National Clinical Guideline Centre

DRAFT FOR CONSULTATION

Fractures (complex): assessment and management

Complex fractures: assessment and management of complex fractures

Clinical guideline <...>

Appendices G - H

August 2015

Draft for consultation

Commissioned by the National Institute for Health and Care Excellence

Royal College of Physicians

The Royal College of Surgeons of England

Royal College of General Practitioners

Royal College of Nursing

NICE accredited

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Funding
National Institute for Health and Care Excellence

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1 # Appendices

Appendix G: Clinical evidence tables

G.1 Open fractures

G.1.1 Limb salvage

Table 1: Kumar 2007[36]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Kumar et al. Salvage versus amputation: utility of mangled extremity severity score in severely injured lower limbs. Indian J Orthop 2007; 41: 183-187	Retrospective and prospective prognostic accuracy studies	25 lower limbs in retrospective study and 36 lower limbs in prospective study.	All 'patients of either sex and any age, who had presented in emergency'. **Inclusion criteria:** Mangled lower limb; Gustilo type IIA femur and tibial fractures with hospital stay >4 days, severe muscle damage, associated nerve injury and major blood loss or bone injury; associated with a fibular	Mangled extremity severity scale(MESS), with threshold set at a score of 7. MESS ≥7 taken as indicator of amputation and <7 as indicator of salvage.	Actual clinical decision to amputate. Amputation decision: 'salvage protocol was abandoned if the general condition of the patient deteriorated or once the severe infection of injured limb was observed or renal failure set in making amputation inevitable'. However it is unclear if this	**MESS (all patients)**		None reported	Included primary amputation but not unreconstructable cases. Amputation decision appears to be based on reasons other than the MESS score (though no blinding was reported) and to be one that is indicative that amputation would have been the correct decision. However it is unclear if this was used in the retrospective arm of the study, so only prospective
						TP	10		
						FN	1		
						FP	1		
						TN	49		
						Sensitivity	0.91(0.59 -0.99)		
						Specificity	0.98(0.89 -0.99)		
						MESS (prospective patients)			
						TP	5		
						FN	1		
						FP	1		
						TN	29		
						Sensitivity	0.83(0.36 -0.97)		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
			fracture and displacement of >50% and comminuted and segmental fracture; Gustilo type IIB or C femur and tibial fractures; Gustilo Type III open pilon fractures; vascular injuries of lower limb except foot. <u>Exclusion criteria:</u> Injured limbs were near-amputation with only a thin bridge of skin remaining and therefore not reconstructible; unreconstructable feet; traumatic limb avulsions; isolated foot/digit injuries;		was used in the retrospective arm of the study.	Specificity	0.97(0.83-0.99)		results have been used in the review.
						MESS (retrospective patients)			
						TP	5		
						FN	0		
						FP	0		
						TN	20		
						Sensitivity	1.0(0.48-1.0)		
						Specificity	1.0(0.83-100)		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
			patients dying <1 week from admission. Mean age 34.5 years						

Table 2: Sheehan 2014[58]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Sheehan et al. Evaluation of the mangled extremity severity score in combat-related type III open tibia fracture. J Orthop Trauma 2014; 0:1-4	Retrospective	155	**Inclusion criteria:** People with combat-related type III open tibia fractures treated definitively in a US military hospital. **Exclusion criteria:** None reported Median age 23 (range 19-34); mostly blast injuries	Mangled extremity severity scale(MESS), with threshold set at a score of 7. MESS ≥7 taken as indicator of amputation and <7 as indicator of salvage. The MESS scores were generated post-hoc from the data, using the Gustilo-Anderson open fracture classification, age, systolic bp, injured extremity	Actual clinical decision to amputate. Amputation decision: it was unclear on what basis the decision was made. However it may not have been made in response to a MESS score, as the pre-calculated MESS score was not amongst the clinical data collected.	**MESS (all patients)**		None reported	No distinction made between primary and secondary amputation. Basis of amputation decision unclear. Appears to be based on reasons other than the MESS score (though no blinding was reported).
						TP	14		
						FN	26		
						FP	14		
						TN	101		
						Sensitivity	0.35 (0.21-0.52)		
						Specificity	0.88(0.80-0.93)		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
				vascular status and extremity soft tissue injury.					

Table 3: Fagelman 2002[18]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Fagelman et al. Mangled extremity severity score in children. J Paediatric Orthop 2002; 22: 182-184	Retrospective cohort	36 injured limbs in unclear number of children (possibly 34).	**Inclusion criteria:** All children from two paediatric trauma centres presenting with open lower extremity long bone fractures between 1885 and 1995; grade IIIB or IIIC open fractures or traumatic amputations **Exclusion criteria:**	Mangled extremity severity scale(MESS), with unreported threshold.	Actual clinical decision to amputate. Amputation decision: Amputation decision: it was unclear on what basis the decision was made. However it may not have been made in response to a MESS score, as the pre-calculated MESS score was not amongst the clinical data	**MESS (all patients)**		None reported	Included primary amputations. Poor reporting of results, with 2x2 table data having to be extracted from the text, and the author's rating of accuracy being incorrect. No threshold for MESS given. Amputation decision appears to be based on reasons other than the MESS score (though no blinding was reported).
						TP	5		
						FN	5		
						FP	0		
						TN	26		
						Sensitivity	0.50(0.19-0.81)		
						Specificity	1.0(0.87-1.0)		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
			Amputations below the ankle All skeletally immature. Main mechanisms of injury were pedestrian versus MVA, motorcycle versus MVA, machinery, and trains. Mean age was 9.5 years.		collected. The researchers admitted that MESS scores could not be excluded as a reason for amputation. The authors also reported that 'no attempt was made to salvage limbs that could possibly have survived. Finally the authors stated that the study omitted 'additional procedures or late amputations performed at outside institutions or in adulthood'.				However possibility that the amputations could have been avoided and that some reportedly salvaged limbs may have gone on to need later, but unrecorded, amputations. Overall, the data is prone to serious bias.

Table 4: Bonanni 1993[3]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Bonanni et al.	Retrospective	58	**Inclusion**	Mangled	Actual clinical	**MESS**		None	Only secondary

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
The futility of predictive scoring of mangled lower extremities. The Journal of Trauma 1993; 34: 99-104	cohort study.	included.	**criteria:** Patients in a level I trauma centre treated for mangled limbs, defined as one of the following: Severe injury to three of the following – integument, bone, nerve and vessel; severe injury of two of four organ systems where the area of lost muscle and skin is > the largest circumference of the extremity and required free muscle transfer; severe injury of two of four organ systems that require surgical intervention; severe injury of two of four	extremity severity scale(MESS), mangled extremity syndrome index (MESI), predictive salvage index (PSI) and limb salvage index(LSI). No thresholds given for any of these.	decision to amputate. Amputation decision: unclear, but probably not made in response to the actual scores as the scores were calculated retrospectively from the patient data.	TP	4	reported	amputations included. Amputation decision appears to be based on reasons other than the predictive scores (though no blinding was reported) and to be one that is indicative that amputation would have been the correct decision.
						FN	14		
						FP	19		
						TN	21		
						Sensitivity	0.22(0.06-0.48)		
						Specificity	0.53(0.36-0.68)		
						MESI			
						TP	1		
						FN	17		
						FP	4		
						TN	36		
						Sensitivity	0.06(0.01-0.27)		
						Specificity	0.90(0.76-0.97)		
						PSI			
						TP	6		
						FN	12		
						FP	12		
						TN	28		
						Sensitivity	0.33(0.13-0.59)		
						Specificity	0.70(0.53-0.83)		
						LSI			

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
			organ systems when bone loss is >5cm and periosteal stripping has occurred. **Exclusion criteria:** Primary amputations – where amputation was never considered as an option; traumatic amputations; isolated foot or digit injury; all dying <1 week from admission. Mean age 32(15); ISS 16; mostly MVAs			TP	11		
						FN	7		
						FP	23		
						TN	17		
						Sensitivity	0.61(0.36-0.83)		
						Specificity	0.43(0.27-0.59)		

Table 5: Slauterbeck 1994[59]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Slauterbeck et al. Mangled Extremity Severity Score: an accurate guide to treatment of the severely injured upper extremity. Journal of Orthopaedic Trauma; 1994; 8:282-285	Retrospective study	37 patients with 43 open fractures	**Inclusion criteria:** Patients sustaining open humerus, radius or ulna fractures, as well as any other mangles upper extremity injuries proximal to the hand where limb viability was in question. **Exclusion criteria:** None reported Age not given; no other details on population	Mangled extremity severity scale(MESS), with threshold set at a score of 7. MESS ≥7 taken as indicator of amputation and <7 as indicator of salvage. **This was slightly adjusted to accommodate limbs without ischaemia- a score of zero was added for no limb ischaemia rather than the standard lowest score of 1 for this.** MESS was calculated retrospectively for each injury without knowledge of	Actual clinical decision to amputate. Amputation decision: this was 'based on the surgeon's clinical judgement. The MESS was not applied to these patients during the course of their treatment.	**MESS** TP FN FP TN Sensitivity Specificity	 9 0 0 34 1.0 (0.66-1.0) 1.0 (0.909-1.0)	None reported	Unclear if secondary or primary; Amputation decision appears to be based on reasons other than the MESS score and to be one that is indicative that amputation would have been the correct decision.

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
				the treatment outcome.					

Table 6: Durham 1996[15]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Durham et al. Outcome and utility of scoring systems in the management of the mangled extremity. Am	Retrospective study	23 UL and 51 LL	**Inclusion criteria:** Patients with severe UL and LL injuries; significant injury to at least 3 of the 4	Threshold Mangled extremity severity scale(MESS), with threshold set at a score of 7. MESS >7 taken	Actual clinical decision to amputate. Amputation decision: 'amputations were necessary because of soft	**MESS - UL**		None reported	Primary amputations not included in accuracy data. Not explicitly stated that amputation
						TP	3		
						FN	0		
						FP	1		
						TN	8		
						Sensitivity	1.0(0.30-1.0)		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
J Surg 1996; 172:569-574			major tissue groups. **Exclusion criteria:** Not reported All had Gustilo type IIIB or IIIC fractures, a severe degloving injury, or a fracture in association with a major nerve injury. 57 males and 12 females; mean age 35(14) years. Most injuries were after MVA or motorcycle collisions; mean ISS 17(11). Mean follow-up was 54 (36) months	as indicator of amputation and ≤7 as indicator of salvage. Note this is different to normal threshold. Mangled extremity Syndrome Index (MESI) (>20 amputation) Predictive Salvage index (PSI) (>8 amputation) Limb Salvage Index (LPI) (>6 amputation)	tissue injury and poor arterial outflow.' For UL injuries. For LL injuries secondary amputations were for sepsis, arterial thrombosis, insensate limb, and nerve transection and contusion.	Specificity	0.89(0.52-0.98)		decision was not based on the prediction score. However the reasons for amputation appear to be purely clinically based and indicate that amputation was probably the correct decision.
						MESI - UL			
						TP	2		
						FN	1		
						FP	0		
						TN	9		
						Sensitivity	0.67(0.12-0.95)		
						Specificity	1.0(0.66-1.0)		
						MESS - LL			
						TP	5		
						FN	1		
						FP	5		
						TN	19		
						Sensitivity	0.83(0.36 – 0.97)		
						Specificity	0.79(0.58-0.93)		
						MESI - LL			
						TP	3		
						FN	3		
						FP	0		
						TN	24		
						Sensitivity	0.50(0.12-0.88)		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
						Specificity	1.0(0.86-1.0)		
						PSI - LL			
						TP	3		
						FN	3		
						FP	1		
						TN	23		
						Sensitivity	0.50(0.12-0.88)		
						Specificity	0.96(0.79-0.99)		
						LSI - LL			
						TP	5		
						FN	1		
						FP	4		
						TN	20		
						Sensitivity	0.83(0.36-0.97)		
						Specificity	0.83(0.58-0.93)		

Table 7: El Sharawy 2005[16]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
El Sharawary et al. Arterial reconstruction after mangled	Prospective study	62	**Inclusion criteria:** Non iatrogenic upper and	Mangled extremity severity scale(MESS),	Actual clinical decision to amputate. Amputation	**MESS (both UL and LLs)**		None reported	Primary amputations not included in accuracy data.
						TP	4		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
extremity: injury severity scoring systems are not predictive of limb salvage. Vascular 2005; 13: 114-119			lower arterial injuries admitted to a vascular unit in Egypt. **Exclusion criteria:** Primary amputations; non-mangled extremity; death within one week of admission Mean age 29(12.5); mostly RTAs	with threshold set at a score of 7. MESS ≥7 taken as indicator of amputation and <7 as indicator of salvage. MESI (threshold was 20)	decision: severe secondary haemorrhage, or massive limb injuries complicated by sepsis	FN	0		Not explicitly stated that amputation decision was not based on the prediction score. However the reasons for amputation appear to be purely clinically based and indicate that amputation was probably the correct decision.
						FP	42		
						TN	16		
						Sensitivity	1.0(0.40-1.0)		
						Specificity	0.28(0.17-0.41)		
						MESI (both UL and LLs)			
						TP	4		
						FN	0		
						FP	38		
						TN	20		
						Sensitivity	1.0(0.40-1.0)		
						Specificity	0.34(0.23-0.48)		

Table 8: Johansen 1990 and Helfet 1990[25,32]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Johansen et al. Objective criteria accurately predict amputation following	Prospective study (There was also a retrospective study, but that was effectively the	26	**Inclusion criteria:** Not reported **Exclusion criteria:**	Mangled extremity severity scale(MESS), with threshold set at a score of 7. MESS ≥7 taken	Actual clinical decision to amputate. Amputation decision: Not reported	**MESS (all patients)**		None reported	Unclear if primary or secondary amputations; Very poorly reported. Unclear if amputation
						TP	12		
						FN	0		
						FP	0		
						TN	14		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
lower extremity trauma. The Journal of Trauma 1990; 30: 568-573 SAME RESULTS IN: Helfet et al. Limb salvage versus amputation. Clinical orthopaedics and related research 1990; 256: 80-86	development al study. The prospective arm is the validation study)		Not reported No population details given.	as indicator of amputation and <7 as indicator of salvage.		Sensitivity	1.0(0.73-1.0)		decision based on reasons other than the MESS score
						Specificity	1.0(0.77-1.0)		

Table 9: Kjorstad 2007[56]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Kjorstad et al. Application of the mangled extremity severity score in a combat setting. Military	Retrospective study	60 extremities in 49 patients	**Inclusion criteria:** All patients with extremity injuries **Exclusion**	Mangled extremity severity scale(MESS), with threshold set at a score of 7. MESS ≥7 taken as indicator of	Actual clinical decision to amputate. Amputation decision: based on 'the experience of the military surgeon	**MESS (all patients)**		None reported	Amputation decision appears to be based on reasons other than the MESS score (though no blinding was reported) and to
						TP	6		
						FN	2		
						FP	1		
						TN	49		
						Sensitivity	0.75(0.59-		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
medicine 2007; 172: 777-781			**criteria:** Deceased patients	amputation and <7 as indicator of salvage.	(based on extent of injury, time from evacuation from the battlefield to treatment, and estimated evacuation time and distance to a higher level of care) and not the MESS…'		0.99)		be one that is indicative that amputation would have been the correct decision.
						Specificity	0.98(0.89-1.0)		

Table 10: Robertson 1991[55]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Robertson et al. Prediction of amputation after severe lower limb trauma. The Journal of Bone and Joint Surgery 1991; 73-B: 816-818	Retrospective study	164 lower extremities in 152 patients	**Inclusion criteria:** All patients with severe lower extremity injuries; required either vascular reconstruction, soft tissue reconstruction by plastic surgeons, or had had major open fractures combined with	Mangled extremity severity scale(MESS), with threshold set at a score of 7. MESS ≥7 taken as indicator of amputation and <7 as indicator of salvage.	Actual clinical decision to amputate. Amputation decision: for secondary amputation based on necrosis or ischaemia in first month and infection and uselessness of limb after two months. For those with primary	**MESS (secondary amputation only)**		None reported	Amputation decision appears to be based on reasons other than the MESS score (though no blinding was reported) and to be one that is indicative that amputation would have been the correct decision.
						TP	16		
						FN	49		
						FP	0		
						TN	43		
						Sensitivity	0.24(0.15-0.37)		
						Specificity	1.0(0.92-1.0)		
						MESS (primary and			

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
			other serious injuries; **Exclusion criteria:** Deceased patients		amputation, decision to amputate based on 'severity of the trauma'.	**secondary amputation)**			
						TP	41		
						FN	54		
						FP	0		
						TN	43		
						Sensitivity	0.43(0.33-0.54)		
						Specificity	1.0(0.92-1.0)		

Table 11: Stewart 2012[62]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Stewart et al. Application of lower extremity injury severity scores in children. J Child Orthop 2012; 6: 427-431	Retrospective study	24 children patients	**Inclusion criteria:** All patients with lower limb trauma; traumatic amputations of the LL; Gustilo IIIB and C compound fractures; Gustilo IIIA compound tibial fractures with >2	Mangled extremity severity scale(MESS), with threshold set at a score of 7. MESS $\geq$7 taken as indicator of amputation and <7 as indicator of salvage. Predictive Salvage index (PSI) (>8	Actual clinical decision to amputate. Amputation decision: not clearly reported	**MESS**		Academic funding	Includes primary amputations – no secondary amputations were performed. Very poorly reported. Unclear if amputation decision based on reasons other than the MESS score
						TP	2		
						FN	1		
						FP	3		
						TN	18		
						Sensitivity	0.66(0.12-0.95)		
						Specificity	0.86(0.64-0.97)		
						LSI			
						TP	2		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
			procedures, severe bone loss, major nerve injury; dysvascular injuries; major soft tissue injuries; severe foot injuries **Exclusion criteria:** Age>16 years or had fused growth plates; impaired GCS; SCI; developmental delay 2 female and 22 male patients; mean age 8.72 years	amputation) Limb Salvage Index (LPI) (>6 amputation) Nerve injury, ischaemia, soft tissue injury, skeletal injury, shock, age system (NISSSA) (≥11 amputation) Hanover fracture scale (HF-98) (≥11 amputation)		FN	1		
						FP	4		
						TN	17		
						Sensitivity	0.66(0.12-0.95)		
						Specificity	0.81(0.58-0.94)		
						PSI			
						TP	3		
						FN	0		
						FP	2		
						TN	19		
						Sensitivity	1.0(0.30-1.0)		
						Specificity	0.90(0.70-0.99)		
						NISSSA			
						TP	2		
						FN	1		
						FP	4		
						TN	17		
						Sensitivity	0.66(0.12-0.95)		
						Specificity	0.81(0.		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
							58-0.94)		
						HFS-98			
						TP	3		
						FN	0		
						FP	5		
						TN	16		
						Sensitivity	1.0(0.30-1.0)		
						Specificity	0.76(0.53-0.92)		

Table 12: Mommsen 2010[44]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Mommsen et al. Traumatic extremity arterial injury in children: epidemiology, diagnostics, treatment and prognostic value of mangled extremity severity score	Retrospective study	44 children	**Inclusion criteria:** Traumatic extremity arterial injuries admitted to a level 1 trauma centre; complete documentation required for calculation of severity scores	Mangled extremity severity scale(MESS), with threshold set at a score of 7. MESS $\geq$7 taken as indicator of amputation and <7 as indicator of salvage.	Actual clinical decision to amputate. Amputation decision: not clearly reported	**MESS (UL)**		None reported	Includes primary and secondary amputation. Very poorly reported. Unclear if amputation decision based on reasons other than the MESS score
						TP	0		
						FN	0		
						FP	0		
						TN	17		
						Sensitivity	-		
						Specificity	1.0 (0.80-1.0)		
						MESS (LL)			
						TP	8		
						FN	0		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
			Exclusion criteria: Age>14 years; venous and iatrogenic vascular lesions			FP	4		
						TN	15		
						Sensitivity	1.0(0.63-1.0)		
			Mean age 9 (3.2) years; 79.6% male; average follow-up 1.7 years; mostly penetrating injuries, blunt extremity trauma and multiple trauma; LL injuries 61.4%.			Specificity	0.79(0.54-0.94)		

Table 13: Brown 2009[5]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Brown et al. Predicting the need for early amputation in ballistic mangled extremity injuries. J	Retrospective study	77 patients with 85 limb injuries	**Inclusion criteria:** Military patients with an abbreviated injury score >1 for lower limb injury;	Mangled extremity severity scale(MESS), with threshold set at a score of 7. MESS ≥7 taken as indicator of	Actual clinical decision to amputate. Amputation decision: not reported	**MESS (secondary only)**		None reported	Primary and secondary amputations included. Very poorly reported. Unclear if amputation decision based
						TP	4		
						FN	3		
						FP	9		
						TN	54		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Trauma 2009; 66: S93-S98			**Exclusion criteria:** Non-body injuries; non-ballistic injuries; closed injuries; traumatic amputation Median age 25(18-42); 53% blast injuries and 47% penetrating fragment injuries; Median ISS 10(4-59)	amputation and <7 as indicator of salvage. MESS was calculated retrospectively for each injury from database		Sensitivity	0.57(0.19-0.90)		on reasons other than the MESS score
						Specificity	0.86(0.75-0.93)		
						MESS (primary and secondary)			
						TP	19		
						FN	3		
						FP	9		
						TN	54		
						Sensitivity	0.86(0.65-0.97)		
						Specificity	0.86(0.75-0.93)		

Table 14: Behdad 2012[1]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes		Source of funding	Comments
						MESS				
						Threshold(amputate if ≥)	**Sensitivity**	**Spec**		
Behdada et al. Evaluation of mangled extremity severity score (MESS) as a	Retrospective study	60 extremities in 49 patients	**Inclusion criteria:** All children with lower extremity long	Mangled extremity severity scale(MESS). No threshold set, so ROC	Actual clinical decision to amputate. Amputation decision: based on the	2	1	0	None reported	No raw data available. Only secondary amputations included. Amputation
						4	1	0.133		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes		Source of funding	Comments
predictor of lower limb amputation in children with trauma. Eur J Pediatric Surg 2012; 22: 465-469			bone fractures; children consecutively admitted to the unit; grade I,IIB and IIIC open fractures due to trauma **Exclusion criteria:** Traumatic amputation; primary amputation Mean age 12.3 amputation group and 11.4 salvage group.	analysis done.	paediatric surgeon's clinical judgement.	5.5	0.867	0.333		decision appears to be based on reasons other than the MESS score (though no blinding was explicitly reported, there is a suggestion of it by reference to the MESS scores being calculated by the research physicians) and to be one that is indicative that amputation would have been the correct decision.
						6.5	**0.733**	**0.533**		
						7.5	**0.533**	**0.666**		
						8.5	0.267	0.867		
						9.5	0.133	0.933		
						11	0	1.0		

Table 15: McNamara 1994[42]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes		Source of funding	Comments
McNamara et al. Severe open fractures	Retrospective study	24 fractured tibias from	**Inclusion criteria:**	Mangled extremity severity	Actual clinical decision to amputate.	**MESS**			None reported	Primary and secondary amputations
						Threshold (amputate	**Sensiti**	**Spec**		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes		Source of funding	Comments
of the lower extremity: a retrospective evaluation of the mangled extremity severity score. Journal of Orthopaedic Trauma 1994; 8: 81-87		14 patients	All patients with type IIIB and C open tibial fractures **Exclusion criteria:** Deceased patients Ages 3-76; mostly MVSa	scale(MESS), with varying thresholds. NISSA with varying thresholds MESS and NISSA calculated retrospectively from raw data.	Amputation decision: based on surgeon's decision, who was blinded from prediction scores. Basis of this decision not reported	**if ≥)**	**vity**			included. Amputation decision based on reasons other than the MESS or NISSA score (blinding of the surgeons from actual prediction scores was reported). Unclear, however, if the decision to amputate was one likely to lead to a correct decision.
						4	1.0	0.46		
						5	0.82	0.69		
						6	0.55	0.92		
						7	**0.55**	**1.0**		
						8	**0**	**-**		
						NISSA				
						Threshold(amputate if ≥)	**Sensitivity**	**Spec**		
						4		0		
						5		0.08		
						6		0.46		
						7	1.0	0.46		
						8	0.91	0.69		
						9	0.81	0.92		
						10	0.54	0.92		
						11	0.36	1.0		
						12	0.27			

Table 16: Rajasekaran 2006[51]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Rajasekeran et al. A score for predicting salvage and	Type of study unclear but possible prospective	109	**Inclusion criteria:** All patients with type IIIA	Mangled extremity severity scale(MESS),	Actual clinical decision to amputate. Amputation	**MESS (all patients)**		None reported	Primary and secondary amputations included.
						TP	3		
						FN	4		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
outcome in Gustilo type-IIIA and type-IIIB open tibial fractures. J Bone Joint Surg (Br) 2006; 88-B:1351-60			and B injuries referred to a tertiary trauma centre; tibial open fractures; within 24 hours of injury **Exclusion criteria:** Debridement or initial procedure at another hospital; complete traumatic amputations; vascular injury requiring vascular reconstruction; severe associated injuries to the foot/ankle 42 Type IIIA and 67 type IIIB; 107 males and 2 females; mean age 34.97	with threshold set at a score of 7. MESS ≥7 taken as indicator of amputation and <7 as indicator of salvage. Ganga scale. Threshold for amputation set at >14.	decision: 'The decision to amputate or undertake salvage was taken independently by a consensus of the senior members of the plastic and orthopaedic teams without any bias or consideration of any score	FP	1		Amputation decision appears to be based on reasons other than the MESS score (though no blinding was reported) and to be one that is indicative that amputation would have been the correct decision. The paper had incorrectly calculated one value. The study also reported AUC to account for accuracy at other thresholds but the AUC values reported appear far too high given the sensitivity and
						TN	101		
						Sensitivity	0.42(0.10-0.81)		
						Specificity	0.99(0.95-1.0)		
						Ganga (all patients)			
						TP	7		
						FN	0		
						FP	3		
						TN	99		
						Sensitivity	1.0(0.59-1.0)		
						Specificity	0.97(0.92-0.99)		
						AUC MESS	0.998		
						AUC GANGA	0.988		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
			years; mostly RTAs and fall from height.						specificity values at the thresholds

Table 17: Doucet 2011[14]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Doucet et al. Combat versus civilian open tibia fractures: the effect of blast mechanism on limb salvage. The journal of Trauma – Injury, Infection and Critical Care. 2011; 70:1241-1247	Retrospective study	850 military fractures in 850 people and 115 civilian fractures in 103 people	**Inclusion criteria:** Open tibia fractures; abbreviated injury score >1 **Exclusion criteria:** Civilian: age 35; 5.9% penetrating; ISS 6.8; 77% male; mostly RTA Military: age 24; 97% penetrating; ISS 15.2; 100% male; mostly explosive injuries	Mangled extremity severity scale(MESS), with threshold set at a score of 7. MESS ≥7 taken as indicator of amputation and <7 as indicator of salvage. MESS score calculated retrospectively from data.	Actual clinical decision to amputate. Amputation decision: not reported	**MESS (MILITARY – primary and secondary)**		None reported	Primary and secondary amputations included. Very poorly reported. Unclear if amputation decision based on reasons other than the MESS score
						TP	15		
						FN	6		
						FP	8		
						TN	74		
						Sensitivity	0.71(0.48-0.89)		
						Specificity	0.90(0.82-0.96)		
						MESS (MILITARY – secondary only)			
						TP	4		
						FN	4		
						FP	8		
						TN	74		
						Sensitivity	0.50(0.16-0.84)		
						Specificity	0.90(0.82-0.96)		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
						MESS (CIVILIAN – primary and secondary)			
						TP	16		
						FN	29		
						FP	42		
						TN	599		
						Sensitivity	0.35(0.22-0.51)		
						Specificity	0.93(0.91-0.95)		
						MESS (CIVILIAN – secondary only)			
						TP	9		
						FN	18		
						FP	42		
						TN	599		
						Sensitivity	0.33(0.17-0.54)		
						Specificity	0.93(0.91-0.95)		

Table 18: Dagum 1999[9]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Dagum et al. Salvage after severe lower-	Retrospective study	40 severe open fractures	**Inclusion criteria:**	Mangled extremity severity	Actual clinical decision to amputate.	**MESS (secondary amputatio**		None reported	Primary and secondary amputations

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
extremity trauma: are the outcomes worth the means? Plast Reconstr Surg 1999; 103: 1212-1220		in 40 patients	Gustilo type IIIB and IIIC open tibial fractures; Requiring soft-tissue coverage by either local muscle or free flap, vascular repair, or both, by the plastic surgery service; Requiring bone fixation, bone grafting or both by orthopaedic surgeons, for leg salvage **Exclusion criteria:** Insufficient data to calculate the amputation risk tools Mean follow-up 7-147 months; mean age 37(15) years; ISS 13(6.6); mostly MVAs	scale(MESS), with threshold set at unreported level Mangled extremity Syndrome Index (MESI) (threshold set at unreported level) Predictive Salvage index (PSI) (threshold set at unreported level) Limb Salvage Index (LPI) (threshold set at unreported level) All were calculated retrospectively from the patient data.	Amputation decision: 'standard indications for amputation in severe open tibial fractures were used; otherwise an attempt at leg salvage was undertaken. The absolute indications for a primary amputation were total or near total leg amputation or complete tibial or sciatic nerve transection. Relative indications were 2 or more of the following: concurrent severe ipsilateral foot injury, large intercalary soft tissue or	**ns)** TP FN FP TN Sensitivity Specificity **MESI (secondary amputations)** TP FN FP TN Sensitivity Specificity **PSI (secondary amputations)** TP FN FP TN Sensitivity Specificity **LSI**	 2 3 4 31 0.40(0.06-0.85) 0.89(0.73-0.97) 0 5 2 33 0.0(0.0-0.52) 0.94(0.81-0.99) 3 2 2 33 0.6(0.15-0.94) 0.94(0.81-0.99) 		included. Amputation decision appears to be based on reasons other than the prediction score (though no blinding was reported) and to be one that is indicative that amputation would have been the correct decision.

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
					bone loss, warm ischaemia time>6 hours and severe concurrent multiple injuries.	**(secondary amputations)**			
						TP	3		
						FN	2		
						FP	6		
						TN	29		
						Sensitivity	0.6(0.15-0.94)		
						Specificity	0.83(0.66-0.93)		

Table 19: Madhuchandra 2015[40]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Madhunchandra et al. Predictability of salvage and outcome of Gustilo and Anderson type-IIIA and type IIIB open tibial fractures using Ganga Hospital Scoring system. Injury, Int J Care Injured 2015; 46: 282-287	Prospective study	40 patients included from an original 44, 3 of which were lost to follow up and one transferred to another hopsitla.	**Inclusion criteria:** >17 years old; open fractures of the tibia irrespective of fracture site; presenting within 24 hours of injury; Class IIA or IIIB. **Exclusion criteria:** Class IIIC injuries, complete traumatic	Ganga Open Injury Severity Score (threshold 14). Scored by consultant doing original debridement.	Actual clinical decision to amputate. Amputation decision: persistent infection and non-union of the fracture	**Ganga (threshold for amputation >14)**		None reported	The decision to amputate in the single patient appears to be valid as an attempt at salvage had been made after consensus of senior surgeons despite a Ganga score above the threshold – thus bias
						TP	1		
						FN	0		
						FP	0		
						TN	39		
						Sensitivity	1.0(0.17-1.0)		
						Specificity	1.0(0.91-1.0)		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
			amputations; initial debridement at another hospital. 38 females and 2 males; 11 type IIIA and 29 type IIIB. RTA in 36 patients, industrial in 3 and farmyard in 1.						resulting from the Ganga score influencing the decision to amputate seems unlikely. Data in paper described in text and the diagnostic accuracy results do not tally. Data in text has been used to derive accuracy data.

Table 20: Krettek 2001[35]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Krettek et al. Hannover fracture scale '98 – re-evaluation and new	Retrospective and prospective study	60 extremities in 49 patients	**Inclusion criteria:** Retrospective: all open long bone fractures of the UL and LL	Mangled extremity severity scale(MESS), with threshold set at	Actual clinical decision to amputate. Amputation decision: ' The therapy itself	**HFS '98 (primary and secondary)**		None reported	Retrospective study used to determine HFS '98 threshold through ROC
						TP	14		
						FN	3		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
perspectives of an established extremity salvage score. Injury. Int J Care Injured 2001; 32: 317-328			admitted between 1994 and 1996 Prospective: all open long bone fractures of the UL and LL admitted between 1996 and 1997 **Exclusion criteria:**	unreported level Hannover Fracture Scale '98 (HFS '98) – threshold set at >11 Hannover Fracture Scale (HFS) with threshold set at unreported level Nerve injury, ischaemia, soft tissue injury, skeletal injury, shock, age system (NISSSA) with threshold set at unreported level Scoring performed in the OR after debridement by surgeon in	was not influenced by the HFS '98 score as no information about the value of this score was available at that time of the study.' However this only applied to HFS '98 in the retrospective review and does not apply to any of the tests in the prospective review. It is stated that patients were involved in the clinical decision making process, which indicates that the risk tool	FP	1		analysis. However discrete results based on a threshold are given for all 4 tools in retrospective analysis. Prospective analysis aimed to measure sensitivity and specificity of each tool at optimal threshold. Only prospective results are given in this review. Both primary and secondary amputations included. Unclear if the risk tool
						TN	69		
						Sensitivity	0.82(0.57-0.96)		
						Specificity	0.99(0.92-1.0)		
						HFS (primary and secondary)			
						TP	15		
						FN	2		
						FP	3		
						TN	67		
						Sensitivity	0.88(0.64-0.98)		
						Specificity	0.96(0.88-0.99)		
						MESS(primary and secondary)			
						TP	14		
						FN	3		
						FP	1		
						TN	69		
						Sensitivity	0.82(0.57-0.96)		
						Specificity	0.99(0.92-1.0)		
						NISSSA(primary and secondary)			
						TP	12		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
				both retrospective and prospective arms. As the surgeon may also have been involved in the later decision to amputate this implies that knowledge of the scores could have affected the decision.	was probably not a major influence on the decision.	FN	5		accuracies were confounded by the risk tool scores.
						FP	1		
						TN	69		
						Sensitivity	0.71 (0.44-0.90)		
						Specificity	0.99(0.92-1.0)		

Table 21: Bosse 2001[4]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Bosse et al. A prospective evaluation of the clinical utility of the lower extremity injury-severity scores. The Journal of Bone and Joint Surgery 2001;	Prospective study	556 extremities in 539 patients	**Inclusion criteria:** High energy trauma of the lower extremity, defined as injuries leading to traumatic amputation below the distal aspect of the	Mangled extremity severity scale(MESS) – threshold set at ≥7 predictive salvage index (PSI) – threshold set	Actual clinical decision to amputate. Amputation decision: all decisions were meant to be made by the attending surgeons. At no point, however,	**HFS '97 (secondary)**		None reported	Included both primary and secondary amputations (within 6 months after injury but after some other treatment associated with
						TP	6		
						FN	49		
						FP	5		
						TN	252		
						Sensitivity	0.11(0.04-0.22)		
						Specificity	0.98(0.96-0.99)		
						PSI (secondary)			

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
83A: 3-14			femur or as injuries associated with some risk of amputation, including Gustilo type IIIB and C tibial fractures, selected type A fractures, dysvascular limbs, major soft tissue injuries to the tibia; severe injuries to the distal tibia or foot. **Exclusion criteria:** <16 years old; >69 years old; psychiatric disorder; CNS injury; 3rd degree burns to injured limb > 1 hand breadth; prior limb amputation or	at ≥8 Limb salvage index(LSI) – threshold set at ≥6 Hannover Fracture Scale '97 (HFS '97) – threshold set at ≥9 Nerve injury, ischaemia, soft tissue injury, skeletal injury, shock, age system (NISSSA) – threshold set at 11 All were graded at the time of at the initial surgical procedure and then again at final closure or secondary	were criteria for amputation described. It was stated that: 'The overall scores for each lower-extremity injury severity scoring system were not tabulated in the study data books, nor were individual patient scores ever revealed to the surgeon.'	TP	20		attempted salvage). Unclear if amputations were clinically unavoidable but unlikely decisions were affected by the index scores.
						FN	35		
						FP	42		
						TN	215		
						Sensitivity	0.36(0.24-0.50)		
						Specificity	0.84(0.79-0.88)		
						MESS (secondary)			
						TP	12		
						FN	43		
						FP	19		
						TN	238		
						Sensitivity	0.22(0.12-0.35)		
						Specificity	0.93(0.89-0.95)		
						NISSSA (secondary)			
						TP	7		
						FN	48		
						FP	4		
						TN	253		
						Sensitivity	0.13(0.05-0.24)		
						Specificity	0.98(0.96-0.99)		
						LSI (secondary)			
						TP	16		
						FN	39		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
			non-ambulatory before the injury; primary treatment received prior to admission to a participating trauma centre; no English or Spanish; unable to attend follow-ups because lived too far away. Age 16-69; 77% male; 64% MVA-related; mean ISS 11.	amputation.		FP	7		
						TN	250		
						Sensitivity	0.29(0.18-0.43)		
						Specificity	0.97(0.94-0.99)		
						HFS '97 (primary and secondary)			
						TP	37		
						FN	63		
						FP	5		
						TN	252		
						Sensitivity	0.37(0.38-0.47)		
						Specificity	0.98(0.96-0.99)		
						PSI(primary and secondary)			
						TP	47		
						FN	53		
						FP	42		
						TN	215		
						Sensitivity	0.47(0.37-0.57)		
						Specificity	0.84(0.79-0.88)		
						MESS(primary and secondary)			
						TP	45		

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
						FN	55		
						FP	19		
						TN	238		
						Sensitivity	0.45(0.35-0.55)		
						Specificity	0.93(0.89-0.95)		
						NISSSA(primary and secondary)			
						TP	33		
						FN	67		
						FP	4		
						TN	253		
						Sensitivity	0.33(0.24-0.434)		
						Specificity	0.98(0.96-0.99)		
						LSI(primary and secondary)			
						TP	51		
						FN	49		
						FP	7		
						TN	250		
						Sensitivity	0.51(0.41-0.61)		
						Specificity	0.97(0.94-0.99)		

Table 22: Ramasamy 2013A[52]

Reference	Study type	No. of patients	Patient characteristics	Risk tool(s)	Reference test	Outcomes	Effect sizes	Source of funding	Comments
Ramamsamy et al. FASS is a better predictor of poor outcome in lower limb blast injury than AIA: implications for blast research. J Orthop trauma 2012; 0:1-7	Retrospective	63 people (89 limbs)	**Inclusion criteria:** Lower leg injury from a military vehicle explosion, leading to either amputation or salvage **Exclusion criteria:** Blast amputations Mean age 26 (5.75) years	Foot and ankle severity score (FASS) Abbreviated injury score (AIS) No thresholds pre-specified so AUC approach was used in analysis.	Actual clinical decision to amputate. Amputation decision: not reported	AUC for FASS (primary and secondary amputations)	0.891(0.807-0.947) FSS threshold of ≥5 found to give optimum balance of sensitivity and specificity	None reported	Primary and secondary amputations included. Unclear if decisions influenced by the scoring systems, and also unclear if amputation was truly clinically indicated.
						AUC for AIS (primary and secondary amputations)	0.783 (0.683 to 0.863) AIS threshold of 3 found to give optimum balance of sensitivity and specificity		

G.1.2 Antibiotics

Table 23: Enninghorst 2011[17]

Study	Enninghorst 2011[17]
Study type	Prospective Cohort
Number of studies (number of participants)	(n=89 blunt trauma patients with open tibial shaft fractures)
Countries and setting	Conducted at the John Hunter Hospital (University of Newcastle affiliated Level 1 trauma center) in New South Wales,

	Australia
Line of therapy	First-line
Duration of study	12-month follow-up
Method of assessment of guideline condition	Orthopedic Trauma Association coding for the fractures
Stratum	-
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis.
Inclusion criteria	Consecutive adult (>18 years) blunt trauma patients with open tibia shaft fractures (Orthopedic Trauma Association code 42A, B and C)
Exclusion criteria	None described
Recruitment/selection of patients	Between 1st January 2007 and 29th December 2009.
Age, gender and ethnicity	For the deep infected group and those that did not have a deep infection respectively: Age – 43.9 (SD 16.3) and 40.9 (SD18.2) years. Gender (M: F) 11:4 and 55:19 .Ethnicity: Not reported. Age and Gender were not given by debridement timing groups.
Indirectness of population	No indirectness
Interventions	A specific protocol was not listed. The papers describes that all patients had an initial washout in the emergency department and antibiotic cover and tetanus prophylaxis. The type of antibiotics and dosing was not described. Patients received their antibiotics at a mean of 1.2 hours (SD 0.3). Timing of antibiotics (time point taken from): Not described. Type of antibiotics used: Not described Duration of antibiotic use: Not described. No intervention timings reported. In the methods section of the paper it describes that the timing to antibiotics was prospectively recorded.
Funding	None described
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Groups not described. Deep infection definition used: If the infection required surgical debridement and long-term IV antibiotics based on infectious disease and service consultation.	

Covariates in the MVA unclear. It is described in the papers that 18 variables examined in this paper were taken into account in the MVA. Variables listed in the univariate logistic regression table: Sex, age, smoking status, ISS, NISS, Trauma team activation, high energy mechanism, contamination (non, mild, heavy), Time from injury to operating room, time from admission to operating room, grade of fracture, initial stabilisation (none, or internal fixation), in hours (8-8) or not, attending surgeon in the operating room, ICU admission and number of procedures. The time to antibiotic treatment and type of fracture were later listed as confounding factors that they had been adjusted for in the MVA. Protocol outcome 1: Deep surgical site infection. (n=89) - Actual outcome: Number of patients with a deep infection; 15 patients (17%) got a deep infection, 4 of which required a late amputation. The paper states that "all patients got their antibiotic prophylaxis in a timely fashion (1.2 hours +/- 0.3 hours) without statistical difference between infected and non-infected cases. No data was given in the univariate logistic regression analysis table. No data was given for the multivariate analysis for the deep infection outcome but the paper describes there to have been 'no identifiable predictors for infection'. Risk of bias: High; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Mortality up to 12 months, Health related quality of life, Return to normal activities, Re-operation (unplanned), Amputation, Functional outcomes and length of stay.

Narrative text and additional information:

The mechanism of injury was primarily road and traffic injuries (n=55, motor vehicle and motor bike crashes and pedestrians struck by vehicles). Thirty-three (37%) patients had multiple injuries. The grade of injuries were grade 1 (n=21), grade 2 (n=27), grade 3a (n=18), grade 3b (n=21) and grade 3c (n=1). The initial fixation of the fractures consisted of intramedullary nailing (n=70), external fixation (n=12), closed reduction and application of plaster (n=3) and percutaneous plating (n=4).

Table 24: Weber 2014[67]

Study	**Weber 2014[67]**
Study type	Prospective Cohort
Number of studies (number of participants)	1 (n=686 patients with 737 fractures)
Countries and setting	Conducted in Canada
Line of therapy	First-line
Duration of study	Followed up >90 days after the original injury.

Method of assessment of guideline condition	Observation of injury
Stratum	-
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis.
Inclusion criteria	Skeletal maturity, long bone open fractures, requiring initial surgical debridement.
Exclusion criteria	Pathologic fractures, penetrating injury, unsalvageable limb injuries, other medical conditions precluding surgical management.
Recruitment/selection of patients	Patients at 3 level 1 trauma centres in Canada
Age, gender and ethnicity	Median (IQR) age: 39.6 (26.5-52.8); 72% male; Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	Established principles of open fracture management used, including initial surgical debridement and fracture fixation with copious irrigation (3 L or more) and debridement of soft tissues and contaminated bone. Surgical fixation was at the surgeon's discretion. This was repeated at intervals of 48 hours until tissues were clean, all non-viable tissue had been removed, and delayed wound closure could occur. Timing of debridement or timing of prophylactic antibiotics was at the discretion of the surgeon, and the effects of timing of antibiotics was evaluated using a multivariable regression adjusting for timing of surgery, transfusion, fracture location, and Gustilo grade. Age and gender were not included in the model.
Funding	None described
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Protocol outcome 1: Deep surgical site infection. (n=89) - Actual outcome: Time to antibiotics: OR 1.0 (95% CI: 0.95-1.05) per increased hour of time to surgery after adjustment for: time to surgery, transfusion, fracture location, and Gustilo grade; Risk of bias: High; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Mortality up to 12 months, Health related quality of life, Return to normal activities, Re-operation (unplanned), Amputation, Functional outcomes and length of stay.

Table 25: Hull 2014[29]

Study	Hull 2014[29]
Study type	Retrospective Cohort
Number of studies (number of participants)	1 (n=364 patients with 459 open fractures)
Countries and setting	Conducted in Canada
Line of therapy	First-line
Duration of study	Followed up up to one year after the original injury, or uncomplicated healing.
Method of assessment of guideline condition	Observation of injury
Stratum	-
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis.
Inclusion criteria	Open fractures.
Exclusion criteria	Hand injuries
Recruitment/selection of patients	Consecutive patients presenting with an open fracture between 2003 and 2007.
Age, gender and ethnicity	Age range 16-85. Mean age similar between those with non-infected and infected fractures (40.1 vs 39.7); 70% male in non-infected and 84.7% male in infected; ethnicity not reported.
Indirectness of population	No indirectness
Interventions	Intravenous antibiotics administered on presentation and continued until the wound is covered definitively, or for at least 24 hours post-operatively in patients with a Gustillo-Anderson G1 fracture. Patients not allergic to penicillin received cefuroxime, and patients with a higher grade fracture received gentamycin and metronidazole/penicillin. Patients allergic to penicillin were given clindamycin or vancomycin rather than cefuroxime. Debridement was undertaken urgently based on the availability of an operating theater. Delays of > 6 hours were often encountered due to the lack of availability and/or the physiological instability of the patient. The timing of wound closure and the method of fixation were left to the discretion of the surgeon.
Funding	Internal academic funding; no commercial funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Protocol outcome 1: Deep surgical site infection - Actual outcome: Time of antibiotic administration: non-significant effect per increased hour delay after adjustment for gross contamination, existence of tibial fracture,	

time to debridement and grade of fracture (low versus high). Age, gender, mechanism of penetration, ASA class, and ISS score had a non-significant association with the outcome.; Risk of bias: Very high; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Mortality up to 12 months, Health related quality of life, Return to normal activities, Re-operation (unplanned), Amputation, Functional outcomes and length of stay.

Table 26: Lack 2015[38]

Study	**Lack 2015[38]**
Study type	Retrospective Cohort
Number of studies (number of participants)	1 (n=137 patients)
Countries and setting	Conducted in USA
Line of therapy	First-line
Duration of study	Followed up up to 90 days after the original injury.
Method of assessment of guideline condition	Observation of injury
Stratum	-
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis.
Inclusion criteria	Open fractures with Gustillo Anderson Grade III.
Exclusion criteria	Missing data; non-reconstructible limbs
Recruitment/selection of patients	Consecutive patients presenting with an open fracture in 2013.
Age, gender and ethnicity	Mean age similar between those with non-infected and infected fractures (40 vs 40.5); gender and ethnicity not reported.
Indirectness of population	No indirectness
Interventions	Definitive fracture fixation and wound management followed basic standard principles. Diaphyseal fractures were treated with intramedullary fixation. Those with intra-articular extension or at the very distal or proximal metaphysis were usually treated with plate and screw fixation. Those with intra-articular extension or at the very distal or proximal metaphysis were usually treated with plate and screw fixation. The standard regimen for antibiotic prophylaxis was Cefazolin (128/137). Other antibiotics used were clindamycin or vancomycin. Temporizing external fixation was used

	when necessary and definitive fixation was performed as soon as the patient and wound were amenable. Wounds were closed when possible and those not able to be closed were treated with negative pressure dressings pending definitive wound coverage.
Funding	Internal academic funding; no commercial funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Protocol outcome 1: Deep surgical site infection - Actual outcome: Time of antibiotic administration: For patients with >66 minutes to antibiotics the adjusted OR for deep infection was 3.78 (95% CIs: 1.26 to 14.11), compared to ≤66 minutes to antibiotics. Adjustment was made for for age, Gustillo-Anderson classification, smoking, presence of diabetes, time to debridement and time to cover Risk of bias: Very high; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Mortality up to 12 months, Health related quality of life, Return to normal activities, Re-operation (unplanned), Amputation, Functional outcomes and length of stay.

G.1.3 Arterial shunts

Table 27: Desai 2012[13]

Study	**Desai 2012[13]**
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=26)
Countries and setting	Conducted in USA; Setting: Level I trauma centre in USA
Line of therapy	First-line
Duration of study	Not clear: certainly extended to length of stay, up to 1 month or more
Method of assessment of guideline condition	Adequate method of assessment/diagnosis

Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	patients at a level I trauma centre with combined lower extremity traumatic injuries requiring both orthopaedic and vascular surgical repair
Exclusion criteria	Traumatic amputations (immediate); death within 24 hours of arrival; did not undergo a revascularisation procedure; insufficient medical records
Recruitment/selection of patients	Retrospective review of patient data
Age, gender and ethnicity	Age - Median (range): 33 (6-80). Gender (M:F): Not reported. Ethnicity: Not reported
Further population details	
Extra comments	Mechanism of injury MVC (n=3), motorcycle collision (n=7), crush (n=3), pedestrian struck by vehicle (n=7), gunshot (n=7), bike struck by vehicle (n=1). Mean GCS score 13.8, mean ISS 15.4, mean MESS 5.6.
Indirectness of population	No indirectness
Interventions	(n=5) Intervention 1: Repair - Shunt, definitive skeletal stabilisation, definitive vascular repair. Temporary shunt to address the vascular injury before definitive vascular repair or orthopaedic stabilisation. Duration Not reported. Concurrent medication/care: Very poorly reported (n=17) Intervention 2: Repair - definitive vascular repair, definitive skeletal stabilisation. Definitive vascular procedure as initial surgical intervention, followed by orthopaedic intervention. Duration Not reported. Concurrent medication/care: Very poorly reported
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SHUNT, DEFINITIVE SKELETAL STABILISATION, DEFINITIVE VASCULAR REPAIR versus DEFINITIVE VASCULAR REPAIR, DEFINITIVE SKELETAL STABILISATION

Protocol outcome 1: Mortality at Define
- Actual outcome: mortality ; Group 1: 0/5, Group 2: 1/17; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Amputation at Define

- Actual outcome: Amputation ; Group 1: 1/5, Group 2: 5/17; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 3: Compartment decompression at Define - Actual outcome: compartment syndrome ; Group 1: 0/5, Group 2: 2/17; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 4: Unplanned re-operation at Define - Actual outcome: vascular reoperation ; Group 1: 1/5, Group 2: 7/17; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life ; Hospitalisation ; Deep infection ; Length of stay

G.1.4 MDT

Table 28: Naique 2006[45]

Study	**Naique 2006[45]**
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=72)
Countries and setting	Conducted in United Kingdom; Setting: UK teaching hospital
Line of therapy	First-line
Duration of study	Follow up (post intervention): 14 months mean follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Gustilo and Anderson classification
Inclusion criteria	Grade IIIB tibial open fractures
Exclusion criteria	Non-grade IIIB; open #s of tibial plateau and ankle
Recruitment/selection of patients	All eligible patients consecutively
Age, gender and ethnicity	Age - Mean (range): 42 (19 to 94). Gender (M:F): 60:12. Ethnicity: Not reported
Further population details	1. Age: 18-65 years. 2. Gustillo Anderson grade: IIIB and worse. 3. Isolated injury: Not applicable / Not stated / Unclear. 4. Wound contamination: Not applicable / Not stated / Unclear.

Extra comments	Grade IIIB tibial open fractures only; cause of injury: RTA (70%), falls from heights (20%), sports (5%), industrial crush injuries (4%) and gunshot injuries (1%).
Indirectness of population	No indirectness
Interventions	(n=25) COMBINED: Combined orthoplastic and plastic teams physically present at initial procedure - Combined in physical realm. Dose/quantity, brand name, extra details. Duration not applicable. Concurrent medication/care: None reported Further details: 1. Grade of surgeon: (n=47) non-combined: Orthopaedic surgeon only involved at initial procedure - Not combined. Initial orthopaedic treatment at another centre before transfer for definitive combined orthopaedic and plastic surgical management. Duration NA. Concurrent medication/care: None reported Further details: 1. Grade of surgeon: Not applicable / Not stated / Unclear
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: COMBINED IN PHYSICAL REALM versus NOT COMBINED Protocol outcome 1: Patient outcomes - return to normal activities at Define - Actual outcome: Enneking limb score; Combined: mean 75 points (SD 15.9); n=25, Non-combined: mean 74 points (SD 15.9); n=47 Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 2: Amputation at Define - Actual outcome: Delayed amputations at up to 19 months; Combined: 1/25, Non-combined: 2/47; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 3: Flap failure at Define - Actual outcome: Flap failures; Combined: 0/25, Non-combined: 6/47; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 4: AE - Deep surgical site bone infection at Define - Actual outcome: Deep infection; Combined: 1/25, Non-combined: 5/47; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at Define; Mortality at Define; Time to definitive cover at Define; length of hospital stay at Define; Further unplanned surgery at Define; Unplanned complexity of soft tissue cover at Define

G.1.5 Optimal timing of debridement

Table 29: CHARALAMBOUS2005A[7]

Study	Charalambous 2005A[7]
Study type	Retrospective Cohort
Number of studies (number of participants)	(n=383 open tibial fractures)
Countries and setting	Conducted in the North West of England, 7 hospitals
Line of therapy	First-line
Duration of study	Followed until there was clinical and radiological evidence of complete bony union or to the time of secondary surgical procedure to promote union.
Method of assessment of guideline condition	Identified through the hospitals' information system via a computer search. Two authors reviewed medical records +/- radiographs using a pre-designed form.
Stratum	-
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis.
Inclusion criteria	Open tibial fractures
Exclusion criteria	Grade 3C injuries (due to vascular injuries needing emergency treatment), patients requiring a limb amputation (as the primary outcome was infection and secondary procedure to promote bony union), isolated medial malleolar fractures
Recruitment/selection of patients	Hospital information system/medical records between January 1992-January 2001
Age, gender and ethnicity	For the early (<6 hours) and the delayed (>6 hours) groups respectively: Age – 31 (range 4-87) and 30 (range 3-88) years. Gender (M: F) 68:32 and 70:30 .Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	Framework: intention to operate as soon as possible, essential antibiotic prophylaxis. Case management was by the surgeon's discretion. Thorough wound cleaning and debridement for all patients. Note: there was no pre-defined protocol. Note: if the injury had been clearly under graded, the grade was adjusted. Timing of surgery definition: Time (in hours) from presentation to A&E to initial surgery. Patients were not included if they had been transferred from outside the local area, so it was estimated that patients arrived within 1 hour of their injury. Note: one patient arrived 24 hours after injury and in this case time of injury rather than the presentation to A&E

	was considered. Intervention 1 (n=184): <6 hours to debridement Intervention 2 (n=199): >6 hours to debridement
Funding	None described

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Early versus delayed debridement (Group 1 <6 hours to debridement, Group 2 >6 hours to debridement)

Deep infection definition used: development of osteomyelitis diagnosed clinically (development of chronic discharging sinus) or radiologically, that required surgical bone debridement. A positive microbiological culture was not considered essential for the diagnosis of superficial or deep infection. Pin site infections were excluded due them being a complication of external fixator devices

Re-operation (unplanned) definition used: secondary surgical procedures (those performed for inadequate radiological and clinical bony union and included bone grafting with or without change in the means of fracture stabilization or fibula osteotomy, or exchange intra-medullary nailing with reaming. Dynamisation of internal or external fixation devices was excluded.

Covariates in the MVA - It is not clear. It is described in the papers that all the variables examined in this paper were taken into account in the MVA. Variables listed in the paper include: Sex, age, mechanism of injury, fracture site, fracture pattern, Gustilo grade, average time to initial antibiotics, length of antibiotic administration, most senior surgeon present at initial surgery, primary surgical procedure and definitive surgical procedure.

Protocol outcome 1: Deep surgical site infection. (n=383)
- Actual outcome: Number of patients with a deep infection; Group 1: n=8/184 Group 2: 8/199; Risk of bias: High; Indirectness of outcome: No indirectness. Note: No MVA was carried out for the deep infection outcome as it was not possible due to the small complication rate in the series. Bivariate analysis: p=1.0, Fisher exact test)

Protocol outcome 2: Re-operation (unplanned) n=383), operated at a median of 180 days (range 41-750 days)
-Actual outcome: Number of patients having secondary procedures; Group 1: n=24/184, Group 2: 20/199; Risk of bias: High; Indirectness of outcome: No indirectness. Bivariate analysis p=0.42, Chi-squared test. MVA p=0.53, no significant difference between the two groups.

Protocol outcomes not reported by the study	Mortality up to 12 months, Health related quality of life, Return to normal activities, Amputation, Functional outcomes and length of stay.

Narrative text/additional information:

The Gustilo grading for the two groups, were as follows: Grade 1 7.6%, Grade 2 10.3%, Grade 3A 59.3% and Grade 3B 22.8% in the early debridement group and Grade 1 9.5%, Grade 2 9.5%, Grade 3A 69.8% and Grade 3B 11.2% for the delayed debridement group. Out of the patients who had delayed debridement the timings were 128 at 6-12 hours, 52 at 12-18 hours, 9 at 18-24hours and 10 at more than 24 hours. The primary surgical procedures consisted of 120 manipulation and cast immobilisation with or without traction, 116 external fixation, 147 internal fixation (75 reamed nails, 53 unreamed nails, 15 screws +/- plate and 4 K wires). The deep infections were found in patients in the less than 6 hours group (n=8), 6-12 hours (n=7) and 1 at 20 hours and 20 minutes. They were all grade 3 fractures apart from 2, grade 2 fractures. Note: one patient died 2 months after injury and was excluded from the further surgical analysis as it was prior to complete bone healing.

Table 30: Davissears 2012[11]

Study	**Davissears 2012[11]**
Study type	Retrospective Cohort
Number of studies (number of participants)	(n=7560 open tibial fractures with no missing data)
Countries and setting	Conducted in the United States of America, 200 hospitals
Line of therapy	First-line
Duration of study	Does not specify follow-up time.
Method of assessment of guideline condition	International Classification of Diseases, Ninth Revision Clinical Modification diagnosis codes for open tibia fractures. Patients were wanted to be admitted near to the time of injury (not transferred), with acute primary injury of an open tibia fracture where immediate amputation was not required. **Note:** Codes for operative procedures (arterial repair, vein repair, nerve repair, placement of an external fixator, open reduction and internal fixation and amputation) where debridement had not been coded for were used for timing of debridement as it was thought to be unlikely a patient would undergo a surgical procedure without adequate debridement of the wound. Debridement codes proximal to the knee and distal to the ankle were also included on the assumption that the tibia fracture would also be debrided at the same time. It was due to reimbursement issues that debridement coding may have been missing.
Stratum	-
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis.
Inclusion criteria	Adults (18 years and older)
Exclusion criteria	Patients having an immediate amputation on day 0 or 1 of being hospital or the timing was not specified, patients with more than one amputation, transfers from other hospitals, patients who discharged against medical advice, patients

	who did not receive an emergency procedure during admission, patients with procedures performed prior to admission (readmissions).
Recruitment/selection of patients	Health Care Utilization Project Nationwide Inpatient Sample administrative database from 2003-2009 (annual stratified probability sample of |20% of all US nonfederal hospital admission from the majority of states (44 in 2009). It is the largest all-payer inpatient care database.
Age, gender and ethnicity	For the amputation and salvage groups respectively: Age – 46.0 (SD 16.3) and 40.3 (SD 15.7) years. Gender (M: F) 84:15 and 5610:1851 .Ethnicity: White (61.6%, 49.5%), Black (11.1%, 13.6%), Hispanic (11.1%, 12.3%), Other (4%, 3.9%), Unspecified (12.1%, 20.7%)
Indirectness of population	No indirectness
Interventions	No protocols described. Timing of surgery definition: Use codes for first emergency procedure whether debridement was specified or not. Days since admission. Intervention 1 (n=3093): Debridement (first surgical procedure) on day 0 Intervention 2 (n=882): Debridement (first surgical procedure) on day 1 Intervention 3 (n=401): Debridement (first surgical procedure) on day 2 Intervention 4 (n=394): Debridement (first surgical procedure) on days 3-4 Intervention 5 (n=600): Debridement (first surgical procedure) on day 5 or greater Intervention 6 (n=2190): Debridement (first surgical procedure) timing unspecified
Funding	None described

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Reference group is Hospital day 0 versus hospital day 1 versus hospital day 2 versus hospital days 3-4 versus hospital day 5 or greater to the first emergency procedure (debridement)

Amputation: amputation occurring at or below the knee and up to the ankle was identified.

Covariates in the MVA- The paper describes on the control variables ($p<0.05$) from the bivariate associations with amputation were included in the final multiple logistic regression model, robustly adjusted for clustered sampling at the hospital level. Model findings were then used to produce adjusted probabilities of amputation as the outcome. Variables inputted into the MVA were: age, sex, race, economic characteristics (insurance types), Injury severity scale score, comorbidities, associated injuries/procedure (arterial injury, tibial nerve injury, complicated open wound, fasciotomy, dislocation (knee or ankle)), admission type (trauma center, non-trauma center, unspecified), location (rural, urban), bed size (small, medium, large), hospital teaching status, hospital volume open tibial fractures per year (in quartiles), median

household income, mechanism of injury. **Note:** Gustilo grading was unable to be captured by the ICD coding. Arterial injury, nerve injury and the presence of a complex wound based on the ICD codes were, but the extent of the soft tissue injury was not able to be recorded. Protocol outcome 1: Amputation. (n=99/7560) - Actual outcome: Number of patients with an amputation; Group 1: n=16/3093, Group 2: n=19/882, Group 3 n=9/401, Group 4 n=10/394, Group 5 n=38/600, Group 6 n=7/2190; Risk of bias: High; Indirectness of outcome: No indirectness. Group 1 as reference in the MVA. Group 2: OR 3.814 (95%CI 1.801-8.074), p<0.001 Group 3: OR 3.816 (95%CI 1.511-9.638), p=0.005 Group 4: OR 4.023 (95%CI 1.832-8.832), p=0.001 Group 5: OR 11.417 (95% CI 5.928-21.991), p<0.001 Group 6: OR 0.611 (95%CI 0.251-1.484), p=0.276	
Protocol outcomes not reported by the study	Mortality up to 12 months, Health related quality of life, Return to normal activities, Deep surgical site infection, Functional outcomes and length of stay.

Narrative text/additional information:

81.5% had blunt trauma.

Table 31: Enninghorst 2011[17]

Study	**Enninghorst 2011[17]**
Study type	Prospective Cohort
Number of studies (number of participants)	(n=89 blunt trauma patients with open tibial shaft fractures)
Countries and setting	Conducted at the John Hunter Hospital (University of Newcastle affiliated Level 1 trauma center) in New South Wales, Australia
Line of therapy	First-line
Duration of study	12-month follow-up
Method of assessment of guideline condition	Orthopedic Trauma Association coding of the fracture

Stratum	-
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis.
Inclusion criteria	Consecutive adult (>18 years) blunt trauma patients with open tibia shaft fractures (Orthopedic Trauma Association code 42A, B and C)
Exclusion criteria	None described
Recruitment/selection of patients	Between 1st January 2007 and 29th December 2009.
Age, gender and ethnicity	For the deep infected group and those that did not have a deep infection respectively: Age – 43.9 (SD 16.3) and 40.9 (SD18.2) years. Gender (M: F) 11:4 and 55:19 .Ethnicity: Not reported. Age and Gender were not given by debridement timing groups.
Indirectness of population	No indirectness
Interventions	A specific protocol was not listed. The papers describes that all patients had an initial washout in the emergency department and antibiotic cover and tetanus prophylaxis. The type of antibiotics and dosing was not described. Patients received their antibiotics at a mean of 1.2 hours (SD 0.3). Timing of surgery definition: Time between the injury and the commencement of surgical treatment. Intervention 1 (n=46): <6hours to debridement Intervention 2 (n=45): >6 hours to debridement In the univariate logistic regression and multivariate analysis time to debridement (time to surgery) is inputted as a continuous variable.
Funding	None described

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Early versus delayed debridement (Group 1 <6 hours to debridement, Group 2 >6 hours to debridement)

Deep infection definition used: If the infection required surgical debridement and long-term IV antibiotics based on infectious disease and service consultation.

Covariates in the MVA - It is not clear. It is described in the papers that 18 variables examined in this paper were taken into account in the MVA. Variables listed in the univariate logistic regression table or described in the paper were: Sex, age, smoking status, ISS, NISS, Trauma team activation, high energy mechanism, contamination (none, mild, heavy), Time from injury to operating room, time from admission to operating room, grade of fracture, initial stabilization (none, or internal fixation), in hours

(8-8) or not, attending surgeon in the operating room, ICU admission, number of procedures, antibiotic timing and type of fracture. Protocol outcome 1: Deep surgical site infection. (n=89) - Actual outcome: Number of patients with a deep infection; 15 patients (17%) got a deep infection, 4 of which required a late amputation. It is unclear how many there were in each group. Time to surgery was presented as a continuous variable and in the univariate logistic regression there was no significant difference between those who developed a deep infection and those that did not (7.87 hours SD 4.7 and 7.95 hours SD 4.5 respectively). The OR was 1 (95% CI 0.88, 1.13) with a p value of 0.9543. There was also no statistically significant different between the infected (deep infection) and non-infected groups for the confounders of age (0.5417) and grade of injury (p=0.9821). No data was given for the multivariate analysis for the deep infection outcome but the paper describes there to have been 'no identifiable predictors for infection'. Risk of bias: High; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Mortality up to 12 months, Health related quality of life, Return to normal activities, Re-operation (unplanned), Amputation, Functional outcomes and length of stay.

Narrative text/additional information:

The mechanism of injury was primarily road and traffic injuries (n=55, motor vehicle and motor bike crashes and pedestrians struck by vehicles). 33 (37%) patients had multiple injuries. The grade of injuries were Grade 1 (n=21), Grade 2 (n=27), Grade 3a (n=18), Grade 3b (n=21) and Grade 3c (n=1). The initial fixation of the fractures consisted of intramedullary nailing (n=70), external fixation (n=12), closed reduction and application of plaster (n=3) and percutaneous plating (n=4).

Table 32: Harley 2002[22]

Study	**Harley 2002[22]**
Study type	Retrospective Cohort
Number of studies (number of participants)	(n=215 open long bone fractures)
Countries and setting	Conducted in Canada, a major teaching hospital and referral trauma centre with transport times often >8 hours from the time of injury
Line of therapy	First-line
Duration of study	Minimum of 12 months post injury, until a definitive procedure for non-union or deep infection was carried out.
Method of assessment of guideline condition	Medical charts, data extraction using a standardized data collection form. Records and radiograph reports were reviewed.

Stratum	-
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis.
Inclusion criteria	Open fracture of a major long bone (femur, tibia/fibula, humerus and forearm)
Exclusion criteria	Patients younger than 14 years, fractures that results from penetrating trauma.
Recruitment/selection of patients	Hospital records between January 1996 and December 1998. 247 fractures in 233 patients were identified but on 215 were included due to mortality related to the trauma (n=5), below the knee amputation due to non-viable foot (n=1) and inadequate follow-up (n=26).
Age, gender and ethnicity	For the early (≤8 hours) and the delayed (>8 hours) groups respectively: Age – 38.7 (SD 17) and 41.3 (SD 20) years, p=0.12. Gender (M) 82 (71%) and 74 (74%). Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	No formal protocol but the following process was carried out: Arrival to the study hospital – soft tissue and bone debridement, pulsed irrigation with a minimum of 3L of sterile saline and skeletal stabilization performed on an emergent basis. All Grade 3 fractures/lower grade fractures based on surgeon preference and wound characteristics may have repeated operative debridements. Antibiotics given: cephalosporin IV, minimum of 48 hours after all operative procedures. Aminoglycoside for all grade 3 injuries, or if a definitive treatment was carried out >8 hours. Penicillin was added based on wound characteristics. Type of fixation was decided by the surgeon. Time of definitive fracture treatment definition (debridement time): Time point was defined as the operative start time of irrigation and surgical debridement, followed by fracture stabilization, by an orthopaedic surgeon in an operating room at this regional trauma referral center. Intervention 1 (n=115): ≤8 hours to debridement/fracture fixation Intervention 2 (n=100): >8 hours to debridement/fracture fixation
Funding	None described

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Early versus delayed debridement (Group 1 ≤8 hours to debridement, Group 2 >8 hours to debridement)

Deep infection definition used: Purulent drainage or osteomyelitis presenting after definitive wound closure and were diagnosed by the responsible surgeon based on clinical suspicion and subsequent deep cultures. For the purposes of our analyses, cellulitis during the course of the primary hospitalization was not considered deep infection.

Covariates in the MVA- Male gender, Age (<25 years, 25-35 years, 35-50 years, >50 years), time (time to definitive management/debridement time), Gustilo grade (1, 2, 3). Antibiotic duration was removed from the final regression model because it was not significant in the presence of the other factors. Injury mechanism, wound closure and ICU stay were not included in the MVA as they were not significant in the univariate analysis. Fracture location and fixation method were not included in the MVA due to having a 0 in the cells for upper extremity and cast/PP. Mean time to definitive treatment was 8 hours 29 minutes (+/- 2 hours 47 minutes). Group 1 mean time to definitive treatment was 5 hours 51 minutes (+/- 1 hour 25 minutes). Group 2 mean time to definitive treatment was 11 hours 15 minute (+/- 3 hours 45 minutes). Protocol outcome 1: Deep surgical site infection. (n=215) - Actual outcome: Number of patients with a deep infection; Group 1: n=10/115 Group 2: 10/100; MVA Odds ratio 0.95 (95% CI 0.36, 2.51). Risk of bias: High; Indirectness of outcome: No indirectness. There were 9 deep infections in tibia/fibula fractures and 1 in the femur in the ≤8 hours to fracture fixation/debridement group and 7 tibia/fibula and 3 femur deep infections in the >8 hours group.	
Protocol outcomes not reported by the study	Mortality up to 12 months, Health related quality of life, Return to normal activities, Re-operation (unplanned), Amputation, Functional outcomes and length of stay.

Narrative text/additional information

For fewer than or equal 8 hours and more than8 hours respectively, the grade of fractures were; grade 1 (n=33, n=27), grade 2 (n=51, n=39), grade 3 (n=31, n=34). The fractures were located in the tibia/fibula (n=61, n=48), femur (n=11, n=17), and upper extremity (n=43, n=35). The fixation methods used to treat the fractures were IM nail (n=39, n=39), ORIF (n=49, n=28), ExFix (n=20, n=24) and other/PP (n=7, n=9). The mechanism of injury was primarily motorcycle, motor vehicle and motorcycle/car/pedestrian injuries (n=109, 51%). 37% (n=81) were due to falls or assaults and 12% (n=25) due to crushing injuries. The reasons why times to definitive treatment were longer was due to long extrication times, extended transportation time, patient instability requiring either neurosurgical or general surgical intervention and operating room delays as a result of a triage system to treat life threatening cases first.

Table 33: Malhotra 2014[41]

Study	Malhotra 2014[41]
Study type	Retrospective Cohort
Number of studies (number of participants)	(404 patients with n=415 blunt trauma open extremity fractures)
Countries and setting	Conducted in Virginia
Line of therapy	First-line

Duration of study	72-month study
Method of assessment of guideline condition	List from the trauma registry of all the open blunt trauma extremity fractures from the American College of Surgeons, verified level 1 trauma center
Stratum	-
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis.
Inclusion criteria	Blunt open extremity fractures
Exclusion criteria	Patients transferred from another hospital, patients with isolated fractures of the wrist and/or ankle, patients whose first debridement and irrigation was delayed beyond 24 hours,
Recruitment/selection of patients	Chart review
Age, gender and ethnicity	For the early (<8 hours) and the delayed (>8 hours) groups respectively: Age – 40 years (SD 1.0) and 35 (SD 1.6) years. Gender (M: F) not reported .Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	Only an antibiotic protocol was listed in the paper. Antibiotic protocol used: Grade 1; first generation cephalosporin, grade 2 and 3; first generation cephalosporin and an aminoglycoside. Extensive contamination (decision made by the surgeon) penicillin would also be given or clindamycin if allergic to penicillin. Antibiotics were continued until 48 hours after wound closure or if the surgeon thought the wound was clean enough not to require further debridement and irrigation. Time to debridement: Not defined. Intervention 1 (n=328): <8hours to debridement, mean 4 hours and 58 minutes, IQR 3 hours 53 minutes - 6 hours 9 minutes) Intervention 2 (n=87): >8 hours to debridement, mean 11 hours and 4 minutes, IQR 8 hours 41 minutes -11 hours 39 minutes)
Funding	None described

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Early versus delayed debridement (Group 1 <8 hours to debridement, Group 2 >8 hours to debridement)

Deep infection definition used: Infections were defined as those requiring parenteral antimicrobial therapy with or without surgical therapy. Superficial wound infections

requiring only outpatient oral antimicrobial therapy were excluded. Baseline characteristic differences- younger age and a higher ISS (Injury Severity Score) in the >8 hours debridement group. Covariates in the MVA - The entire data set was used. Assuming this includes all the variables in the baseline characteristics table, it would have included; age, ISS, RTS, SBP, lactate and Gustilo grade. Protocol outcome 1: Deep surgical site infection. (n=415) - Actual outcome: Number of patients with a deep infection; Group 1: n=35/328 Group 2: 17/87; Risk of bias: High; Indirectness of outcome: No indirectness. MVA: Delay of >8 hours RR 2.035 (95%CI 1.022-4.4054), P<0.05	
Protocol outcomes not reported by the study	Mortality up to 12 months, Health related quality of life, Return to normal activities, Reoperation (unplanned), Amputation, Functional outcomes and length of stay.

Narrative/additional information:

There were 129 upper and 286 lower extremity fractures. The grading of the fractures for the less than 8 hours and more than 8 hours until debridement were as follows: grade 1 (n=64, n=22), grade 2 (n=128, n=34), grade 3a (n=90, n=22), grade 3b (n=38, n=9) and grade 3c (n=8, n=0). The mechanisms of injury and fixation used were not described.

Table 34: Noumi 2005[46]

Study	**Noumi 2005[46]**
Study type	Retrospective Cohort
Number of studies (number of participants)	(n=88 patients with 89 open femoral shaft fractures)
Countries and setting	Conducted in Kitsato University Hospital, Japan
Line of therapy	First-line
Duration of study	Followed up between 2-12 years after the original injury.
Method of assessment of guideline condition	Medical records. Roentgenograms were available for 85 fractures. Deep infection rate assessed by use of clinical charts and radiographs.
Stratum	-
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis.

Inclusion criteria	Open femoral shaft fractures treated with locked IMN
Exclusion criteria	None described.
Recruitment/selection of patients	Patients were treated at the Department of Orthopedic Surgery and Trauma Centre between 1988 and 2001.
Age, gender and ethnicity	Not reported by debridement time, but age and gender were controlled for in the MVA. Mean age – 24.8 years (range 15-62). Gender (M: F) 72:16.Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	No protocol was used for the type of fixation used; they were based on decisions by the orthopaedic staff, interval since injury, degree of contamination, extent of injury to the soft tissue and degree of associated vital organ injuries. The patients received one of three different treatments; immediate IMN at the time of initial debridement (n=36), delayed IMN following non-operative treatment such as skeletal traction or splint (n=44) or delayed IMN following external fixation (n=9). Patients were also divided into reamed (n=67) and unreamed (n=22) IMN. Kitasat cylinder nails (reamed IMN) and AO/ASIF unreamed Femoral Nails were used. Antibiotics: IV cephalosporin (sometimes combined with an aminoglycoside for type 3 fractures) started in emergency room and continued for 72 hours. Post resuscitation, and required emergency surgical procedures completed, irrigation and debridement of the open wound was carried out. Debridement repetition at 48 hour intervals until the wound was clean and devitalized tissue resected. Timing of debridement definition: Not described. Intervention 1 (n=76): ≤6hours to debridement Intervention 2 (n=13): >6 hours to debridement
Funding	None described

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Early versus delayed debridement (Group 1 ≤6 hours to debridement, Group 2 >6 hours to debridement)

Deep infection definition used: Infection involving tissue below the muscular fascia (according to Delinger1988[12]).

Covariates in the MVA- age (numerical data), sex (male or female), Gustilo type (I+II or III), fracture grade by AO type (A or B+C), fracture site (proximal site + distal site or middle site), reamed versus unreamed nailing, debridement time (≤6 hours or >6 hours), existence of multiple trauma (ISS<18 or ISS≥18), and existence of floating knee injury (+ or -). Note: although the authors felt that skin closure (immediate versus delayed) was important for deep infection rates, they thought it was concomitant with Gustilo type or debridement time so not included. Protocol outcome 1: Deep surgical site infection. (n=89) - Actual outcome: Number of patients with a deep infection; Group 1: n=4/76 Group 2: 1/13. Regression coefficient -0.563, OR 0.569, probability 0.789; Risk of bias: High; Indirectness of outcome: No indirectness. Deep infection organisms: 2 staphylococcus aureus and MRSA, 2 MRSA alone and 1 staphylococcus aureus alone. They occurred in one Gustilo grade 2 (1/43) and four in grade 3 (4/24). Predictive logistic regression equation for deep infection: log (1-p)/p=0.101 x age – 11.253 x sex – 4.402 x Gustilo type+2.146 x fracture grade by AO type +0.128 x fractures site – 1.330 x treatment type 1+ 0.901 x R versus UR -0.563 x debridement time – 0.426 x existence of multiple trauma + 1.725 x existence of floating knee injury – 5.070 (p<0.05)	
Protocol outcomes not reported by the study	Mortality up to 12 months, Health related quality of life, Return to normal activities, Re-operation (unplanned), Amputation, Functional outcomes and length of stay.

Narrative text/additional information

Mechanism of injury was primarily due to motor vehicle accidents (n=81), of which 59 were motorcycle, 16 passengers or drivers in cars and 6 were pedestrians stuck by the vehicles. Seven patients fell from a height. The grade of fractures were grade 1 (n=22), grade 2 (n=43), grade 3a (n=12), grade 3b (n=7) and grade 3c (n=5). The fractures were located in the proximal third for 15 fractures, middle third for 60 fractures and distal third for 14.

Table 35: Hull 2014[29]

Study	**Hull 2014[29]**
Study type	Retrospective Cohort
Number of studies (number of participants)	1 (n=364 patients with 459 open fractures)
Countries and setting	Conducted in Canada
Line of therapy	First-line

Duration of study	Followed up up to one year after the original injury, or uncomplicated healing.
Method of assessment of guideline condition	Observation of injury
Stratum	-
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis.
Inclusion criteria	Open fractures.
Exclusion criteria	Hand injuries
Recruitment/selection of patients	Consecutive patients presenting with an open fracture between 2003 and 2007.
Age, gender and ethnicity	Age range 16-85. Mean age similar between those with non-infected and infected fractures (40.1 vs 39.7); 70% male in non-infected and 84.7% male in infected; ethnicity not reported.
Indirectness of population	No indirectness
Interventions	Intravenous antibiotics administered on presentation and continued until the wound is covered definitively, or for at least 24 hours post-operatively in patients with a Gustillo-Anderson G1 fracture. Patients not allergic to penicillin received cefuroxime, and patients with a higher grade fracture received gentamycin and metronidazole/penicillin. Patients allergic to penicillin were given clindamycin or vancomycin rather than cefuroxime. Debridement was undertaken urgently based on the availability of an operating theater. Delays of > 6 hours were often encountered due to the lack of availability and/or the physiological instability of the patient. The timing of wound closure and the method of fixation were left to the discretion of the surgeon.
Funding	Internal academic funding; no commercial funding

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

Protocol outcome 1: Deep surgical site infection
- Actual outcome: Time to debridement: OR 1.033 (95% CI: 1.01-1.057) per increased hour of time to surgery after adjustment for gross contamination, existence of tibial fracture and grade of fracture (low versus high). Age, gender, mechanism of penetration, ASA class, ISS score and time of antibiotic administration were not included in the final model as they had a non-significant association with the outcome.; Risk of bias: Very high; Indirectness of outcome: No indirectness.

When the analysis was stratified by the grade/contamination status of tibial fractures, the effect of delay on deep infection increased with the grade and contamination.

Protocol outcomes not reported by the study	Mortality up to 12 months, Health related quality of life, Return to normal activities, Re-operation (unplanned), Amputation, Functional outcomes and length of stay.

Table 36: Weber 2014[67]

Study	Weber 2014[67]
Study type	Prospective Cohort
Number of studies (number of participants)	1 (n=686 patients with 737 fractures)
Countries and setting	Conducted in Canada
Line of therapy	First-line
Duration of study	Followed up >90 days after the original injury.
Method of assessment of guideline condition	Observation of injury
Stratum	-
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis.
Inclusion criteria	Skeletal maturity, long bone open fractures, requiring initial surgical debridement.
Exclusion criteria	Pathologic fractures, penetrating injury, unsalvageable limb injuries, other medical conditions precluding surgical management.
Recruitment/selection of patients	Patients at 3 level 1 trauma centres in Canada
Age, gender and ethnicity	Median (IQR) age: 39.6 (26.5-52.8); 72% male; Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	Established principles of open fracture management used, including initial surgical debridement and fracture fixation with copious irrigation (3 L or more) and debridement of soft tissues and contaminated bone. Surgical fixation was at the surgeon's discretion. This was repeated at intervals of 48 hours until tissues were clean, all non-viable tissue had been removed, and delayed wound closure could occur. Timing of debridement or timing of prophylactic antibiotics was at the discretion of the surgeon, and the effects of each of these primary factors was evaluated using a multivariable regression adjusting for each other, transfusion, fracture location, and Gustillo grade. Age and gender were not included in the model.
Funding	None described
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Protocol outcome 1: Deep surgical site infection. (n=89) - Actual outcome: Time to surgery: OR 0.97 (95% CI: 0.9-1.06) per increased hour of time to surgery after adjustment for time to antibiotics, transfusion, fracture location,	

and Gustillo grade; Risk of bias: High; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Mortality up to 12 months, Health related quality of life, Return to normal activities, Re-operation (unplanned), Amputation, Functional outcomes and length of stay.

Table 37: Lack 2015[38]

Study	**Lack 2015[38]**
Study type	Retrospective Cohort
Number of studies (number of participants)	1 (n=137 patients)
Countries and setting	Conducted in USA
Line of therapy	First-line
Duration of study	Followed up up to 90 days after the original injury.
Method of assessment of guideline condition	Observation of injury
Stratum	-
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis.
Inclusion criteria	Open fractures with Gustillo Anderson Grade III.
Exclusion criteria	Missing data; non-reconstructible limbs
Recruitment/selection of patients	Consecutive patients presenting with an open fracture in 2013.
Age, gender and ethnicity	Mean age similar between those with non-infected and infected fractures (40 vs 40.5); gender and ethnicity not reported.
Indirectness of population	No indirectness
Interventions	Definitive fracture fixation and wound management followed basic standard principles. Diaphyseal fractures were treated with intramedullary fixation. Those with intra-articular extension or at the very distal or proximal metaphysis were usually treated with plate and screw fixation. Those with intra-articular extension or at the very distal or proximal metaphysis were usually treated with plate and screw fixation. The standard regimen for antibiotic prophylaxis was Cefazolin (128/137). Other antibiotics used were clindamycin or vancomycin. Temporizing external fixation was used when necessary and definitive fixation was performed as soon as the patient and wound were amenable. Wounds were closed when possible and those not able to be closed were treated with negative pressure dressings pending definitive

	wound coverage.
Funding	Internal academic funding; no commercial funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Protocol outcome 1: Deep surgical site infection - Actual outcome: Time of debridement: A non-significant effect of debridement time was found after adjustment for confounders. Adjustment was made for for age, Gustillo-Anderson classification, smoking, presence of diabetes, time to antibiotics and time to cover Risk of bias: Very high; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Mortality up to 12 months, Health related quality of life, Return to normal activities, Re-operation (unplanned), Amputation, Functional outcomes and length of stay.

G.1.6 Fixation

RCT

Table 38: Benson 1983

Study	**Benson 1983[2]**
Study type	RCT (Patient randomised; random selection of numbers, double blind)
Number of studies (number of participants)	(n=78 patients with n=82 open fractures)
Countries and setting	Conducted in America; Setting: University of California, Davis Medical Center
Line of therapy	First-line
Duration of study	Followed until the wound and fracture was healed. No time given.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults 18 years or over
Inclusion criteria	None described

Exclusion criteria	Wounds which were open for (>24 hours), wounds contaminated by river or lake water, lawnmower injuries, high velocity gunshot wounds (previous study showed these wounds to have high infection rate when closed primarily), if closure of the wound was deemed physically impossible
Recruitment/selection of patients	Patients had to be able to supply written consent prior to involvement.
Age, gender and ethnicity	Age – mean 30.4±14.7 years. Gender (M: F) 69:9 .Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	Four groups of patients. Two received IV 5 day course of cefazolin, the other two groups received clindamycin. One of each group was left open for a delayed primary closure and the other was closed immediately. Cefazolin or clindamycin dose was diluted in 100ml of sterile saline and infused every 6 hours over a 10-16 minute period. Protocol: 1-5g traumatized tissue excided, put in sterile tube which is loosely capped, then put into a miniature anaerobic jar (kept at room temp). They were processed within 24 hours. Once debridement started antimicrobics were commenced. Degree of contamination assessed by orthoplastic surgeon or senior orthoplastic resident at debridement. Irrigation with normal saline. Multiple extremity wounds were treated in the same way. Open wounds returned to theatre in 4-6 days for wound evaluation, further debridement and delayed primary closure. Fractures of extremity wounds were treated as per principles of the University of California, Davis, Department of Orthopaedic Surgery.
Funding	Cefazolin provided by Smith Kline and French Laboratories, Clindamycin by Upjohn Company. Grants from all three companies
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Primary versus delayed closure (Group 1 Cefazolin primary closure, Group 2 Cefazolin delayed closure, Group 3 Clindamycin primary closure, Group 4 Clindamycin delayed closure) Note: time from injury to debridement was: 5.38±3.50 hours for the primary closures, 5.53±3.1 hours for the delayed closures. Delayed primaries from injury to closure were 5.9±4.6 days. 2 patients were excluded as they only took oral cephalexin postoperatively. Protocol outcome 1: Deep surgical site infection (infection involving the bone) (n=76) - Actual outcome for Adults 18 years or over: Number of patients with a deep infection; Group 1: n=0/22 Group 2: 1/20 Group 3: 0/18, Group 4: 1/16; Risk of bias: Very high; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Mortality at 1,12 months, health-related quality of life, amputation, flap failure, length of hospital stay, further

	unplanned surgery and return to normal activities

Cohort studies

Table 39: Liu 2012[39]

Study	**Liu 2012[39]**
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=103 patients with open limb fractures, n=105 free-flap constructions of which 42 had exposed metalware)
Countries and setting	Conducted in Australia; Setting: Plastics and Reconstructive Surgery Unit (PRSU) at the Royal Melbourne Hospital
Line of therapy	First-line
Duration of study	One year follow-up
Method of assessment of guideline condition	Clinical information from patient records cross-referenced with the RMH Trauma Registry and the Victorian Orthopaedic Trauma Outcomes Registry.
Stratum	Duration of exposed metalware prior to free-flap coverage (Group 1: within 1 day, Group 2: 2-7 days and Group 3: >7 days)
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis
Inclusion criteria	Consecutive patients who underwent free-flap construction between June 2002 and July 2009 for open lower limb trauma. They were identified from the PRSU free-flap database.
Exclusion criteria	None stated
Recruitment/selection of patients	Consecutive, June 2002- July 2009 on the PRSU free flap database
Age, gender and ethnicity	Age -Mean (SD): Group 1; 37.7 (2.9) years, Group 2; 41.2 (2.4) years, Group 3: 45.7 (2.5) years. Gender (M:F): Group 1 20:4, Group 2: 33:6, Group 3: 38:4 . Ethnicity: Not described.
Interventions	(n=14) Intervention 1: ≤1 day of exposed metalware to free-flap reconstruction. (n=14) Intervention 2: 2-7 days of exposed metalware to free-flap reconstruction. (n=14) Intervention 3: >7 days of exposed metalware to free-flap reconstruction. Process: Resuscitation, debridement and fracture stabilisation in theatre, NPWT (vacuum assisted closure) or moist

	gauze dressing applied to open fractures. Serial debridement in theatre until wound vitality was adequate, then free-flap transfer. Use of NPWT, timing and method of skeletal fixation and soft tissue reconstruction was at the discretion of the surgeon. IV antibiotics given from presentation to at least 72 hours post wound closure. The exposed metalware group consisted of patients who had undergo staged fixation (external then internal fixation, n=15) and internal fixation (n=27). The other patients had either external fixation alone or no fixation.
Funding	None described
Definitions: Soft tissue and deep metal infection: presence of clinical signs of infection (increasing erythema and/or suppurative discharge from the wound as assessed by a PRSU surgeon, orthopaedic surgeon or infectious diseases physician, with positive cultures from soft tissues and fixation hardware. Osteomyelitis was identified acutely by clinical evidence with positive cultures from bone and chronically by x-ray MRI or CT imaging. Partial flap loss: debridement occurred for partial flap necrosis. Total flap loss: required complete removal of the free-flap. Covariates in the MVA: age, gender, smoking, ISS (injury severity score), GA (Gustilo and Anderson score) and ASA (American Society of Anaesthesiology) scores, injury location, flap type, method of fracture fixation and use of NPWT. RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ≤1 days versus 2-7 days versus >7 days of exposed metalware to free flap reconstruction Protocol outcome 1: Flap failure (total or partial) - Actual outcome: Flap failure (total or partial); Group 1: 0/ 14, Group 2: 5/14, Group 3; 7/14. MVA: Delay of >7 days (compared with ≤ 1 day) independently predicted higher flap take-backs and flap failure OR 10.8 (95%CI 1.69-68.94).Risk of bias: Very high; Indirectness of outcome: Serious indirectness The following were not MVA adjusted: Deep surgical site infection (infection involving the bone) - Actual outcome: Osteomyelitis; Group 1: 1/ 14, Group 2: 2/14, Group 3; 9/14 Length of hospital stay - Actual outcome: Length of stay, days (SEM); Group 1: 26.6 (2.8), Group 2: 30.0 (4.8), Group 3; 49.0 (5.4). Further unplanned surgery - Actual outcome: Post flap operations, mean (SEM); Group 1: 0.9 (0.4), Group 2: 1.4 (0.7), Group 3; 2.5 (0.5)	
Protocol outcomes not reported by the study	Mortality at 1,12 months, health-related quality of life, amputation and return to normal activities

Narrative text/ additional information:

Overall, injury mechanisms included RTAs (64.3%, 57.1% and 64.3% for groups 1, 2 and 3, respectively), work accidents (21.4%, 14.3% and 14.3%), recreational accidents (14.3%, 14.3% and 14.3%), and other (0%, 14.3% and 7.1%). All of the injuries were Gustilo and Anderson grade III (a, b and c). Injuries were in the proximal 1/3, middle 1/3 and distal 1/3 of the tibia/fibular or the foot.

Grade: Operative reports for the patients were independently reviewed by two PRU surgeons who were blinded to the timing of the free-flap reconstruction.

Table 40: Schemitsch 2012[57]

Study	**Schemitsch 2012[57]**
Study type	Retrospective cohort study based on data from a prospective RCT
Number of studies (number of participants)	1 (n=1226 patients with tibial shaft fractures, n=392 open fractures)
Countries and setting	Data from the SPRINT trial which involved 29 clinical centres in Canada, United States and the Netherlands.
Line of therapy	1st line
Duration of study	One year follow-up post injury
Method of assessment of guideline condition	Clinical assessment
Stratum	Primary closure, delayed closure (staged)
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis
Inclusion criteria	Skeletal maturity, an open or closed tibial shaft fracture (Tscherne Type 0 to 3, Gustilo-Anderson Type I to IIIB), amenability of the fracture to surgical repair with an intramedullary nail, and informed consent.
Exclusion criteria	Tibial shaft fractures not amenable to reamed or undreamed nailing, pathologic fractures, patients likely to be lost before completing adequate follow-up, patients who were not skeletally mature, and patients who had not provided consent.
Recruitment/selection of patients	Sprint RCT trial recruitment: Randomization by a 24 hour toll free telephone system. Randomization was stratified by the center and the severity of soft-tissue injury (open, closed, or both open and closed) in randomly permuted blocks of 2 and 4. Double blinded. Patients with a bilateral fracture were assigned the same treatment for both fractures. Patients were randomised to reamed or unreamed IMN. All patients had the same postoperative care protocol.
Age, gender and ethnicity	Only given overall, not by closure group. Age -Mean (SD): 39.5 (16.0) years, Gender (M:F): 904:322 Ethnicity: White

	n=986, Black n=109, Hispanic n=46, Asian n=33, Native n=23, Other n=29.
Interventions	(n=239) Intervention 1: Primary closure: Performed at the time of the intramedullary nailing (n=100) Intervention 2: Delayed closure: Open wound with repeat irrigation and debridement and no other documented wound procedures, although they may have had negative pressure wound therapy (NPWT). There was also a third group, additional soft-tissue reconstruction (n=61); they had documentation of a delayed wound closure procedure, including split thickness skin grafts, fasciocutaneous flaps, rotational muscle flaps or free flaps. Note: It is unclear the time from injury to primary and delayed closure, as this was not reported in the paper. Process: Patients were randomized to receive a reamed intramedullary nail or an undreamed intramedullary nail. Two investigators independently identified a number of variables from the SPRINT trial data. Factors included in the model needed to have at least 30 occurrences to be included. There were 219 events in the trial, so the MVA was adapted using the most highly ranked variables of importance, to ensure a stable model (at least 10 events per variable). See below for MVA variables that were included. A second model was also performed which only included the open fractures to enable the wound closure variable to be investigated (thought to confound with open/ closed fractures). Antibiotic protocol: Pre-op IV cephalosporin and an aminoglycoside (continued 72 hours post op). Surgeon decided on any specific antibiotics. Recommended antibiotics were: Gustilo grade I and II: IV cephalosporin, Grade III (as per Grade I and II) plus aminoglycoside (gentamicin). Badly contaminated wounds would have the addition of penicillin to a cephalosporin and aminoglycoside. Irrigation and debridement repeated as necessary. Delayed wound closure, split-thickness skin-grafting, or reconstruction with muscle flaps (for Type-IIIB injuries only) was performed by seven days following the initial surgery.
Funding	Research grants from: Canadian Institutes of Health Research, National Institutes of Health, Orthopaedic Research and Education Foundation of the American Academy of Orthopaedic Surgeons, Orthopaedic Trauma Association, Hamilton Health Sciences Research Grant, Zimmer, and in part by a Canada Research Chair in Musculoskeletal Trauma at McMaster University. The funding sources had no role in influencing the trail or the manuscript.
The mechanism of injury which were of a high energy were; motor vehicle accidents (n=256), pedestrian/motor vehicle accidents (n=248), motorcycle accident (n=143), direct blunt trauma (n=84), crush injury (n=64) and snowmobile accident (n=1). The low energy injuries were primarily due to falls (n=355). There were 22 bilateral fractures (1.8%). The AO/OTA fracture classification of the fractures were grade A (n=687), grade B (n=362), and grade C (n=177). There were 206 of the open fractures that were treated with reamed nailing, and 194 unreamed. The time from injury to surgery was <6 hours for 207 patients, 6-24 hours for 606 and >24 hours for 405 patients (there was some missing data for this variable). Composite primary outcome (further unplanned surgery: Bone-grafting, implant exchange or removal, debridement of bone and soft tissue because of deep infection, fracture dynamisation (due to locking screw removal), removal of locking screws because of screw breakage or loosening, autodynamisation (breaking of a locking screw	

that resulted in the fracture collapsing), fasciotomy, failure of the construct (broken nail), and hematoma drainage. Covariates in the MVA: smoking status, open fracture, fracture gap, mechanism of injury, reamed intramedullary nailing, age, location of fracture, isolated fracture, type of wound coverage, NSAID use, AO/OTA fracture classification, number of locking screws, postoperative weight bearing status, time from injury to surgery and nail material. Total 15 covariates. RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Primary closure versus delayed closure Protocol outcome 1: Further unplanned surgery - Actual outcome: Composite measure (see definition above); adjusted OR 0.62 (95% CI 0.23-1.70) See below for calculation. Risk of bias: High; Indirectness of outcome: None Note: the adjusted OR for primary versus delayed primary coverage has been calculated indirectly from the following comparisons reported in the paper: Primary versus additional soft tissue reconstruction adjusted OR 0.18 (95%CI 0.09-0.35), p<0.001 Delayed primary versus additional soft tissue reconstruction adjusted OR 0.29 (95% CI 0.14-0.62), p=0.001 Calculation of the Primary versus delayed value by indirect treatment comparisons method: Converting the above results to natural logs: Primary versus additional soft tissue reconstruction adjusted ln OR (SE): -1.7148 (0.3537) Delayed primary versus additional soft tissue reconstruction adjusted ln OR (SE): -1.2379 (0.3716) Primary versus delayed ln OR = -1.7148 minus -1.2379 = -0.4769 Therefore Primary versus delayed OR = exp -0.4769 = 0.6207 The variance of the ln OR primary versus delayed would be the sum of the variances of the two constituent comparisons As variance = SE squared, then Variance ln OR primary versus delayed = 0.3537 squared + 0.3716 squared = 0.26318 Therefore SE of ln OR primary versus delayed = SQRT 0.26318 = 0.513017 The values for ln OR (SE) primary versus delayed are therefore -0.4769 (0.513017), which were input into RevMan using the Generic inverse Variance method.	
Protocol outcomes not reported by the study	Mortality at 1,12 months, health-related quality of life, deep surgical site infection (infection involving the bone) amputation, flap failure (total or partial), length of hospital stay and return to normal activities

Table 41: Jenkinson 2014[31]

Study	**Jenkinson 2014[31]**

Study type	Retrospective cohort study using propensity matching
Number of studies (number of participants)	1 (n=146 patients with open fractures, n=66 tibial fractures)
Countries and setting	Canada
Line of therapy	First-line
Duration of study	One year follow-up post injury
Method of assessment of guideline condition	Clinical assessment
Stratum	Primary closure, delayed closure (staged)
Subgroup analysis within study	Not applicable.
Inclusion criteria	Open extremity fracture
Exclusion criteria	Hand and pelvic fractures; grade IIIb and IIIc fractures
Recruitment/selection of patients	Consecutive patients treated for an open extremity fracture from 2003-2007 at a level I trauma centre in Canada.
Age, gender and ethnicity	Only given overall, not by closure group. Age: Mean 40.7 years, Gender: 68.8% male
Interventions	(n=73) Intervention 1: Primary closure. Second look debridement done on discretion of surgeon based on impression of adequacy of the debridement (n=73) Intervention 2: Delayed closure. Second look debridement after 48 hours was performed routinely Both groups had IV antibiotics on arrival until at least 24 hours post closure. Sefazolin was used, or clindamycin if necessary. Gentamicin was added if it was a Grade III open fracture. Debridements were done urgently. Fixation method and time of closure were at the discretion of the treating physicians. To adjust for confounding by indication a propensity score matched cohort study was developed from the original dataset of 262 with primary closure and 87 with delayed closure. Injury characteristics were used in a logistic regression to predict the likelihood of the need for treatment with delayed wound closure. Factors included in the propensity scoring were: age, sex, debridement delay, grade of fracture, contamination, site of fracture and ASA class.
Funding	None
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Primary closure versus delayed closure	

Protocol outcome 1: Deep infection Primary closure 3/73, delayed closure 13/73	
Protocol outcomes not reported by the study	Mortality at 1,12 months, health-related quality of life, further unplanned surgery, amputation, flap failure (total or partial), length of hospital stay and return to normal activities

Table 42: Gopal 2004[20]

Study	**Gopal 2004[20]**
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=33 patients with open tibial fractures 29 adults and 4 children)
Countries and setting	UK
Line of therapy	First-line
Duration of study	Mean: 46 months
Method of assessment of guideline condition	Clinical assessment
Stratum	Primary closure, delayed closure (staged)
Subgroup analysis within study	Not applicable.
Inclusion criteria	Severe open tibial fractures of grade IIIb or IIIc
Exclusion criteria	Severe head injuries
Recruitment/selection of patients	Consecutive patients undergoing a fix and flap protocol between 1996 and 2000.
Age, gender and ethnicity	Age: adults – 48 years, children – 13 years; Gender: 25 men/4 women and 2 boys and 2 girls
Interventions	ADULTS (n=29, 30 fractures): (n=12 fractures) Intervention 1: Primary closure in a single fix and flap procedure, comprising radical debridement, skeletal stabilisation (normally internal) with a muscle flap.

	(n=18 fractures) Intervention 2: Immediate debridement and internal fixation with soft tissue cover between 48-72 hours. For 8 subjects cover was only attempted at 72 hours+ because of severe head injury No multivariable analysis but both groups were adequately similar for age and grade of fracture. The high head injury prevalence in the delayed group could be a serious confounder. CHILDREN: Unclear
Funding	None
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Primary closure versus delayed closure Only adult results given as results for children by group were not reported Protocol outcome 1: deep infection Primary closure 0/12, delayed closure 2/18 Functional results were reported but the immediate group was changed to include people having cover up to 72 hours, so these results have not been reported.	
Protocol outcomes not reported by the study	Mortality at 1,12 months, hospital stay, further unplanned surgery, amputation, flap failure (total or partial), and return to normal activities

Table 43: Hertel 1999[26]

Study	**Hertel 1999[26]**
Study type	Prospective cohort study
Number of studies (number of participants)	1 (n=29 patients with open lower leg fractures)
Countries and setting	Switzerland
Line of therapy	First-line
Duration of study	Mean: 47 months
Method of assessment of guideline condition	Clinical assessment
Stratum	Primary closure, delayed closure (staged)
Subgroup analysis within study	Not applicable.

Inclusion criteria	Open lower leg fractures of grade IIIb or IIIc
Exclusion criteria	Not reported
Recruitment/selection of patients	Consecutive patients between 1988 and 1995.
Age, gender and ethnicity	Age: 28/27; male79%/80%
Interventions	(n=14) Intervention 1: Immediate reconstruction - adequate debridement, definitive skeletal stabilisation in 11 and preliminary external stabilisation in 3. Immediate soft tissue coverage was done with a local muscle flap in 8 and a free muscle flap in 7. In 5 a primary cancellous bone graft was added. (n=15) Intervention 2: Delayed reconstruction – primary debridement, mostly preliminary stabilisation with an external fixator and soft tissue reconstruction between days 1 and 9 after injury. Soft tissue coverage was achieved with a local muscle flap in 7 and a free muscle flap in 8. Definitive skeletal stabilisation was obtained immediately in 3, at the time of cover in 1 and at a 3rd intervention in 12 patients. No cancellous bone graft was used. No multivariable analysis but both groups were adequately similar for age and grade of fracture. They were also similar for sex, type of trauma, associated general injuries, type of fracture, arterial lesions, tendon ruptures and soft tissue reconstruction. CHILDREN: Unclear
Funding	None

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Primary closure versus delayed closure
Only adult results given as results for children by group were not reported

Deep infection
Primary closure 0/14, delayed closure 4/15
Return to weight bearing (mean (range)
Primary closure 5(3-8 months), delayed closure 3.9(2-7) months
Number of operations (mean (range)
Primary closure 1.6(1-3), delayed closure 3.9(2-7)

Flap failure
Primary closure 0/14, delayed closure 0/15

Amputation Primary closure 0/14, delayed closure 0/15	
Protocol outcomes not reported by the study	Mortality at 1,12 months, hospital stay, further unplanned surgery, amputation, flap failure (total or partial), and return to normal activities

Table 44: Wei 2014[68]

Study	**Wei 2014[68]**
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=80 patients with open tibial fractures)
Countries and setting	China
Line of therapy	First-line
Duration of study	Mean: 33-38 months
Method of assessment of guideline condition	Clinical assessment
Stratum	Primary closure, delayed closure (staged)
Subgroup analysis within study	Not applicable.
Inclusion criteria	Open tibial fractures of grade IIIa or IIIb; age >18; soft tissue wounds treated with VAC; fractures treated with IF and EF methods
Exclusion criteria	Immediate amputation; PVD, diabetes, immune dysfunction.
Recruitment/selection of patients	Consecutive patients between 2005 and 2011.
Age, gender and ethnicity	Age: 36/43; male67%/73%
Interventions	(n=27) Intervention 1: Primary wound closure – One stage debridement, internal fixation and cover, using NPT. (n=22) Intervention 2: Delayed wound closure – primary debridement at same time as internal fixation, with direct cover of wound with non-adherent sponge and intermittent suction via a vacuum assisted colure. Final wound coverage

	about 7 days later depending on soft tissue status. No multivariable analysis but both groups were adequately similar for age and grade of fracture. They were also similar for sex, type of trauma, time to debridement and fixation methods. CHILDREN: Unclear
Funding	None
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Primary closure versus delayed closure Only adult results given as results for children by group were not reported Deep infection Primary closure 5/27, delayed closure 6/22 Amputation Primary closure 1/27, delayed closure 3/22 Osteomyelitis Primary closure 3/27, delayed closure 4/22	
Protocol outcomes not reported by the study	Mortality at 1,12 months, hospital stay, further unplanned surgery, flap failure (total or partial), and return to normal activities

G.1.7 Cover

RCT

Table 45: Benson 1983

Study	**Benson 1983[2]**
Study type	RCT (Patient randomised; random selection of numbers, double blind)
Number of studies (number of participants)	(n=78 patients with n=82 open fractures)

Countries and setting	Conducted in America; Setting: University of California, Davis Medical Center
Line of therapy	First-line
Duration of study	Followed until the wound and fracture was healed. No time given.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults 18 years or over
Inclusion criteria	None described
Exclusion criteria	Wounds which were open for (>24 hours), wounds contaminated by river or lake water, lawnmower injuries, high velocity gunshot wounds (previous study showed these wounds to have high infection rate when closed primarily), if closure of the wound was deemed physically impossible
Recruitment/selection of patients	Patients had to be able to supply written consent prior to involvement.
Age, gender and ethnicity	Age – mean 30.4 +/-14.7 years. Gender (M: F) 69:9 .Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	Four groups of patients. Two received IV 5 day course of cefazolin, the other two groups received clindamycin. One of each group was left open for a delayed primary closure and the other was closed immediately. Cefazolin or clindamycin dose was diluted in 100ml of sterile saline and infused every 6 hours over a 10-16 minute period. Protocol: 1-5g traumatized tissue excided, put in sterile tube which is loosely capped, then put into a miniature anaerobic jar (kept at room temp). They were processed within 24 hours. Once debridement started antimicrobics were commenced. Degree of contamination assessed by orthopaedic surgeon or senior orthopaedic resident at debridement. Irrigation with normal saline. Multiple extremity wounds were treated in the same way. Open wounds returned to theatre in 4-6 days for wound evaluation, further debridement and delayed primary closure. Fractures of extremity wounds were treated as per principles of the University of California, Davis, Department of Orthopaedic Surgery.
Funding	Cefazolin provided by Smith Kline and French Laboratories, Clindamycin by Upjohn Company. Grants from all three companies

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Primary versus delayed closure (Group 1 Cefazolin primary closure, Group 2 Cefazolin delayed closure, Group 3 Clindamycin primary closure, Group 4 Clindamycin delayed closure)

Note: time from injury to debridement was: 5.38 +/-3.50 hours for the primary closures, 5.53 +/-3.1 hours for the delayed closures. Delayed primaries from injury to

closure was 5.9 +/-4.6 days. 2 patients were excluded as they only took oral cephalexin postoperatively. Protocol outcome 1: Deep surgical site infection (infection involving the bone) (n=76) - Actual outcome for Adults 18 years or over: Number of patients with a deep infection; Group 1: n=0/22 Group 2: 1/20 Group 3: 0/18, Group 4: 1/16; Risk of bias: Very high; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Mortality at 1,12 months, health-related quality of life, amputation, flap failure, length of hospital stay, further unplanned surgery and return to normal activities

Cohort studies

Table 46: Hohmann 2007

Study	**Hohmann 2007[27]**
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=95 patients with open tibial fractures)
Countries and setting	South Africa
Line of therapy	First-line
Duration of study	One year follow-up post injury
Method of assessment of guideline condition	Clinical assessment
Stratum	Primary closure, delayed closure (staged)
Subgroup analysis within study	Not applicable.
Inclusion criteria	Isolated open tibial fractures (Grade 1,2 and 3A) treated at two different hospitals
Exclusion criteria	Grade IIIb and IIIc fractures, polytrauma and associated injuries, significant unrelated co-morbid conditions, history of surgery in past 6 months, delayed presentation > 24 hours, admission to ICU.

Recruitment/selection of patients	Consecutive patients fulfilling inclusion at two major trauma referral centres in Greater Johannesburg area.
Age, gender and ethnicity	Age: 33.4/30.2; Gender: 72%/83% male
Interventions	(n=46) Intervention 1: Primary closure (mean 7.2 hours), done at Helen Josef Hospital by a single surgeon. Fracture stabilised with unreamed AO nail after early initial debridement and primary wound closure. IV antibiotics on arrival until 72 hours post-surgery (n=49) Intervention 2: Delayed closure, done at Johannesburg hospital by one surgeon. Early surgical debridement and stabilisation in a plaster splint. IV antibiotics (cefazolin 1 g three times a day). Repeat debridement at 48 hours with closure if possible (but mean closure was at 9.3 days) and unreamed AO nail inserted for fracture stabilisation. No multivariable analysis, but both groups were adequately similar for age and grade of fracture.
Funding	None
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Primary closure versus delayed closure Protocol outcome 1: Hospital stay Primary closure mean(range): 8.6 (3-20) days, delayed closure 15.4 (4-52) days Infection : immediate 2/46 and delayed 1/49	
Protocol outcomes not reported by the study	Mortality at 1,12 months, deep infection health-related quality of life, further unplanned surgery, amputation, flap failure (total or partial), and return to normal activities

Table 47: Gopal 2004

Study	**Gopal 2004[20]**
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=33 patients with open tibial fractures 29 adults and 4 children)
Countries and setting	UK
Line of therapy	First-line
Duration of study	Mean: 46 months

Method of assessment of guideline condition	Clinical assessment
Stratum	Primary closure, delayed closure (staged)
Subgroup analysis within study	Not applicable.
Inclusion criteria	Severe open tibial fractures of grade IIIb or IIIc
Exclusion criteria	Severe head injuries
Recruitment/selection of patients	Consecutive patients undergoing a fix and flap protocol between 1996 and 2000.
Age, gender and ethnicity	Age: adults – 48 years, children – 13 years; Gender: 25 men/4 women and 2 boys and 2 girls
Interventions	ADULTS (n=29, 30 fractures): (n=12 fractures) Intervention 1: Primary closure in a single fix and flap procedure, comprising radical debridement, skeletal stabilisation (normally internal) with a muscle flap. (n=18 fractures) Intervention 2: Immediate debridement and internal fixation with soft tissue cover between 48-72 hours. For 8 subjects cover was only attempted at 72 hours+ because of severe head injury No multivariable analysis, but both groups were adequately similar for age and grade of fracture. The high head injury prevalence in the delayed group could be a serious confounder. CHILDREN: Unclear
Funding	None
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Primary closure versus delayed closure Only adult results given as results for children by group were not reported Protocol outcome 1: deep infection Primary closure 0/12, delayed closure 2/18 Functional results were reported but the immediate group was changed to include people having cover up to 72 hours, so these results have not been reported.	
Protocol outcomes not reported by the study	Mortality at 1,12 months, hospital stay, further unplanned surgery, amputation, flap failure (total or partial), and return to normal activities

Table 48: Hertel 1999

Study	**Hertel 1999[26]**
Study type	Prospective cohort study
Number of studies (number of participants)	1 (n=29 patients with open lower leg fractures)
Countries and setting	Switzerland
Line of therapy	First-line
Duration of study	Mean: 47 months
Method of assessment of guideline condition	Clinical assessment
Stratum	Primary closure, delayed closure (staged)
Subgroup analysis within study	Not applicable.
Inclusion criteria	Open lower leg fractures of grade IIIb or IIIc
Exclusion criteria	Not reported
Recruitment/selection of patients	Consecutive patients between 1988 and 1995.
Age, gender and ethnicity	Age: 28/27; male79%/80%
Interventions	(n=14) Intervention 1: Immediate reconstruction - adequate debridement, definitive skeletal stabilisation in 11 and preliminary external stabilisation in 3. Immediate soft tissue coverage was done with a local muscle flap in 8 and a free muscle flap in 7. In 5 a primary cancellous bone graft was added. (n=15) Intervention 2: Delayed reconstruction – primary debridement, mostly preliminary stabilisation with an external fixator and soft tissue reconstruction between days 1 and 9 after injury. Soft tissue coverage was achieved with a local muscle flap in 7 and a free muscle flap in 8. Definitive skeletal stabilisation was obtained immediately in 3, at the time of cover in 1 and at a 3rd intervention in 12 patients. No cancellous bone graft was used. No multivariable analysis, but both groups were adequately similar for age and grade of fracture. They were also similar for sex, type of trauma, associated general injuries, type of fracture, arterial lesions, tendon ruptures and soft tissue reconstruction. CHILDREN: Unclear
Funding	None

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Primary closure versus delayed closure Only adult results given as results for children by group were not reported Deep infection Primary closure 0/14, delayed closure 4/15 Return to weight bearing (mean (range) Primary closure 5(3-8 months), delayed closure 3.9(2-7) months Number of operations (mean (range) Primary closure 1.6(1-3), delayed closure 3.9(2-7) Flap failure Primary closure 0/14, delayed closure 0/15 Amputation Primary closure 0/14, delayed closure 0/15	
Protocol outcomes not reported by the study	Mortality at 1,12 months, hospital stay, further unplanned surgery, amputation, flap failure (total or partial), and return to normal activities

Table 49: Liu 2012[39]

Study	**Liu 2012[39]**
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=103 patients with open limb fractures, n=105 free-flap constructions)
Countries and setting	Conducted in Australia; Setting: Plastics and Reconstructive Surgery Unit (PRSU) at the Royal Melbourne Hospital
Line of therapy	First-line
Duration of study	One year follow-up
Method of assessment of guideline condition	Clinical information from patient records cross-referenced with the RMH Trauma Registry and the Victorian Orthopaedic

	Trauma Outcomes Registry.
Stratum	Adults
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis
Inclusion criteria	Consecutive patients who underwent free-flap construction between June 2002 and July 2009 for open lower limb trauma. They were identified from the PRSU free-flap database.
Exclusion criteria	None stated
Recruitment/selection of patients	Consecutive, June 2002- July 2009 on the PRSU free flap database
Age, gender and ethnicity	Age -Mean (SD): Group 1(≤3days to cover); 37.7 (2.9) years, Group 2 (4-7 days to cover); 41.2 (2.4) years, Group 3 (>7 days to cover): 45.7 (2.5) years. Gender (M:F): Group 1 20:4, Group 2: 33:6, Group 3: 38:4 . Ethnicity: Not described.
Interventions	(n=24) Intervention 1: ≤3 days to free flap reconstruction cover. (n=39) Intervention 2: 4-7 days to free flap reconstruction cover.. (n=42) Intervention 3: >7 days to free flap reconstruction cover.. Process: Resuscitation, debridement and fracture stabilisation in theatre, NPWT (vacuum assisted closure) or moist gauze dressing applied to open fractures. Serial debridement in theatre until wound vitality was adequate, then free-flap transfer. Use of NPWT, timing and method of skeletal fixation and soft tissue reconstruction was at the discretion of the surgeon. IV antibiotics given from presentation to at least 72 hours post wound closure.
Funding	None described

Definitions:

Soft tissue and deep metal infection: presence of clinical signs of infection (increasing erythema and/or suppurative discharge from the wound as assessed by a PRSU surgeon, orthopaedic surgeon or infectious diseases physician, with positive cultures from soft tissues and fixation hardware. Osteomyelitis was identified acutely by clinical evidence with positive cultures from bone and chronically by x-ray MRI or CT imaging.

Partial flap loss: debridement occurred for partial flap necrosis.

Total flap loss: required complete removal of the free-flap.

Covariates in the MVA: age, gender, smoking, ISS (injury severity score), GA (Gustilo and Anderson score) and ASA (American Society of Anaesthesiology) scores, injury location, flap type, method of fracture fixation and use of NPWT.

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ≤3 days versus 4-7 days versus >7 days of exposed metalware to free flap reconstruction

MVA results (note the potential outcome reporting bias, where because the original grouping of >7 days did not show significant differences to <3 days, the researchers

opted to present the results of a >14 days compared with <3 days analysis. Flap failure (total or partial) - Actual outcome: Flap failure (total or partial); Group 1: 3/24, Group 2: 12/39, Group 3; 15/42. MVA: Delay of >14 days (compared with ≤ 1 day) independently predicted higher flap take-backs OR 7.41 (95%CI 1.56-35.18).Risk of bias: Very high; Indirectness of outcome: Serious indirectness Deep surgical site infection (infection involving the bone) - Actual outcome: deep infection Group 1: 1/24, Group 2: 6/39, Group 3; 12/42. MVA: Delay of >14 days (compared with ≤ 3 days) independently predicted higher rates of deep infection OR 10.53 (95%CI 1.11-99.83).Risk of bias: Very high; Indirectness of outcome: Serious indirectness Osteomyelitis Group 1: 1/24, Group 2: 3/39, Group 3; 9/42. MVA: Delay of >14 days (compared with ≤ 3 days) independently predicted higher rates of deep infection OR 11.50 (95%CI 1.19-111.51).Risk of bias: Very high; Indirectness of outcome: Serious indirectness **The following were not analysed with an MVA (or it was unclear) and these are not included in the review because of large differences in age at baseline (up to 8 years):** Mean (SEM) number of post-flap operations were Group 1: 0.5(0.2), Group 2: 1.1(0.3), Group 3; 1.6(0.3). Mean (SEM) length of stay (days) was Group 1: 20(1.6), Group 2: 24.8(1.6), Group 3; 36.2(3.0). Length of hospital stay - Actual outcome: Length of stay, days (SEM); Group 1: 26.6 (2.8), Group 2: 30.0 (4.8), Group 3; 49.0 (5.4). Further unplanned surgery - Actual outcome: Post flap operations, mean (SEM); Group 1: 0.9 (0.4), Group 2: 1.4 (0.7), Group 3; 2.5 (0.5)	
Protocol outcomes not reported by the study	Mortality at 1,12 months, health-related quality of life, amputation and return to normal activities

Table 50: Webb 2007[66]

Study	**Webb 2007[66]**
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=105 patients with Gustilo type-IIIA-C tibial open fractures, who underwent limb salvage). 85 Gustilo IIIB, 17 Gustilo IIIA and 4 Gustilo IIIC.
Countries and setting	Probably USA; setting unclear but patients were enrolled in the Lower extremity Assessment Project (LEAP).
Line of therapy	First-line
Duration of study	2-7 year follow-up

Method of assessment of guideline condition	Gustilo grading
Stratum	Adults
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis
Inclusion criteria	Gustilo type III A,B or C
Exclusion criteria	Co-existing limb-threatening foot, ankle, pilon or knee injuries; segmental fractures of proximal or distal tibia; <2 years of follow-up; delayed amputation
Recruitment/selection of patients	All eligible patients from the LEAP database
Age, gender and ethnicity	Not described; however an MVA was reported to have been carried out
Interventions	Intervention 1: ≤3 days to soft tissue cover. Intervention 2: >3 days to soft tissue cover. Most cover was performed with free or rotational muscle flaps; only 3 were performed with fasciocutaneous flap but group make-up unclear Process: No other details of care given in the paper
Funding	Academic funding but no commercial conflicts of interest
Covariates in the MVA: Not well reported but included time to debridement, sociodemographic variables, injury characteristics and severity (all available injury descriptors). Hence all likely confounders were almost certainly well-covered. However, the requirement of 10 events per variable in the MVA was clearly not met. No data were presented for relevant outcomes, but paper reported that: "timing of soft-tissue coverage (3 days or less after the injury as compared with more than three days after the injury had no apparent effect on clinical or functional outcome". Outcomes included days in hospital and total number of surgical procedures.	
Protocol outcomes not reported by the study	Mortality at 1,12 months, health-related quality of life, amputation and return to normal activities

Table 51: Dalleyrand2014 2007[8]

Study	**Dalleyrand, 2014[8]**
Study type	Retrospective cohort study

Number of studies (number of participants)	1 (n=69 patients with tibial (n=45), plateau (n=17) and pilon (n=12) open fractures
Countries and setting	Probably USA; academic trauma centre
Line of therapy	First-line
Duration of study	More than 3 months follow-up. Median 14 months (range 3-59 months).
Method of assessment of guideline condition	Clinical assessment
Stratum	Mixed ages (15-76 years)
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis
Inclusion criteria	Acute open tibial fracture (including shaft, plateau and pilon) requiring flap for initial soft-tissue coverage.
Exclusion criteria	Treatment for breakdown of previously closed wound; follow-up < 3 months.
Recruitment/selection of patients	All eligible patients from the medical records in a single trauma centre in a 4 year time span
Age, gender and ethnicity	No group data for the timing of coverage 'groups' but a propensity analysis performed covering all likely confounders. Overall age 36 (range 15-76); 53:21 gender ratio.
Interventions	Intervention 1: 1-7 days to soft tissue cover. Intervention 2: >7 days to soft tissue cover. Process: No other details of care given in the paper
Funding	Academic funding but no commercial conflicts of interest
Covariates in the MVA: propensity scores calculated for propensity to go into each of the two soft tissue cover groups. It included: gender, age, ISS, zone of injury, mechanism of injury, use of negative wound pressure therapy, use of antibiotic bead pouch and rotational nature of the flap. Further analysis using logistic regression included fracture classification. Infection: After MVA adjustment, the effect of **one day of flap delay** on the odds of infection[a] was not significant between 1 and 7 days: OR: 0.94(0.65-1.36)[p=0.73] but was significant after 7 days: OR: 1.155(1.03-1.29)[p=0.011].	
Protocol outcomes not reported by the study	Mortality at 1,12 months, health-related quality of life, amputation and return to normal activities

(a) Not specified if deep or superficial, so taken as superficial.

Table 52: Pollak2010[49]

Study	Pollak2010[49]
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=315 patients with high energy lower extremity injury and open fracture)
Countries and setting	Probably USA; setting unclear but patients were enrolled in the Lower extremity Assessment Project (LEAP).
Line of therapy	First-line
Duration of study	More than 3 months follow-up.
Method of assessment of guideline condition	Clinical assessment
Stratum	Mixed ages (16-69 years)
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis
Inclusion criteria	16-69 years; admitted to one of 8 participating level 1 trauma centres for the treatment of limb-threatening lower extremity trauma distal to the femur; Gustilo type IIIA-C open tibial, ankle, pilon and foot fractures.
Exclusion criteria	GCS<15 at 21 days after hospitalisation or discharge; spinal cord deficit; previous amputation; third degree burns; transferred to treatment centre . 24 hours post injury; No English/Spanish; psychiatric disorder; active military duty..
Recruitment/selection of patients	A sub-set of the LEAP database.
Age, gender and ethnicity	No group or overall age/gender or ethnicity data for the timing of coverage 'groups' but a multivariable analysis performed covering all likely confounders.
Interventions	The time to soft tissue cover was one of the covariates in the MVA. All patients were managed by a protocol that included aggressive fracture debridement, antibiotic coverage, fracture stabilisation, repeat debridement and early soft-tissue coverage
Funding	Academic funding but no commercial conflicts of interest
Covariates in the MVA: Not well reported but included time to debridement, sociodemographic variables, health habits and fracture classification. However, the requirement of 10 events per variable in the MVA was possibly not met. Infection: After MVA adjustment, the effect of timing of cover was not an independent predictor of the development of serious infection requiring rehospitalisation. The mean time from debridement to cover of those with major infection was 4.4(3.3) days and 5.7(4.9) for those without major infection.	

Protocol outcomes not reported by the study	Mortality at 1,12 months, health-related quality of life, amputation and return to normal activities

Table 53: Wei 2014[68]

Study	**Wei 2014[68]**
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=80 patients with open tibial fractures)
Countries and setting	China
Line of therapy	First-line
Duration of study	Mean: 33-38 months
Method of assessment of guideline condition	Clinical assessment
Stratum	Primary closure, delayed closure (staged)
Subgroup analysis within study	Not applicable.
Inclusion criteria	Open tibial fractures of grade IIIa or IIIb; age >18; soft tissue wounds treated with VAC; fractures treated with IF and EF methods
Exclusion criteria	Immediate amputation; PVD, diabetes, immune dysfunction.
Recruitment/selection of patients	Consecutive patients between 2005 and 2011.
Age, gender and ethnicity	Age: 36/43; male67%/73%
Interventions	(n=27) Intervention 1: Primary wound closure – One stage debridement, internal fixation and cover, using NPT. (n=22) Intervention 2: Delayed wound closure – primary debridement at same time as internal fixation, with direct cover of wound with non-adherent sponge and intermittent suction via a vacuum assisted colure. Final wound coverage about 7 days later depending on soft tissue status. No multivariable analysis but both groups were adequately similar for age and grade of fracture. They were also similar for sex, type of trauma, time to debridement and fixation methods. CHILDREN: Unclear

Funding	None
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Primary closure versus delayed closure Only adult results given as results for children by group were not reported Deep infection Primary closure 5/27, delayed closure 6/22 Amputation Primary closure 1/27, delayed closure 3/22 Osteomyelitis Primary closure 3/27, delayed closure 4/22	
Protocol outcomes not reported by the study	Mortality at 1,12 months, hospital stay, further unplanned surgery, flap failure (total or partial), and return to normal activities

Table 54: Lack 2015[38]

Study	**Lack 2015[38]**
Study type	Retrospective Cohort
Number of studies (number of participants)	1 (n=137 patients)
Countries and setting	Conducted in USA
Line of therapy	First-line
Duration of study	Followed up up to 90 days after the original injury.
Method of assessment of guideline condition	Observation of injury
Stratum	-
Subgroup analysis within study	Not applicable. Controlled for by multivariate analysis.
Inclusion criteria	Open fractures with Gustillo Anderson Grade III.
Exclusion criteria	Missing data; non-reconstructible limbs

Recruitment/selection of patients	Consecutive patients presenting with an open fracture in 2013.
Age, gender and ethnicity	Mean age similar between those with non-infected and infected fractures (40 vs 40.5); gender and ethnicity not reported.
Indirectness of population	No indirectness
Interventions	Definitive fracture fixation and wound management followed basic standard principles. Diaphyseal fractures were treated with intramedullary fixation. Those with intra-articular extension or at the very distal or proximal metaphysis were usually treated with plate and screw fixation. Those with intra-articular extension or at the very distal or proximal metaphysis were usually treated with plate and screw fixation. The standard regimen for antibiotic prophylaxis was Cefazolin (128/137). Other antibiotics used were clindamycin or vancomycin. Temporizing external fixation was used when necessary and definitive fixation was performed as soon as the patient and wound were amenable. Wounds were closed when possible and those not able to be closed were treated with negative pressure dressings pending definitive wound coverage.
Funding	Internal academic funding; no commercial funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Protocol outcome 1: Deep surgical site infection - Actual outcome: Time of antibiotic administration: For patients with >5 days to cover the adjusted OR for deep infection was 7.39 (95% CIs: 2.54 to 27.04), compared to ≤5 days to cover. Adjustment was made for for age, Gustillo-Anderson classification, smoking, presence of diabetes, time to debridement and time to antibiotics Risk of bias: Very high; Indirectness of outcome: No indirectness.	
Protocol outcomes not reported by the study	Mortality up to 12 months, Health related quality of life, Return to normal activities, Re-operation (unplanned), Amputation, Functional outcomes and length of stay.

G.1.8 Definitive dressings after debridement

Table 55: Rasool 2013[53]

Study	Rasool 2013[53]
Study type	RCT (Patient randomised; Parallel)

Study	Rasool 2013[53]
Number of studies (number of participants)	(n=50)
Countries and setting	Conducted in Pakistan; Setting: Hospital
Line of therapy	First-line
Duration of study	Intervention time: Up to 40 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Grade II, IIIA, IIIB open tibial fractures
Exclusion criteria	Gustilo type I, IIIC, gunshot injuries, and contraindications for wound VAC use
Recruitment/selection of patients	Recruited from March 2010 until March 2012
Age, gender and ethnicity	Age - Range: 10-40 years. Gender (M:F): 35/15. Ethnicity:
Further population details	1. Age: Not applicable/Not stated/Unclear (Mixed). 2. Grade of fracture: Not applicable/Not stated/Unclear (Mixed).
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Dressings - Negative pressure dressing. VAC therapy. Continuous negative pressure of 125 mm of mercury was applied to the wound.. Duration Until appearance of 100% granulation tissue over the wound. Concurrent medication/care: All patients received irrigation, sharp debridement, tetanus prophylaxis and empirical systemic antibiotics against staphylococci. Dressings were changed 3 times a week. Further details: 1. Setting: Acute care (n=25) Intervention 2: Dressings - Standard dry/saline/antiseptic dressing. Saline soaked dressing. Duration Until appearance of 100% granulation tissue over the wound. Concurrent medication/care: All patients received irrigation, sharp debridement, tetanus prophylaxis and empirical systemic antibiotics against staphylococci. Dressings were changed 3 times a week. Further details: 1. Setting: Acute care
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NEGATIVE PRESSURE DRESSING versus STANDARD DRY/SALINE/ANTISEPTIC DRESSING Protocol outcome 1: Wound healing at 6 weeks	

Study	Rasool 2013[53]
- Actual outcome: Wound healed within 30 days at .; Group 1: 25/25, Group 2: 13/25; Risk of bias: ; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at .; Re-operation (unplanned)/amputation at .; Function at .; Deep infection (bone) at .; Wound infection at .; Tissue necrosis at .; Return to normal activities at .

Table 56: Stannard 2009[61]

Study	Stannard 2009[61]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=58 (with 62 open fractures))
Countries and setting	Conducted in United Kingdom; Setting: Level 1 trauma centre
Line of therapy	First-line
Duration of study	Follow-up (post intervention): 14-67 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Severe open fracture (heavily contaminated type II/IIIA, severe soft tissue injury type IIIA, all types IIIB and IIIC). Over 18 years of age, consent
Exclusion criteria	Open fractures that could be closed after initial surgery and did not require serial debridements, infected open fractures, a surgical incision that cannot be treated with NPWT, prisoners, pregnancy, did not consent, unable to complete protocol.
Recruitment/selection of patients	Recruited from June 2001 until August 2006
Age, gender and ethnicity	Age - Other: Not reported. Gender (M:F): 39/19. Ethnicity:
Further population details	1. Age: Adults (18-65 years) 2. Grade of fracture: Not applicable/Not stated/Unclear (Mixed).
Extra comments	Intervention groups: well matched for time to wound closure. Grade of fracture was similar between groups though the NPWT group. Mean age of the groups was not reported.
Indirectness of population	No indirectness
Interventions	(n=35) Intervention 1: Dressings - Negative pressure dressing. Vacuum-assisted closure (VAC) system. Duration Until wound closure or coverage. Concurrent medication/care: Patients had irrigation and debridement every 46 to 72 hours followed by dressing replacement. This was continued until the wound was ready for closure or coverage. All

Study	Stannard 2009[61]
	patients were given prophylactic IV antibiotics until 24 hours after closure or coverage. Patients were given either a broad spectrum cephalosporin or an aminoglycoside plus a first generation cephalosporin as prophylaxis. Patients who developed infections received antibiotics based on the sensitivity of their culture. Mean time to initial debridement was 5.9 hours. Further details: 1. Setting: Acute care (n=23) Intervention 2: Dressings - Standard dry/saline/antiseptic dressing. Saline wet to moist dressing. Duration Until wound closure. Concurrent medication/care: Patients had irrigation and debridement every 46 to 72 hours followed by dressing replacement. This was continued until the wound was ready for closure or coverage. All patients were given prophylactic IV antibiotics until 24 hours after closure or coverage. Patients were given either a broad spectrum cephalosporin or an aminoglycoside plus a first generation cephalosporin as prophylaxis. Patients who developed infections received antibiotics based on the sensitivity of their culture. Mean time to initial debridement was 7.7 hours. Further details: 1. Setting: Acute care
Funding	Principal author funded by industry (Grant from Kinetics Concepts Inc.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NEGATIVE PRESSURE DRESSING versus STANDARD DRY/SALINE/ANTISEPTIC DRESSING

Protocol outcome 1: Quality of life at .
- Actual outcome: SF36 mental component score at 3 months; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome: SF36 mental component score at 12 months; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome: SF36 physical component score at 3 months; Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome: SF36 physical component score at 12 months; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Deep infection (bone) at .
- Actual outcome: Deep infection at 11 weeks; Group 1: 2/35, Group 2: 7/23; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 4: Wound healing at 6 weeks
- Actual outcome: Wound healed ready for closure at .; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 5: Return to normal activities at .
- Actual outcome: Length of stay in hospital at .; Risk of bias: Very high; Indirectness of outcome: No indirectness

Study	Stannard 2009[61]
Protocol outcomes not reported by the study	Re-operation (unplanned)/amputation at .; Function at .; Tissue necrosis at .

G.2 Pelvic fractures

G.2.1 Decision for pelvic binders

Table 57: Gross 2005[21]

Reference	Study type	No. of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Gross EA and Niedens BA. Validation of a decision instrument to limit pelvic radiography in blunt trauma. The Journal of Emergency Medicine 2005; 28: 263-266	Diagnostic	973	'Level one' trauma patients, defined as people brought in by the emergency services. USA	This tool involved 5 criteria: • GCS <14 • Complaint of pelvic pain • Pelvic tenderness on examination • Distracting injury • Clinical intoxication If one or more were present the test was positive for pelvic fracture. In this study the tool was used to predict who should be sent for X-ray.	Antero-posterior X-ray	Not stated	**Risk tool versus X-ray (all fractures)**		Maricopa medical foundation	Blinding not reported.
							TP	60		
							FN	2		
							FP	477		
							TN	434		
							Sensitivity	0.97		
							Specificity	0.48		
							Positive predictive	0.11		
							Negative predictive	1.00		
							Risk tool versus X-ray (clinically important fractures)			
							TP	62		
							FN	0		

Reference	Study type	No. of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
							FP	477		
							TN	434		
							Sensitivity	1.00		
							Specificity	0.48		
							Positive predictive	0.12		
							Negative predictive	1.00		

G.2.2 Pelvic imaging

Table 58: [37]

Reference	Study type	No. of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcome measures (Index/Ref)	Effect sizes	Source of funding	Comments
[37]	Prospective	451	All identified with pelvic fractures of dislocations. 14% of these underwent operative intervention. GCS 15, MVA in 39%, hit by vehicle in 41% Inclusion: <18 years; presenting <24 hours after blunt torso trauma;	Plain film X-ray interpreted by board radiologists.	Review of all medical records, including CT scans. Also appears X rays were included, which may have increased concordance between index and reference tests. Telephone follow up also	Not reported	**Pelvic fractures X-ray in all children**		Not reported	Decision to X ray made at discretion of physicians – thus possible that some fractures were not included, which may have affected
							sensitivity	0.78 (0.73 to 0.82)		
							Pelvic fractures X-ray in children 0-12			
								0.73 (0.66 to 0.79)		

Reference	Study type	No. of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcome measures (Index/Ref)	Effect sizes	Source of funding	Comments
			plain X rays obtained. Exclusion: penetrating injury; neurological disease; pregnancy; transferred from an outside facility and had an abdominal CT or diagnostic peritoneal lavage.		used		**Pelvic fractures** **X-ray in children 13-17**			results, if there was an association between clinical suspicion and X-ray detection.
								0.82 (0.76 to 0.87)		

Table 59: [64]

Reference	Study type	No. of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcome measures (Index/Ref)	Effect sizes	Source of funding	Comments
[64]	Retrospective	17	Patients (8 women, 9 men; age range,	Plain film X-ray including	A musculoskeletal radiologist	Not reported	**Area under ROC**		Not reported	Only the area under
							X-ray	0.92		

Reference	Study type	No. of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcome measures (Index/Ref)	Effect sizes	Source of funding	Comments
			18-87 years) with known or suspected pelvic fractures. Sixteen patients had an injury to both hips, one had an injury to a single hip. Fifteen of the fractures were displaced and 18 were comminuted. Inclusion criteria biased towards more complex cases, as these cases were those who required imaging for planning surgery. Images of both patients injured and non-injured hips were included in the study.	anterior-posterior pelvis and frog-leg lateral views (if available) of the hips. Not available for all cases (27 out of 33 hips). Radiographs selected to be as near to time of injury as possible.	reviewed all images (X-ray, CT, 3DCT), clinical history, and follow-up examinations. In 'many' cases the follow-up included plain-films.		**Comminuted fractures X-ray**			the ROC was reported for all pelvic fractures. Sensitivity and specificity was provided for comminuted fractures only
							Sensitivity	0.77		
							Specificity	0.67		

G.2.3 Pelvic cystourethrogram

Table 60: Chan 2006[6]

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
Chan 2006[6]	**Study type:** Retrospective cohort study **Data source:** Patient records **Setting:** Level 1 Trauma Center **Country:** USA **Recruitment:** January 1st 2000 until December 31st 2004	n=234 **Inclusion criteria:** Trauma patients with suspected bladder rupture after an initial CT with contrast, who consequently underwent CT cystography **Exclusion criteria:** None	**Male: Female** 142:92 **Mean (range):** 42 years (3-94) 163 (70%) patients had pelvic fractures	**Index test** CT with contrast followed by CT cystography. Bladder refilled between initial CT and CT cystography 4-MDCT and 16-MDCT used **Reference standard** Operative findings and the progress of the patient's clinical condition during hospital stay and subsequent clinical follow-up (length of follow-up not stated). **Target conditions** Bladder injury: extraperitoneal rupture, intraperitoneal rupture, combined rupture.	**Bladder injury**[a] TP FP TN FN Sensitivity Specificity PPV NPV	 18 0 206^ 0 1 (0.81-1) 1 (0.98-1) 1 1	**Source of funding:** No funding stated **Limitations:** • Unreliable reference standard
					Extraperitoneal rupture[a] TP FP TN FN Sensitivity Specificity PPV NPV	 11 0 212^ 1 0.92 (0.62-1.0) 1 (0.98-1.0) 1 1	
					Intraperitoneal rupture[a] TP FP TN FN Sensitivity Specificity PPV NPV	 5 1 218^ 0 1 (0.48-1.0) 1 (0.98-1.0) 0.83 1	

(a) 8 patients who had a positive test were treated conservatively/died before surgery and so bladder injury was not definitively confirmed. For the purposes of the diagnostic calculations, these are assumed to be correct diagnoses.
(b) 216 patients had negative tests but 10 died and were lost to follow-up. They have been removed from the analysis.

Table 61: Horstman 1991[28]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Statistical measures and 2x2 tables				Comments
Horstman 1991[28]	**Study type:** retrospective cohort study **Data source:** Medical records **Setting:** Hospital **Country:** USA Recruitment: Approximately 1985-1990.	n=25 **Inclusion criteria:** People who had both CT and conventional cystography as initial evaluation of blunt trauma. No details as to why patients had both CT cystography and conventional cystography **Exclusion criteria:** None detailed	**Male: Female** Not detailed **Age:** 6-81 years old 4 of 5 (80%) people with bladder rupture had pelvic fracture	**Index test** Conventional cystography. Unclear if any other imaging was carried out beforehand. All patients had CT cystography as well but radiographers interpreting conventional cystography were blinded to those results. **Reference standard** Operative findings, later imaging for 5 positive (conventional cystography 10-12 days later) and clinical follow-up (negatives). Length of follow-up not stated. **Target condition** Bladder rupture		Ref std +	Ref std -	Total	**Source of funding:** No funding stated **Limitations:** • Unreliable reference standard • Selection bias: no explanation of why these patients received both CT cystography and conventional cystography.
					Index test +	5	1	6	
					Index test -	0	19	19	
					Total	5	20		
					Sensitivity		1 (0.48-1.0)		
					Specificity		0.95 (0.75-1.0)		
					PPV		0.83		
					NPV		1		

Table 62: Quagliano 2006[50]

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
Quagliano 2006[50]	**Study type:** Prospective cohort study **Setting:** Trauma centre **Country:** USA **Recruitment:** October 1994-March 2003	n=212 (non-consecutive) **Inclusion criteria:** Haemodynamically stable people with blunt torso trauma who were considered at risk for bladder injury (gross haematuria, pelvic fracture, high clinical suspicion) after abdominal/pelvic CT. **Exclusion criteria:** None detailed.	**Male: Female** Not detailed **Mean age:** Not detailed Unclear how many patients had pelvic fracture	**Index test** Abdominal/pelvic CT (single/dual/quadruple) followed by conventional retrograde cystogram. Bladder refilled between initial CT and conventional cystography Patients also received a CT cystogram in between initial CT and conventional cystogram. Results not reported here because not all scans were done using MDCT. Radiologist interpreting conventional cystogram was not blinded to CT cystogram results. **Reference standard** Surgical findings, later imaging (conventional cystography) and clinical follow-up were used as the reference standard. Length of follow-up not stated. Target condition Bladder injury: extraperitoneal rupture, intraperitoneal rupture, combined rupture.	**Bladder injury** TP FP TN FN Sensitivity Specificity PPV NPV **Extraperitoneal rupture** TP FP TN FN Sensitivity Specificity PPV NPV **Intraperitoneal rupture** TP FP TN FN Sensitivity Specificity PPV NPV	 18 0 193 1 0.95 (0.74-1.0) 1 (0.98-1.0) 1 0.995 13 0 1 198 0.93 (0.66-1.0) 1 (0.98-1.0) 1 0.995 5 0 0 207 1 (0.48-1.0) 1 (0.98-1.0) 1 1	**Source of funding:** Funding not stated **Limitations:** • Unreliable reference standard • Index test: radiologist not blinded to CT cystography results • Selection bias: non-consecutive patients and towards end of study conventional cystograms were only ordered when CT results were inconclusive

G.2.4 Pelvic haemorrhage control

Table 63: Katsura 2013[33]

Study	Nationwide observational study from the Japan Trauma Data Bank trial: Katsura 2013[33]
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=317)
Countries and setting	Conducted in Japan; Setting: Data from patients that met the inclusion criteria from 87 emergency hospitals in Japan.
Line of therapy	Unclear
Duration of study	Intervention + follow-up: 6 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Adjusted comparison between the two groups using 3 different models
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Blunt Trauma patients who had both pelvic fractures and positive FAST results. Eligible patients included those who underwent either Laparotomy or TAE as the initial therapeutic intervention
Exclusion criteria	1) penetrating trauma patients, 2) unsalvageable severe head injury (head AIS >5), 3) patients who underwent a different initial therapeutic intervention, 4) patients who were dead on arrival, 5)unknown hospital discharge disposition
Recruitment/selection of patients	Patients who met inclusion criteria
Age, gender and ethnicity	Age - Mean (SD): Lap: 48.7 and TAE 48.9. Gender (M:F): M:F 185:132. Ethnicity: Japanese
Further population details	
Extra comments	Retrospective cohort study using data derived from the prospectively maintained Japan Trauma Data Bank (JTDB) from 2004 to 2010. Total of 317 patients from 87 institutions that submitted data were analysed Concurrent medication/care: M:F ratio= 86:37 . LAP group had a higher proportion of men, a higher mean ISS and a higher mean abdominal AIS score than the TAE group. The LAP group had a lower mean GCS score and was more likely to present with a lower mean systolic blood pressure (SBP) Concurrent medication/care: M:F ratio= 99: 95. TAE group had a higher mean pelvic AIS score and showed better probability of survival than the LAP group. Approximately 50% of the patients who were hypotensive in the ED underwent TAE as the initial therapeutic intervention
Indirectness of population	No indirectness
Interventions	(n=123) Intervention 1: Other - any other treatment. Group of patients that had Laparotomy as the first therapeutic

Study	Nationwide observational study from the Japan Trauma Data Bank trial: Katsura 2013[33]
	intervention after presentation with a pelvic fracture and positive FAST result. Duration 6 years. (n=194) Intervention 2: Arterial embolization (interventional radiology) - arterial embolization. Group of patients that had trans-arterial embolization as the first therapeutic intervention after presentation with a pelvic fracture and positive FAST result. Duration 6 years
Funding	Academic or government funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LAP versus TAE Protocol outcome 1: Mortality at Define - Actual outcome: In-hospital mortality at 6 years; Group 1: 50/102, Group 2: 52/102; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at Define; Re-bleeding rates at Define; Need for further intervention at Define; Volume of blood lost/Number of transfusions required at Define; Time to definitive control of haemorrhage at Define; Need for rescanning at Define; Adverse effects at Define; Pain/Discomfort at Define; return to normal activities at Define; Length of stay at Define

G.3 Pilon fractures

G.3.1 Pilon early fixation

Table 64: Davidovitch 2011[10]

Study	Davidovitch 2011[10]
Study type	Non-randomised study
Number of studies (number of participants)	1 (n=46)
Countries and setting	Conducted in USA; Setting: ED or tertiary care centre receiving ED referrals
Line of therapy	First-line
Duration of study	Follow-up (post intervention): 18-22 months

Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	acute fractures of the distal tibial plafond (OTA type 43 C fracture)
Exclusion criteria	Type A or B OTA type 43 fractures; incomplete chart/ X ray data;
Recruitment/selection of patients	Retrospective analysis of patient notes
Age, gender and ethnicity	Age - Mean (SD): 42.5. Gender (M:F): 30:16. Ethnicity: Not stated
Further population details	None
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: repair - definitive fixation within 24 hours. Possible that definitive fixation may have not been until a mean of 4.6 days but reporting was very unclear and it's possible that the 4.6 days may relate only to fibular repair. Definitive fixation was external fixation that consisted of angle ankle joint spanning, single hinged device and limited internal fixation with or without fibular fixation. Following reduction, cannulated screws were placed across fracture lines for compression. Surgeon was fellowship trained (n=26) Intervention 2: repair - temporary fixation and then definitive fixation at >7 days. Definitive fixation at mean of 13.3 days after temporary external fixation. Temporary fixation was done with a spanning external fixator (n-18) with or without fixation of the fibular fracture or done with in a splint (n=8).
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DEFINITIVE FIXATION WITHIN 24 HOURS versus TEMPORARY FIXATION AND THEN DEFINITIVE FIXATION AT >7 DAYS

Protocol outcome 1: Deep infection
- Actual outcome: Deep infection; Group 1: 2/20, Group 2: 3/26; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Unplanned surgery
- Actual outcome: Number of surgeries; Group 1: mean 1.5 number of surgeries (SD 0.738); n=20, Group 2: mean 2.1 number of surgeries (SD 0.738); n=26; Risk of bias:

Very high; Indirectness of outcome: No indirectness Protocol outcome 3: Function - Actual outcome: AOFAS total score; Group 1: mean 77.1 (SD 14.4); n=20, Group 2: mean 72.4 (SD 21); n=26; AOFAS 0-100 Top=High is good outcome; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome: SMFA function index; Group 1: mean 25.8 (SD 15.2); n=20, Group 2: mean 34.3 (SD 19.1); n=26; SMFA function index 0-100 Top=High is poor outcome; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life ; Hospitalisation ; Mortality ; Amputation ; Pain ; Return to normal activities ; Length of stay

Table 65: Harris 2006[23]

Study	**Harris 2006[23]**
Study type	Non-randomised study
Number of studies (number of participants)	1 (n=79)
Countries and setting	Conducted in USA; Setting: level one trauma centre in Ohio, USA
Line of therapy	First-line
Duration of study	Follow-up (post intervention): 26 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Fractures of the tibial plafond
Exclusion criteria	None reported
Recruitment/selection of patients	Retrospective review of patient data
Age, gender and ethnicity	Age - Mean (range): 25 (17 to 81). Gender (M:F): 45:31. Ethnicity: Not reported
Further population details	None
Indirectness of population	No indirectness

Interventions	(n=16) Intervention 1: Closed reduction and splinting, followed by definitive fixation at mean of 7.6 days. Definitive treatment consisted of limited open articular reduction and wire ring external fixation. (n=63) Intervention 2: Closed reduction and splinting, followed by definitive repair (ORIF) at a mean of 11.2 days. Out of the 63 patients, fibular fixation and temporary external fixation or splinting was applied before the definitive ORIF in 56.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: POP AND THEN DEFINITIVE FIXATION FROM >24 HOURS TO 7 DAYS versus POP AND THEN DEFINITVE FIXATION AT > 7 DAYS Protocol outcome 1: Deep infection - Actual outcome: Deep infection ; Group 1: 1/16, Group 2: 0/63; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 2: Unplanned surgery - Actual outcome: secondary procedures ; Group 1: 4/16, Group 2: 4/63; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 3: Function - Actual outcome: Foot function Index subscale total score at 98 weeks; Group 1: mean 0.4 (SD 0.305); n=16, Group 2: mean 0.23 (SD 0.305); n=63; Foot Function Index Subscale 0-1 Top=High is poor outcome; Risk of bias: Very high; Indirectness of outcome: No indirectness - Actual outcome: Musculoskeletal function assessment scores at 98 weeks; Group 1: mean 34 (SD 23.5); n=16, Group 2: mean 20.9 (SD 23.5); n=63; Musculoskeletal Function assessment 0-100 Top=High is poor outcome; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life ; Hospitalisation ; Mortality ; Amputation ; Pain ; Return to normal activities ; Length of stay

Table 66: Koulouvaris 2007[34]

Study	**Koulouvaris 2007[34]**
Study type	Non-randomised study
Number of studies (number of participants)	1 (n=55)
Countries and setting	Conducted in Greece
ine of therapy	1st line

Duration of study	Follow-up (post intervention): up to 11 years
Method of assessment of guideline condition	Not reported
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	None
Indirectness of population	None
Interventions	(n=42) Intervention 1: definitive fixation within 24 hours. Immediate definitive external fixation. In 20 patients a half pin external fixator with ankle spanning was fitted. In 22 patients a single ankle sparring ring hybrid external fixator with tensioned wires was fitted. After primary reduction and plating of the fibula, reconstruction of the articular surface of the tibia was performed through a small arthrotomy. After surgery patients used a splint for 2 weeks (n=13) Intervention 2: fibular fixation and placement of a medial spanning external fixator in all 13 patients. After an average of 12 days, the external fixator was removed and internal fixation of the fractures was carried out. Via a short distal skin incision, the plate was introduced subcutaneously, pushed proximally and fixed by screws inserted via stab incisions. Hardware was removed 2 years after the primary surgery
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DEFINITIVE FIXATION WITHIN 24 HOURS versus TEMPORARY FIXATION AND THEN DEFINITIVE FIXATION AT >7 DAYS

Protocol outcome 1: Unplanned surgery
- Actual outcome: Further surgery ; Group 1: 0/42, Group 2: 1/13; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcome 2: Return to normal activities
- Actual outcome: Return to leisure activities ; Group 1: 35/42, Group 2: 12/13; Risk of bias: Very high; Indirectness of outcome: No indirectness

Protocol outcomes not reported by the study	Quality of life ; Hospitalisation ; Mortality ; Amputation ; Deep infection ; Function ; Pain ; Length of stay

Table 67: Tang 2014[63]

Study	**Tang 2014[63]**
Study type	Non-randomised study
Number of studies (number of participants)	1 (n=46}
Countries and setting	Conducted in China
Line of therapy	1st line
Duration of study	Follow-up (post intervention): mean 25.8 months
Method of assessment of guideline condition	Not reported
Stratum	Closed
Subgroup analysis within study	Not applicable
Inclusion criteria	Unilateral AO/OTA type C closed pilon fractures, age 18-65 years; ORIF treatment and folwo up for >1 year
Exclusion criteria	Open fracture, pathological fracture, other fractures affecting the target ankle rehabilitation, AO soft tissue injuries grade 4 or above, compartment syndrome, neurovascular insufficiency, no follow up data, cancer, diabetes and immunodeficiency.
Age, gender and ethnicity	Age 45.11/44.26 . Gender (M:F): 17.6:1 Ethnicity: Chinese
Further population details	None
Indirectness of population	None
Interventions	(n=42) Intervention 1: definitive fixation within 36 hours. Immediate definitive ORIF (n=13) Intervention 2: Delayed ORIF fixation until 1-2 weeks after temporary external fixation.
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DEFINITIVE FIXATION WITHIN 24 HOURS versus TEMPORARY FIXATION AND THEN DEFINITIVE FIXATION AT >7 DAYS Protocol outcome 1: Deep infection - Actual outcome: Deep infection ; Group 1: 0/23, Group 2: 1/23; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 2: Hospital stay - Actual outcome: Hospital stay ; Group 1: 7.6(2.6) days, Group 2: 15.2 (4.2) days; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 3: Function (fair/poor) - Actual outcome: Deep infection ; Group 1: 0/23, Group 2: 0/23; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life ; Hospitalisation ; Mortality ; Amputation ; Deep infection ; Function ; Pain ; Length of stay

G.3.2 Pilon fixation

Staged internal fixation versus external fixation – RCT

Table 68: Wang2010

Study	**Wang2010[65]**
Study type	Randomised controlled trial
Number of studies (number of participants)	n=60 fractures in 60 patients. 56 were successfully followed up and included in the study.
Countries and setting	Unclear, assumed to be the hospital that the author is from; Traumatology Department, Peking, China.
Line of therapy	First-line
Duration of study	Two-year follow-up
Method of assessment of guideline condition	Diagnosis and classification of tibial plafond fractures by 2 senior surgeons looking at radiographic and CT images. These surgeons were not involved in the patients surgery.
Stratum	Staged ORIF versus external fixation. NOTE: staging used calcaneal skeletal traction rather than external fixation.
Subgroup analysis within study	None

Inclusion criteria	Adults older than 18 years, closed type B3 and C Pilon fractures based on AO/OTA classification, both two staged ORIF and LIFEF were suitable for the fracture, no episodes of compartment syndrome.
Exclusion criteria	Ages at or younger than 18 years, type A or B1 or B2 Pilon fracture, history of peripheral angiopathy and/or arthritis in the injured leg, concomitant injuries to the brain, chest and/or abdomen, only one or none of the techniques was suitable for the fracture, AO soft tissue grade 4 or above injuries, open fractures, compartment syndrome was relieved by fasciotomy, associated with diabetes and pathologic fractures.
Recruitment/selection of patients	Patients were recruited from January 2005- June 2007
Age, gender and ethnicity	For the staged ORIF and external fixation groups respectively: Age – mean 40.1 SD 10.7 (range 22-62), mean 37.2 SD 10.9 (range 18-57) years. Gender (M: F) 25:2 and 26:3 .Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	Randomised (patients randomly allocated a number using a Statistical Package for Social Sciences (SPSS). No allocation concealment as the odd numbers were allocated to group 1 and even to group 2. Unblinded. First stage: Calcaneal skeletal traction (transverse Steinmann pin) was carried out on all patients. Staged ORIF: 10-14 days post injury External fixation: 11-15 days after injury. Both groups had fibula fracture stabilisation with a plate or Kirschner wire carried out first. The Steinmann pin was then removed. ORIF group: anteromedial approach, complete replacement of articular surface (internal fixation (locking compression plates combined with screws or Kirschner wires). Allografting carried out in 8 cases. External fixation group: Standard dynamic axial fixator (Orthofix Srl) system with 4 external pins. Intra operative fluoroscopy was used for pin insertion guidance. Positioning template used to find centre of talar dome, Kirschner wire inserting to fix template and axis of template handle to be parallel to the tibia. Two further Kirschner wires inserted to calcaneus and talar, external frame installed. Pre- drilling technique and non-HA coated pins used. Lag screws or Kirschner wire were used for additional stabilisation and articular reconstruction once tibia length restored. 12 allografts. Antibiotic protocol: Cefotiam (IV), 30 mg/kg every 12 hours for 3 days after calcaneal skeletal traction and fracture fixations. Iodophor treatment of pin tracts twice a week (in hospital), saline post discharge. Monthly radiographs until fracture healed. 6 monthly follow-up until 2 yrs. Weight bearing: partial from callus formation on radiograph (external fixation group also had dynamisation then,

	loosening of bolts), full weight bearing on bone union (external fixator removed). Intervention 1 (n=27): Open reduction and internal fixation (ORIF) Intervention 2 (n=29): External fixation
Funding	None described
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Staged ORIF versus external fixation Definitions: Wound infection: Signs and symptoms of infection around the wound. Chronic osteomyelitis: presence of chronic drainage from sinuses, fistulas, ulcers or X-ray evidence. Protocol outcome 1: Surgical site infection. (n=56) - Actual outcome: Number of patients with wound infections; Group 1: n=2/27 Group 2: n=0/29. Risk of bias: High; Indirectness of outcome: No indirectness. - Actual outcome: Osteomyelitis; Group 1: n=1/27 Group 2: n=0/29. Risk of bias: High; Indirectness of outcome: No indirectness. Group 1: 2 wound infections (Staph aureus in one wound), 1 pin site infection. Group 2: 0 wound infections. 12 pin site infections. All pin site infections occurred in the calcaneus and talus. Bacteria positive in 9 cases: Staph aureus n=5, *Staphylococcus epidermidis* n=2, *Haemophilus influenza* n=1, *Pseudomonas aeruginosa* n=1. All infections were treated by IV antibiotics. Patient with wound infection developed chronic osteomyelitis (required additional surgery, 15 days of antibiotic treatment). No patient needed the metalwork removing.	
Protocol outcomes not reported by the study	Health-related quality of life, ankle fusion, unplanned further surgery, wound breakdown, patient reported outcome (return to normal activities)

Table 69: Wyrsch 1996

Study	**Wyrsch 1996** [65]
Study type	Randomised controlled trial
Number of studies (number of participants)	n=39 patients.
Countries and setting	Department of orthopaedics and rehabilitation, Vanderbilt University Medical Centre, Nashville
Line of therapy	First-line
Duration of study	3 years + follow-up (Average 3 years)

Method of assessment of guideline condition	Unclear
Subgroup analysis within study	None
Inclusion criteria	Patients who had sustained an intra-articular fracture of the tibial plafond, which was classified with the system of Ruedi and Allgower. The indications for an operation included an open fracture and unacceptable alignment of the fracture (defined as a joint space or incongruity of the articular surface of more than two millimeters) or malreduction (greater than 10 degrees in any plane), or both, of the tibia and fibula.
Exclusion criteria	Patients who had an acceptable reduction of the fracture, sever osteoporosis, an inability to walk, or neuropathic joint, transfemoral amputation secondary to compartment syndrome.
Recruitment/selection of patients	Patients were recruited from January 1990 – December 1992
Age, gender and ethnicity	For the staged ORIF and external fixation groups respectively: Age – mean 38.84 SD 13.5, mean 37.65 SD 10.9.709. Gender (M: F) 2:1 and 2:1.Ethnicity: Not reported
Indirectness of population	No indirectness
Interventions	All patients with an open fracture underwent initial debridement, followed by immediate stabilisation (unclear exact method) at an average of 3 hours after injury. Closed fractures were treated with reduction and application of a splint, followed by operative treatment within 48 hours unless severe swelling or fracture blisters were present. If the operation was delayed for more than 48 hours, the patient was placed in skeletal traction or was elevated in a Bohler-Braun frame. Average time from injury to operative procedure was 5 days. Antibiotics were administered pre and post-operatively, antibiotics were administered parenterally to all patients. Patients with a closed fracture received cephalexin, 1 gram every 8 hours. Gentamicin was added to the regime for patients with open fractures. Group 1 - ORIF group: 2 separate incisions were made to stabilise the tibia and fibula. The fracture of the fibula was reduced through a lateral incision and stabilised with a plate or IM rod. After open reduction of the distal articular surface of the tibia and inspection of the talar dome, a buttress plate was applied to stabilise the fracture (type varied with surgeon including Dynamic compression plate, cloverleaf plate, mini-fragment T-plate).Post-operatively the lower extremity was immobilised for 2-3 weeks in a plaster splint Group 2 - External fixation group: A limited internal fixation combined with external fixation; an Orthofix fixator (EBI Medical, Parsippany, New Jersey) or a Synthes AO fixator (Paoli, Pennsylvania. The fixator was kept in place for an average of 10 weeks and removed once evidence of bone callus formation was found.

	Intervention 1 (n=19): Open reduction and internal fixation (ORIF) Intervention 2 (n=20): External fixation
Funding	None described

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Staged ORIF versus external fixation

Definitions:
Wound infection: Signs and symptoms of infection around the wound.
Chronic osteomyelitis: presence of chronic drainage from sinuses, fistulas, ulcers or X-ray evidence.

Protocol outcome 1: Surgical site infection (n=39)
- Actual outcome: Number of patients with wound infections; Group 1: n=5/19 Group 2: n=6/20. Risk of bias: Very high; Indirectness of outcome: No indirectness.
- Actual outcome: Osteomyelitis; Group 1: n=3/19 Group 2: n=0/20. Risk of bias: Very high; Indirectness of outcome: No indirectness.

Protocol outcome 2: Unplanned Surgery (n=39)
- Actual outcome: Number of additional unplanned surgeries (n per patients; Group 1: mean (SD) 1.47 (2.12), n=19; Group 2: mean (SD) 0.3 (0.57), n=20. Risk of bias: Very high; Indirectness of outcome: No indirectness.
- Actual outcome: Number of additional unplanned surgeries; Group 1: n=9/19 Group 2: n=4/20. Risk of bias: Very high; Indirectness of outcome: No indirectness.

Protocol outcome 3: Wound breakdown (n=39)
- Actual outcome: Wound breakdown; Group 1: n=6/19 Group 2: n=0/20. Risk of bias: Very high; Indirectness of outcome: No indirectness.

Protocol outcome 4: Ankle fusion (n=39)
- Actual outcome: Wound breakdown; Group 1: n=0/19 Group 2: n=1/20. Risk of bias: Very high; Indirectness of outcome: No indirectness.

Protocol outcome 5: Amputation (n=39)
- Actual outcome: Wound breakdown; Group 1: n=3/19 Group 2: n=0/20. Risk of bias: Very high; Indirectness of outcome: No indirectness.

Protocol outcomes not reported by the study	Health-related quality of life, ankle fusion, , wound breakdown, patient reported outcome (return to normal activities)

Staged internal fixation versus external fixation – Cohort

Table 70: Richards 2012

Study	Richards2012[54]
Study type	Prospective Cohort (initially was designed as an RCT but changed due to low accrual (strict inclusion criteria of isolated fractures, patient and surgeon concerns about changing surgeons)
Number of studies (number of participants)	n=45
Countries and setting	Level 1 Trauma centre, United States of America
Line of therapy	First-line
Duration of study	Follow-up was for 12months. 18 (69%) in the external fixation group had 12 month follow-up, 27 (79%) in the staged ORIF group.
Method of assessment of guideline condition	Not specifically listed. Presumed to be clinical and radiographic examination by the surgeons
Stratum	Staged ORIF versus external fixation
Subgroup analysis within study	None
Inclusion criteria	Aged 18 years or older, had sustained an isolated unilateral open or closed plafond fracture, independently ambulatory prior to injury, English competent, granted consent..
Exclusion criteria	Pathologic fractures, prolonged steroid use, renal failure, pre-existing symptomatic ankle arthritis, Paget's disease, ankle injuries that precluded ORIF or external fixation, decreased mental status type IIIC open tibia plafond fractures, transient patients without a fixed address, patients not living in the immediate vicinity, prisoners.
Recruitment/selection of patients	Patients who were treated at the Trauma center between June 2002 and June 2006. Initially randomised by sealed opaque envelopes after initial external fixation to receive definitive ORIF or definitive external fixation by a surgeon who felt comfortable with that method. This was changed to a prospective cohort design due to low accrual (see reasons above in study type section).
Age, gender and ethnicity	For the staged ORIF and external fixation groups respectively: Age – 46.9 (13.1)years, 40.6 (13.3)years. Gender (M: F) Not described .Ethnicity: Not described. No significant difference was found between the groups for open fractures (%) or fracture classification (C1-3).
Indirectness of population	No indirectness
Interventions	Initial external fixation, followed by definitive ORIF (and removal of external fixator) or reduction via limited ORIF and external fixation until union.

	Staged ORIF: initial bridging external fixation with delayed joint fixation via minimal incisions at approximately 2 weeks post injury. Limited exposure of distal tibia articular surface; percutaneous plating and screw fixation was used. Immediate or delayed bone grafting with allograft or autograft at surgeons discretion. Definitive external fixation: 2 weeks post injury visualisation of the joint by an incision. Screws were used for restabilisation of the articular surface. Length of time of external fixation use was up to the surgeon. Elective removal of fixator once healed. After 2 weeks, posterior splint removal with active and passive movement, with as tolerated weight bearing. Intervention 1 (n=27): Staged Open reduction and internal fixation (ORIF) Intervention 2 (n=18): External fixation
Funding	Funded in part by a grant from the Orthopaedic Trauma Association and an EBI Educational Grant.
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Staged ORIF versus external fixation Protocol outcome 1: Health-related quality of life (n=45) -Actual outcomes: SF-36 (Physical Function) at 6 months; Group 1: mean 49.7 (30.1), Group 2: mean 25.5 (18.0). Reported to be no significant difference at 3 and 12 months, but data was not given. Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Ankle fusion, unplanned further surgery, wound breakdown, patient reported outcome (return to normal activities)

G.4 Other

G.4.1 Identifying vascular compromise

Table 71: Busquets2004

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Busquets et al. Helical Computed	Retrospective	N=97 CTAs carried out on 95	Inclusion: Patients older than 16 years who	**CTA (Computed Tomographic**	**CA (standard cathether**	Unclear	**CT angiography versus mixed**		Not reported	Indirect population (36% with

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Tomographic Angiography for the Diagnosis of Traumatic Arterial Injuries of the Extremities. The Journal of TRAUMA Injury, Infection and Critical Care. 2004; 56: 625-628.	cohort Patients listed on the Trauma registry, American College of Surgeons, Chicago	patients Adults	underwent a CTA for evaluation of suspected vascular injury to the upper or lower extremities (July 1998-April2001). They were identified through medical records, ICD coding, and trauma registry. 70% due to blunt trauma. Diminished pulse n=20, unilateral combined femur and tibia fracture (floating knee) n=34, nerve deficit or proximity wounds to vascular structures n=32, hard signs of arterial injury (ischemia, expanding hematoma or significant	**Angiography)** GE CTI helical scanner (GE Medical Systems), 120ml of non-ionic Optiray 320 contrast, using an 18 gauge catheter into the antecubital vein (injection rate 3-4 ml/sec using a power injector). Transverse views, collimation of 2-3mm with a scan delay to target the area of interest. Image reconstruction: 1-1.5mm (50% collimation width) intervals. Standard shaded surface displays, maximum intensity projection, curved planor reformation and volume	**angiography)** **Or** **Surgery** **Or** **CA & surgery** for those with abnormal CTAs And **Clinical follow up** for those with normal CTAs No information on the methodology of the CA or what surgery was performed		**procedures for the detection of arterial injury** TP FN FP TN sens spec +ve pred -ve pred	 25 0 0 72 100% 100% 100% 100%		fractures) No specific gold standard comparison No blinding reported Adult and young person population

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			bleeding) n=9. 86% male. Mean ISS 11.4 +/- 2.4. Mean age 31 +/- 5.6 years Lower extremity injuries: 81% Upper extremity injuries: 19% No ankle brachial indices were performed.	rendring techniques were used to make 2D and 3D images of the arteries. Note: patients with arterial spasm were considered to have a normal study if no other abnormality was detected.						

Additional narrative information:

Out of the penetrating wounds, the reasons for the injuries were: gunshot wounds (79%) and stab wounds (21%).

The 25 abnormal CTA results were found to be 21 arterial occlusions, 2 intimal defects, and 2 pseudoaneurysm. These were shown by arteriography, surgery or a combination of the two procedures. 10 normal CTAs had normal arteriography. The paper describes that the remaining 62 normal CTAs, had no further radiographic evaluation and that there were no missed or delayed diagnosis of arterial injuries in the group. The follow up was for a mean of 8 +/-3.1 months and was available for 84% of the cohort.

There were two deaths (caused by associated injuries) and 5 below the knee amputations (post-surgical arterial repair). The reasons for the amputations were delay in arrival to the emergency department resulting in prolonged limb ischemia (n=3), necrotizing fasciitis after repair of popliteal artery injury secondary to multiple fracture (n=1) and non-functional limb secondary to an associated nerve injury (n=1).

Table 72: Lynch1991

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Lynch et al. Can Doppler Pressure Measurement Replace "Exclusion" Arteriography in the Diagnosis of Occult Extremity Arterial Trauma? 1991. Ann. Surg. 214 (6): 737-741.	Prospective cohort Emergency department, Seattle, United States of America.	N=100 injured limbs in 93 patients All patients underwent: a history, examination, baseline laboratory examinations, measurement of Doppler systolic arterial blood pressure at the ankle or wrist, distal to an injury thought to threaten the extremity'	Inclusion: Trauma victims with blunt or penetrating extremity trauma (including all injuries between the neck and the wrist and between the inguinal ligament and the ankle) Exclusion: Patients who underwent contrast arteriography solely to localize the site of an obvious arterial injury. Baseline characteristics: Male/ female: 86/7 Age range (11-62), mean 26.2 years. Injuries: gunshot wound (n=58),	**1. Doppler (ABPI)** – Arterial pressure index was calculated (API) Doppler device was a Medasonics brand.	**1. Arteriography** Transfemoral approach, the Seldinger technique, an automated dye injector and biplane images. No further information given. Arterial pressure >0.9 was classed as normal. **2. Later Clinical outcome** 94% returned to the vascular clinic for examination and repeat	Unclear	**Doppler (ABPI) versus arteriography** TP FN FP TN sens spec +ve pred -ve pred **Doppler (ABPI) versus later clinical outcome** TP FN FP TN sens spec +ve pred -ve pred **Contrast arteriography versus later clinical**	 20 3 2* 75 87% 97% 91% 96% 20 1** 2 77 95% 97% 91% 99%	Not reported	Indirect population (22% with fractures or dislocations) No blinding reported Note: mixed adult and child population and majority male (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
		s artery. They then underwent contrast arteriography.	stab wounds (n=16), fractures/dislocations (n=22) and other (n=4).		Doppler measurement follow up.		**outcome**			
							Sens	100%		
							Spec	97.5%		
							+ve pred	91%		
							-ve pred	100%		
							*Two of the positive API with abnormal arteriography turned out to be false positives, and on surgical exploration there was no vessel injury. **Small profunda femoris artery pseudoaneurysm			

Additional narrative information:

Patients either had immediate or delayed operation or inpatient observation depending on their clinical outcome and arteriographic findings with a follow up appointment at the vascular clinic for all. Fourteen patients had an intervention; 9 arterial reconstructions, 2 fasiotomies, 1 therapeutic embolization. 86 arteriograms resulted in observation only (normal or minimally abnormal arteriograms).

Table 73: Mills2004

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Mills et al. The Value of the Ankle-Brachial Index for Diagnosing Arterial Injury After Knee Dislocation: A Prospective Study. 2004. 56 (6): 1261-1265.	Prospective cohort	N=52 admitted to the author's level 1 Trauma centre (October 1998-February 2002) 38 patients with knee dislocation to evaluate for potential arterial injury met the inclusion criteria.	Inclusion: Age: 15-74 years Knee dislocation Exclusion: Presented to the authors' institution >24 hours after injury (n=7), bilateral upper extremity injuries precluding adequate brachial pressure measurements (n=1), vascular injury treated at an outside institution before transfer (n=5). Mechanism of injury: motor vehicle accident (n=19), pedestrian struck by vehicle (n=11), industrial accidents (n=2), fall from	**1.Doppler (ABPI)** Systolic blood pressures were taken for all extremities using the Doppler and a standardized blood pressure cuff. ABI was calculated. ABI <0.9 was the cut off used for arterial injury. 2. **Clinical assessment (pulse examination)**	**Conventional angiography (ABI <0.9)or clinical follow up or arterial duplex ultrasonography (ABI>0.9)** 11 patients had an ABI <0.9; 9 underwent emergency arteriography and consequent surgical intervention, 2 had expansile knee haematomas and underwent surgical exploration and revascularisation with reverse saphenous	Unclear	**Doppler (ABPI) versus conventional angiography and later clinical outcomes/ duplex ultrasonography** TP FN FP TN sens spec +ve pred -ve pred **Pulse examination (clinical assessment) versus later clinical outcomes/ duplex ultrasonography** TP	 11 0 0 27 100% 100% 100% 100% 10		Indirect population (5/11 fractures, 45%). All knee dislocations No blinding No specific gold standard reference

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
			significant height (n=3), sport athletics injury (n=2), morbidly obese patient who sustained a dislocation stepping from bed (n=1).		vein grafting for a transected popliteal artery.		FN	1*		
							FP	3		
							TN	24		
							sens	91%		
							spec	89%		
							+ve pred	77%		
							-ve pred	96%		
							* This patient had palpable pulses but an ABI of 0.74. They had chronic 90% stenotic lesion of the superficial femoral artery and an intimal flap limiting popliteal artery flow.			

Additional narrative information:

Arterial injuries included: six popliteal artery occlusions, one popliteal artery transection, one common femoral artery thrombosis with peroneal artery thrombosis and one superficial femoral artery high grade chronic stenosis with an intimal flap that altered the popliteal artery flow. They all had surgical revascularization and reverse saphenous vein grafting and one patient angioplasty (superficial femoral artery stenosis). Average follow up for those with arterial damage was 12 months, range 8-24 months. One patient who had an amputation had an ABI of 0.25 with a popliteal artery occlusion. The 27

patients with normal ABI (>0.9), had no evidence of vascular injury detected on daily serial clinical examination or arterial duplex ultrasonography. They had an average follow up of 19 months with a range of 4-36 months.

There was no significant difference (p=0.94) in the ages between the patients with and without vascular injury (35.5 +/- 4.64, range 16-74 years and 35.9 +/-3.13, range 15-74 years respectively).

Out of the patients with fractures (tibial plateau or supracondylar femur fracture), there were 3 (3/5, 60%) patients with a vascular injury.

Table 74: Soto 1999

Reference	Study type	Number of patients	Patient characteristics	Index test	Reference test	Time between tests	Outcomes (Index/Ref)	Effect sizes	Source of funding	Comments
Soto JA et al. Diagnostic performance of helical CT Angiography in trauma to large Arteries of the Extremities. Journal of Computer Assisted Tomography 1999; 23: 188-196	Prospective cohort	N=43 45 fulfilled the inclusion criteria but 2 were excluded as the index test was not of diagnostic standard.	Inclusion: Age: people aged 16-60 years with suspected arterial injury to limbs; haemodynamically stable and one or more of pulse deficit, expanding haematoma, pulsatile bleeding, major neurological deficit, ischaemic extremity and bruit/thrill over wound. Exclusion: Suspected arterial injury below	**Helical CTA with iodized contrast** injected through 18 gauge catheter. 3mm slices for axilla and 5mm slices for other area. Carried out by 2 fellowship-trained radiologists blinded to reference test result	**Conventional angiography.** Selective catheterisation and serial imaging with cut-film techniques. Minimum of 2 orthogonal planes obtained on every patient. Done by one radiologist, but not stated clearly if this was before the index (though stated that "helical CTA…was completed	Within 6 hours	**CTA angiography versus conventional angiography – reader one**		Quimica Schering, Bogota, Colombia. Thus possible outcome reporting bias.	Indirect population (7/43 fractures, 16.3%). Unclear blinding
							TP	17		
							FN	2		
							FP	0		
							TN	24		
							sens	90%		
							spec	100%		
							+ve pred	100%		
							-ve pred	92%		
							CTA angiography versus conventional angiography – reader two			
							TP	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
			elbows or ankle; >1 extremity injured; orthopaedic hardware in situ; previous history of AEs to contrast, diabetes, hypertension, cardiac, peripheral vascular or renal disease. Mechanism of injury: gunshot (n=28), stabbing (n=10); open fracture (n=7). Injuries in axilla (n=5), arm (n=8), thigh (n=16) and lower leg (n=16).		within 6 hours of conventional angiography…" which suggests it was); however still possible it could have been after the index test, the lack of reporting of blinding of the reference tester to index test findings is a limitation.		FN FP TN sens spec +ve pred -ve pred	0 0 24 100% 100% 100% 100%		

G.4.2 Detecting compartment syndrome

Table 75: Harris 2006[24]

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Effect sizes	Comments
Harris IA et al. Continuous compartment	RCT	• 197 people with 200	• Conducted in the UK	Continuous compartment pressure monitoring	No continuous compartment pressure	Average follow-up 8 months	Sensory loss (neurological dysfunction)	5/71 5/84	• Sensory loss at very high

Reference	Study type	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Effect sizes	Comments
pressure monitoring for tibia fractures: does it influence outcome?		fractures • n=100 fractures in each arm Inclusion criteria: • 10 years and over • Extra-articular fracture of tibia • Presenting within 24 hours of injury	• Recruited between June 2000 and August 2003 • 18 people classified at major trauma (ISS>15) Monitored group: • Mean age: 37 • M:F - 83:17 • Unconscious: 6 Unmonitored group: • Mean age: 31 • M:F - 82:18 • Unconscious: 3	(hourly for 36 hours) • Surgical team was called if difference between diastolic blood pressure and compartment pressure (ΔP) <30 mmHg. • Compartment syndrome then diagnosed by clinical examination	monitoring (for 36 hours) • Routine post-operative examination • Compartment syndrome then diagnosed by clinical examination Unconscious patients in both groups diagnosed by ΔP <30	(3-24). Follow-up rate was 89%. (9 lost in monitored and 14 lost in unmonitored	Contracture (muscle/joint contracture) Length of stay (median days) 0 fasciotomies performed in monitored group and 5 in unmonitored group	1/71 3/84 8 6	risk of bias due to performance, attrition and detection bias • Contracture at high risk of bias due to attrition • Length of stay at very high risk of bias due to performance and attrition bias Funding not stated

Table 76: Janzing 2001[30]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Statistical measures and 2x2 tables		Comments
Janzing 2001[30]	**Study type:** Prospective diagnostic accuracy study **Setting:** Hospital	n=100 (104 fractures) **Inclusion criteria:** Children, young people and adults with tibial fractures (including polytrauma)	**Male: Female** 64:33 **Mean age:** 33 years **Attrition** 2 patients died and 3 moved and were lost to	**Index test** Compartment pressure monitoring (anterior compartment) using Stryker or Kordiag portable pressure monitors. Monitored for 24 hours and at least 24 hours post-operatively for surgical patients. Compartment pressure checked every hour for 6 hours and then	Clinical symptoms ICP>30 mmHg DBP-ICP<30 mmHg DBP-CP<20 mmHg	Sensitivity: 0.67 Specificity: 0.89 Sensitivity: 0.83 Specificity: 0.42 Sensitivity: 0.89 Specificity: 0.65 Sensitivity: 0.61	**Source of funding:** Monitors lent by Stryker-Howmedica **Limitations:** High risk of bias due to the reference

	Country: Belgium **Recruitment:** Consecutive patients. August 1996 to November 1997.	**Exclusion criteria:** Monitoring equipment not available, people unwilling to enter study ICP = intracompartmental pressure DBP = diastolic blood pressure MAP = mean arterial pressure	follow-up. Full outcome data available for 95 patients (with 97 fractures).	every 3 hours until 24 hours. **Reference standard** Those patients who underwent fasciotomy or had residual symptoms (sequelae) consistent with compartment syndrome were considered to have had compartment syndrome. The decision to do a fasciotomy appeared to have been taken on the basis of clinical symptoms and compartment pressure but no details were given in the paper. Follow-up for residual symptoms - mean days: 393 (range 365-810) **Target condition** Compartment syndrome	MAP-ICP<30 mmHg MAP-ICP<30 mmHg more than 1 hour Symptoms and DBP-ICP<30 mmHg Symptoms and MAP-ICP<30 mmHg	Specificity: 0.81 Sensitivity: 0.39 Specificity: 0.92 Sensitivity: 0.33 Specificity: 0.99 Sensitivity: 0.61 Specificity: 0.97 Sensitivity: 0.28 Specificity: 0.99	standard. No clear criteria for when fasciotomies were carried out

Table 77: McQueen 2013[43]

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Statistical measures and 2x2 tables				Comments
McQueen 2013[43]	**Study type:** Retrospective diagnostic accuracy study **Data source:** Trauma unit	n=979 (850 analysed) 129 patients excluded (127 lost to follow-up and 2 due to early amputation unrelated to	**Male: Female** 598:252 **Mean age:** 38 years old (range: 12 to 94)	**Index test** Compartment pressure monitoring (anterior compartment). Measured by transducer through a static column of saline for at least 24 hours. A positive test was diastolic blood pressure minus intracompartmental pressure		Ref std +	Ref std -	Total	**Source of funding:** No biomedical funding **Limitations:** Very high risk of
					Index test +	141	11	152	
					Index test -	9	689	698	
					Total	150	700		

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Statistical measures and 2x2 tables		Comments
	database **Setting:** Orthopaedic trauma unit **Country:** UK **Recruitment:** Consecutive. From 1998 to 2007	compartment syndrome) **Inclusion criteria:** Children, young people and adults with tibial diaphyseal fractures	152 patients had a fasciotomy, 698 patients did not.	<30 mmHg for 2 hours. **Reference standard** People were considered to have compartment syndrome if: • The escape of muscles at fasciotomy was seen along with colour change in the muscles or muscle necrosis was documented by the operating surgeon. (It was considered incorrect if it was possible to close the fasciotomy wounds primarily at 48 hours). • Those who did not undergo fasciotomy had sequelae consistent with compartment syndrome during the follow-up period (mean 59 weeks) **Target condition** Compartment syndrome	Sensitivity Specificity (with 95% confidence intervals)	0.94 (0.89 to 0.97) 0.98 (0.97 to 0.99)	bias due to reference test (confirming compartment syndrome after fasciotomy is unreliable) and attrition (129 patients lost to follow-up)
					PPV NPV PLR NLR (with 95% confidence intervals)	0.93 (0.88 to 0.96) 0.99 (0.98 to 0.99) 60 (33 to 108) 0.06 (0.03 to 0.12)	

G.4.3 Information and support

Table 78: Forsberg 2014[19]

Study	Forsberg 2014[19]
Aim	To describe people's experiences of suffering a lower limb fracture and undergoing surgery.
Population	People with a lower limb fracture who had surgery and spent time in a hospital in Northern Sweden. Five women and four men; aged 24–72 years; 6 employed and 3 pensioners; 6 with children; causes: a car accident and different fall traumas relating to work or leisure; femur fractures (n=2), tibia/fibula fractures (n=4), ankle fractures (n=4); 7 had surgery with regional anaesthesia, 2 had general anaesthesia.

Study	Forsberg 2014[19]
Methods	Purposive sampling: 9/30 agreed to participate. Personal semi-structured interviews, held between 1 month and 1 year after surgery. Held at home (n=6), the university (n=2) or workplace (n=1). Interviews lasted 30–60 minutes, transcribed verbatim by the paper author, and analysed using qualitative content analysis. There was no mention of triangulation, member checking or any other methods to measure trustworthiness of findings. Very high risks of bias due to lack of methods to ensure trustworthiness and long duration after surgery for some.
Themes with findings	<u>Information desired whilst waiting for surgery</u> Worry while waiting for surgery 'depended on what they did not know would happen'. Most participants 'lacked information about time intervals, routines in the ward and the medical care of a fracture'. Participants agreed that 'an approximate time schedule would have been desirable'. Some 'participants wished that they could have gotten written information: "I lacked information/what is the plan…wanted a document to read…an ordinary fracture...then this and this will happened..."
	<u>Information desired during surgery</u> During surgery, those with regional anaesthesia reported 'feelings of curiosity and desired to know what was occurring…they appreciated when the staff narrated what they were doing and why: "I heard them banging and I felt when I was…I said what are you doing and they said [orthopaedic] now we are spiking the long nail in". When 'staff promised to give sedative drugs if the sense of being awake became unbearable, participants could see a possible way out of a situation they had not chosen'.
	<u>Information desired post-surgery</u> Awake patients 'said it was a comfortable feeling to arrive at the PACU, often having already been informed about the outcome of the surgery. Patients who had had a GA 'expressed great need for orientation in time and space and a desire to know the outcome of the surgery'. Patients felt it was professional when staff behaviours included 'explaining which kind of drug was being administered when giving pain relief, why an apparatus was sounding or how long the stay would be'. Some 'participants stated that laying there not knowing how long they would stay in the PACU was a real strain'. Participants wished to know about the metalwork inserted into their body. Being shown 'a similar material or an X-ray ….was described ….as helpful for understanding what had been done and remembering the information they had been given. Participants described the importance of being treated as a person and not as 'the fracture'. They wanted staff members to speak directly to them and not about them and their diagnosis'. When staff offered 'suggestions of solutions like repositioning the fractured limb to relieve the pain, or informing participants that they could decide when they wanted pain relief, this contributed to a sense of involvement.'
	<u>Information prior to discharge</u> Patients were insecure about being able to do post-discharge tasks, such as using their mobility device or blood thinners, after discharge. 'Participants remembered learning best when staff in the ward gradually explained things while participants were doing them

Study	Forsberg 2014[19]
	Information post-discharge Patients felt that it 'was difficult to assess for themselves what was normal during recovery, although they received much verbal information from various professionals. Some participants received conflicting information, but stated that it also was difficult to remember. They emphasised the importance of getting individual coherent written information in connection with discharge from the hospital'.

Table 79: Sleney 2014[60]

Study	Sleney 2014[60]
Aim	To explore experiences of patients after injury and identify implications for clinical care and support within the hospital setting and primary care
Population	This was an indirect population as not all had fractures; however, although there was no detailed breakdown on the injury types, the results section appeared to be mainly consisting of themes relating to people with fractures. The population was: people aged >5 years attending an emergency department or admitted to hospital following a wide range of injuries.
Methods	Purposive sampling: 89 included out of 140. The study aimed to get participants from 3 centres in Bristol, Surrey and Swansea, with quotas in each centre and within the following age ranges: 5–24,25–59 and 60+. There were also attempts to ensure an equal gender ratio and a cross-section of injury types. Individual semi-structured interviews with thematic qualitative analysis. The topic guide in the interviews was guided by the research aims and also 5 pilot interviews. For children aged <12 (n=8) a parent or carer was interviewed. Interviews were transcribed verbatim and imported into the computer-assisted qualitative data analysis software NVivo7 to allow in-depth thematic content analysis. One researcher carried out all data analysis. Triangulation of researcher interpretations was used.
Themes with findings	General Information 'they had been given about treatment or aftercare' was viewed positively by inpatients. What was very valued were the efforts of particular members of staff who 'had taken time to explain the treatment that they were to receive or had received and to answer questions and this was much valued'. Some patients 'received conflicting information from different hospital departments over whether or not they should receive physiotherapy. This was confusing for patients and unsettling in what was already a stressful situation'. For many participants, the information that they received in relation to their injury met their needs. Information from consultants and other health professionals about procedures and likely outcomes inspired confidence for many of the participants: ''…the consultant he was... absolutely on the ball and that's one thing I have to say, he instilled confidence..., you know he kept me fully informed and made sure that I knew what was going on'' In one or two cases, the language used by healthcare professionals was reported to be too technical for the participant to fully understand although this was not necessarily regarded as problematic: ''I had a letter sent to the doctor with everything stating on it and a copy given to me so I could read it as well. Not that I could fully understand all the terms, but I got the gist of it.''

Study	Sleney 2014[60]
	More significantly many participants had received some information but would have welcomed more. In the majority of cases, this related to treatment or aftercare. Participants wanted answers to questions such as when improvements would be noticeable, when they could or should use an injured limb as normal and whether mobility and strength would improve with time. Such questions may be complex to answer from a clinical perspective but are central to the patient's desire to return to normal life and their ability to manage their injury in the interim: ''The hardest thing I thought was not any feedback because there was no one there saying like now you can start lifting light weights, now you can do this. Just after they straightened my arm out they just left me. I was ringing them up and they were just saying 'Just take your time it is a big injury (...) back on track. The only thing that has got me back on track is my ambition not so much push myself but made sure I was doing things and made sure my arm was all right and trained it up really. Some guidance might have...If I had some feedback from the doctors I might have been recovered quicker maybe, I don't know.'' With regard to surgery, some participants reported that whilst information was provided beforehand to gain consent if an operation was required, they were not necessarily in a fit state to take this in. Some participants would have liked to have also seen a member of the surgical team after the operation: ''...I must admit maybe it is just norm but the follow up from the operation was pretty non-existent, in other words I don't know what do you expect? Do you expect the surgeon to come round, sit down and have a long chat with you? I guess he's rather busy. But I must admit he was conspicuous by his absence". Some participants had been given written information, for example about caring for plaster casts or danger signs to look for in the case of a head injury, and this was felt to be useful. More verbal information would also have been welcomed by some, whilst a few participants said that written information was useful to take home because they had found it difficult to take in verbal information from staff while they were in the hospital. <u>Social support after discharge</u> In the vast majority of cases, participants did have at least one person to support them on discharge from hospital. This was usually a family member, friend or neighbour. In one particular case, however, a participant with a dislocated knee had no family and no friends that lived close by. She had moved into her flat a week previously, did not know anyone in the area and her telephone was not yet connected. The discharge process took no account of these circumstances: ''I had nothing, no particular food or anything, my car was left at [name of hospital] Hospital, so and I live four miles from a local shop, I live in a very rural area on my own. There was no questions about that aspect; you know it's all very well discharging people but what are you discharging them to particularly with a massive injury, which it was. In fact it was so debilitating that it – an arm is quite different, you can walk around with your arm – but with a leg, particularly as I had steps to negotiate to my flat as well. I was totally bed bound, absolutely bed bound, massive pain. [...] I had really minimal support and I think that what is worrying is that the patient is not really looked at as a whole but only, in my respect, I was 'a knee' but you know that knee inhabits a person and that person needs to have some sort of support, whether it's food, just being kept in touch with.'' In some cases where participants were older and their children had left home, it was mainly their partner who helped them and this could be problematic if the partner was unwell at the time or in hospital themselves. The quote below is an extreme but not isolated example of the lengths people might have to go to in order to cope: ''So then I had my leg in plaster and my wife had a severe chest infection and was in bed so I then had to, we are in a ground floor flat, so I had to then take food into her on my crutches [...] In one pocket I had a mug and in the other pocket I had a thermos flask and in my mouth I was holding a bag with things like boiled eggs, bread and butter and so on and then at one point we noticed that the bag had on it ''Help the Aged''. (laughing) We are quite versatile you know in our family.''

Study	Sleney 2014[60]
	Rehabilitation Participants who had received no physiotherapy said that they were unsure what to do to improve the strength and mobility of their injured limb or what to expect in terms of the likely completeness or speed of recovery. They were also unsure how much they should use the injured limb or when they would be able to put pressure on it, for example start playing sport again or resume a physically demanding job: ''You don't really know how much you know you have to push it yourself, how much you can bend things and force things to get it going. It was only my daughter mainly because she's got a sports science degree and has been involved with injuries herself and it was only from that experience and her experience that we knew basically what we needed to do anyway.'' 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. These participants all had fractures.

Table 80: Okonta 2011[48]

Study	Okonta 2011[48]
Aim	To explore the experience of patients with traumatic fractures treated for more than 6 months at a Doctors On Call for Service (DOCS) hospital in The Republic of Congo.
Population	Patients with fractures treated for more than 6 months at a Doctors On Call for Service (DOCS) hospital in The Republic of Congo.
Methods	Purposive sampling: details not given. 'Free-attitude' interviews transcribed verbatim in French and evaluated using content analysis. Interviews lasted 50-90 minutes. Data saturation reached after the 6th interview. For each interview a separate relative, who was the main caregiver, was interviewed to 'validate' the information given by the patient. However this failed to validate researcher's analytical interpretations. Another researcher independently listened to all the tapes and transcribed the texts for agreement on the categories used in identification of themes. It is unclear if this person triangulated the data or was the sole person analysing the data.
Themes with findings	'Most of the participants were not informed about their condition and the management plan and were therefore not part of decision making: "they did not inform me how long the nail will stay in my bone"; "if I was informed about the duration of my hospital stay I would manage my financial resources accordingly".' 'Most patients disclosed their needs and their expectations of caregivers: "we need to get information about the steps of treatment"; …"we need reassurance by doctors".

Table 81: O'Brien 2010[47]

Study	O'Brien 2010[47]
Aim	To describe patients' experience of distraction splinting and to identify key issues in patient adherence to their splint wear and exercise programme.

Study	O'Brien 2010[47]
Population	People who had sustained an intra-articular finger fracture within the previous eight years that was treated with distraction splinting at the research hospital, and who were on the database of a previous quantitative study. 18 were identified as eligible and 12 agreed to participate. 6 were women; age 24–50; 11 PIP#, 1DIP#;0.2–7.8 years post-injury; 5 ball sport, 3 fall, 2 bicycle accident, 1 crush, 1 stub.
Methods	Personal semi-structured interview conducted by first author of study; interviews completed in hand department (n=10), home (n=1) or by phone (n=1). Interviews transcribed verbatim. Two parallel analytical strategies were used for all analysis of interview transcripts. The first author conducted a manual analysis and developed preliminary findings. Transcripts were also entered into a computer data management program (nVIVO Version 2.0; QSR International, Melbourne, VIC, Australia) and were independently analysed by the second author. For the phenomenological component of this study, a systematic process for coding data was used in which specific statements were analysed and categorized into clusters of meaning that represented a phenomenon of interest. To develop an explanatory framework for predicting treatment adherence, grounded theory's method of comparison using three stages of coding was used. The first stage involved open coding: examining and comparing data, then developing coding categories that reflected the content of the data collected. The data were then reassembled into groupings based on patterns and relationships between the categories and patient report of adherence to treatment (axial coding). Finally, the central or core category was identified and described. The themes, patterns, categories, descriptive examples, and quotations identified through the analysis formed the basis of the interpretation of the findings. For both analyses, the authors compared emergent themes and categories to review thematic and conceptual consistency, and any disagreements were resolved by consensus moderation. To ensure trustworthiness of the results, the researchers also ''member checked'' the emerging themes and categories with two of the interviewees to ensure that the interpretation of the findings were an accurate representation of the participants' accounts of their experience.
Themes with findings	One participant was relieved to find that her splint was not as big as the ''banjo'' style splint that she was expecting: I was told that I would have a distraction splint. I didn't really understand what that involved so I looked it up online and the picture was some huge enormous thing and my big concern was how on earth would I manage with that, and when I learned that the splint I was going to have was a lot more compact I was relieved. Although most found the explanation of the treatment and its rationale clear and logical at the time it was given, it is worth noting how easily the individual's belief in the legitimacy of the treatment approach could be undermined by the contrary opinions of others. There were also some patients who believed that their treatment was ''experimental'' and that they were not given any other option. This appeared to be underpinned by the belief that they should have received a much simpler treatment, such as an operation to pin the fracture. "I was expecting that firstly they would put some plaster on it… They didn't explain anything [in the Emergency Department]. They were experimenting, I believe, on that day... It seemed like quite a new thing that they were going through, and I didn't really know what the reason was and why they were doing it and all that. That said, obviously they explained to an extent, but I didn't really know the technicalities of this and what other options are available and that sort of thing.

Appendix H: GRADE tables

H.1 Open fractures

H.1.1 Arterial shunts

Table 82: Clinical evidence profile: Shunt, definitive skeletal stabilisation, definitive vascular repair versus definitive vascular repair and definitive skeletal stabilisation

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Shunt	Immediate repair	Relative (95% CI)	Absolute	Quality	Importance
Mortality												
1	Observational	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious imprecision[b]	none	0/5 (0%)	1/17 (5.9%)	OR 0.27 (0 to 29.45)	42 fewer per 1000 (from 59 fewer to 589 more)	VERY LOW	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Deep infection												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Amputation												
1	Observational	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious imprecision[b]	none	1/5 (20%)	5/17 (29.4%)	RR 0.68 (0.1 to 4.55)	94 fewer per 1000 (from 265 fewer to 1000 more)	VERY LOW	CRITICAL
Compartment syndrome												
1	Observational	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious imprecision[b]	none	0/5 (0%)	2/17 (11.8%)	OR 0.26 (0.01 to 7.61)	84 fewer per 1000 (from 116 fewer to 386 more)	VERY LOW	CRITICAL
Other vascular surgery												
1	Observational	Very	No serious	No serious	Very serious	none	1/5	7/17	RR 0.49 (0.08 to	210 fewer per 1000	VERY	CRITICAL

		serious[a]	inconsistency	indirectness	imprecision[b]		(20%)	(41.2%)	3.07)	(from 379 fewer to 852 more)	LOW	
Length of stay												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Hospitalisation												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

(a) Non-randomised study. Reasonable matching for key and other main confounders but some residual confounding very likely
(b) 95% CIs crossed both MIDs, making the point estimate very imprecise

H.1.2 MDT

Table 83: Clinical evidence profile: Combined orthoplastic versus non-combined

Quality assessment							Proportion (%) with an event or mean(SD) (n)		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Combined**	**Not combined**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Amputations												
1 Naique 2006	Retrospective cohort	Very serious risk of bias[a]	No serious inconsistency	No serious indirectness	Very serious imprecision[b]	None	1/25 (4%)	2/47 (4.3%)	RR 0.94 (0.09 to 9.87)	3 fewer per 1000 (from 39 fewer to 377 more)	VERY LOW	CRITICAL
Flap failure												
1 Naique 2006	Retrospective cohort	Very serious risk of bias[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	None	0/25 (0%)	6/47 (12.8%)	Peto OR 0.19 (0.03 to 1.1)	130 fewer per 1000 (from 240 fewer to 20 less)	VERY LOW	CRITICAL

Quality assessment							Proportion (%) with an event or mean(SD) (n)		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Combined**	**Not combined**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Deep infection												
1 Naique 2006	Retrospective cohort	Very serious risk of bias[a]	No serious inconsistency	No serious indirectness	Very serious imprecision	None	1/25 (4%)	5/47 (10.6%)	RR 0.38 (0.05 to 3.04)	66 fewer per 1000 (from 101 fewer to 216 more)	VERY LOW	CRITICAL
Enneking limb score (Better indicated by lower values)												
1 Naique 2006	Retrospective cohort	Very serious risk of bias[a]	No serious inconsistency	No serious indirectness	Serious imprecision[b]	None	75(15.9) (25)	74(15.9) (47)	-	MD 1 higher (6.71 lower to 8.71 higher)	VERY LOW	CRITICAL
Time to definitive cover												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Unplanned complexity of soft tissue cover												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Length of stay												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Further unplanned surgery												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Return to normal activities												
0	-	-	-	-	-	-	-	-	-	-	-	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 in this non-randomised study were likely selection bias, performance bias, and detection bias.

(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 both MIDs were crossed by one or both of the 95% CIs. Default MIDs were set at RRs of 0.75 and 1.25.

H.1.3 Optimal timing of debridement

Table 84: Clinical evidence profile: Early versus delayed debridement in open fractures (all ORs are MVA-adjusted)

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Early debridement	Delayed debridement	Relative (95% CI)	Absolute	Quality	Importance
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Deep surgical site infection (OR) ≤ 6 hours versus > 6 hours												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	4/76 (5.3%)	1/35 (2.9%)	OR 1.76 (0.03 to 109.26)	21 more per 1000 (from 28 fewer to 734 more)	VERY LOW	CRITICAL
Deep surgical site infection (OR) ≤ 8 hours versus >8 hours												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	10/115 (8.7%)	10/100 (10%)	OR 0.95 (0.36 to 2.51)	5 fewer per 1000 (from 62 fewer to 118 more)	VERY LOW	CRITICAL
Deep surgical site infection (RR) < 8 hours versus > 8 hours												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	35/328 (10.7%)	17/87 (19.5%)	RR 0.49 (0.25 to 0.98)	100 fewer per 1000 (from 4 fewer to 147 fewer)	VERY LOW	CRITICAL
Deep surgical site infection (OR) later versus earlier debridement												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	NA	NA	0R 0.97 (0.90 to 1.06)	Not estimable	VERY LOW	CRITICAL
Amputation - Day 0 versus Day 1												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	16/3093 (0.52%)	19/882 (2.2%)	OR 0.26 (0.12 to	16 fewer per 1000 (from 9	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Early debridement**	**Delayed debridement**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
									0.56)	fewer to 19 fewer)		
Amputation - Day 0 versus Day 2												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	16/3093 (0.52%)	9/401 (2.2%)	OR 0.26 (0.10 to 0.66)	17 fewer per 1000 (from 8 fewer to 20 fewer)	VERY LOW	CRITICAL
Amputation - Day 0 versus Days 3 and 4												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	16/3093 (0.52%)	10/394 (2.5%)	OR 0.25 (0.11 to 0.55)	19 fewer per 1000 (from 11 fewer to 23 fewer)	VERY LOW	CRITICAL
Amputation - Day 0 versus Day 5 or greater												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	16/3093 (0.52%)	38/600 (6.3%)	OR 0.09 (0.05 to 0.17)	57 fewer per 1000 (from 52 fewer to 60 fewer)	VERY LOW	CRITICAL
Amputation - Day 0 versus timing not specified												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	16/3093 (0.52%)	7/2190 (0.32%)	OR 1.64 (0.67 to 3.98)	2 more per 1000 (from 1 fewer to 9 more)	VERY LOW	CRITICAL
Return to normal activities												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Unplanned reoperation												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Functional outcomes												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Length of stay												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Early debridement	Delayed debridement	Relative (95% CI)	Absolute		
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

(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 in the weighted average number of serious methodological limitation across studies were two or more. Methodological limitations in this non-randomised study were likely selection bias, performance bias, and detection bias.

(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 both MIDs were crossed by one or both of the 95% CIs. Defaults MIDs were set at RRs/ORs of 0.75 and 1.25.

H.1.4 Fixation

Definitive fixation and immediate cover versus definitive fixation and staged cover

Table 85: Clinical evidence profile: RCT – definitive fixation and immediate cover (primary) versus definitive fixation and staged cover (delayed) of open fractures

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Primary cover	Delayed cover	Relative (95% CI)	Absolute		
Deep infection- all antibiotics												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/40 (0%)	2/36 (5.6%)	Peto OR 0.12 (0.01 to 1.94)	49 fewer per 1000 (from 55 fewer to 47 more)	VERY LOW	CRITICAL

(a) Very serious risk of selection bias, due to no reporting of allocation sequence and limited reporting of baseline characteristics in each group, higher attrition than event rates and no blinding for patients , health care professionals and outcome assessors in terms of the early/delayed grouping.

(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 both MIDs were crossed by one or both of the 95% CIs. Default MIDs were set at 0.75 and 1.25.

Table 86: Clinical evidence profile: cohort studies –immediate cover (primary) versus staged cover (delayed) of open fractures

Quality assessment	Raw data	Adjusted effects	Quality	Importance

No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Primary cover**	**Delayed cover**	**Relative (95% CI)**	**Absolute**		
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Deep infection												
3	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	8/112	21/113	RR: 0.37 (0.18 to 0.74)	112 fewer per 1000 (from 36 fewer to 146fewer)	VERY LOW	CRITICAL
Amputation												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/27	3/22	RR: 0.27 (0.03 to 2.43)	99 fewer per 1000 (from 132 fewer to 194 more)	VERY LOW	CRITICAL
Flap failure												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	None	None	0/28	7/29	Adjusted OR (95% CIs): 0.09 (0.01 to 0.59).	-	VERY LOW	CRITICAL
Length of stay												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Return to normal activities												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Further unplanned surgery												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	-	-	Adjusted OR (95% CIs) [estimated from indirect treatment comparisons methods]: 0.62 (0.23 to 1.70)	-	VERY LOW	IMPORTANT

(a) Very serious risk of selection bias, due non-randomisation, with inevitable residual confounding. Although multivariable analysis was carried out, there were insufficient events per variable for validity of analyses in two of the cohorts. Performance bias was also present.

(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 both MIDs were crossed by one or both of the 95% CIs. Default MIDs were set at 0.75 and 1.25.

Definitive fixation and immediate cover versus staged fixation and staged cover

Table 87: Clinical evidence profile: cohort studies –immediate cover (primary) versus staged cover (delayed) of open fractures

Quality assessment							Raw data		Adjusted effects			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Primary cover**	**Delayed cover**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Deep infection												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	None	None	0/14	4/15	Peto OR 0.11 (0.01 to 0.91)	270 fewer per 1000 (from 500 fewer to 30 fewer)	VERY LOW	CRITICAL
Flap failure												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Not estimable	None	0/14	0/14	Not estimable	-	VERY LOW	CRITICAL
Number of further operations (mean and range given)												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Unclear	None	1.6 (1-3)	3.9 (2-7)	-	-2.3 (CIs not estimable)	VERY LOW	IMPORTANT
Return to weight bearing (months) (mean and range given)												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Unclear	None	5 (3-8)	9.6 (3.5 to 17))	-	-4.6 (CIs not estimable)	VERY LOW	IMORTANT
Amputation												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Not estimable	None	0/14	0/15	Not estimable	Not estimable	VERY LOW	CRITICAL
Length of stay												

Quality assessment							Raw data		Adjusted effects		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Primary cover	Delayed cover	Relative (95% CI)	Absolute		
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

(a) Very serious risk of selection bias, due non-randomisation, with inevitable residual confounding. Although multivariable analysis was carried out, there were insufficient events per variable for validity of analyses in two of the cohorts. Performance bias was also present.

(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 both MIDs were crossed by one or both of the 95% CIs. Default MIDs were set at 0.75 and 1.25.

H.1.5 Cover

Immediate versus 3 days

Table 88: Clinical evidence profile: immediate versus 3 days

Quality assessment							Raw data		Adjusted effects		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Primary cover	Delayed cover	Relative (95% CI)	Absolute		
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Deep infection												
2	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	None	Very serious	0/26	5/25	Peto OR 0.11 (0.02 to 0.71)	200 fewer per 1000 (from 380 fewer to 10 fewer)	VERY LOW	CRITICAL
Flap failure												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Not estimable	None	0/14	0/14	Not estimable	-	VERY LOW	CRITICAL
Number of further operations (mean and range given)												
1	Cohort	Very	No serious	No serious	Unclear	None	1.6 (1-3)	3.9 (2-7)	-	-2.3 (CIs not estimable)	VERY LOW	CRITICAL

		serious[a]	inconsistency	indirectness								
Amputation												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Not estimable	None	0/14	0/15	Not estimable	Not estimable	VERY LOW	CRITICAL
Length of stay												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Superficial wound infection												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Return to weight bearing (months) (mean and range given)												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Unclear	None	5 (3-8)	9.6 (3.5 to 17))	-	-4.6 (CIs not estimable)	VERY LOW	IMORTANT

(a) Very serious risk of selection bias, due non randomisation, with inevitable residual confounding. Although multivariable analysis was carried out, there were insufficient events per variable for validity of analyses in two of the cohorts. Performance bias was also present.

(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 both MIDs were crossed by one or both of the 95% CIs. Default MIDs were set at 0.75 and 1.25.

Immediate versus 7 days

Table 89: Clinical evidence profile: immediate versus 7 days

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Primary cover**	**Delayed cover**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Deep infection (RCT)												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/40 (0%)	2/36 (5.6%)	Peto OR 0.12 (0.01 to 1.94)	49 fewer per 1000 (from 55 fewer to 47 more)	VERY LOW	CRITICAL
Deep infection (cohort)												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	5/27	6/22 (27.3%)	RR: 0.68 (0.24 to 1.93)	87 fewer per 1000 (from 207 fewer to 254 more)	VERY LOW	CRITICAL

Amputation (cohort)												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/27	3/22 (13.6%)	RR: 0.27 (0.03 to 2.43)	99 fewer per 1000 (from 132 fewer to 194 more)	VERY LOW	CRITICAL
reoperation												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
function												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Flap failure												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Length of stay												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Superficial wound infection												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Return to normal activities												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

(a) Very serious risk of selection bias, due to no reporting of allocation sequence and limited reporting of baseline characteristics in each group, higher attrition than event rates and no blinding for patients , health care professionals and outcome assessors in terms of the early/delayed grouping.

(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 both MIDs were crossed by one or both of the 95% CIs. Default MIDs were set at 0.75 and 1.25.

Immediate versus more than 7 days

Table 90: Clinical evidence profile: immediate versus more than 7 days

Quality assessment							Raw data		Adjusted effects			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Primary cover**	**Delayed cover**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Deep infection												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

amputation												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
function												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Flap failure												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Return to normal activities												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Hospital stay (days) (mean and range given)												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Unclear	None	8.6(3-20)	15.4 (4-52)	-	-6.8 (CIs not estimable)	VERY LOW	IMPORTANT
Infection (not specified as deep)												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious imprecision	None	2/46	1/49	2.13 (0.2 to 22.71)	23 more per 1000 (from 16 fewer to 443 more)	VERY LOW	IMPORTANT

(a) Very serious risk of selection bias, due to no reporting of allocation sequence and limited reporting of baseline characteristics in each group, higher attrition than event rates and no blinding for patients , health care professionals and outcome assessors in terms of the early/delayed grouping.

More than 14 days versus less than 3 days

Table 91: Clinical evidence profile: more than 14 days versus less than 3 days

Quality assessment							Raw data		Adjusted effects			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Primary cover**	**Delayed cover**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Deep infection												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	None	None	-	-	Adjusted OR 7.41 (1.56 to 35.18)	-	VERY LOW	CRITICAL
Osteomyelitis												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[B]	None	-	-	Adjusted OR 10.53 (1.11 to 99.83)	-	VERY LOW	CRITICAL

Flap take-backs												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[B]	None	-	-	Adjusted OR 11.5 (1.19 to 111.51)	-	VERY LOW	CRITICAL
amputation												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
function												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Flap failure												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Length of hospital stay												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Superficial wound infection												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Return to normal activities												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

(a) Very serious risk of selection bias, due non randomisation, with inevitable residual confounding. Although multivariable analysis was carried out, there were insufficient events per variable for validity of analyses.

(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 both MIDs were crossed by one or both of the 95% CIs. Default MIDs were set at 0.75 and 1.25.

More than 5 days versus less than 5 days

Table 92: Clinical evidence profile: more than 5 days versus less than 5 days

Quality assessment							Raw data		Adjusted effects			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Primary cover**	**Delayed cover**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Deep infection												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	None	None	-	-	Adjusted OR 7.39 (2.54 to 27.04)	-	VERY LOW	CRITICAL

function												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Flap failure												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
amputation												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Length of hospital stay												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Superficial wound infection												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Return to normal activities												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

Timing as a continuous outcome

Table 93: Clinical evidence profile: effects of delay on outcomes in two discrete sub-groups defined by time of cover

Quality assessment							Raw data		Adjusted effects			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Primary cover	Delayed cover	Relative (95% CI) Odds of increment (day) rise in cover delay	Absolute	Quality	Importance
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Deep infection in those with cover from 1-7 days												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	None	None	-	-	Adjusted OR 0.94 (0.65 to 1.36)	-	VERY LOW	CRITICAL
Deep infection in those with cover >7 days												
1	Cohort	Very serious[a]	No serious inconsistency	No serious indirectness	Serious imprecision[B]	None	-	-	Adjusted OR 1.155 (1.03 to 1.29)	-	VERY LOW	CRITICAL
Amputation												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
reoperation												

0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
function												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Falp failure												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Length of stay												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Superficial wound infection												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Return to normal activities												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

(a) Very serious risk of selection bias, due non randomisation, with inevitable residual confounding.
(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 both MIDs were crossed by one or both of the 95% CIs. Default MIDs were set at 0.75 and 1.25.

H.1.6 Definitive dressings after debridement

Table 94: Clinical evidence profile: NPWT versus standard dressing

Quality assessment							No. of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**NPWT**	**Standard dressing**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life at 3 months (measured with: SF36 physical component; range of scores: 0-100; Better indicated by higher values)												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	35	23	-	MD 11.4 higher (2.67 to 20.13 higher)	VERY LOW	CRITICAL
Deep infection at 11 weeks												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	2/35 (5.7%)	30.4%	RR 0.19 (0.04 to 0.83)	246 fewer per 1000 (from 52 fewer to 292 fewer)	VERY LOW	CRITICAL
Wound healed within 30 days (assessed with: appearance of 100% granulation tissue over the wound)												

Quality assessment							No. of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**NPWT**	**Standard dressing**	**Relative (95% CI)**	**Absolute**		
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	25/25 (100%)	52%	RR 1.89 (1.3 to 2.74)	463 more per 1000 (from 156 more to 905 more)	LOW	CRITICAL
function												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Wound infection												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Reoperation / amputation												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Wound healing												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Tissue necrosis												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Return to normal activities												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

(a) The majority of evidence was from studies at very high risk of bias
(b) Confidence interval crossed one MID
(c) Confidence interval crossed both MIDs

H.2 Pelvic fractures

H.2.1 Pelvic haemorrhage control

Table 95: Clinical evidence profile: TAE versus LAP

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**LAP**	**TAE**	**Relative (95% CI)**	**Absolute**		
Mortality-Odds Ratio (follow-up 6 years; assessed with: Japan Trauma Data Bank)												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	50/123	52/194	OR 1.13 (0.63 to 2.03)[c]	NA	VERY LOW	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Re-bleeding												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Further intervention												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Volume of blood lost / number of transfusions												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Time to definitive control												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Need for rescanning												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Adverse events												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
pain												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Return to normal activities												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Length of stay												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

(a) Downgraded for selection and attrition bias
(b) Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MID's.
(c) Adjusted for age, gender, number of co-morbidities, systolic blood pressure (SBP),Glasgow coma scale (GCS), injury Severity Score (ISS) and abbreviated injury scale (AIS)

H.3 Pilon fractures

H.3.1 Pilon early fixation

MIXED OPEN/CLOSED STRATUM

Table 96: Clinical evidence profile: Definitive fixation within 24 hours versus temp fixation plus definitive fixation at more than 7 days

Quality assessment							No. of patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Definitive fixation within 24 hours	Temporary fixation plus definitive fixation at >7 days	Relative (95% CI)	Absolute	Quality	Importance
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Number of surgeries (Better indicated by lower values)												
1	Observational	Very serious[a]	No serious inconsistency	Serious indirectness[b]	Serious[c]	None	1.5(0.738)[20]	2.1(0.738)[26]	-	MD 0.6 lower (1.03 to 0.17 lower)	VERY LOW	CRITICAL
Function - AOFAS (Better indicated by higher values)												
1	Observational	Very serious[a]	No serious inconsistency	Serious indirectness[b]	Serious[c]	None	77.1(14.4)[20]	72.4(21)[26]	-	MD 4.7 higher (5.55 lower to 14.95 higher)	VERY LOW	CRITICAL
Function - SMFA (Better indicated by lower values)												
1	Observational	Very serious[a]	No serious inconsistency	Serious indirectness[b]	Serious[c]	None	25.8(14.4)[20]	2.1(0.738)[26]	-	MD 8.5 lower (18.41 lower to 1.41 higher)	VERY LOW	CRITICAL
People with unplanned surgery												
1	Observational	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c]	None	0/42 (0%)	1/13 (7.7%)	OR 0.01 (0 to 1.47)	76 fewer per 1000 (from 77	VERY LOW	CRITICAL

										fewer to 32 more)		
Amputation												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Deep infection												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Pain												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Return to normal activities												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Return to normal activities												
1	Observational	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[c]	None	35/42 (83.3%)	12/13 (92.3%)	RR 0.9 (0.73 to 1.11)	92 fewer per 1000 (from 249 fewer to 102 more)	VERY LOW	IMPORTANT
Hospitalisation												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

(a) Risk of bias very serious because of non-randomised design and a lack of adjustment for important confounders.
(b) Indirectness serious because intervention may have been given at a later time than specified in the protocol.
(c) Imprecision serious if CIs crossed one MID and very serious if CIs crossed both MIDs

Table 97: Clinical evidence profile: temporary fixation plus definite fixation at more than 24 hours to 7 days versus temporary fixation and definitive fixation at more than 7 days

Quality assessment							No. of patients		Effect			
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Temporary fixation plus definitive fixation at >24 hrs to 7 days versus temporary fixation and definitive fixation at >7 days**	**Control**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Deep infection												

1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	1/16 (6.3%)	0/63 (0%)	OR 139.42 (1.06 to 18295.53)	60 more per 1000 (from 70 less to 200 more)	VERY LOW	CRITICAL
Unplanned surgery												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	4/16 (25%)	4/63 (6.3%)	RR 3.94 (1.1 to 14.06)	187 more per 1000 (from 6 more to 829 more)	VERY LOW	CRITICAL
Foot function index (Better indicated by lower values)												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	0.4(0.305)[16]	0.23|(0.305)[63]	-	MD 0.17 higher (0 to 0.34 higher)	VERY LOW	CRITICAL
Musculoskeletal function assessment score (Better indicated by lower values)												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	34(23.5)[16]	20.9(23.5)[63]	-	MD 13.1 higher (0.21 to 25.99 higher)	VERY LOW	CRITICAL
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
amputation												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
function												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
pain												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
hospitalisation												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Return to normal activities												

0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Length of stay												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

(a) Risk of bias very serious because of non-randomised design and a lack of adjustment for important confounders.
(b) Imprecision serious as CIs crossed one MID

CLOSED STRATUM

Table 98: Clinical evidence profile: temporary fixation plus definite fixation at more than 24 hours to 7 days versus temporary fixation and definitive fixation at more than 7 days

Quality assessment							No. of patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Temporary fixation plus definitive fixation at >24 hrs to 7 days	temporary fixation and definitive fixation at >7 days	Relative (95% CI)	Absolute	Quality	Importance
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Deep infection												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	0/23 (0%)	1/23 (4.4%)	OR 0.14 (0 to 6.82)	38 fewer per 1000 (from 44 less to 195 more)	VERY LOW	CRITICAL
Function												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Not estimable	None	0/23 (0%)	0/23 (0%)	Not estimable	Not estimable	VERY LOW	CRITICAL

amputation											
0	-	-	-	-	-	-	-	-	-	-	CRITICAL
function											
0	-	-	-	-	-	-	-	-	-	-	CRITICAL
pain											
0	-	-	-	-	-	-	-	-	-	-	CRITICAL
hospitalisation											
0	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Return to normal activities											
0	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Hospital stay											
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	7.6(2.6)[23]	15.2|(4.2)[23]	-	MD 7.6 lower (9.62 to 5.58 lower)	VERY LOW	IMPORTANT

(c) Risk of bias very serious because of non-randomised design
(d) Imprecision serious if CIs crossed one MID and very serious if CIs crossed 2 MIDs

H.3.2 Pilon fixation

Table 99: Clinical evidence profile: Staged ORIF versus external fixation

Quality assessment							No. of patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Staged ORIF	External fixation	Relative (95% CI)	Absolute	Quality	Importance
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

Surgical site infection												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	7/46 (15.2%)	2.5%	RR 5.29 (0.97 to 28.8)	107 more per 1000 (from 1 fewer to 695 more)	VERY LOW	CRITICAL
Osteomyelitis												
2	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	4/46 (8.7%)	0%	OR 8.52 (1.15 to 63.01)[3]	90 more per 1000 (from 0 more to 180 more)	VERY LOW	CRITICAL
Ankle fusion												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	0/20 (0%)	5.3%	OR 0.14 (0.0 to 7.18)[3]	45 fewer per 1000 (from 53 fewer to 234 more)	VERY LOW	CRITICAL
Unplanned further surgery (Continuous) (Better indicated by lower values)												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	19	20	-	MD 1.17 higher (0.18 to 2.16 higher)	VERY LOW	CRITICAL
Unplanned further surgery (Dichotomous)												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	9/19 (47.4%)	20%	RR 2.37 (0.87 to 6.42)	274 more per 1000 (from 26 fewer to 1000 more)	VERY LOW	CRITICAL
Wound breakdown												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	6/19 (31.6%)	0%	OR 10.63 (1.91 to 59.23)[3]	320 more per 1000 (from 10 more to 520 more)	LOW	CRITICAL
Amputation												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	3/19 (15.8%)	0%	OR 8.73 (0.85 to 89.36)[3]	160 more per 1000 (from 0 more to 340 more)	LOW	CRITICAL
Return to normal activities												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

(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 limitations across studies were two or more.

(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 both MIDs were crossed by one or both of the 95% CIs. Default MIDs were set at RRs of 0.75 and 1.25.

(c) Peto odds ratio.

Table 100: Clinical evidence profile: Staged (temporary external fixation) ORIF versus external fixation

Quality assessment							Proportion (%) with an event or mean (SD)[n]		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Staged ORIF	External fixation	Relative (95% CI)	Absolute	Quality	Importance

Health-related quality of life (follow-up 12 months; Better indicated by lower values)												
1	Observational studies	Very seriousa	No serious inconsistency	Serious[b]	Serious[c]	None	49.7 (30.1) [27]	25.5 (18) [18]	-	MD 24.2 higher (10.13 to 38.27 higher)	VERY LOW	CRITICAL
Surgical site infection												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Ankle fusion												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Unplanned further surgery												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Wound breakdown												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Return to normal activities												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

(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 limitations across studies were two or more. Methodological limitations in these non-randomised studies were likely selection bias, performance bias and detection bias.

(b) Staged ORIF rather than ORIF as per the protocol. Temporary external fixation was used to wait for the soft tissue swelling to decrease.

(c) 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 both MIDs were crossed by one or both of the 95% CIs. Default MIDs were set at RRs of 0.75 and 1.25.

H.4 Other

H.4.1 Detecting compartment syndrome

Table 101: Clinical evidence profile: continuous compartment pressure monitoring versus no compartment pressure monitoring

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Monitored	Unmonitored	Relative (95% CI)	Absolute		
Mortality												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Sensory loss (follow-up mean 8 months)												
1	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	5/71 (7%)	6%	RR 1.18 (0.36 to 3.92)	11 more per 1000 (from 38 fewer to 175 more)	VERY LOW	CRITICAL
Contracture (follow-up mean 8 months)												
1	Randomised trials	Serious[c]	No serious inconsistency	No serious indirectness	Very serious[b]	None	1/71 (1.4%)	3.6%	RR 0.39 (0.04 to 3.71)	22 fewer per 1000 (from 35 fewer to 98 more)	VERY LOW	CRITICAL
Neurological dysfunction												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Muscle/joint contracture												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
amputation												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

function												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Deep infection												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Neuropathic ulcers												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Un`planned surgery												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Missed compartment syndrome												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Length of stay												
0	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

(a) The majority of evidence was from studies at very high risk of bias
(b) Confidence interval crossed both MIDs
(c) The majority of evidence was from studies at high risk of bias

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