain score other than zero were then given the study drug in a 1-ml intravenous bolus. Patients were then reassessed every 5 minute (normal flight protocol, with automated monitor and clinical evaluation) during transport with a complete set of vital signs (including pulse oximetry) and another numeric pain score. During each reassessment, a 1-ml bolus of the study drug was given for any pain score >0. Duration Not reported. Concurrent medication/care: Not reported Further details: 1. Dose: Low Dose (0.71 micrograms/kg).
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MORPHINE versus FENTANYL Protocol outcome 1: Pain levels - Actual outcome for Adults 18 years or over: Final pain score at mean 40 minute; Group 1: mean 5.8 (SD 2.7); n=103, Group 2: mean 5.5 (SD 2.4); n=97; Numeric Pain Scale 0-10 Top=High is poor outcome; Risk of bias: Low; Indirectness of outcome: No indirectness. Protocol outcome 2: Adverse effects (Nausea, Respiratory depression, hallucinations). - Actual outcome: Incidence of nausea of vomiting at mean 40 minute; Group 1: 0/103, Group 2: 0/97; Risk of bias: Low; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Health-related quality of life; Level of consciousness; Patient reporting outcomes (psychological wellbeing).

Table 85: Tran 2014

Study	Tran 2014 [89]
Study type	RCT (Patient randomised; Parallel)

Study	Tran 2014 [89]
Number of studies (number of participants)	(n=312)
Countries and setting	Conducted in Vietnam; Setting: Prehospital: Patients who were referred to the Quang Tri Provincial General Hosptial, which is surgical referral centre following transfer from a community hospital.
Line of therapy	First-line
Duration of study	Intervention and follow-up: 18 Months, September 2007- March 2009
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Mixed population
Inclusion criteria	Trauma patients transferred to the Quang Tri Provincial Hospital
Exclusion criteria	Objections to pain treatment by the patient or the patient's family, comatose patients, patients given in-field anaesthesia for invasive life support measures, deep unconsciousness upon first infield contact, infants less than 30 months of age, and patients with a pre-hospital evacuation time of less than 10 minutes.
Age, gender and ethnicity	Age - Mean (SD): 36.2 years (not reported). Gender (M: F): 3:1. Ethnicity: Not stated
Indirectness of population	No indirectness
Interventions	(n=142) Intervention 1: Intramuscular Opiates - Morphine. Administered in one single intramuscular dose of 10mg for adults and 5mg for children. (n=170) Intervention 2: Intravenous Ketamine. Administered as slow intermittent intravenous doses of 0.2-0.3 mg/kg.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MORPHINE versus KETAMINE Protocol outcome 1: Pain levels - Actual outcome for Adults 18 years or over: Change in pain score; Group 1: mean 3.1; n=139, Group 2: mean 3.5; n=169; Visual analogue score Scale 0-10 Top=High is poor outcome; Risk of bias: Very high; Indirectness of outcome: Serious indirectness. (Cannot be meta-analysed) Protocol outcome 2: Adverse effects (Nausea, Respiratory depression, hallucinations). - Actual outcome: Incidence of nausea of vomiting; Group 1: 27/139, Group 2: 8/169; Risk of bias: High; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Health-related quality of life; Level of consciousness; Patient reporting outcomes (psychological wellbeing).

G.8 Documentation

Table 86: Deckelbaum 2009[24]

Study	Deckelbaum 2009[24]
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=7753)
Countries and setting	Conducted in USA
Line of therapy	Mixed line
Duration of study	Intervention and follow up: In hospital
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Not stated
Exclusion criteria	Not stated
Age, gender and ethnicity	Age - Mean (SD): 36.4 (18) versus 36.9 (19). Gender (M:F): 75% male. Ethnicity: Not stated
Further population details	1. Age: Not applicable / Not stated / Unclear
Extra comments	Trauma and burn patients. Data collected between 2003.2006. USA
Indirectness of population	--
Interventions	(n=4038) Intervention 1: electronic medical record. No details. Duration Not relevant. Concurrent medication/care: No details (n=3481) Intervention 2: No electronic medical record. No details. Duration Not relevant. Concurrent medication/care: No details
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ELECTRONIC MEDICAL RECORD versus NO ELECTRONIC MEDICAL RECORD

Protocol outcome 1: Mortality at 30 days
- Actual outcome: Mortality at In hospital; Group 1: 304/4038, Group 2: 312/3481; Risk of bias: High; Indirectness of outcome: No indirectness

Study	Deckelbaum 2009[24]
Protocol outcome 2: Missing data at Define - Actual outcome: Floor notes at In hospital; Group 1: 3553/4038, Group 2: 35/3481; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Procedure notes at In hospital; Group 1: 3529/4038, Group 2: 2715/3481; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Resuscitation notes at In hospital; Group 1: 3604/4038, Group 2: 2820/3481; Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: ICU notes at In hospital; Group 1: 3678/4038, Group 2: 2785/3481; Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 3: Delay in diagnosis at Define - Actual outcome: Delay in diagnosis at Not relevant; Group 1: 304/4038, Group 2: 312/3481; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Mortality at 24 hours; Mortality at 1 year; Quality of life at Define; Psychological well-being at Define; Complications at Define; Time to transfer at Define; Length of stay at Define

G.9 Information and support

Table 87: Gabbe 2013[36]

Study (ref id)	Gabbe 2013[36]
Aim	To investigate injured patients' experiences of trauma care to inform improvements in service delivery.
Population	Adults (18 or more) who had been treated through the Victoria State Trauma System. Patients in the VSTR or VOTOR (see below) who were blunt trauma patients, patients at least 12-24 months after injury, aged 18 or over, and who had received definitive care at an adult trauma MTC. Purposive sampling was used to ensure sample reflected the diversity of registry patients. The target was 120 with 60 of each sex, with even representation of registries, hospitals and compensatory status across three age groups (18-44, 45-64, ≥65 years). n = 120; Male 52.5%, female 47.5%. Mean age 48.6 (SD 17.6), 40% 18-44 years, 40% 45-64 years, 20% ≥65 years. 90% blunt trauma patients. MOI: 20% MVC, 15.7% Motorbike crash, 26.6% fall, 13.3% cyclist, 10.8% pedestrian, 10% other, 4.2% struck/collision, 3.3% horse-related.
Setting	The Victoria State Trauma System. All 138 trauma-receiving hospitals have a system level of designation. One paediatric and two adult hospitals are defined as major trauma centres. Used the Victorian State Trauma registry (VSTR) which collects data on all major trauma patients in Victoria, and the Victorian Orthopaedic Trauma Outcomes Registry (VOTOR) which collects data on adult orthopaedic trauma patients with a length of stay over 24 hours admitted to four hospitals.
Study design	Qualitative interview study
Methods and	Individual in-depth, semi-structured telephone interviews were used to enable participants to speak freely about their experiences. All interviews

Study (ref id)	Gabbe 2013[36]
analysis	were conducted between 1 April 2011 and 31 January 2012. Three experienced interviewers completed the interview using a topic guide with prompts about key issues for exploration (including issues relating to injury treatment such as: What information or advice did you receive about your injury? If you didn't receive information, what information would you have liked to have received and from whom?) Thematic analysis to identify important thematic groupings and the relationships between them. This involved (1) reading each transcript and listening to the recorded interview if appropriate to make sense of the interview data, 2) re-examining the transcript as a component of all interviews to make sense of what was being said by the participants as a group. 22% of interviews were double-coded to enable cross-checking of coding and interpretation of data. Each researcher generated and collated these codes into tentative themes. The emerging coding frame was discussed and developed throughout the process. The coding frame was based on common topics, patterns, and relationships emerging from the transcripts. The themes in the coding frame were allowed to be revised and refined in an iterative process. This constant comparison method was used to ensure reliability. Transcripts were revisited a number of times to ensure consistency of meaning of individual responses.
Themes with findings	**Setting 1. Hospital care**
	Quality of care. The overall impression of the hospital care received was positive, with a sense of being fortunate to receive high-quality care.
	Delays. Orthopaedic trauma patients perceived their lesser injury severity as a key factor in the delays to surgery that were common. Delays experienced by all participants were common and were perceived to prolong their time spent in hospital and their overall recovery.
	Communication. Most participants reported issues with communication and receipt of information. Common factors were timings, lack of engagement of the patient and the impersonal nature of the process. Common issues were: a lack of information about diagnosis or incorrect prognosis; inability to absorb information because of the effects of the injury or associated treatments (e.g. medication); insufficient explanation of the risks of treatment options, or providing treatment options without sufficient information to make an informed decision; conflicting information provided by clinicians; and limited engagement of the patient in decision making.
	Setting 2. Hospital-discharge and post-discharge care
	Preparation for discharge. Many felt ill prepared for discharge either emotionally, physically or as a result of insufficient information about their limitations and post-discharge care.
	Lack of coordinated care. There was a consistent theme of a lack of coordination of care, and the absence of a consistent point of contact for patients about their on-going management.
Limitations and applicability of evidence	The researchers follow clear methods to ensure the validity and rigour of their qualitative analysis. However of note is that there is no explicit mention of reflexivity. The researchers do not detail their professional backgrounds or provide insight into how this may have influenced the interview and analysis process. The researchers provide an in-depth analysis of the themes that emerged in participants talk about their time in trauma service care. The inclusion of questions that directly relate to our review protocol, and a research aim clearly in line with the current topic and wider trauma service delivery sphere, makes this evidence highly applicable. While their context is slightly larger (including discharge) some of the themes are still relevant to our specific trauma ED setting.

Table 88: Leske 2013[54]

Study (ref id)	Leske 2013[54]
Aim	To describe family experiences of 'family presence during resuscitation' option after trauma from motor vehicle crashes and gunshot wounds.
Population	Family members of trauma patients aged 18 years and older, who required resuscitation prior to admission to the surgical intensive care unit (SICU). Convenience sample of family members defined as "a group of individuals bonded by biological, legal, or social relationships". One family member per patient and had only one critically injured patient in the family. n=28 family members. 71% female. Mean age 47 years (SD 13 years, range 21-75 years). Predominantly self-identified as white (82%). Most were either a spouse (29%) or parent (29%) of the injured person (child 18%, sibling 7% and other 18%). Information about the injured family members: 22 MVC's, 6 GSW. 18 arrived by ambulance, 10 arrived by Flight for Life. Excluded family members of people younger than 18, and those patients with cardiac, burns, suicidal and brain injuries because they were admitted to other units or specialised facilities. Family members were also excluded if there was a fatality in the traumatic event.
Setting	Family members recruited from a major level 1 adult trauma centre in the American Midwest within two days of the injured person being admitted into the SICU. Data was collected from October 2010 to June 2012.
Study design	A descriptive, qualitative design allowing the researcher to determine a 'social reality'.
Methods and analysis	Interviews lasted between 30-60 minutes, were undertaken in a quiet, private room and were transcribed verbatim. The interviews focused on the experience of being present with a family member undergoing medical care after trauma. Participants were enrolled until no new data emerged from the interviews (saturation). The interview transcripts were analysed using qualitative content analysis (translating text into meaning through coding and theme identification).
Themes with findings	**Theme 1: Role of the healthcare professional**
	a) **Multiple people helping the patient.** Many participants described being overwhelmed by the number of HCP involved with their family members, but ultimately being relieved staff were so focussed on helping their family member.
	b) **Assessment of damages**. Many participants mentioned recognising what the HCP were doing, for example, rolling them over, cutting off clothing, splinting, putting in IV's and chest tubes. All felt it was comforting or reassuring to be able to "see everything".
	c) **Professionalism and teamwork**. Many participants valued the professionalism and teamwork of the HCP's on the trauma teams. *Note: Examples provided here included "very informative", "I was kept informed as things were being done", and "gratitude for the information the health care professionals provided".*
	Theme 2: Role of the family member
	a) **Provide information to the medical team and other family members**. Family members felt they provided key information about things, such as medical history, medications and insurance. And act as go-betweens to other family members outside of the resuscitation room.
	b) **Ensure the team is doing their job.** This theme reflected family members' wishes to be constantly informed and up to date with the latest, and

Study (ref id)	Leske 2013[54]
	have the ability to actually see what was being done. c) **Close proximity to provide physical and emotional comfort**. Acknowledge that the patient may be afraid and that they can provide the emotional comfort needed to help them survive the experience. Note: included in this theme is a clear message that most participants, while being happy with their decision to be present in the resuscitation room, felt that it may not be the best for all people, and should only be offered as an opportunity, not something that was encouraged for everyone.
Limitations and applicability of evidence	There is no explicit mention of reflexivity. The researchers do not detail their professional backgrounds or provide insight into how this may have influenced the interview and analysis process. For instance, if they came across as health professionals within the hospital environment, then perhaps participants may have felt slightly overwhelmed and this may have affected how they described their experiences. This is especially important given that the participants were recruited very shortly after what was very likely to have been a highly stressful and scary experience. The investigators offer a very limited explanation of the key themes identified. Sometimes they rely heavily on participant's quotes, which in themselves do not enlighten the reader as to how the key themes were identified and narrowed down. A more in-depth analysis of how the participants' talk relates to the key themes identified would have been helpful. For example in the 'professionalism and teamwork' category under the larger theme of the 'role of the healthcare professional', many of the quotes listed as examples of this theme mention the information that the trauma team provided to the family members. However, no further exploration of this idea is offered by the authors, it is only the quotes themselves that give us a hint of this critical aspect of the participants' interaction with the medical team. Investigator identified pros: Rigor and trustworthiness were ensured through: • Addressing transferability by providing thick description of the research context to allow readers to make informed judgements • Peer debriefing to meet credibility requirements. Researchers shared experienced with the study team to address judgements and emotions that could affect analysis. This was an attempt to reduce bias based on preconceived ideas and beliefs. • A stepwise approach to analysis enhanced dependability so that future researchers could replicate the work. • Maintaining an audit trail of all data collected and analyses performed in order to ensure that the conclusions reflected the experiences of the participants rather than the researcher Investigator self-identified limitations: written field notes rather than audio-taped interviews meant that there was no opportunity for repeat listening to the interview for others to offer interpretation. The population and setting of this study are directly applicable to our review question. However the study being focused on a more generally descriptive experience, rather than explicitly exploring what the family members wanted and felt about their experience, slightly limits applicability. While some of the themes feature ideas about information and support that would be appreciated, these are not adequately explored by the study authors. One minor concern is that this is US based and therefore concerns about medical insurance may have added to participants' anxiety.

Table 89: McGahey-Oakland 2007[56]

Study (ref id)	McGahey-Oakland 2007[56]
Aim	To describe the experiences of family members whose children underwent resuscitation in a children's hospital emergency department and identify critical information about family experiences to improve circumstances for future families.
Population	English and Spanish-speaking adult family members of children undergoing resuscitation prior to arrival at the ED. n=10 family members (seven mothers, two fathers, and one great grandmother). Six Hispanic, two White and two Black with a mean age of 35.9 (SD 11.9, range 23-65 years). Information about the injured/ill family members: three children had chronic illnesses, seven experienced acute life-threatening events. All 10 children died after the resuscitation event. The time-lapse between the child's resuscitation and the interview ranged from 1 to 2 years. Participants were identified through a performance improvement activity of the hospital's cardio-pulmonary resuscitation committee, including medical record review. English and Spanish-speaking adult family members of children undergoing resuscitation prior to arrival at the ED.
Setting	Large paediatric tertiary hospital in Texas between March 2002 and April 2003.
Study design	Descriptive, retrospective survey and qualitative one-to-one interview study.
Methods and analysis	The Parkland Family Presence During Resuscitation/Invasive Procedures Unabridged Family Survey (FS) and five investigator-developed questions about their experience being present during resuscitation were used. The survey includes 22 open-ended questions about family presence during resuscitation. Interviews were approximately one hour long. Audio of the interviews was transcribed verbatim. Three investigators independently identified emerging themes and categories were established when investigators came together.
Themes with findings	**Theme 1. It's my right to be here.** All participants felt it was an unequivocal right, an innate and instinctual responsibility as a parent to be present with their child. They were the central person in their child's life and many felt they were the link between the child and other family members. *Note: Many participants recognised that not all family members may want to be present but that it was important to give them the option. And many agreed that although they believed they should be there, if their presence would be detrimental to the child then it would be appropriate for the medical team to ask them to leave.*
	Theme 2. Connection and comfort makes a difference. Many believed that their presence provided strength for the children and helped them not to be too afraid. Physical presence was also felt to help the family member with their later grieving.
	Theme 3. Seeing is believing. Being able to see the medical team undertaking resuscitation seemed to reassure family members that all possible options were being attempted to save their child. It also made family members realise the severity of their child's condition. All family members interviewed believed that this experience was superior to receiving updates from the waiting room.
	Theme 4. Getting in. There were different experiences of how the family members came to be present. Some were explicitly invited, while for others it was more of a passive process where they were in the room and not asked to leave. Without having a formal 'family presence' policy in place, it is left up to staff discretion and this can result in inconsistent treatment of family members.

Study (ref id)	McGahey-Oakland 2007[56]
	Theme 5. Information giving. Many family members felt that the most important thing was them being with their child and that time for receiving information was after the event rather than during. S*ome indicated that having a family facilitator with them to explain things <u>when requested</u> would have been helpful*. The family members made it clear that they their questions would be answered at a later point. Also mentioned under this theme were conversations around organ donation and that family members expressed the importance of not being pressured in their decision.
Limitations and applicability of evidence	There is no explicit mention of reflexivity. The researchers do not detail their professional backgrounds or provide insight into how this may have influenced the interview and analysis process. For instance, if they came across as health professionals or connected to the hospital, then perhaps participants may have felt slightly overwhelmed and this may have affected how they described their experiences. This is especially important given that the participants were talking about an experience connected with the extremely emotional event of losing a child. Author-recognised limitations were the small sample size and time lag between the event and the interview which may have 'altered recall'. This study may not be directly application to our review question due to the population. This paper was a very specific population of family members of children who died after the resuscitation event that the family members were present for. This limits the applicability of the findings in respect to our review protocol and population of interest. It is not necessarily clear whether the 70% of the population that were brought to hospital because of an "acute life-threatening event" could be defined as trauma patients. Another reason this study may not be directly applicable is that some of the content in the themes is related to the different healthcare system in America compared with the UK (for example worries that specifically relate to limited financial resources [lack of medical insurance] and the effect that may have on the care provided).

Table 90: Sleney 2014[83]

Study (ref id)	Sleney 2014[83]
Aim	To explore experiences of patients after injury and identify implications for clinical care and support within the hospital setting and primary care.
Population	n=89 people who had experienced trauma from three hospitals. 53 had been admitted as hospital inpatients following injury and 36 had been treated in the ED and either discharged or referred for a follow-up appointment. Included 19 people aged between 5-17 years old. 40 males and 49 females. For children aged under 12 (8) a parent or carer was interviewed.
Setting	Three centres across England between September 2005 and April 2008. Part of the larger UK Burden of Injury Study.
Funding	Study funded by the Department of Health
Study design	Semi-structured telephone administered qualitative interviews.
Methods and analysis	All interviews were recorded, transcribed and the researchers performed an in-depth thematic content analysis with assistance from NVivo 7. One researcher carried out all analysis and a senior researcher checked the validity of the coding and theme development in 20 of the 89 interviews. The researcher read through each transcript and coded sentences or paragraphs under broad general headings or more specific areas. The codes were then explored in more detail using NVivo and paper transcripts, and were revisited on a number of occasions, comparing and contrasting comments between difference participants and within individual transcripts to check consistency of meaning. This constant comparison technique

Study (ref id)	Sleney 2014[83]
	is a well-recognised means of ensuring reliability.
Themes with findings	**Theme 1. Positive experiences of care in hospital.** Positive aspects of care mentioned across participants include promptness or otherwise of treatment, interactions with hospital staff, the general care and comfort they experienced, and the information they had been given about their treatment or aftercare. Many participants reported that particular members of staff (surgeons, ward staff, nurses or physiotherapists) had taken the time to explain the treatment they were to receive or had received and to answer questions. This was much valued.
	Theme 2. Negative experiences of care in hospital. Most negative comments related to the severe time pressures that hospital staff seemed to be under. While mostly being sympathetic to the situation, participants observed that it took a long time for nurses to answer call bells. And there were reports of instances of staff being thoughtless, inconsiderate towards their feelings or rude. Other negative comments about care were that staff hadn't listed to participants reported that something was wrong. This made participants feel vulnerable or not in control.
	Theme 3. Delays in receiving appropriate care. Some participants reported that due to bed shortages they had been put on general medical wards rather than specialist surgical wards and staff had been unsure how to treat them (for example: no adequate pain medication or long waits until diagnoses). Sometimes people reported that these delays in care made them feel depersonalised.
	Theme 4. Communication amongst hospital staff. Some participants reported lack of communication between staff members which resulted in less than adequate care (for example: lengthy waits for pain medication of confusion over appropriate treatment). Others reported feeling unsettled in an already stressful situation when they received conflicting information, particularly around the need for physiotherapy, from different departments.
	Theme 5. Communication of information to patients. For many participants, the information they received in relation to their injury met their needs. In a minority of cases, the language used by the healthcare professional was reported as too technical to fully understand. Of more importance was that many participants would have welcomed more information, mostly in relation to treatment or aftercare (for example: when would improvements be noticed, when can they use their injure limb as normal, and whether mobility and strength would improve?). Some of these may be complex for the clinical perspective but are central to the injured person's desire to return to normal life. For some participants conflicting or lack of information related to perceived problems with treatment. Both verbal and written information were felt to be useful, especially written to take home with them as more difficult to 'take it all in' in the hospital situation.
	Theme 6. Social support after discharge. In the majority of cases participants had at least one person to support them on discharge from hospital. However one person, with no family or friends near as she had just moved to the area, felt that the discharge process took no account of her circumstances. Similarly for those whose support person may have been unwell themselves. The participants mentioned feeling more like the hospital was seeing their injury walk out the door on discharge rather than taking into account the whole context of the person experiencing the injury.
	Theme 7. Pain management. Only a few participants mentioned that they felt their pain had not been managed well while in hospital.
	Theme 8. Low emotional state. Many participants reported that their injury affected them emotionally, either in the immediate instance or longer-lasting timeframes. *Note: no mention of how/if this was related back to hospital experience.*
	Theme 9. Loss of confidence. Some participants reported being more cautious since their injury. *Note: no mention of how/if this was related back*

Study (ref id)	Sleney 2014[83]
	to hospital experience.
	Theme 10. Rehabilitation and the central role of physiotherapy. Participants who were not offered physiotherapy talked about how they were unsure what to do to improve strength and mobility or what to expect in terms of likely completeness or speed of recovery. Others who did receive physiotherapy felt it ended too soon, often just as it seemed to be making a difference. A number of participants reported that it was a physiotherapist that had helped them most in their recovery and provided the most useful information or advice.
Limitations and applicability of evidence	Author-reported limitations: most of the participants were inpatients which would relate to the severity of their injury requiring them to have a longer interaction with clinicians and prolonged recovery. One minor limitation is that although the authors' conclusion states that "trauma patients' recovery needs to be supported by information protocols" this is the only occasion where they specifically identify that the unintentional injury population involved in the study are considered trauma patients (no specific information if the three centres where the study is set are MTC's). This study is highly applicable for our review question. It is a recent study based in the UK and focuses directly on our population of interest. While not asking specifically what information and support the injured patients would have liked to receive, the semi-structured interview guide focused on areas which could promote this type of information coming up in conversation (for example, experience of care received, what hindered or facilitated recovery including access to health care, social and emotional support).

Appendix H: Economic evidence tables

H.1 Assessment and management of haemorrhage

H.1.1 Haemostatic agents

Table 91: Roberts 2013[76]

Roberts I, Shakur H, Coats T, Hunt B, Balogun E, Barnetson L et al. The CRASH-2 trial: a randomised controlled trial and economic evaluation of the effects of tranexamic acid on death, vascular occlusive events and transfusion requirement in bleeding trauma patients. Health Technology Assessment. 2013; 17(10):1-79. (Guideline Ref ID ROBERTS2013)				
Study details	**Population and interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CEA (health outcome: Life years gained) **Study design:** Probabilistic decision analytic model. **Approach to analysis:** Markov model estimating the gain in life years of a cohort of trauma patients with haemorrhage who receive tranexamic acid (TXA) compared with placebo. Mortality data from within CRASH-2 trial. Cycle lengths of 1 year,	**Population:** Trauma patients with significant haemorrhage or at risk of significant haemorrhage and who were within 8 hours of injury.[(a)] **Cohort settings:** Start age: 18, 22, 30, 42 and 75 years Male: NR **Intervention 1:** Placebo (0.9% saline), same dose and timing **Intervention 2:** TXA, loading dose 1g over	**Total costs (mean per patient):** Intervention 1: £2,127 Intervention 2: £2,158 Incremental (2-1): £31 (95% CI NR; p=NR) **Currency and cost year:** 2009 US dollars (presented here as 2009 UK pounds[(b)]) **Cost components incorporated:** • TXA • Saline and IV infusion • Nurse time (cost per hour for preparing and administering TXA)	**Life years (mean per patient):** Intervention 1: 23.407 Intervention 2: 24.162 Incremental (2-1): 0.755 (95% CI NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** £42 per life year gained (da) 95% CI: NR Probability Intervention 2 cost-effective (WTP threshold of £65 ($100) per LY gained/Max WTP threshold of £163 per LY gained): 80%/100%[(d)] **Analysis of uncertainty:** One-way sensitivity analysis was undertaken on the: • **Relative risk of death with tranexamic acid** Increasing the relative risk of death for TXA to 0.95 resulted in an incremental cost per life year gained of £110. Reducing the relative risk to 0.81 resulted in an ICER of £28 per life year gained. • **Cost of tranexamic acid** If the cost of TXA was as low as £2, the incremental

patients are either alive or dead. **Perspective:** UK NHS **Time horizon/Follow-up:** Lifetime **Treatment effect duration:** 12 months **Discounting:** Costs: None[(c)] ; Outcomes: 3.5%	10 minutes then infusion of 1g over 8 hours	• Non-ICU stay cost per day		cost per life year gained would be £17. If the cost of TXA was as high as £30, the cost per life year gained would be £56. • **Cost of additional non-ICU stay and cost per non-ICU day** If the cost of non-ICU stay is reduced to £59, the ICER reduces to £30 per life year gained. With a non-ICU stay cost of £512, the ICER increases to £54 per life year gained. • **Increase in non-ICU hospital stay following TXA** When the additional ICU stay from TXA is increased to 0.08 days, the cost per life year gained rises to £56. • **Effect of using different parametric survival functions.** Using a log-normal parametric function reduced the cost per life year to £25. A probabilistic sensitivity analysis was performed with 1000 simulations. The net benefit was calculated using a threshold of £163($250) per life year to produce a CEAC.

Data sources

Health outcomes: The CRASH-2 trial recorded data up to 28 days or death, a parametric survival function was fitted to extrapolate mortality over 12 months following injury. In the statistical analysis three covariates were explored (age, sex and GDP). The cumulative hazard rate implied that after trauma the hazard rate decreases over time, the probability of dying increases with age, and GDP coefficients were found to be highly significant, but sex was not found to be influential for the hazard rate. (The hazard rate decreases to almost zero in the first 40 days after hospital admission and remains constant for the rest of the year). Risk of death during the first year following trauma in the tranexamic group was estimated by multiplying the cumulative hazard for the placebo group by the relative risk reduction in all-cause mortality estimated by the CRASH-2 trial (RR=0.87 (95% CI 0.81 to 0.95). Beyond 12 months, the risk of death is assumed to be equal whether or not the patient received TXA, and is equal to the risk of death for the relevant age-sex group in the general population.

Quality-of-life weights: n/a **Cost sources:** Cost per day in non-ICU facility ($429) from NHS reference costs 2008-2009. Tranexamic acid cost ($5.70/g) and IV infusion and saline bag prices (IV administration set $4.35) from BNF 2009. Cost per hour of nursing ($38) from Unit costs of Health and Social Care. Cost of syringe (syringes and needles $0.23) from Dziekan et al.
Comments
Source of funding: UK National Institute for Health Research Health Technology Assessment programme, Pfizer, the Bupa Foundation and the J P Moulton Charitable Foundation. **Limitations:** The model only takes into account the effect on mortality and does not consider adverse events, which could impact cost effectiveness (for example the clinical review found that there is a reduction in the number of MI's/strokes for tranexamic acid which would impact resource use, however this is just within the boundary of not being clinically important (0.76 RR). Does not use QALYs. Analysis does not allow for future health service savings, as CRASH-2 trial showed that after 28 days the proportion of patients reporting no symptoms at discharge was significantly higher in TXA group than in placebo group. Therefore, if TXA arm are patients more likely to survive without disability then the study undervalues the potential cost saving arising from the administration of TXA as healthier people will use future health care services less. Only includes costs which the CRASH-2 trial found evidence of a difference for (between the two arms); TXA cost and non-ICU stay cost.
Overall applicability: Partially applicable **Overall quality:** Potentially serious limitations

Abbreviations: BNF: British National Formulary; CEA: cost-effectiveness analysis; CEAC: cost-effectiveness acceptability curve; 95% CI: 95% confidence interval; da: deterministic analysis; ICER: incremental cost-effectiveness ratio; ICU: intensive care unit; NR: not reported; pa: probabilistic analysis; QALYs: quality-adjusted life years; TXA: tranexamic acid; WTP = Willingness to Pay

(a) Significant haemorrhage indicated by systolic blood pressure (BP) < 90mmHg, heart rate > 110 beats per minute or both.

(b) Converted using 2009 purchasing power parities[70]. This study assessed three different settings (UK, India and Tanzania) so all costs were converted to US dollars in the study using purchasing power parities (OECD and Penn World Table, accessed 2010). Where necessary, the US Consumer Price Index was used to inflate prices (US Department of Labor, accessed 30th January 2009).

(c) Costs were not discounted as the costs associated with giving tranexamic acid occur within the year following trauma (for example reduction on number of strokes may result in long term cost savings compared with placebo).

(d) The threshold presented in the analysis was $100 per life year. The CEAC showed values the probability for thresholds up to $250 per life year. The thresholds presented were converted to 2009 UK pounds.

Table 92: Morris 2007 [63]

Morris S, Ridley S, Munro V, Christensen MC. Cost effectiveness of recombinant activated factor VII for the control of bleeding in patients with severe blunt trauma injuries in the United Kingdom. Anaesthesia. United Kingdom 2007; 62(1):43-52. (Guideline Ref ID MORRIS2007)				
Study details	**Population and interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA **Study design:** Model	**Population:** 16 to 64 years of age with blunt trauma, who received 6 units of RBC	**Total costs (mean per patient):** Intervention 1: £57,639 Intervention 2: £70,882	**Total QALYs (mean per patient):** Intervention 1: 9.88 Intervention 2: 10.59	**ICER (Intervention 2 versus Intervention 1):** £18,825 per QALY (da) 95% CI: NR

based on patient level data **Approach to analysis:** Model based on patient level data from two randomised placebo-controlled phase II trials. Data was supplemented with additional UK data to estimate costs and benefits (mortality and QoL). **Perspective:** UK NHS **Time horizon/Follow-up:** Lifetime **Treatment effect duration:** 30 days **Discounting:** Costs: 3.5% ; Outcomes: 3.5%	within 4 hours of admission. **Cohort settings:** N: 143 Mean age: 34 Male: 70% **Intervention 1:** Placebo **Intervention 2:** Recombinant activated factor VII, 3 injections (200, 100 and 100 micrograms/kg). Second and third injections given 1 hour and 3 hours after the initial dose.	Incremental (2−1): £13,243 (95% CI £1973 – £24,516; p=0.02) **Currency and cost year:** 2004 UK pounds **Cost components incorporated:** • drug acquisition costs • RBC • fresh frozen plasma • platelets • cryoprecipitate • surgical procedures undertaken (including fixed costs covering overheads and consumables and a variable cost) • ICU days and regular inpatient days • Long-term costs of annual health expenditure per capita, and rehabilitation costs	Incremental (2-1): 0.70 (95% CI -1.5 – 2.9; p=0.54) **Life years (mean per patient):** Intervention 1: 14.75 Intervention 2: 15.80 Incremental (2-1): 1.05 (95% CI -2.3 – 4.4; p=0.54)	£12,613 per life year gained Probability Intervention 2 cost-effective (£20k/£30k threshold): 52%/61% **Analysis of uncertainty:** **Difference in mortality risk** Baseline = 5% • 10%: £8,990 per QALY. • 6%: £14,983 per QALY. • 4%: £22,474 per QALY. • 3%: £29,966 per QALY. • 1%: £89,897 per QALY. **Cost per surgical procedure** Baseline = £6.40 per minute plus £788 • Costs halved: £18,692 per QALY. • Costs doubles: £19,091 per QALY. **Long-term trauma-related costs** Baseline = £1654 per year with an additional £10,000 in first year. • £1,654 in first year only with no additional cost: £15,754 per QALY. • £1,654 per year with an additional £20,000 in first year: £19,545 per QALY. **Life expectancy** Baseline = no adjustment from residual general population life expectancy. • 90% of general population residual life expectancy: £20,614 per QALY **Health state utilities** Baseline = 0.67 each year following trauma

				• 0.67 in first year followed by UK age- and gender-specific norms: £15,406 per QALY **Multivariate analysis** Two multivariate sensitivity analysis were performed with the following parameter values: • Utility of 0.67 in first year with UK population norms for remaining years of life. • 90% of general population residual life expectancy. • Long-term trauma-related costs per patient: **Analysis 1** - £1654 in first year and £0 in subsequent years; **Analysis 2** - £20,000 + £1,654 in first year and £1654 in subsequent years. **Analysis 1:** £12,893 per QALY **Analysis 2:** £21,412 per QALY

Data sources

Health outcomes: Mortality data and resource use data within the first 30 days was taken from Boffard et al[10]. Survival after 30 days was estimated using a three stage approach: Stage 1 – Data from TARN was used to model survival up to the time of hospital discharge (max time to hospital discharge among TARN cohort was 90 days) or death in hospital; survivors in the trial at 30 days were assigned a survival probability based on the probability of survival for a matched cohort of patients in TARN. Stage 2 – Data was used from a cohort of 166 trauma patients admitted to the intensive care unit of the Western Infirmary, Glasgow between 1985-92, alive at 90 days post trauma. This cohort was followed until 1997 giving a follow-up period of 5 years, thus the probability of survival at 5 years was modelled using logistic regression (survival at 5 years was the binary variable and regressed against gender, age, and whether or not the patient was still in the intensive care unit 30 days post trauma). Stage 3 – UK life tables were used (for 2002-4) to generate age and gender specific residual life expectancy for each patient alive at 5 years post trauma. Same life expectancy was assumed at 5 years as for the general population.

Quality-of-life weights: A utility of 0.67 was applied to all survivors. This was taken from a published study using a cross sectional survey design (Seguin et al[81])

Cost sources: For the first 30 days resources from the Boffard trial were costed up, for post 30 days length of hospital stay data was taken from TARN.

Source of the cost of the intervention is unclear (£462.88/mg). Blood product costs from the National Blood Service (UK) (RBC = £131.80/unit, FFP = £0.13/ml, platelets = £0.99/ml, cryoprecipitate = £0.91/ml). Surgical and inpatient costs also from UK sources; (NHS reference costs 2004) (cost of ICU day = £1328, cost of inpatient day = £176), fixed theatre cost from Guidance to the Methods of Technology Appraisal; NICE, 2004 (variable theatre cost of £6.40 per minute and fixed cost of £788).

Long term healthcare costs (from 90 days till death) were estimated using the mean annual health expenditure per capita in the UK of £1,654 (OHE Compendium of Health Statistic; OHE, 2006). Baseline estimates also included £10,000 in the first year for rehabilitation costs.

Comments

Source of funding: Original trial and cost effectiveness study funded by Novo Nordisk (manufacturers of intervention).

Limitations: Adverse events not included (of the intervention and consequences from blood transfusions). Original trial the data is taken from is stated to be underpowered to detect mortality and study sample comprised of 143 patients. Potential conflict of interest from the authors and funders (First two authors have received fees from the company, and third and fourth authors are employees of the company).

Other: Extrapolation methods to predict probability of survival post 30 days are not explained enough to identify whether there may be any issues such as the previous stages in the 3 stage process are affecting the probability derived for the later stages. Also the populations compared within TARN and Scottish data have been stated as being older and less severely injured than the patients in the trial. How applicable is this study to a low risk population? Are the confounders used in the regression analysis appropriate?; "these were chosen because they were collected by Boffard and also included in the Scottish data". Large uncertainty around cost effectiveness. No information given on structure of the model.

Overall applicability: Directly applicable **Overall quality: Potentially serious limitations**

Abbreviations: BNF, British National Formulary; CUA, cost-utility analysis; CEAC, cost-effectiveness acceptability curve; 95% CI, 95% confidence interval; da, deterministic analysis; ICER, incremental cost-effectiveness ratio; ICU, intensive care unit, NR, not reported; pa, probabilistic analysis; QALYs, quality-adjusted life years; RBC, red blood cells, FFP, fresh frozen plasma

Table 93: Rossaint 2007

Rossaint R, Christensen M, Choong P, Boffard K, Riou B, Rizoli S et al. Cost-Effectiveness of Recombinant Activated Factor VII as Adjunctive Therapy for Bleeding Control in Severely Injured Trauma Patients in Germany. Eur J Trauma Emerg Surg.: Urban & Vogel. 2007; 33(5):528-538. (Guideline Ref ID ROSSAINT2007)

Study details	Population and interventions[a]	Costs	Health outcomes	Cost effectiveness
Economic analysis: CUA (health outcome = QALY) **Study design:** Model based on patient level data **Approach to analysis:** Model based on patient level data from two randomised placebo-controlled phase II trials. Data was supplemented with additional German data to	**Population:** 16 to 64 years of age with blunt trauma, who received 6 units of RBC within 4 hours of admission. **Cohort settings:** N: 143 Mean age: 34 Male: 70% **Intervention 1:** Placebo **Intervention 2:** Recombinant activated factor VII, 3 injections (200, 100 and	**Total costs (mean per patient):** Intervention 1: £48,344 Intervention 2: £63,175 Incremental (2−1): £14,831 (95% CI: £5,492 - £24,171; p<0.01) **Currency and cost year:** 2005 Euro (presented here as 2005 UK pounds) [(b)] **Cost components incorporated:** • drug acquisition costs • RBC	**QALYs (mean per patient):** Intervention 1: 8.94 Intervention 2: 9.63 Incremental (2-1): 0.69 (95% CI: -1.27 – 2.64; p=0.49) **Life years (mean per patient):** Intervention 1: 11 Intervention 2: 11.85 Incremental (2-1): 0.85 (95% CI: -1.52 – 3.21; p=0.48)	**ICER (Intervention 2 versus Intervention 1):** £21,613 per QALY (da) 95% CI: NRs Probability Intervention 2 cost-effective (£20k/£30k threshold): 48%/60% [(c)] **Analysis of uncertainty:** An estimate of the uncertainty around the ICER was generated using bootstrapping with replacement. *One way sensitivity analyses:* The incremental cost per QALY is most sensitive to the difference in mortality risk between the intervention and placebo at 30 days, and the discount rate.

estimate costs and benefits (mortality and QoL). **Perspective:** Third party payer perspective **Time horizon/Follow-up:** Lifetime **Treatment effect duration:** 30 days **Discounting:** Costs = 5%; Outcomes = 5%	100 micrograms/kg). Second and third injections given 1 hour and 3 hours after the initial dose.	• fresh frozen plasma • platelets • cryoprecipitate • surgical procedures undertaken (including fixed costs covering overheads and consumables and a variable cost) • ICU days and regular inpatient days • Long-term costs of annual health expenditure per capita, and rehabilitation costs		**Difference in mortality risk at 30 days** Baseline = 5% • 4% = £29,201 • 3% = £38,935 • 2% = £58,402 • 1% = £116,804 **Discount rate** Baseline = 5% • 0% = £9,831 • 3% = £16,497 • 10% = £34,805 **Long-term trauma-related costs** Baseline = £2,128 per year. • €0 in the first year and all subsequent years: £18,681 per QALY. • £2,128 (€2,900) per year with an additional £7,339 (€10,000) in first year: £22,031 per QALY. **Life expectancy** Baseline = Assumed trauma patients have 90% of the age and gender specific residual life expectancy of the general population. • 80% of general population residual life expectancy: £24,319 per QALY • 100% of general population residual life expectancy: £19,449 per QALY **Health state utilities** Baseline = 0.67 in the first year after trauma, and assumed equal to the age and gender specific population norms for the German population for the remaining years of life.

				• 0.67 for remaining years of life: £26,061 per QALY

Data sources

Health outcomes: Differences in mortality and resource use for the first 30 days were taken from Boffard et al[10]. Secondary data sources were used to estimate survival post 30 days. The life years for all 30 day survivors were calculated using the following two stage approach: Stage 1 – Patients from the German Trauma Registry (a cohort of 358) were identified based on the inclusion and exclusion criteria from Boffard, and patients from the trial who were alive at 30 days were assigned an individual survival probability for the period until hospital discharge or death based on a set of patient characteristics developed from the patient level data in the trauma registry. Markers with the greatest explanatory power to predict mortality that were included in the model were; multiple organ failure, ISS ≥16, and in the ICU at day 30. Stage 2 – for the period after discharge, German life table data for the general population (http://www.mortality.org) were used to generate age and gender specific residual life expectancy for each individual patient assumed to be discharged alive from the hospital after day 30 (it was assumed trauma patients have 90% of the age and gender specific residual life expectancy of the general population for the remaining years of their life).

Quality-of-life weights: For the first year post injury it was assumed patients have a utility of 0.67 (Seguin et al[81]). For the remaining years of life the utility was assumed equal to the age and gender specific norms for the population (reference states this data is from Novo Nordisk – the manufacturer)

Cost sources: For the first 30 days, resource use from the Boffard trial was costed up. Blood product costs are from the German Red Cross (through oral communication, May 2005). Surgical costs are from a study on costs (Pape 2003). ICU costs were from the same paper which calculated ICU costs based on a scoring system comprising 28 measures of medical treatment received when on ICU. Applying this model to patients in the 30 day trial provided a cost of €35 per point on the 28 point score.

For the 30 days post trauma until hospital discharge home or death, cost data from the German Trauma Registry was used. Included were regular inpatient ward costs, ICU costs (including time spent on a ventilator) and inpatient rehab costs. Patient groups used to predict treatment costs for patients surviving to discharge were (with corresponding treatment costs from day 30 to discharge); 'patients on regular inpatient ward at day 30 + no severe extremity injury' = €7,872, 'patients on regular inpatient ward day at day 30 + severe extremities injury' = €12,079, 'patients in ICU at day 30 + no multiple organ failure' = €22,135, 'patients in ICU at day 30 + multiple organ failure' = €32,261.

Long term healthcare costs were estimated for the period of hospital discharge until death. These costs were approximated using the mean annual healthcare expenditure per capita in Germany of €2,900 (from the Federal Statistics office Germany).

Comments

Source of funding: Trial funded by Novo Nordisk, the manufacturer of the product.

Limitations: Does not include adverse events, focus is on mortality. Original trial the data is taken from is stated to be underpowered to detect mortality and study sample comprised of 143 patients. Potential conflict of interest from the authors and funders (Most of the authors have received funds from Novo Nordisk).

Other: Large uncertainty around cost effectiveness. Not clear as to the source of utility data for the years following the first year. Are the confounders appropriate? Is it possible that the staging process of identifying the mortality post 30 days has limitations such as the previous stages in the staging process are affecting the probability derived for the later stages?

Overall applicability: Directly applicable **Overall quality: Potentially serious limitations**

Abbreviations: CUA, cost-utility analysis; CEAC, cost-effectiveness acceptability curve; 95% CI, 95% confidence interval; da, deterministic analysis; ICER, incremental cost-effectiveness ratio; ICU, intensive care unit; NR, not reported; pa, probabilistic analysis; QALYs, quality-adjusted life years; RBC, red blood cells

(a) Population and interventions data not explained in the published paper. Detail in this column taken from Morris 2007 which used the same RCT to estimate effect.

(b) Not all the cost sources state the dates, therefore 2005 was chosen as it is stated this is when communication occurred with the German Red Cross who provided the costs on blood products. Converted using 2005 purchasing power parities[70].

(c) These probabilities of being cost effective were read off from the cost effectiveness acceptability curve, with around €27,200 being equal to £20,000, and €40,900 being equal to £30,000.

Table 94: Pohar 2009

S. L. Pohar, E. Tsakonas, G. Murphy, D. Anderson, D. Carney, C. Moltzan, and R. Banks. Recombinant activated Factor VII in treatment of hemorrhage unrelated to hemophilia: a systematic review and economic evaluation. Anonymous. Anonymous. Canada: Ottawa: Canadian Agency for Drugs and Technologies in Health (CADTH). 2009. (Guideline Ref ID POHAR2009)				
Study details	**Population and interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome = QALY) **Study design:** Model based on patient level data **Approach to analysis:** Decision tree model based on patient level data from two randomised placebo-controlled phase II trials. Data was supplemented with additional data to estimate costs and benefits (mortality and QoL). **Perspective:**	**Population:** 16 to 64 years of age with blunt trauma, who received 6 units of RBC within 4 hours of admission. **Cohort settings:** N: 143 Mean age: 34 Male: 70% **Intervention 1:** Placebo **Intervention 2:** Recombinant activated factor VII, 3 injections (200, 100 and 100 micrograms/kg). Second and third injections given 1 hour and 3 hours after the initial dose.	**Total costs (mean per patient):** ***Undiscounted (only 1 year costs):*** Intervention 1: £41,075 Intervention 2: £61,416 Incremental (2−1): £20,342 (95% CI: NR; p=NR) **Currency and cost year:** 2008 Canadian Dollars (presented here as 2008 UK pounds) [(a)] **Cost components incorporated:** • Drug acquisition costs • RBC • hospital costs • inpatient physician	**QALYs (mean per patient):** **Undiscounted:** Intervention 1: 23.30 Intervention 2: 24.98 Incremental (2-1): 1.68 (95% CI: NR; p=NR) **Discounted:** Intervention 1: NR Intervention 2: NR Incremental (2-1): NR (95% CI: NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** Not reported in study (da or pa) 95% CI: NR Calculated using undiscounted costs and QALYS: £12,108 per QALY Probability Intervention 2 cost-effective (£20k/£30k threshold): 36%/52% [b] **Analysis of uncertainty:** *One way sensitivity analyses:* As the ICER was not reported, the sensitivity analysis results are reported as the percentage change impact on the non-reported ICER. Analyses were conducting on the following: • Discount rate • Mortality risk difference at 30 days • Mortality rate form 30 days to discharge

Canadian publicly funded healthcare system **Time horizon/Follow-up:** Lifetime **Treatment effect duration:** 30 days **Discounting:** Costs = 0%; Outcomes = 5%		consultations • long term care • inpatient rehab • post-acute care physician consultation • physiotherapy and occupation therapy		(changed both for same group and also varied for the two groups). • Patient weight • Difference in RBC transfusion units between the two groups • Drug cost • Hospital costs • In patient physician costs • Reduced LoS in factor 7 patients • Long term care costs • Utility • Residual life expectancy at discharge • Two way analyses on utility and residual life expectancy The parameter with the largest impact on the ICER is the mortality risk difference at 30 days. With only a 1% difference in risk then the ICER increases by 354%. With a 10% difference in risk the ICER decreases by 42%. (Baseline is 5%).

Data sources

Health outcomes: Treatment outcome probabilities (mortality at 30 days) were based on Boffard et al. Estimates of patient outcomes after 30 days were taken from other sources; death in hospital after 30 days was taken from another economic evaluation (Rossaint 2007). The probabilities of being discharged to different locations (long term care facility, in patient rehab, home care) were taken from Boffard and the Canadian Institute for Health Information (Ottawa, Canada. Discharge Abstract Database 2006-7). Estimates of the proportion of patients who live in the community and use physiotherapy and occupational therapy were taken from a published source (Gabbe et al). It was assumed that the survivors of a major trauma had 90% of the age and gender specific life expectancy of the general population.

Median number of RBC units by treatment group that was reported by Boffard did not permit the estimation of differences so average RBC units were used for these patients estimated from the data in the Rossaint study.

Hospital length of stay was based on durations reported in Boffard and those estimated by Rossaint after 30 days. Average 6 month length of stay assumed in a long term care facility. Inpatient rehabilitation length of stay from Canadian Institute for Health Information (CIHI) (Inpatient rehabilitation in Canada, 2006-2007). One in hospital physician visit per patient per day was assumed.

Post acutely, an average of 15 physician consults was estimated for each patient. One weekly physiotherapy and occupational therapy session in six months was

assumed.

Quality-of-life weights: A utility of 0.67 was identified from the literature (Seguin et al). It is stated the mean ISS in the group of patients from this study was 22 whereas the mean ISS in Boffard was 32, however because the mean ISS in Boffard included 27% of all patients who died who likely had higher ISS, then 0.67 was felt to be a reasonable reflection of QoL for patients who survived discharge from hospital. Data from a Canadian study (Brenneman et al) suggested an improvement in QoL (using the SF-36) of around 25% in the first year after injury. Thus it was assumed patients would experience a 25% improvement in utility in the first year after injury increasing the utility score to 0.84. A final assumption was made that a 5% improvement in quality of life would be experienced in the second year post injury resulting in a utility value of 0.88. Utility values were left at 95% of the population norm for the remainder of life expectancy.

Cost sources: Cost of factor 7 from the Canadian Pharmacists Association (C$1,100.27/mg). Per day hospital costs were estimated using resource intensity weights that were obtained from tabulations provided by the Canadian Institute for Health Information Discharge Abstract Database (2006-7) and using the average cost per weighted hospital case in Canadian hospitals (C$1,191/day). The cost of a physician consultation was based on the average fees charged by general surgeons and general physicians for non-emergency consultations in Quebec and Ontario (C$60/visit). The cost of blood transfusions was from a published study; Amin (2004) (C$308.26/transfusion). Cost per day for long term care was from a published study; Wodchis (2007) (C$315/day). Cost of an inpatient rehab stay estimated from published cost data for a Canadian setting (Mahomed 2008) (C$306/day). Home care cost per patient estimated using data on total public sector expenditures for home care and the estimated number of publicly funded home care per 1000 population in Canada (Canadian Institute for Health Information (CIHI). Public-sector expenditures and utilization of home care services in Canada: exploring the data) (C$4,863/per episode of service).
Post acutely: cost of a physician consultation estimated from the average rates charged by GP's in Ontario and Quebec (C$51.55). Cost of physiotherapy and occupational therapy based on sources estimated from across Canada (C$65/session).
All costs obtained from sources that were dated before 2008 were inflated to 2008 Canadian Dollars using the Canadian Consumer Price Index.

Comments

Source of funding: Not stated, however it is a Canadian Health Technology Assessment thus publicly funded.

Limitations: No adverse events considered ("thromboembolic events ad their potential impact on cost effectiveness were not considered"). Costs beyond one year were not considered. Not possible to work out the ICER as average discounted QALYs for both groups or incremental QALYs were not reported. Original trial the data is taken from is stated to be underpowered to detect mortality and study sample comprised of 143 patients. Some of the limitations which apply to Rossaint study may also apply here as data was used from the Rossaint paper.

Other: Cost effectiveness uncertain (although actual ICER not reported).

Overall applicability: Partially applicable **Overall quality: Very serious limitations**

Abbreviations: CUA, cost-utility analysis; CEAC, cost-effectiveness acceptability curve; 95% CI, 95% confidence interval; da, deterministic analysis; ICER, incremental cost-effectiveness ratio; ICU, intensive care unit; NR, not reported; pa, probabilistic analysis; QALYs, quality-adjusted life years; QoL, quality of life; RBC, red blood cells

(a) Converted using 2008 purchasing power parities[70].

(b) These probabilities of being cost effective were read off from the cost effectiveness acceptability curve, with around C$37,600 being equal to £20,000, and C$56,300 being equal to £30,000.

H.1.2 Anticoagulation reversal

Table 95: Guest 2010[41]

Guest JF, Watson HG, Limaye S. Modelling the cost-effectiveness of prothrombin complex concentrate compared with fresh frozen plasma in emergency warfarin reversal in the United Kingdom. Clinical Therapeutics. United Kingdom 2010; 32(14):2478-2493. (Guideline Ref ID GUEST2010)				
Study details	**Population and interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome: QALY) **Study design:** Probabilistic decision analytic model. **Approach to analysis:** Decision tree capturing the success of reversal of warfarin for each type of haemorrhage, and the probability of requiring an additional warfarin reversal treatment when the initial attempt is unsuccessful. **Perspective:** UK NHS **Time horizon:** Lifetime. Most costs occur within 1 year, except for the	**Population:** Indirect population: Patients with a life-threatening intracranial, gastrointestinal, or retroperitoneal haemorrhage. (The most applicable population to that of the guideline was felt to be intracranial haemorrhage). **Cohort settings:** Start age: 65 Male: n/a **Intervention 1[(a)]:** 3 units fresh frozen plasma (FFP) plus 10 mg vitamin K (3 to 5 hours after arrival at hospital) **Intervention 2[(a)]:** 30 units/Kg Prothrombin complex concentrate (PCC)	**Total costs (mean per patient):** **Intracranial haemorrhage[(b)]:** • Intervention 1: £11,142 • Intervention 2: £14,388 • **Incremental (2−1): £3246** (95% CI NR; p=NR) **Gastrointestinal haemorrhage:** • Intervention 1: £7824 • Intervention 2: £8225 • **Incremental (2−1): £401** (95% CI NR; p=NR) **Retroperitoneal haemorrhage:** • Intervention 1: £7730 • Intervention 2: £8264 • **Incremental (2−1): £534** • (95% CI NR; p=NR) **Currency and cost year[(c)]:** 2007-2008 UK pounds	**QALYs (mean per patient):** **Intracranial haemorrhage:** • **Incremental: 2.1 QALYs** (95% CI NR; p=NR) **Gastrointestinal haemorrhage:** • **Incremental: 0.14 QALYs** (95% CI NR; p=NR) **Retroperitoneal haemorrhage:** • **Incremental: 0.71 QALYs** (95% CI NR; p=NR)	**ICER (Intervention 2 versus Intervention 1):** **Intracranial haemorrhage:** **£1,600 per QALY gained** (da) 95% CI: NR Probability Intervention 2 cost-effective (£10K threshold): ≥95% **Gastrointestinal haemorrhage** **£2900 per QALY gained** (da) 95% CI: NR Probability Intervention 2 cost-effective (£10K threshold): ≥90% **Gastrointestinal haemorrhage** **£800 per QALY gained** (da) 95% CI: NR Probability Intervention 2 cost-effective (£10K threshold): ≥95% **Analysis of uncertainty:** PSA with 10,000 iterations was performed, with variation in probabilities, utilities, unit costs and resource use in the model.

rehabilitation for intracranial haemorrhage (but average length of this not stated). States that the expected length of survival was incorporated to calculate life years gained, however unclear as to whether this means a lifetime horizon **Treatment effect duration:** Lifetime **Discounting:** Costs: NR; Outcomes: NR	plus 5mg vitamin K (1 to 3 hours after arrival at hospital)	**Cost components incorporated:** • Ambulance transportation • Diagnostic tests: ○ CT scans ○ Endoscopy ○ Ultrsanograms ○ Full blood count ○ Basic biochemistry ○ Evaluation of coagulation • Hospital admissions: ○ Accident and emergency admission ○ Neurosurgical/gastrointestinal/general medical wards ○ High-dependency unit ○ Intensive treatment unit ○ Stroke unit ○ Stroke rehabilitation • Drugs/Blood products: ○ PCC ○ Vitamin K ○ FFP ○ Platelets ○ Red blood cells		Deterministic sensitivity analysis was also performed on the probability of survival following warfarin reversal with PCC; the initial dose of PCC; the probability of second warfarin reversal; utility scores; age and resource use. The ICER for gastrointestinal haemorrhage was very sensitive to the probability of survival following PCC treatment. With a probability of 0.972, the ICER increased to almost £16,000 per QALY whereas increase the probability to 0.998 brought the ICER down to around £1500 per QALY. Again for gastrointestinal bleeding, the ICER was very sensitive to the initial dose of PCC. When this was varied between 15 and 50 units/kg, the ICER ranged from being dominant to £11,300 per QALY. All sensitivities for all types of haemorrhage resulted in a cost per QALY of ≤ £16,000 for treatment with PCC.

Data sources

Health outcomes: Mortality rates for each type of haemorrhage were estimated from various published studies[(d)] (including controlled trials, retrospective cohorts and observational studies) found in a systematic literature search using Medline (between years 1998-2008). Mean values used in the model for patients who received FFP were 46%, 3% and 29% for intracranial, gastrointestinal and retroperitoneal haemorrhage respectively. For patients treated with PCC, the mean mortality rate used in the model was 24% for those with an intracranial haemorrhage. Mortality rates following PCC treatment were only found for intracranial haemorrhage so assumptions were made for gastrointestinal and retroperitoneal haemorrhage. These values were 2% and 24% respectively. The mortality rates were combined with the life expectancy of a 65 year old, found to be 18.9 years (ONS, deaths registered in 2007) to calculate the expected number of life years for a patient.

Probabilities for the success of warfarin reversal were elicited from a panel of 9 consultant physicians (6 haematologists and 3 anaesthetists) as well as 2 clinical authors

of this study (Watson and Limaye). For the success of PCC a probability of 0.95 was given; for FFP the value was 0.65. It was also assumed that for those requiring a second reversal following an initial attempt with FFP, 95% would have FFP again and the rest would have PCC. All patients initially on PCC who require a second reversal have PCC. An arbitrary standard deviation of 10% was applied to assess uncertainty around probabilities.

Resource use: If an intracranial haemorrhage was suspected, patients would undergo a CT. After successful warfarin reversal, 5% of patients will undergo craniotomy and then be admitted to a neurosurgical intensive treatment ward for around 2 days. Most other patients would be admitted to a high dependency unit (HDU) for around 2 days followed by admission to a stroke unit or medical ward, length of hospital stay could vary depending on rehab needed.

If gastrointestinal haemorrhage is suspected, patients undergo an endoscopy. Those confirmed as having a gastrointestinal haemorrhage would receive a mean of 8 units of red blood cells, and 10% would also receive 2 units of platelets. After successful reversal most patients would undergo endoscopy, after which 10% would be admitted to a HDU for around 5 days, also all patients would be admitted to a gastrointestinal medical ward for around 7 days.

If retroperitoneal haemorrhage is suspected, patients would have an abdominal ultrasonogram followed by a CT scan. About 90% of patients who are confirmed as having a retroperitoneal haemorrhage would have a mean of 6 units of blood. After successful reversal, around 10% of patients would be admitted to a HDU for 5-7 days, additionally all patients would be admitted to a general medical ward for around 10 days.

Quality-of-life weights: Utility values for stroke and gastrointestinal haemorrhage were found in two systematic reviews – Sandercock et al (2002) and Leontiadis et al (2007). These gave separate values for patients who were dependent on a carer or were independent following an intracranial haemorrhage. The study stated that 42% of these patients are expected to be independent and 52% dependent. The utility for independent patients was given as 0.74 and for dependent, 0.38. For gastrointestinal patients utilities were separated for when patients are hospitalised and when they are at home. These were given as 0.45 and 0.78 respectively. No utilities were found for retroperitoneal haemorrhage so it was assumed that this would be the same as for gastrointestinal haemorrhage. The utilities used are all derived using the EQ-5D directly elicited from patients.

Cost sources: NHS reference costs 2009-2010, National Audit Office, Drug Tariff 2009, and BNF (accessed September 2009).

Comments

Source of funding: CSL Behring (manufacturers of Prothrombin complex concentrate brand Beriplex).

Limitations: The population is only specified as patients with a haemorrhage who are on anti-coagulant therapy using warfarin, and not those with a traumatic injury.

Resource use and probabilities of successful reversal and type of intervention used for second reversal were based on the results of individually interviewing a group of consultant physicians as well as two clinical authors of the study and so were based on assumptions. Another author conducted the interviews and consensus of the model inputs was reached in a meeting comprising 5 of the interviewees and 2 additional clinicians.

Mortality rates used were taken as an average of the values found in the studies without weighting by the sample size of the study. Only 3 studies were used for mortality rates of gastrointestinal haemorrhage using FFP and only 2 for retroperitoneal haemorrhage, of which one did not report sample size. Mortality rates for intracranial haemorrhage following treatment with PCC were based on 7 studies with very small sample sizes (between 3 and 23) and a weighted mean was not used. With the exception of intracranial haemorrhage, mortality rates using PCC were assumed and sensitivity analyses did not use a wide range of values. For gastrointestinal haemorrhage, the highest mortality rate used was only 2.8% which gave the highest ICER of £16,000 per QALY.

The model only incorporated mortality over a short time period and did not include the chance of a second haemorrhage. NHS costs were only included in the first year following haemorrhage (except rehabilitation for intracranial haemorrhage). Methodology unclear at times, for example in relation to the time horizon.

Other: Weighted mean values for mortality rates were not used because two studies did not report sample size. The study reported that weighted values based on the studies that reported a sample size were either the same or differed by 1 percentage point and so it would not have an effect on the results.

Overall applicability: Partially applicable **Overall quality:** Potentially/Very serious limitations

Abbreviations: 95% CI, 95% confidence interval; BNF, British National Formulary; CUA, cost–utility analysis; da, deterministic analysis; FFP, fresh frozen plasma; ICER, incremental cost-effectiveness ratio; NR, not reported; ONS, Office of National statistics; PCC, prothrombin complex concentrate; QALYs, quality-adjusted life years; HDU, High Dependency Unit

(a) Second PCC dosage following initial PCC is 15 to 20 units/kg 3 to 5 hours after arrival to ED. Second FFP dosage following initial FFP is 3 to 5 units 6 to 8 hours after arrival to ED. Second reversal with PCC following FFP has dosage of 500 units.

(b) Includes stroke rehabilitation.

(c) Unit costs from earlier years were inflated to 2008 using the health services inflation index.

(d) Flaherty et al (2006), Zubkov et al (2007), Rosand et al (2004), Cavallini et al (2008), Fric-Shamji et al (2008), Neau et al (2001), Berwaerts et al (2000), Sjalander et al (2003), Gage et al (2001),Wilcox and Truss (1988), Thomopoulos et al (2005), Rubin et al (2003), Andrade et al (2003), Ivascu et al (2005), Sjoblom et al (2001), Yasaka et al (2002), Cartmill et al (2000), Boulis et al (1999),Lankiewicz et al (2006), Vigue et al (2007), Bertram et al (2000).

Appendix I: GRADE Tables

I.1 Assessment and management of haemorrhage

I.1.1 Pelvic binders

Table 96: Pelvic binder versus no binder

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Pelvic binder	No binder	Relative (95% CI)	Absolute	Quality	Importance
Mortality												
1	Observational studies	Serious[a]	No serious inconsistency	Serious[b]	Very serious[c]	None	0/153 (0%)	4/432 (0.9%)	OR 0.26 (0.03 to 2.4)	7 fewer per 1000 (from 9 fewer to 13 more)	VERY LOW	CRITICAL
Mortality (adjusted)												
1	Observational studies	No serious risk of bias	No serious inconsistency	Serious[b]	Very serious[c]	None	-	-	OR 0.9 (0.31 to 2.6)	-	VERY LOW	CRITICAL
Volume of blood (pRBC) transfused (Better indicated by lower values)												
1	Observational studies	Serious[a]	Serious4	Serious[b]	No serious imprecision	None	62 91	388 44	-	MD 0.11 lower (0.16 lower to 0.66 higher MD 1.56 lower (1.67 lower to 1.44 lower)	VERY LOW	CRITICAL
Volume of total blood products transfused (Better indicated by lower values)												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	6	5	-	MD 6.49 lower (15.56 lower to 2.58 higher)	VERY LOW	CRITICAL
Need for massive transfusion (>6 units pRBC in 24 hours)												
1	Observational	No	No serious	Serious[b]	Very	None	-	-	OR 1.4	-	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Pelvic binder	No binder	Relative (95% CI)	Absolute		
	studies	serious risk of bias	inconsistency		serious[c]				(0.58 to 3.38)			

(a) Downgraded by one increment if the majority of the evidence was at high risk of bias and downgraded by two increments if the majority of the evidence was at very high risk of bias
(b) Downgraded by one increment if the confidence interval crossed one MID or by two increments if the confidence interval crossed both MIDs
(c) The majority of the evidence was from studies in an in-hospital setting in a population of confirmed pelvic fractures
(d) Heterogeneity, I^2 100%, unexplained by subgroup analysis therefore random effects model used.

I.1.2 Haemostatic agents

Table 97: Clinical evidence profile: tranexamic acid versus standard care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Tranexamic acid versus standard care	Control	Relative (95% CI)	Absolute		
Mortality (follow-up 28 days)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	1463/10060 (14.5%)	16%	RR 0.91 (0.85 to 0.97)	14 fewer per 1000 (from 5 fewer to 24 fewer)	HIGH	CRITICAL
MI/Stroke (follow-up 28 days)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[1]	None	92/10060 (0.91%)	1.2%	RR 0.76 (0.58 to 1)	3 fewer per 1000 (from 5 fewer to 0 more)	MODERATE	CRITICAL
Pulmonary embolus (follow-up 28 days)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[a]	None	72/10060 (0.72%)	0.7%	RR 1.01 (0.73 to	0 more per 1000 (from 2 fewer to 3	LOW	CRITICAL

									1.41)	more)		
Deep vein thrombosis (follow-up 28 days)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[1]	None	40/10060 (0.4%)	0.4%	RR 0.98 (0.63 to 1.51)	0 fewer per 1000 (from 1 fewer to 2 more)	LOW	CRITICAL
Blood products transfusion (follow-up 28 days)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	5067/10060 (50.4%)	51.3%	RR 0.98 (0.96 to 1.01)	10 fewer per 1000 (from 21 fewer to 5 more)	HIGH	CRITICAL

(a) Outcomes were downgraded by one increment if the weighted average number of serious methodological limitations across studies was one, and downgraded by two increments if the weighted average number of serious methodological limitation across studies were two or more. Methodological limitations comprised one or more of the following: unclear allocation concealment, the lack of blinding, or inadequate allowance for drop-outs in the analysis. Cross-over studies were not downgraded for selection bias, as the effects of such bias would only be expected to exert effects via an order effect, and so selection bias would be less serious a limitation than in a parallel trial.

Table 98: Clinical evidence profile: Recombinant factor VIIa versus standard care

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Recombinant factor VIIa versus standard care**	**Control**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality (follow-up mean 30 days)												
2	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	66/401 (16.5%)	20.6%	RR 0.95 (0.7 to 1.28)	10 fewer per 1000 (from 62 fewer to 58 more)	VERY LOW	CRITICAL
MI/Stroke (follow-up mean 90 days)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[b]	None	5/270 (1.9%)	1.7%	RR 1.07 (0.31 to 3.67)	1 more per 1000 (from 12 fewer to 45 more)	LOW	CRITICAL
Venous thromboembolic adverse events - Blunt (follow-up mean 90 days)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[a]	None	29/224 (12.9%)	9.6%	RR 1.36 (0.81 to 2.25)	34 more per 1000 (from 18 fewer to 120 more)	MODERATE	CRITICAL

Venous thromboembolic adverse events - Penetrating (follow-up 90 days)											
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[b]	None	0/46 (0%)	10%	Peto OR 0.11 (0.01 to 0.8)	88 fewer per 1000 (from 18 fewer to 99 fewer)	MODERATE	CRITICAL
Pulmonary embolism (follow-up mean 90 days)											
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[b]	None	9/270 (3.3%)	2.8%	RR 1.21 (0.47 to 3.09)	6 more per 1000 (from 15 fewer to 59 more)	LOW	CRITICAL
Thrombotic adverse events (follow-up 30-90 days)											
2	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[b]	None	44/409 (10.8%)	7.3%	RR 1.1 (0.74 to 1.63)	7 more per 1000 (from 19 fewer to 46 more)	LOW	CRITICAL
Red blood cells (follow-up mean 2 days; Better indicated by lower values)											
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[b]	None	267	287	-	MD 1.45 lower (3.11 lower to 0.21 higher)	MODERATE	CRITICAL
Platelets (follow-up 2 days; Better indicated by lower values)											
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[b]	None	267	287	-	MD 0.46 lower (1.58 lower to 0.66 higher)	MODERATE	CRITICAL
Fresh Frozen Plasma (follow-up 2 days; Better indicated by lower values)											
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	267	287	-	MD 2.66 lower (4.02 to 1.29 lower)	HIGH	CRITICAL
Cryoprecipitate (follow-up 2 days; Better indicated by lower values)											
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[b]	None	267	287	-	MD 0.49 lower (1.15 lower to 0.18 higher)	MODERATE	CRITICAL
Sepsis (follow-up 2 days)											
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[b]	None	37/270 (13.7%)	11.5%	RR 0.86 (0.58 to 1.28)	16 fewer per 1000 (from 48 fewer to 32 more)	LOW	CRITICAL

(a) Outcomes were downgraded by one increment if the weighted average number of serious methodological limitations across studies was one, and downgraded by two increments if the weighted average number of serious methodological limitation across studies were two or more. Methodological limitations comprised one or more of the following: unclear allocation concealment, the lack of blinding, or inadequate allowance for drop-outs in the analysis. Cross-over studies were not downgraded for selection bias, as the effects of such bias would only be expected to exert effects via an order effect, and so selection bias would be less serious a limitation than in a parallel trial.

(b) Outcomes were downgraded by one increment if the upper or lower 95% CI crossed the lower MID or the upper or lower 95% CI crossed the upper MID. Outcomes were downgraded by two increments if the upper CI simultaneously crossed the upper MID and the lower CI crossed the lower MID. Default MIDs were set at RRs of 0.75 and 1.25 for dichotomous variables, and at 0.5 of the control group weighted mean standard deviation either side of the null line for continuous variables.

I.1.3 IO/IV access

Table 99: IO versus central IV

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**IO versus central IV**	**Control**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Time to establish access (Better indicated by lower values)												
1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[a]	None	40	40	-	MD 6.5 lower (10.97 to 2.03 lower)	VERY LOW	CRITICAL
Adverse events - Failed first attempt												
1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[a]	None	6/40 (15%)	16/40 (40%)	RR 0.38 (0.16 to 0.86)	248 fewer per 1000 (from 56 fewer to 336 fewer)	VERY LOW	CRITICAL
Adverse events (including infection, bleeding, thrombosis, compartment syndrome, pneumothorax)												
1	Observational studies					None	0/40 (0%)	0/40 (0%)	not pooled	not pooled		CRITICAL
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Health-related quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

Patient-reported outcomes (psychological well-being)												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

(a) Downgraded by one increment if the confidence interval crossed one MID or by two increments if the confidence interval crossed both MIDs.

I.1.4 Volume resuscitation

Table 100: Clinical evidence profile: Permissive Hypotension versus Resuscitation with normotension as aim – Pre-hospital

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Pre-hospital**	**Control**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality (follow-up mean 30 days)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[a]	None	86/289 (29.8%)	37.5%	RR 0.79 (0.63 to 1)	79 fewer per 1000 (from 139 fewer to 0 more)	MODERATE	CRITICAL
Length of ICU Stay (Better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	238	227	-	MD 1 lower (3.51 lower to 1.51 higher)	HIGH	CRITICAL
Multi-organ Failure (follow-up mean 30 days)												
1	Randomised trials	Serious[b]	No serious inconsistency	No serious indirectness	Serious[a]	None	55/238 (23.1%)	30.4%	RR 0.76 (0.56 to 1.03)	73 fewer per 1000 (from 134 fewer to 9 more)	LOW	IMPORTANT
Mortality at 24 hours and 12 Months – no evidence												
Health related quality of life – no evidence												
Neurological outcome– no evidence												
Blood product use– no evidence												
Time to definitive control of haemorrhage– no evidence												
Patient reported outcomes : Pain/discomfort, return to normal activities, psychological wellbeing– no evidence												

(a) Downgraded by one increment if the confidence interval crossed one MID
(b) Downgraded by one increment if the majority of the evidence was at high risk of bias.

Table 101: Clinical evidence profile: Permissive Hypotension versus Resuscitation with normotension as aim – In-hospital

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**In Hospital**	**Control**	**Relative (95% CI)**	**Absolute**		
Mortality (follow-up mean 24 hours)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[a]	None	3/55 (5.5%)	3.6%	RR 1.5 (0.26 to 8.63)	18 more per 1000 (from 27 fewer to 275 more)	LOW	CRITICAL
Mortality (follow-up mean 30 days)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[a]	None	4/55 (7.3%)	7.3%	RR 1 (0.26 to 3.8)	0 fewer per 1000 (from 54 fewer to 204 more)	LOW	CRITICAL
Time to definitive control of haemorrhage (Better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[a]	None	52	53	-	MD 0.4 lower (1.02 lower to 0.22 higher)	MODERATE	IMPORTANT
Mortality at 12 Months – no evidence												
Health related quality of life – no evidence												
Neurological outcome – no evidence												
Blood product use – no evidence												
Length of ICU Stay – no evidence												
Patient reported outcomes : Pain/discomfort, return to normal activities, psychological wellbeing – no evidence												

(a) Downgraded by one increment if the confidence interval crossed one MID or by two increments if the confidence interval crossed both MIDs

Table 102: Clinical evidence profile: Permissive Hypotension versus Resuscitation with normotension as aim – In-hospital (Combined)

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Permissive Hypotension	Normotension	Relative (95% CI)	Absolute		
Mortality (follow-up mean 24 hours)												
2	Randomised trials	Very serious[a]	Serious[b]	Serious	Serious[c]	None	54/344 (15.7%)	84/364 (23.1%)	RR 0.69 (0.51 to 0.93)	72 fewer per 1000 (from 16 fewer to 113 fewer)	VERY LOW	CRITICAL
Mortality (follow-up mean 30 days)												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	90/344 (26.2%)	120/364 (33%)	RR 0.80 (0.64 to 1.0)	66 fewer per 1000 (from 119 fewer to 0 more)	VERY LOW	CRITICAL
Length of ICU Stay (Better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	238	227	-	MD 1 lower (3.51 lower to 1.51 higher)	HIGH	CRITICAL
Multi-organ Failure (follow-up mean 30 days)												
1	Randomised trials	Serious[b]	No serious inconsistency	No serious indirectness	Serious[a]	None	55/238 (23.1%)	30.4%	RR 0.76 (0.56 to 1.03)	73 fewer per 1000 (from 134 fewer to 9 more)	LOW	IMPORTANT
Time to definitive control of haemorrhage (Better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[a]	None	52	53	-	MD 0.4 lower (1.02 lower to 0.22 higher)	MODERATE	IMPORTANT
Mortality at 12 Months – no evidence												
Health related quality of life – no evidence												
Neurological outcome – no evidence												
Blood product use – no evidence												
Patient reported outcomes : Pain/discomfort, return to normal activities, psychological wellbeing – no evidence												

(a) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
(b) Downgraded by 1 or 2 increments because the point estimate varies widely across studies, unexplained by subgroup analysis.
(c) Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs.

Table 103: Clinical evidence profile: Permissive Hypotension versus Resuscitation with normotension as aim – Penetrating Injury

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pre-hospital	Control	Relative (95% CI)	Absolute	Quality	Importance
Mortality (follow-up mean 30 days)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[a]	None	86/289 (29.8%)	37.5%	RR 0.79 (0.63 to 1)	79 fewer per 1000 (from 139 fewer to 0 more)	MODERATE	CRITICAL
Length of ICU Stay (Better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	238	227	-	MD 1 lower (3.51 lower to 1.51 higher)	HIGH	CRITICAL
Multi-organ Failure (follow-up mean 30 days)												
1	Randomised trials	Serious[b]	No serious inconsistency	No serious indirectness	Serious[a]	None	55/238 (23.1%)	30.4%	RR 0.76 (0.56 to 1.03)	73 fewer per 1000 (from 134 fewer to 9 more)	LOW	IMPORTANT
Mortality at 24 hours and 12 Months – no evidence												
Health related quality of life – no evidence												
Neurological outcome – no evidence												
Blood product use – no evidence												
Time to definitive control of haemorrhage – no evidence												
Patient reported outcomes : Pain/discomfort, return to normal activities, psychological wellbeing – no eevidence												

(a) Downgraded by one increment if the confidence interval crossed one MID
(b) Downgraded by one increment if the majority of the evidence was at high risk of bias.

I.1.5 Fluid replacement

Table 104: Clinical evidence profile: Plasma: platelet: red blood cells

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Plasma: Platelet: Red blood cells 1:1:1**	**1:1:2**	**Relative (95% CI)**	**Absolute**		
Mortality - 24 hours												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[a]	None	43/338 (12.7%)	17%	RR 0.75 (0.52 to 1.08)	43 fewer per 1000 (from 82 fewer to 14 more)	MODERATE	CRITICAL
Mortality - 30 days												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[a]	None	75/338 (22.2%)	26%	RR 0.85 (0.65 to 1.11)	39 fewer per 1000 (from 91 fewer to 29 more)	MODERATE	CRITICAL
Transfusion-related metabolic complication (follow-up 30 years)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[a]	None	53/338 (15.7%)	17.3%	RR 0.91 (0.65 to 1.28)	16 fewer per 1000 (from 61 fewer to 48 more)	LOW	CRITICAL
Transfusion-associated circulatory overload (follow-up 30 days)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[a]	None	1/338 (0.3%)	0/342 (0%)	OR 7.48 (0.15 to 376.84)	0 (from 10 fewer to 10 more)	LOW	CRITICAL
Achieved haemostasis												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	291/338 (86.1%)	267/342 (78.1%)	RR 1.1 (1.03 to 1.18)	78 more per 1000 (from 23 more to 141 more)	HIGH	IMPORTANT
Discharged home (follow-up 30 days)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[a]	None	118/338 (34.9%)	105/342 (30.7%)	RR 1.14 (0.92 to 1.41)	43 more per 1000 (from 25 fewer to 126 more)	MODERATE	IMPORTANT
Mortality 12 months – no evidence												
Health-related quality of life – no evidence												
Length of intensive care stay – no evidence												

Time to definitive control of haemorrhage – no evidence												
Patient-reported outcomes – no evidence												

Downgraded by one increment if the confidence interval crossed one MID or by two increments if the confidence interval crossed both MIDs.

Table 105: Clinical evidence profile: Crystalloid: PRBC

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**High ratio crystalloid: PRBC**	**Low ratio crystalloid: PRBC**	**Relative (95% CI)**	**Absolute**		
Mortality (in hospital)												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	-[c]	-	OR 0.9 (0.58 to 1.45)	NA[d]	VERY LOW	CRITICAL
Nosocomial infection												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	-[c]	-	OR 1.3 (0.68 to 2.5)	NA[d]	VERY LOW	CRITICAL
Multiple organ failure												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	-[c]	-	OR 1.7 (1.2 to 2.6)	NA[d]	VERY LOW	CRITICAL
Acute respiratory distress syndrome												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision[b]	None	-[c]	-	OR 2.2 (1.5 to 3.1)	NA[d]	VERY LOW	CRITICAL
Mortality 24 hrs, 12 months – no evidence												
Health-related quality of life – no evidence												
Length of intensive care stay – no evidence												
Time to definitive control of haemorrhage – no evidence												
Patient-reported outcomes – no evidence												

(a) Survivor bias accounted for by excluding early mortality
(b) Downgraded by one increment if the confidence interval crossed one MID or by two increments if the confidence interval crossed both MIDs.
(c) No adjusted data presented

(d) Generic inverse variance used

Table 106: Clinical evidence profile: Crystalloid: crystalloid

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	0.9% NaCl	Plasma Lyte A	Relative (95% CI)	Absolute	Quality	Importance
Mortality (in hospital)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[a]	None	4/17 (23.5%)	3/14 (21.4%)	RR 1.08 (0.28 to 4.18)	17 more per 1000 (from 154 fewer to 681 more)	LOW	CRITICAL
Mortality 24 hrs, 12 months – no evidence												
Health-related quality of life – no evidence												
Length of intensive care stay – no evidence												
Acute transfusion reaction – no evidence												
Time to definitive control of haemorrhage – no evidence												
Patient-reported outcomes – no evidence												

(a) Downgraded by one increment if the confidence interval crossed one MID or by two increments if the confidence interval crossed both MIDs.

I.2 Control of haemorrhage in hospital

I.2.1 Haemorrhage protocols

Table 107: Clinical evidence profile: Fixed ratio transfusion protocol versus Laboratory-guided transfusion protocol

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Fixed ratio	Lab-guided	Relative (95% CI)/ Median (IQR)	Absolute	Quality	Importance
Mortality (all cause) (follow-up 28 days)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Fixed ratio**	**Lab-guided**	**Relative (95% CI)/ Median (IQR)**	**Absolute**		
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[a]	None	11/37 (29.7%)	3/32 (9.4%)	RR 3.17 (0.97 to 10.38)	204 more per 1000 (from 3 fewer to 882 more)	MODERATE	CRITICAL
Mortality (exsanguination) (follow-up 28 days)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[b]	None	8/37 (21.6%)	3/32 (9.4%)	RR 2.31 (0.67 to 7.97)	123 more per 1000 (from 31 fewer to 655 more)	LOW	CRITICAL
RBC units used (follow-up 12 hours; measured with: median total units per patient (IQR); better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision[d]	None	37	32	Median difference5 = 0 higher (from 5 fewer to 2.5 more Fixed ratio median units (IQR) = 7 (6-10); Lab-guided median units (IQR) = 7 (6-14)		HIGH	CRITICAL
Frozen plasma units used (follow-up 12 hours; measured with: median total units per patient (IQR); better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision[d]	None	37	32	Median difference5 = 2 higher (from 0 more to 4 more) Fixed ratio median units (IQR) = 6 (4-8); Lab-guided		HIGH	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Fixed ratio**	**Lab-guided**	**Relative (95% CI)/ Median (IQR)**	**Absolute**		
									median units (IQR) = 4 (3-8)			
Platelet units used (follow-up 12 hours; measured with: median total units per patient (IQR); better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision[d]	None	37	32	Median difference5 = 4 higher (from 3 fewer to 6 more) Fixed ratio median units (IQR) = 8 (4-8); Lab-guided median units (IQR) = 4 (0-8)		HIGH	CRITICAL
Cryoprecipitate units used (follow-up 12 hours; measured with: median total units per patient (IQR); better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision[d]	None	37	32	Median difference5 = ns Fixed ratio median units (IQR) = 0 (0-0); Lab-guided median units (IQR) = 0 (0-10)		HIGH	CRITICAL
Deep vein thrombosis (follow-up 28 days)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious	None	3/37 (8.1%)	0/32 (0%)	OR 6.83 (0.68 to 68.35)	81 more per 1000 (from 20 fewer to 182 more)[2]	LOW	CRITICAL
Plasma wasted (follow-up 12 hours)												
1	Randomised	No	No serious	No serious	No serious	None	86/390	30/289	RR 2.12 (1.44 to	116 more	HIGH	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Fixed ratio	Lab-guided	Relative (95% CI)/ Median (IQR)	Absolute		
	trials	serious risk of bias	inconsistency	indirectness	imprecision		(22.1%)	(10.4%)	3.13)	per 1000 (from 46 more to 222 more)		
Patient reported outcomes (psychological wellbeing) – no evidence												
Length of intensive care stay– no evidence												
Adverse effects: over-transfusion related morbidity, transfusion-reactions, and infections – no evidence												

(a) Downgraded by one increment as confidence interval crossed one MID
(b) Downgraded by two increments as confidence interval crossed two MIDs
(c) Peto odds ratio
(d) Imprecision could not be assessed as raw data reported as median and IQR
(e) Median difference and confidence intervals estimated using bootstrapping (10,000 simulations) as reported by the study authors

I.2.2 Whole-body CT

Table 108: Clinical evidence profile: Full Body versus selective Imaging

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Full Body CT versus Selective Imaging	Control	Relative (95% CI)	Absolute		
Mortality (timing of exposure 30 days)												
1	Observational studies[a]	Serious[b]	No serious inconsistency	No serious indirectness	Serious[c]	None	-		OR 0.68 (0.45 to 1.03)	-	VERY LOW	CRITICAL
Mortality at 24 hours/12 months (no evidence found)												
Health related quality of life (no evidence found)												
Blood Product Use (no evidence found)												

Length of intensive care stay (no evidence found)
Time to definitive control of haemorrhage (no evidence found)
Time to surgery (no evidence found)
Patient reported welcomes (no evidence found)
Long-term radiation (no evidence found)
Delayed/Missed Injury (no evidence found)

(a) Case-control
(b) Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
(c) Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs.

I.2.3 Interventional radiology

Table 109: Clinical evidence profile: Endovascular repair versus operative repair for aortic injury for major trauma

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Operative repair versus endovascular repair for aortic injury**	**Control**	**Relative (95% CI)**	**Absolute**		
Mortality (in hospital)												
1	Observational studies	No serious risk of bias	No serious inconsistency	Very serious[a]	No serious imprecision	None	125	68	OR 8.42 (2.76 to 25.69)[2]	-[c]	VERY LOW	CRITICAL
Any systemic complication												
1	Observational studies	No serious risk of bias	No serious inconsistency	Very serious[a]	Very serious[d]	None	125	68	OR 1.41 (0.75 to 2.65)[b]	-[c]	VERY LOW	CRITICAL
ICU length of stay (Better indicated by lower values)												
1	Observational studies	No serious risk of bias	No serious inconsistency	Very serious[a]	No serious imprecision[e]	None	125	68	-	MD 1.28 higher (2.41 lower to 4.97 higher)[2]	VERY LOW	CRITICAL

Hospital length of stay (Better indicated by lower values)												
1	Observational studies	No serious risk of bias	No serious inconsistency	Very serious[a]	No serious imprecision[e]	None	125	68	-	MD 4.77 higher (5.33 lower to 14.87 higher)[2]	VERY LOW	CRITICAL
Blood transfusion units -(Better indicated by lower values)												
1	Observational studies	No serious risk of bias	No serious inconsistency	Very serious[a]	No serious imprecision[e]	None	125	68	-	MD 4.98 higher (0.14 to 9.82 higher)[2]	VERY LOW	CRITICAL
Mortality at 24 hours, 12 months – no evidence												
Failure rate or re-intervention rate – no evidence												
Health-related quality of life – no evidence												
Time to definitive control of haemorrhage – no evidence												
Patient-reported outcomes – no evidence												

(a) Some patients did not undergo immediate repair
(b) GIV, generic inverse variance method used in RevMan. Absolute risks and benefits cannot be calculated.
(c) No unadjusted data presented
(d) Downgraded by one increment if the confidence interval crossed one MID or by two increments if the confidence interval crossed both MIDs.
(e) Imprecision could not be assessed as no raw adjusted data presented

Table 110: Operative repair versus endovascular repair for aortic injury for major trauma

Quality assessment							**No of patients**		**Effect**		**Quality**	**Importance**
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Operative repair	Endovascular	Relative (95% CI)	Absolute		
Any systemic complication (all patients)												
1	observational studies	no serious risk of bias	no serious inconsistency	very serious[a]	Serious[b]	none	56[c]	50	OR 0.33 (0.11 to 0.99)3	[d]	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Operative repair	Endovascular	Relative (95% CI)	Absolute		
ICU length of stay (adj) (Better indicated by lower values)												
1	observational studies	no serious risk of bias	no serious inconsistency	very serious[a]	no serious imprecision	none	56	50	-	MD 1.85 higher (4.09 lower to 7.79 higher)	VERY LOW	CRITICAL
Mortality at 24 hours, 12 months – no evidence												
Failure rate or re-intervention rate – no evidence												
Health-related quality of life – no evidence												
Blood transfusion – no evidence												
Time to definitive control of haemorrhage – no evidence												
Patient-reported outcomes – no evidence												

(a) Some patients did not undergo immediate repair
(b) Imprecision could not be assessed as no raw adjusted data presented
(c)No unadjusted data presented
(d)GIV, generic inverse variance method used in RevMan. Absolute risks and benefits cannot be calculated.

Table 111: Clinical evidence profile: Endovascular repair versus operative repair for pelvic injury for major trauma

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Endovascular repair versus operative repair for pelvic injury	Control	Relative (95% CI)	Absolute		
Mortality (In hospital) - Multiple regression analysis												

1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[a]	None	-	-	OR 1.20 (0.61 to 2.36)	GIV	VERY LOW	CRITICAL
Mortality (In hospital) - Propensity scoring												
1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[a]	None	-	-	OR 1.13 (0.63 to 2.03)	GIV	VERY LOW	CRITICAL
Mortality at 24 hours, 12 months – no evidence												
Health-related quality of life – no evidence												
Failure rate or re-intervention rate – no evidence												
Adverse effects – no evidence												
Blood product use – no evidence												
Length of intensive care stay – no evidence												
Time to definitive control of haemorrhage – no evidence												
Patient-reported outcomes – no evidence												

Note: GIV, generic inverse variance method used in RevMan. Absolute risks and benefits cannot be calculated.

(a) Downgraded by one increment if the confidence interval crossed one MID or by two increments if the confidence interval crossed both MIDs.

I.3 Warming

Table 112: Clinical evidence profile: CAVR versus Conventional Care

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**CAVR**	**Conventional warming**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality (follow-up mean 24 hours)												
1	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	4/29 (13.8%)	42.9%	RR 0.32 (0.12 to 0.88)	292 fewer per 1000 (from 51 fewer to 378 fewer)	LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	CAVR	Conventional warming	Relative (95% CI)	Absolute	Quality	Importance
Mortality at 1 month/ 12 months - no evidence												
Health-related quality of life – no evidence												
Length of intensive care stay – no evidence												
Adverse effects: Skin burns - no evidence												
Adverse effects: Hyperthermia – no evidence												
Adverse effects: Infection - no evidence												
Neurological outcome – no evidence												
Patient reported outcome (pain/discomfort, return to normal activity, psychological wellbeing) – no evidence												

(a) Downgraded by one increment if the majority of evidence was at high risk of bias
(b) Downgraded by one increment if the confidence interval crossed one MID

I.4 Pain

I.4.1 Pain management

Table 113: Clinical evidence profile: Morphine versus ketamine

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Morphine	Ketamine	Relative (95% CI)	Absolute	Quality	Importance
Pain Levels (follow-up 30 minutes; measured with: Final Pain Score; range of scores: 0-100; Better indicated by lower values)												
1	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	32	33	-	MD 5.4 higher (3.2 to 7.6 higher)	MODERATE	CRITICAL
Pain Levels (follow-up mean 47 minutes; measured with: Change in Pain Score; range of scores: 0-10; Better indicated by lower values)												
1	Randomised	Serious[a]	No serious	No serious	Serious	None	65	70	-	MD 2.40 higher	LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Morphine**	**Ketamine**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
	trials		inconsistency	indirectness	imprecision					(1.40 to 3.40 higher)		
Quality of life (follow-up mean 1 month: measured with :SF36 Physical Component; range of scores 0-100; better indicated by higher values)												
1	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	50	47	-	MD 1.1 lower (5.48 lower to 3.28 higher)	MODERATE	CRITICAL
Quality of life (follow-up mean 1 month: measured with :SF36 Mental Component; range of scores 0-100; better indicated by higher values)												
1	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	50	47	-	MD 0.0 lower (5.02 lower to 5.02 higher)	MODERATE	CRITICAL
Nausea (assessed with: Incidence of Nausea)												
3	Randomised trials	Serious[a]	Very serious inconsistency[b]	No serious indirectness	Very serious[c]	None	17/117 (14.5%)	11/123 (8.9%)	RR 1.79 (0.36 to 9.52)	71 more per 1000 (from 57 fewer to 762 more)	VERY LOW	CRITICAL
Hallucinations (assessed with: Incidence of Hallucinations)												
2	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	0/85 (0%)	6/90 (6.7%)	OR[f] 0.14 (0.03 to 0.68)	70 fewer per 1000 (from 130 fewer to 10 fewer)	MODERATE	CRITICAL
Loss of consciousness (assessed with: Ramsey Score)												
1	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	2/32 (6.3%)	7/33 (21.2%)	RR 0.29 (0.07 to 1.31)	151 fewer per 1000 (from 197 fewer to 66 more)	VERY LOW	CRITICAL
Loss of consciousness (assessed with: Glasgow Coma Scale)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[c]	None	1/65 (1.6%)	3/70 (4.3%)	OR[f] 0.39 (0.05 to 2.82)	30 fewer per 1000 (from 80 fewer to 30 more)	LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Morphine	Ketamine	Relative (95% CI)	Absolute		
Patient Satisfaction (assessed with: Patient Satisfaction)												
1	Randomised trials	Serious[a]	No serious inconsistency	Serious[d]	Serious[e]	None	22/32 (68.8%)	18/33 (54.5%)	RR 1.26 (0.82 to 1.57)	142 more per 1000 (from 82 fewer to 469 more)	VERY LOW	IMPORTANT

(a) The majority of evidence was at high risk of bias
(b) Heterogeneity, I2 = 70, p=0.04, unexplained by subgroup analysis
(c) The confidence interval crossed the MID by two increments
(d) Scale used to measure patient outcomes was not adequately specified
(e) The confidence interval crossed one MID
(f) Peto odds ratio

Table 114: Clinical evidence summary: Morphine versus acetaminophen

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Morphine	Acetaminophen	Relative (95% CI)	Absolute		
Pain Levels (follow-up 15 minutes; measured with: Final Pain Score; range of scores: 0-100; Better indicated by lower values)												
1	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	27	28	-	MD 8.3 lower (18.26 lower to 1.66 higher)	LOW	CRITICAL
Pain Levels (follow-up 30 minutes; measured with: Final Pain Score; range of scores: 0-100; Better indicated by lower values)												
1	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	27	28	-	MD 8.5 lower (22.42 lower to 5.42 higher)	LOW	CRITICAL
Pain Levels (follow-up 60 minutes; measured with: Final Pain Score; Better indicated by lower values)												
1	Randomised	Serious[a]	No serious	No serious	Serious[b]	None	27	27	-	MD 8.9 lower	LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Morphine	Acetaminophen	Relative (95% CI)	Absolute		
	trials		inconsistency	indirectness						(22.3 lower to 4.5 higher)		
Incidence of Adverse Events (follow-up 60 minutes; assessed with: Incidence of Adverse Event)												
1	Randomised trials	Serious[c]	No serious inconsistency	Serious[d]	Serious[b]	None	8/28 (28.6%)	2/27 (7.4%)	RR 3.86 (0.9 to 16.55)	212 more per 1000 (from 7 fewer to 1000 more)	VERY LOW	CRITICAL
Patient Satisfaction (follow-up 60 minutes; assessed with: 4 Point Likert Scale)												
1	Randomised trials	Serious[c]	No serious inconsistency	No serious indirectness	Serious[b]	None	14/26 (53.8%)	9/25 (36%)	RR 1.50 (0.79 to 2.81)	180 more per 1000 (from 76 fewer to 652 more)	LOW	IMPORTANT
Health-related quality of life – no evidence												

(a) Risk of selection bias - continuous outcome not matched at baseline
(b) The confidence interval crossed one MID
(c) The majority of the evidence was at high risk of bias
(d) Evidence on Adverse Events grouped and not reported per condition

Table 115: Clinical evidence summary: Intermediate-dose morphine versus high-dose morphine

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Intermediate-dose morphine	High-dose morphine	Relative (95% CI)	Absolute		
Pain Levels (follow-up 60 minutes; measured with: Final Pain Score; range of scores: 0-10; Better indicated by lower values)												
1	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	100	100	-	MD 0.49 lower (1.2 lower to 0.22 higher)	MODERATE	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Intermediate-dose morphine	High-dose morphine	Relative (95% CI)	Absolute	Quality	Importance
Nausea (follow-up 60 minutes; assessed with: Incidence of Nausea)												
1	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	8/100 (8%)	10/100 (10%)	RR 0.8 (0.33 to 1.94)	20 fewer per 1000 (from 67 fewer to 94 more)	VERY LOW	CRITICAL
Loss of consciousness (follow-up 60 minutes; assessed with: Glasgow Coma Score [Under 14])												
1	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	4/100 (4%)	5/100 (5%)	RR 0.8 (0.22 to 2.89)	10 fewer per 1000 (from 39 fewer to 95 more)	VERY LOW	CRITICAL
Health-related quality of life – no evidence												
Patient Satisfaction – no evidence												

(a) The majority of the evidence was at very high risk of bias
(b) The majority of evidence was at high risk of bias
(c) The confidence interval crossed the MID by two increments

Table 116: Clinical evidence summary: Morphine versus fentanyl

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Morphine	Fentanyl	Relative (95% CI)	Absolute	Quality	Importance
Pain Level (follow-up 60 minutes; measured with: Final Pain Score; range of scores: 0-10; Better indicated by lower values)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	103	97	-	MD 0.3 higher (0.41 lower to 1.01 higher)	HIGH	CRITICAL
Pain Level (follow-up 30 minutes; assessed with: Change in Pain Score [Dichotomised])												
1	Randomised trials	No serious risk of	No serious inconsistency	No serious indirectness	Serious	None	38/54 (70.4%)	40/54 (74.1%)	RR 0.95 (0.75 to	37 fewer per 1000 (from	MODERATE	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Morphine**	**Fentanyl**	**Relative (95% CI)**	**Absolute**		
		bias							1.20))	185 fewer to 148 more)		
Nausea (follow-up 60 minutes; assessed with: Incidence of Nausea)												
2	Randomised trials	Serious[b]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/157 (0%)	3/151 (2%)	OR[d] 0.13 (0.01 to 1.28)	20 fewer per 1000 (from 50 fewer to 10 more)	VERY LOW	CRITICAL
Respiratory Depression (follow-up 30 minutes; assessed with: Requirement for supplementary Oxygen)												
1	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[c]	None	2/54 (3.7%)	1/54 (1.9%)	OR[d] 1.97 (0.2 to 19.38)	20 more per 1000 (from 40 fewer to 80 more)	LOW	IMPORTANT
Loss of consciousness (assessed with: Ramsay Scale)												
1	Randomised trials	Serious[b]	No serious inconsistency	No serious indirectness	Very serious[c]	None	2/54 (3.7%)	5/54 (9.3%)	RR 0.40 (0.08 to 1.97)	56 fewer per 1000 (from 85 fewer to 90 more)	VERY LOW	CRITICAL
Health-related quality of life – no evidence												
Patient Satisfaction- no evidence												

(a) The evidence interval crossed one MID.
(b) The majority of evidence is at high risk of bias
(c) The confidence interval crosses two increments
(d) Peto odds ratio

Table 117: Clinical evidence summary: Morphine (intramuscular) versus ketamine (intravenous)

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	IM morphine	IV Ketamine	Relative (95% CI)	Absolute		
Nausea (follow-up 60 minutes; assessed with: Incidence of Nausea)												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	27/139 (19%)	8/169 (10%)	RR 4.1 (1.93 to 8.79)	143 more per 1000 (from 42 more to 358 more)	LOW	CRITICAL
Loss of consciousness – no evidence												
Health-related quality of life – no evidence												
Patient Satisfaction – no evidence												

I.5 Documentation

Table 118: Clinical evidence profile: checklist versus no checklist

Quality assessment							No. of patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Checklist	No checklist	Relative (95% CI)	Absolute	Quality	Importance
Mortality												
1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[a]	None	34/824 (4.1%)	26/798 (3.3%)	RR 1.27 (0.77 to 2.09)	9 more per 1000 (from 7 fewer to 36 more)	VERY LOW	CRITICAL
Complications												
1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[a]	None	26/824 (3.2%)	23/798 (2.9%)	RR 1.09 (0.63 to 1.9)	3 more per 1000 (from 11 fewer to 26 more)	VERY LOW	CRITICAL
ICU length of stay (Better indicated by lower values)												

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Checklist**	**No checklist**	**Relative (95% CI)**	**Absolute**		
1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision[b]	None	824	798	Median pre 2 versus post 1, p=0.01	-	LOW	IMPORTANT
Hospital length of stay (Better indicated by lower values)												
1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision[b]	None	824	798	Median pre 2 versus post2, p <0.001	-	LOW	IMPORTANT
Hospital length of stay (ISS > 16) (Better indicated by lower values)												
1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision[b]	None	824	798	Median pre 5 versus post 3, p=0.02	-	LOW	IMPORTANT
Mortality at 24 hours, 12 months – no evidence												
Health-related quality of life – no evidence												
Patient-reported outcomes. – no evidence												
Missing data – no evidence												
Timing of transfers – no evidence												

(a) Outcomes were downgraded by one increment if the upper or lower 95% CI crossed the lower MID or the upper or lower 95% CI crossed the upper MID. Outcomes were downgraded by two increments if the upper CI simultaneously crossed the upper MID and the lower CI crossed the lower MID. Default MIDs were set at RRs of 0.75 and 1.25 for dichotomous variables, and at 0.5 of the control group weighted mean standard deviation either side of the null line for continuous variables.

(b) Peto odds ratio

(c) No variance data provided

Table 119: Clinical evidence profile: Electronic medical record versus no electronic medical record

Quality assessment	No. of patients	Effect	Quality	Importance

No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Electronic medical record**	**Non EMR**	**Relative (95% CI)**	**Absolute**		
Mortality												
3	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	304/4038 (7.5%) 164/2835 2/100	164/2835 (5.8%) 190/3161 5/100	RR 0.84 (0.72 to 0.98) RR 0.96 (0.79 to 1.18) RR 0.40 (008 to 2.01)	9 fewer per 1000 (from 1 fewer to 16 fewer) 2 fewer (from 13 fewer to 11 more) 30 fewer (from 46 fewer to 51 more)	VERY LOW	CRITICAL
Requiring severe surgery												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	47/100 (47%)	53/100 (53%)	RR 0.89 (0.67 to 1.17)	58 fewer per 1000 (from 175 fewer to 90 more)	VERY LOW	CRITICAL
Delay in diagnosis												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	95/3161 (3%)	61/2835 (2.2%)	RR 1.4 (1.02 to 1.92)	9 more per 1000 (from 0 more to 20 more)	VERY LOW	CRITICAL
Complications - Airway complication												
1	Observational studies	None	No serious inconsistency	No serious indirectness	Very serious[b]	None	20/2835 (0.71%)	22/3161 (0.7%)	RR 1.01 (0.55 to 1.85)	0 more per 1000 (from 3 fewer to 6 more)	VERY LOW	CRITICAL
Complications - Cardiac arrest												
1	Observational studies	None	No serious inconsistency	No serious indirectness	Very serious[b]	None	41/2835 (1.4%)	55/3161 (1.7%)	RR 0.83 (0.56 to	3 fewer per 1000 (from	VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Electronic medical record**	**Non EMR**	**Relative (95% CI)**	**Absolute**		
									1.24)	8 fewer to 4 more)		
Complications - Wound infection												
1	Observational studies	None	No serious inconsistency	No serious indirectness	Serious[b]	None	39/2835 (1.4%)	50/3161 (1.6%)	RR 0.87 (0.57 to 1.32)	2 more per 1000 (from 7 fewer to 5 more)	VERY LOW	CRITICAL
Complications - Drug complication												
1	Observational studies	None	No serious inconsistency	No serious indirectness	No serious imprecision	None	5/2835 (0.18%)	20/3161 (0.63%)	RR 0.28 (0.10 to 0.75)	5 fewer per 1000 (from 2 fewer to 6 fewer)	LOW	CRITICAL
Completed data - Floor notes												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	3553/4038 (88%)	35/3481 (1%)	RR 87.51 (62.93 to 121.7)	870 more per 1000 (from 623 more to 1000 more)	VERY LOW	IMPORTANT
Completed data - Procedure notes												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	3529/3715 (95%)	2715/3481 (78%)	RR 1.22 (1.19 to 1.24)	172 more per 1000 (from 148 more to 187 more)	VERY LOW	IMPORTANT
Completed data - Resuscitation notes												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	3604/3715 (97%)	2820/3481 (81%)	RR 1.2 (1.18 to 1.22)	162 more per 1000 (from 146 more to 178 more)	VERY LOW	IMPORTANT

Quality assessment							No. of patients		Effect			
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Electronic medical record**	**Non EMR**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Completed data - ICU notes												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	3678/3715 (99%)	2785/3481 (80%)	RR 1.24 (1.22 to 1.26)	192 more per 1000 (from 176 more to 208 more)	VERY LOW	IMPORTANT
Missing data - Demographics												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	3/357 (0.84%)	123/350 (35.1%)	RR 0.02 (0.01 to 0.07)	344 fewer per 1000 (from 327 fewer to 348 fewer)	VERY LOW	IMPORTANT
Missing data - Diagnosis												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	3/357 (0.84%)	41/350 (11.7%)	RR 0.07 (0.02 to 0.23)	109 fewer per 1000 (from 90 fewer to 115 fewer)	VERY LOW	IMPORTANT
Missing data - Mechanism of injury												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	8/357 (2.2%)	98/350 (28%)	RR 0.08 (0.04 to 0.16)	258 fewer per 1000 (from 235 fewer to 269 fewer)	VERY LOW	IMPORTANT
Missing data - Treatment plan												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	19/357 (5.3%)	167/350 (47.7%)	RR 0.11 (0.07 to 0.18)	425 fewer per 1000 (from 391 fewer to 444 fewer)	VERY LOW	IMPORTANT
Length of stay emergency dept. (Better indicated by lower values)												

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Electronic medical record**	**Non EMR**	**Relative (95% CI)**	**Absolute**		
1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	100	100	-	MD 79 lower (98.92 lower to 59.08 lower)	LOW	IMPORTANT
Time between admission and completion of care (Better indicated by lower values)												
1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	100	100	-	MD 49 lower (67.91 lower to 30.09 lower)	LOW	IMPORTANT
Time between completion of care and exit from ED (Better indicated by lower values)												
1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	100	100	-	MD 31 lower (35.92 lower to 26.08 lower)	LOW	IMPORTANT
Mortality at 24 hours, 12 months – no evidence												
Health-related quality of life – no evidence												
Patient-reported outcomes. – no evidence												

(a) What was recorded probably changed as well as the format

(b) Outcomes were downgraded by one increment if the upper or lower 95% CI crossed the lower MID or the upper or lower 95% CI crossed the upper MID. Outcomes were downgraded by two increments if the upper CI simultaneously crossed the upper MID and the lower CI crossed the lower MID. Default MIDs were set at RRs of 0.75 and 1.25 for dichotomous variables, and at 0.5 of the control group weighted mean standard deviation either side of the null line for continuous variables.

(c) Peto odds ratio

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