TABLE E-1 Study Outcomes*

Authors	Year	Time from Injury to Debridement *(hr)*	Infection Rate for Early and Late Debridement *(%)*	Definition of Infection	Antibiotics Given	Timing of Antibiotics	Initial Procedures	Type of Definitive Fixation	Wound Management Strategy
Dellinger et al.[33]	1988	Infected, 5.0. Non-infected, 5.7	NR	Cellulitis: clinical symptoms, resolved with antibiotic treatment without opening the wound. Superficial wound infection: above the fascia, treatment with antibiotics + opening the wound, without exposure of underlying bone and/or hardware. Deep infection: below the muscular fascia, antibiotics with operative management (acute: <4 wk duration, chronic: >4 wk duration)	Seattle site, 3 arms: (1) cefonicide sodium 2 g IV × 1; (2) cefonicide sodium 2 g IV × 1, followed by cefonicide sodium 1 g IV every 24 hr for 5 d; (3) cefamandole nafate 2 g IV × 1, followed by cefamandole nafate 1 g IV every 6 hr for 5 d. Calgary site: cefamandole nafate 2 g IV × 1 + cefamandole nafate 1 g IV × 1 in PACU, followed by randomization to (1) no additional antibiotics, or (2) cefamandole nafate 1 g IV	All received antibiotics within 12 hr of injury. Mean interval from injury to antibiotics: 2.1 ± 1.5 hr (range, 0.2-9 hr)	Vascular repair (n = 12), fasciotomy (n = 6), “at least some” internal fixation (n = 118), internal + external fixation (n = 17), external fixation only (n = 48), casting/splinting/traction only (n = 80)	NR	Traumatic wounds were left open at initial procedure; closed later by delayed primary closure, skin grafts, flaps, or secondary intention

					every 6 hr for 3 d. Stated total for both sites: (1) 2 doses of cefamandole, n = 57; (2) 1 d of cefonicide, n = 26; (3) 3 d of cefamandole or cefazolin, n = 65; (4) 4-5 d of antibiotics, n = 92				
Patzakis and Wilkins[32]	1989	12	6.8, 7.1	Clinical suspicion of wound infection + positive Gram stain on intraoperative culture	(1) Penicillin IV + streptomycin IM for 10 d, (2) cephalothin IV for 10 d, (3) cephalothin IV for 5 d + cephalexin orally for 5 d, (4) cefamandole IM + tobramycin IM for 3-5 d	Started within 3 hr: n = 364 (infection in 17, 4.7%). Treatment >3 hr: n = 661 (infection in 49, 7.4%)	Primary internal fixation, n = 22 (infection in 2, 9%)	NR	Primary wound closure (infection in 10.6%), delayed wound closure (infection in 13.4%), or partial wound closure (infection in 9.0%). No significant differences among groups. A portion of the patients were randomized to primary or secondary closure
Bednar and Parikh.[20]	1993	6	9, 3.4	Deep infection: cellulitis, purulent drainage, or	G-A types I, II, and IIIA: Ancef. Types IIIB and IIIC:	NR	Plating (n = 45), IMN (n = 29), external fixation (n = 8)	NR	NR

				culture-positive osteomyelitis presenting >6 wk after injury with no evidence of primary infection	Ancef + gentamicin or tobramycin. Given for 48 hr				
Kindsfater and Jonassen[21]	1995	5	7, 38	Osteomyelitis or positive bone cultures	Cefazolin or cephalothin 1 g IV given within 3 hr of injury + addition of aminoglycoside (not given within 3 hr of injury) for 48-72 hr. Antibiosis adjusted on basis of operating room cultures once available	NR	Cast immobilization (n = 8), plate fixation (n = 8), external fixation (n = 15), reamed IMN (n = 4), unreamed IMN (n = 12)	Debrided >5 hr (late): cast immobilization (n = 4), plate fixation (n = 1), external fixation (n = 15), reamed IMN (n = 4), unreamed IMN or flexible IMN (n = 8). Debrided <5 hr (early): cast immobilization (n = 4), external fixation (n = 7), unreamed IMN (n = 4)	G-A type II: primary closure (n = 4), delayed primary closure (n = 16), STSG (n = 3), secondary intention (n = 2; one of these developed osteomyelitis and necessitated fasciocutaneous flap). Type IIIA: delayed primary closure (n = 7), STSG (n = 6). Type IIIB/C: free flap (n = 6), STSG (n = 2), BKA (n = 1)
Ikem et al.[34]	2001	Infected: 7.8 for tibia and 13.7 for femur. Non-infected: 6.1 for tibia and 5.1 for femur	Significantly different, p = 0.008	Delayed union: fracture-healing at 4-6 mo. Nonunion: no union by 8 mo	Ampicillin, cloxacillin, and gentamicin for 72 hr	NR	Fasciotomy, partial fibulectomy, and bone-grafting were performed in all open tibial and fibular fractures. Tibia: above the knee plaster cast (n = 39), Steinmann pins incorporated into	NR	Primary closure, delayed primary closure

							plaster casting, external fixation. Femur: skeletal traction, external fixation		
Harley et al.[30]	2002	8	Tibia and fibula: 8, 7. Femur: 1, 3	Deep infection: purulent drainage or osteomyelitis after definitive wound closure, diagnosed by deep cultures. Nonunion: fracture requiring an additional stabilization procedure because of radiographic evidence of nonunion or failure of primary fixation	First-generation cephalosporin IV for 48 hr. Aminoglycoside added for G-A type III or if definitive treatment was carried out after >8 hr. Penicillin was added on basis of wound characteristics	NR	Surgeon preference. IMN, internal plate fixation, external fixation, percutaneous pinning	NR	Regional flap transfers (n = 12), free flap (n = 9)
Khatod et al.[22]	2003	6	19, 19	Clinical suspicion + positive cultures. Pin-track infections excluded	Cefazolin IV (all but one patient), gentamicin for G-A types II and III. Penicillin added for farm or marine injuries for 48-72 hr	NR	Primary amputation, casting, external fixation, IMN, plate and screw fixation	NR	Wounds initially were left open. Delayed primary closure, skin grafting, or flap coverage was obtained at the second debridement as indicated
Ashford et al.[23]	2004	6	17, 11	NR	Flucloxacillin 1 g IV every 6 hr or cefuroxime	NR	External fixation (n = 23), primary amputation (n = 2), unreamed IMN (n =	NR	Primary closure (n = 4) to free flaps, secondary

					750 mg IV every 8 hr + gentamicin 240 mg IV daily		2). Halfway through study the unreamed tibial nail was introduced to the practice and used in place of casting		intention (n = 18), prophylactic fasciotomy (n = 2)
Spencer et al.[24]	2004	6	10.1, 10.9	Clinical signs (erythema, swelling, pain) and confirmation with deep cultures obtained either at secondary procedure to treat infection/nonunion or from discharging wounds	Cephradine 1 g IV ± metronidazole	All patients received antibiotics within 4 hr of injury	IMN (n = 35 of lower extremity), ORIF (n = 43), external fixation (n = 15), plaster of Paris casting and Kirschner wires (distal radial fractures) (n = 25)	NR	Wounds were left open initially, then referrals to another facility for plastic surgery closure was made after initial debridement or as soon as sufficient patient stability was obtained
Charalambous et al.[25]	2005	6	28.8, 25.6	Superficial infection: cellulitis or pus involving the soft-tissue area of the traumatic wound in the absence of clinical or radiographic features of osteomyelitis. Deep infection: osteomyelitis, diagnosed by the development of a chronic discharging sinus or radiologic	NR	NR	Manipulation and casting with or without traction (n = 120), external fixation (n = 116), internal fixation (n = 147 including reamed IMN [n = 75], unreamed IMN [n = 53])	NR	NR

				evidence, that necessitated surgical bone debridement. Pin-site infections were excluded. A positive culture was not necessary for diagnosis					
Noumi et al.[26]	2005	6	5.3, 2.9	Deep infection: infection below the muscular fascia. Fracture-healing: determined radiographically. Nonunion: lack of clinical or radiographic healing 12 mo after injury, requiring a second procedure	Cephalosporin, ± aminoglycoside (G-A type III), for 72 hr	NR	Surgeon preference. Immediate IMN (reamed and unreamed), skeletal traction, external fixation	Those who had initial skeletal traction or external fixation received delayed IMN, reamed and unreamed. G-A types I and II underwent a closed technique IMN, and III underwent an open technique	G-A types I and II: immediate skin closure, exclusive of those debrided >6 hr from injury. Type III: delayed closure (delayed primary closure, delayed skin grafts, or local skin flaps)
Al-Arabi et al.[27]	2007	6	7.8, 9.6	Deep infection: clinical diagnosis of swelling, erythema, discharging wounds, pain, ± culture results. Cultures were obtained either at secondary procedures for nonunion or	Cefuroxime 1 g IV (+ metronidazole 500 mg IV for heavily contaminated wounds)	Patients placed into groups of <2, <4, <6, <8, <12, or >12 hr. Two patients received antibiotics >24 hr (also	Surgeon preference	NR	Primary or delayed wound closure (with return to the operating room at 48 hr). Those requiring plastic surgery for wound cover were transferred to

				from discharging wounds. Superficial infections were recorded but not included in the analysis as "infected" cases		delayed debridement time >24 hr); both became infected			an outside center for definitive management
Reuss and Cole.[31]	2007	8	10, 8	Osteomyelitis or deep infection: by clinical examination after definitive closure procedures requiring operative intervention or irrigation and debridement ± removal of hardware. Nonunion: fracture that had radiographic evidence of nonunion and required operative intervention >6 mo after ultimate fixation	Cefazolin (+ aminoglycoside for highly contaminated wounds) for 36 hr	NR	External fixation exchanged later with IMN (n = 33), reamed IMN (n = 46), splint + ORIF exchanged later with IMN (n = 2)	All patients who initially received external fixation or splint/ORIF were converted to IMN	Primary closure and fasciocutaneous flaps
Sungaran et al.[28]	2007	0-6, 6-12, and 12-24	7.7, 1.3, 0	Infection: prolongation or reinitiation of antibiotic therapy because of wound changes, or the requirement for further surgical	NR	NR	NR	NR	NR

				debridement for cellulitis, purulent collections, chronic infections, or osteomyelitis					
Tripuraneni et al.[29]	2008	6, 6-12, 12-24, and >24	10.8, 9.5, 5.6, 0	Infection: positive intraoperative tissue or fluid culture, or clinical evidence of purulence requiring operative debridement even with negative cultures	Cefazolin (+ 1 dose of gentamicin for grossly contaminated wounds) for 24-48 hr postoperatively following the definitive procedure	NR	IMN (n = 167), external fixation (n = 30), long leg cast (n = 10), Steinmann pins + long leg cast (n = 3). Five fractures initially treated with an external fixator were later converted to a plate and screw construct (1) or intramedullary nail (4).	Five patients initially treated with an external fixator were converted to definitive fixation by ORIF (n = 1) or IMN (n = 4)	NR
Pollak et al.[19]	2010	<5, 5-10, and >10	28, 29.1, 25.8	Any infection: diagnosis of infection treated on an inpatient or outpatient basis. Major infection: diagnosis of infection or osteomyelitis resulting in rehospitalization. External fixator pin-track infections were included only if they involved the open fracture site. Repeat debridements for necrosis were	NR	Time to arrival at definitive trauma center, maximum of 24 hr. Patients with prolonged pre-hospital time >2 hr were significantly more likely to develop infection. Patients transferred	IMN, external fixation, ORIF	NR	All wounds were initially left open and had a repeat debridement

				defined as infection only if given the diagnosis by the attending surgeon. Culture results were assessed if available		from initial receiving institutions to the definitive trauma center <3 hr were significantly less likely to have infection than those transferred 11-24 hr after the injury			

*NR = not reported, IV = intravenous, PACU = post-anesthesia care unit, IM = intramuscular, G-A = Gustilo-Anderson, IMN = intramedullary nail, STSG = split-thickness skin graft, BKA = below-knee amputation, and ORIF = open reduction and internal fixation.

TABLE E-2 Demographics of Included Studies*

Authors	Year	Mean Age	Level of Evidence	Mean Duration of Follow-up	Fractures Studied	No. of Open Fractures	Gustilo-Anderson Types Included	Definition of Early vs. Late Debridement	Injury Severity
Dellinger et al.[33]	1988	33 ± 16 yr (range, 14-88 yr)	II	>21 d	Upper or lower extremity	263	I-IIIC	Injury-to-operation interval: 5.0 ± 2.0 for infected patients vs. 5.7 ± 3.2 for uninfected patients (range, 0.3-23 hr)	ISS: 16 ± 8 for infected patients vs. 15 ± 7 for uninfected patients. APACHE II score: 7 ± 4 for infected patients vs. 6 ± 6 for uninfected patients
Patzakis and Wilkins[32]	1989	55 children (range, 5 mo-17 yr); mean age of adults NR	II	NR	Tibia or non-tibia	1104	I-III	Early: 0-12 hr. Late: >12 hr	NR
Bednar and Parikh[20]	1993	34 yr (range, 16-63 yr)	III	18 mo (range, 6-38 mo)	Lower extremity	81	I-IIIC	Mean, 8.8 hr (range, 3-30 hr). Early: 0-6 hr. Late: 6-20 hr	NR
Kindsfater and Jonassen[21]	1995	34.5 yr (range, 8-71 yr)	III	19.6 mo (range, 6-48 mo)	Tibia	47	II-IIIC	Early: 2.6-4.9 hr. Late: 5.2-104 hr	Mean ISS: 11.9 (range, 9-22) for patients with osteomyelitis vs. 14.5 (range, 9-50) for uninfected. Mean ISS: 11.3 (range, 9-22) for patients debrided <5 hr vs. 15.9 (range, 9-50) for >5 hr
Ikem et al.[34]	2001	32 yr (range, 4-78 yr)	II	18 mo	Lower extremity	59	I-IIIB	Tibia: time to debridement 6.1 ± 3.2 hr for non-infected vs. 7.8 ±	NR

								3.8 hr for infected. Femur: 5.1 ± 2.1 hr for non-infected vs. 13.7 ± 4.0 hr for infected	
Harley et al.[30]	2002	40 yr (range, 15-89 yr)	III	Minimum, 12 mo. Followed until clinical and radiographic union or until a definitive procedure for nonunion or deep infection	Upper or lower extremity	215	I-IIIC	8 hr threshold (mean time, 8 hr 29 min ± 2 hr 47 min. 54% <8 hr)	NR
Khatod et al.[22]	2003	34 yr (range, 6-90 yr)	III	10.23 mo (range, 2-67 mo). Followed until complete wound/fracture-healing	Tibia	106	I-IIIC	Early: 0-6 hr. Late: 0->12 hr	NR
Ashford et al.[23]	2004	33.9 yr (range, 16-64 yr)	III	16 mo (range, 9-28 mo)	Tibia	48	I-IIIB	Early: 0-6 hr. Late: 6-36 hr; six patients arrived from >500 km from the hospital and all took >24 hr to arrive	NR
Spencer et al.[24]	2004	45 yr (range, 4-98 yr)	II	Follow-up until radiographic union or infection/nonunion occurred	Long bone	115	I-IIIB	Early: 0-6 hr. Late: 6-9.5 hr	The study center was not a Level-I trauma center. Patients with multiple injuries or severe head injuries were transferred either immediately or after initial stabilization. These patients were excluded (n = 17)
Charalambous et al.[25]	2005	Debrided <6 hr: 31 yr. Debrided >6 hr: 30	III	Follow-up until radiographic union or time of a secondary surgical procedure to promote union	Tibia. Isolated medial malleolar fractures	383	I-IIIB. (IIIC was excluded since emergency debridement	Time defined as between presentation to hospital and debridement,	NR

		yr			excluded		was automatic)	except for one patient who clearly reached the hospital >24 hr after injury. Early: 0-6 hr. Late: 6- >24 hr	
Noumi et al.[26]	2005	24.8 yr (range, 15-62 yr)	III	36 mo (range, 2-12 yr)	Femur	89	I-IIIC	Early: 0-6 hr. Late: >6 hr	Mean ISS: 20.3 (range, 16-41)
Al-Arabi et al.[27]	2007	41 yr	II	Follow-up until radiographic union or confirmed nonunion	Long bone	248	I-IIIB	Early: 0-6 hr. Late: 6-24 hr	NR
Reuss and Cole[31]	2007	>17 yr	III	14.4 mo (range, 5 wk - 61 mo)	Tibia	81	I-IIIC	Early: 1-8 hr. Late: 8-47 hr 48 min	NR
Sungaran et al.[28]	2007	NR	III	NR	Tibia	161	I-III	Early: 0-6 hr. Late: 6-24 hr	NR
Tripuraneni et al.[29]	2008	39.2 yr (range, 8-73 yr)	III	10.2 mo (range, 2 wk to 52 mo)	Tibia	215	I-IIIC	Early: 0-6 hr. Late: 6- >24 hr	NR
Pollak et al.[19]	2010	range, 16-69 yr	II	Minimum, 3 mo	Lower extremity	307	IIIA-IIIC	Early: 0-5 hr. Late: 5- >10 hr	NR

*ISS = Injury Severity Score, and NR = not reported.