Gray Areas

Unpacking diabetic foot infections and sacral osteomyelitis

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Objectives

- Summarize updates on recent literature/guidelines in sacral osteomyelitis and diabetic foot infections.

Glossary

- CRP – c-reactive protein
- DFI – diabetes-related foot infection
- DFO – diabetes-releated osteomyelitis of the foot
- DFU – diabetes-related foot ulcer
- IDSA – Infectious Diseases Society of America
- IWGDF - International Working Group on the Diabetic Foot
- ESR – erythrocyte sedimentation rate
- PCT – procalcitonin
- PCR – polymerase chain reaction

Clinical Infectious Diseases
IDSA GUIDELINES

IWGDF/IDSA Guidelines on the Diagnosis and Treatment of Diabetes-related Foot Infections (IWGDF/IDSA 2023)

Éric Senneville,[1,2] Zaina Albalawi,[3] Suzanne A. van Asten,[4] Zulfiqarali G. Abbas,[5] Geneve Allison,[6] Javier Aragón-Sánchez,[7] John M. Embil,[8] Lawrence A. Lavery,[9] Majdi Alhasan,[10] Orhan Oz,[11] Ilker Uçkay,[12] Vilma Urbančič-Rovan,[13] Zhang-Rong Xu,[14] and Edgar J. G. Peters[15,16,17]

- Diagnose on clinical symptoms/signs
- Assess severity
- Treat?
- Hospitalize?

- Consider cultures: Bone, ulcer biopsy, ulcer swab
- Empiric treatment
- Evaluate for pseudomonas coverage

Assessing Infection

Table 1.
The classification system for defining the presence and severity of foot infection in a person with diabetes.[a]

Senneville et al, IWGDF/IDSA Guidelines on the Diagnosis and Treatment of Diabetes-related Foot Infections

Clinical classification of infection, definitions	IWGDF/IDSA classification
No systemic or local symptoms or signs of infection	1/Uninfected
Infected: At least two of these items are present: Local swelling or induration Erythema >0.5 but <2 cm[b] around the wound Local tenderness or pain Local increased warmth Purulent discharge	2/Mild
And, no other cause of an inflammatory response of the skin (e.g., trauma, gout, acute charcot neuro-arthropathy, fracture, thrombosis, or venous stasis)	
Infection with no systemic manifestations and involving: Erythema extending ≥2 cm[b] from the wound margin, *and/or* Tissue deeper than skin and subcutaneous tissues (e.g., tendon, muscle, joint, and bone)[c]	3/Moderate
Infection involving bone (osteomyelitis)	Add "(O)"
Any foot infection with associated systemic manifestations (of the systemic inflammatory response syndrome [SIRS]), as manifested by ≥2 of the following: Temperature, > 38°C or <36°C Heart rate, > 90 beats/min Respiratory rate, > 20 breaths/min, *or* PaCO2 < 4.3 kPa (32 mmHg) White blood cell count >12,000/mm^3, *or* < 4G/L, *or* >10% immature (band) forms	4/Severe
- Infection involving bone (osteomyelitis)	Add "(O)"

The presence of clinically significant foot ischaemia makes both diagnosis and treatment of infection considerably more difficult.

a infection refers to any part of the foot.

b in any direction, from the rim of the wound.

c if osteomyelitis is demonstrated in the absence of ≥2 signs/symptoms of local or systemic inflammation, classify the foot as either grade 3(O) (if <2 SIRS criteria) or grade 4(O) if ≥2 SIRS criteria) (see text).

File:Diabetic Wound after HBOT.JPG. (2026, January 2). *Wikimedia Commons*. Retrieved February 26, 2026, from https://commons.wikimedia.org/w/index.php?title=File:Diabetic_Wound_after_HBOT.JPG&oldid=1140796668. (cropped)

File:Cellulitis Left Leg.JPG. (2025, October 24). *Wikimedia Commons*. Retrieved February 26, 2026, from https://commons.wikimedia.org/w/index.php?title=File:Cellulitis_Left_Leg.JPG&oldid=1104246199. (cropped)

File:OSC Microbio 09 02 foot.jpg. (2025, October 19). *Wikimedia Commons*. Retrieved February 26, 2026, from https://commons.wikimedia.org/w/index.php?title=File:OSC_Microbio_09_02_foot.jpg&oldid=1101736012.

Treatment of Diabetes-related foot infection (DFI)

- Is antimicrobial therapy needed?
  - Don’t treat clinically uninfected ulcers
- 1-2 weeks initially
  - Re-assess prior to more Abx
- Tissue culture better than swab
- Consider targeting aerobic Gram + organisms to start
- Pseudomonas coverage likely only needed if grown from recent culture

- **If mild:** cephalexin, cefadroxil, dicloxacillin, amoxicillin + doxycycline
- **If Moderate:** amox/clav, levo/moxi-floxacin, +/- metronidazole, clinda + cipro

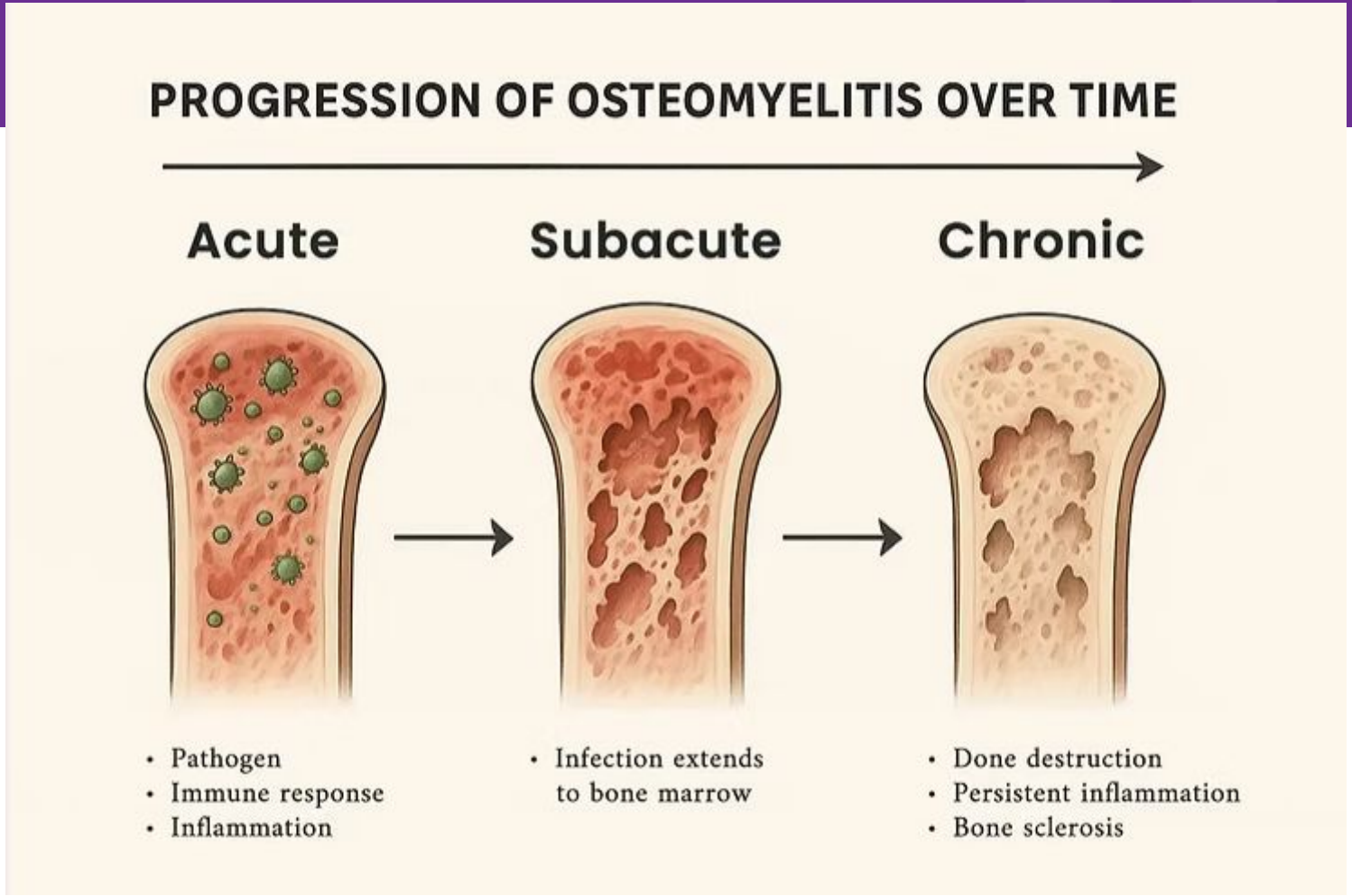
- **If MRSA present:** TMP/SMX, Amox + doxy, Linezolid, Clindamycin

DFI continued, Oral vs IV

- Oral versus intravenous antibiotics for bone and joint infection. New Eng J Med
- Using the Comparing Oral versus Parenteral Antimicrobial Therapy (COPAT) Clinical Trial to Influence Institutional Practice Transformation Towards Earlier Transition to Oral Antibiotics. Clin Infect Dis.
- Three versus six weeks of antibiotic therapy for diabetic foot osteomyelitis: A prospective, randomized, non-inferiority pilot trial. Clin Infect Dis. Nov 26 2020
- Six-week versus twelve-week antibiotic therapy for nonsurgically treated diabetic foot osteomyelitis: a multicenter open-label controlled randomized study. Diabetes care.
- Antibiotics versus conservative surgery for treating diabetic foot osteomyelitis: a randomized comparative trial. Diabetes care.

Osteomyelitis

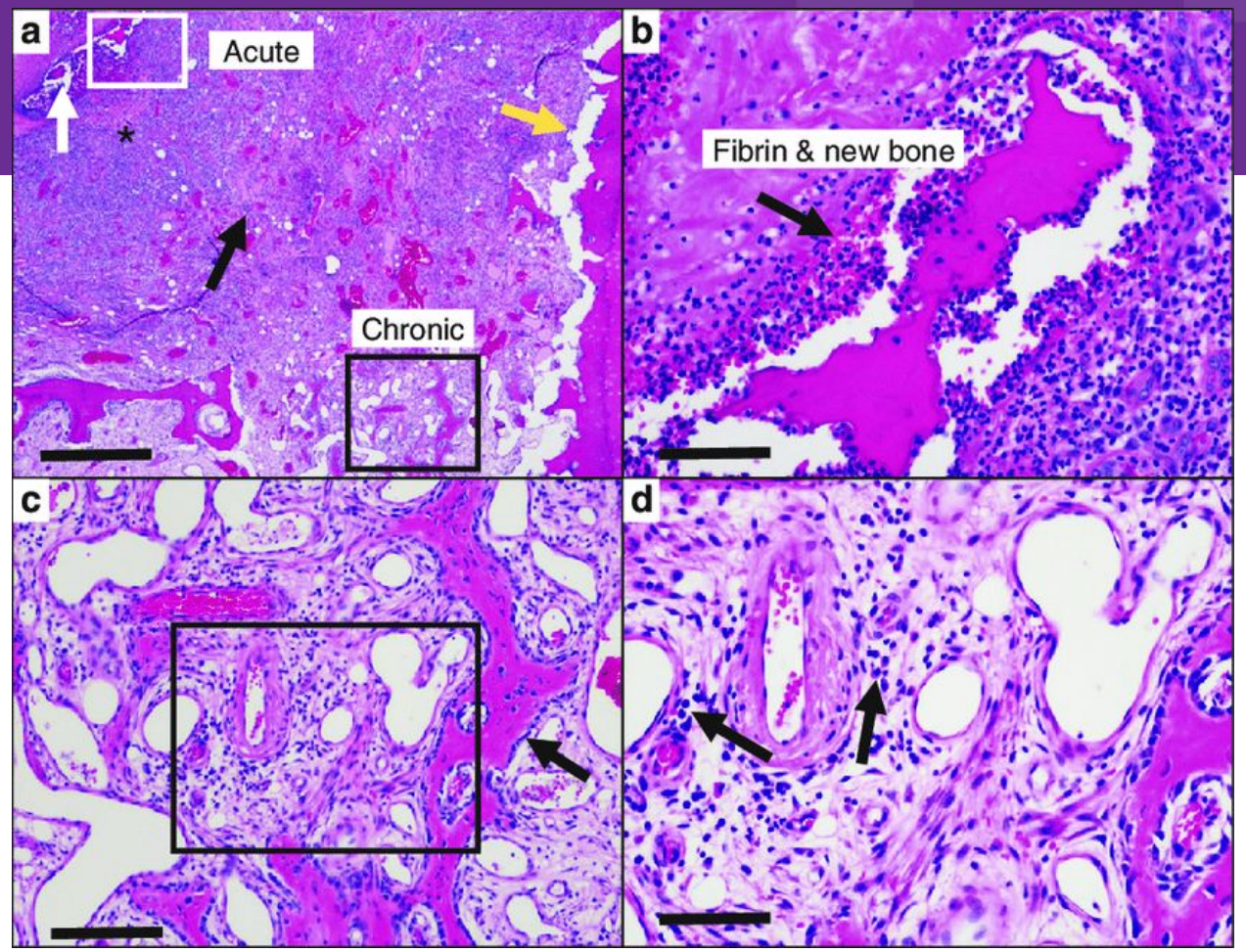
- Large inoculum of bacteremia
- Trauma
- Ischemia
- Foreign bodies
- Hematogenous spread



https://www.sharedhealthservices.com/post/osteomyelitis-in-non-healing-diabetic-foot-ulcers

Acute Osteomyelitis

- Usually within two weeks of disease onset
- Ultimately based on histopathological findings
- Typical local inflammatory symptoms
- One study of 50 patients showed higher remission (56% vs 22% with bone culture-based antibiotics.
- Recent study showed similar outcomes in bone biopsy vs ulcer bed biopsy, even when growth discordant



Evolving concepts in bone infection: redefining “biofilm”, “acute vs. chronic osteomyelitis”, “the immune proteome” and “local antibiotic therapy” - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Histologic-features-of-acute-and-chronic-osteomyelitis-exist-in-the-same-lesion_fig4_334464269 [accessed 2 Mar 2026]

Statpearls: Osteomyelitis
https://www.ncbi.nlm.nih.gov/books/NBK532250/

Diagnosing Diabetic Foot Osteomyelitis (DFO)

Table 1: Pooled Point Estimates of Sensitivity, Specificity, and Likelihood Ratios for Diagnostic Tests for Osteomyelitis

Test	Sensitivity	Specificity	+LR*	-LR*	Reference
Osteomyelitis without PJI					
X-rays	70%	82%	3.9	0.4	45
CT Scans	70%	90%	7.0	0.3	45
MRI	96%	81%	5.1	0.05	45
Nuclear Medicine Scintigraphy†	84%	71%	2.9	0.2	45
White Cell Tagged Scans	87%	95%	17.4	0.1	45
PET	85%	93%	12.1	0.2	45
SPECT	95%	82%	5.3	0.06	45
ESR	49%-79%	50-80%	1.6-3.8	0.3-0.4	46-48
CRP	45%-76%	59%-71%	1.1-2.6	0.3-0.8	46-48
Biopsy (histopathology)	52%	>99%	>50	0.5	49
DFO					
X-rays	62%	78%	2.8	0.5	50
MRI	93%-96%	75%-84%	3.7-6.0	0.05-0.09	50,51
Nuclear Medicine Scintigraphy†	85%	68%	2.7	0.2	50
White Cell Tagged Scans	91%-92%	75%-92%	3.6-11.5	0.09-0.1	51
PET	84%	93%	12.0	0.2	50
ESR	60%-81%	56%-90%	1.4-8	0.2-0.7	52-55
CRP	49%-76%	55%-80%	1.1-3.8	0.3-0.9	52-54,56
Probe-to-bone	87%	83%	5.1	0.2	57

- Superficial culture
- Deep tissue culture
- Bone biopsy
- Concordance at best ~50%, usually better with Staph aureus

Treating Osteomyelitis - Surgery

- Complete resection vs partial resection
  - Based on histopathology
  - Residual osteo vs No residual osteo
  - NRO had shorter duration of therapy (21 vs 37 days), more amputations (90% vs 61%)
  - At 12 months, no difference in ulcer at same site, hospitalization, re-infection including with OM, time to wound healing.
  - Successful treatment in 87% patients both groups
- RCTs for diabetic osteo with debridement
  - Three weeks similar to 6 weeks by Gariani et al.
  - 10 days post surgery vs 90 days, Lazaro-Martinez et al.

Lavery et al. Post hoc analysis of two RCTs. Done in moderate and severe infections.
Gariani et al. Prospective, randomized trial 3 v 6 weeks
Lazaro-Martinez et al. 10 vs 90 d

Treating Osteomyelitis - Duration

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IDSA Infectious Diseases Society of America
hivma hiv medicine association
OXFORD

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Table 5. Duration of antibiotic therapy according to the clinical situation.

	Route	Duration
Infection severity (skin and soft tissues)		
Class 2: Mild	Oral	1–2 weeks
Class 3/4: Moderate/severe	Oral/initially iv	2–4 weeks[a]
Bone/joint		
Resected	Oral/initially iv	2–5 days
Debrided (soft tissue infection)	Oral/initially iv	1–2 weeks
Positive culture or histology of bone margins after bone resection	Oral/initially iv	3 weeks
No surgery or dead bone	Oral/initially iv	6 weeks

Abbreviation: iv, intravenous.

[a]10 days following surgical debridement.

Oral vs. IV Abx for Osteomyelitis

Author	Yr	N	Regimen (Oral vs. IV)	Success
Greenberg	'87	30	Ciprofloxacin vs. std IV	50% (7/14) v 65% (11/16)
Gentry	'90	59	Ciprofloxacin vs. βL+aminoglyc	77% (24/31) v 79% (22/28)
Mader	'90	26	Ciproflox vs. βL/clinda+aminoglyc	79% (11/14) v 83% (10/12)
Gentry	'91	33	Ofloxacin vs. cephalosporin	74% (14/19) v 86% (12/14)
Gomis	'99	32	Ofloxacin vs. imipenem	69% (11/16) v 50% (8/16)
Schrenzel	'04	39	Fleroxacin+rifampin v βL/vanco	82% (18/22) v 65% (11/17)
Euba	'09	48	TMP-SMX+rifampin vs. cloxacillin	81% (17/21) v 77% (21/27)
Li	'19	1054	Std oral vs. std IV	87% (457/527) v 85% (450/527)
Manning	'22	60	PJI/DAIR: Std oral vs. std IV	71% (22/31) v 76% (22/29)
METRC*	'25	233	Std oral vs. std IV	63% (73/115) v 64% (76/118)
Juskowich	'25	73	Std oral vs. std IV	98% (45/46) v 100% (20/20)
Total (N=11 RCT)		1,687		82% (699/856) v 80% (663/824)

*Fracture-related infections; treatment success was a secondary endpoint; Success = absence of osteo at long term follow up (most studies >1 year); std = standard of care, protocol specified; all RCTs comparing oral to IV-only are in adults; 9 other adult & 10 pediatric RCTs or quasi-exptl studies comparing mostly oral vs. mostly oral; refs at https://www.bradspellberg.com/oral-antibiotics

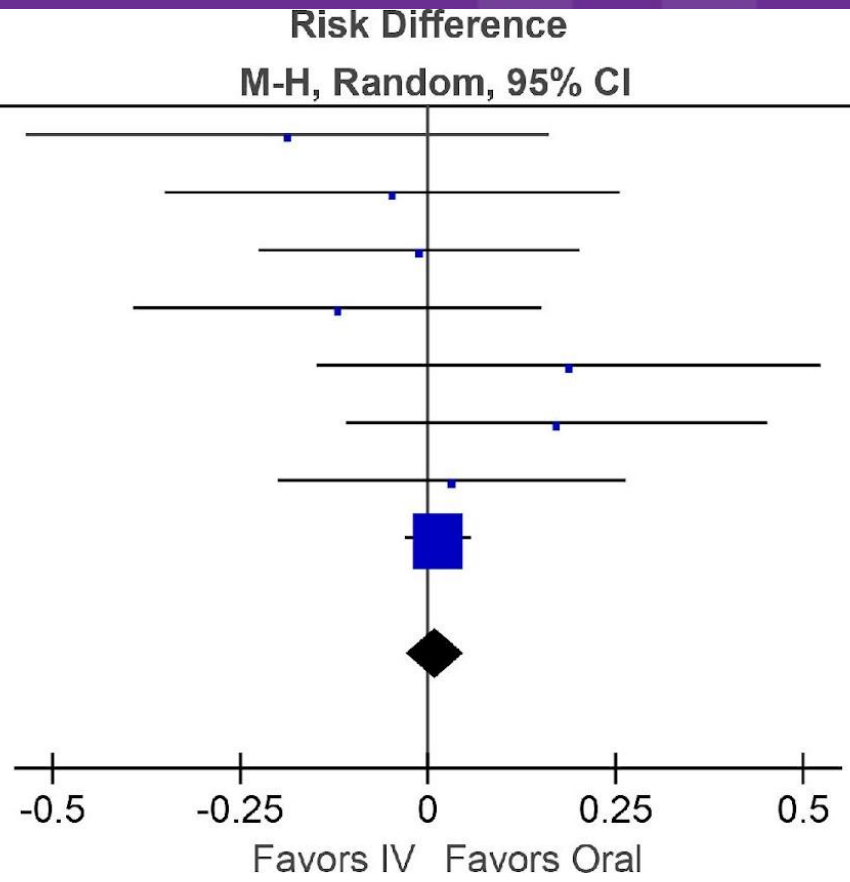
https://static.wixstatic.com/media/8e982b_77d7ff22e70848c8a11a42d12370f826~mv2.jpg/v1/fill/w_803,h_604,al_c,q_85,usm_0.66_1.00_0.01,enc_avif,quality_auto/Tables_Page_1.jpg
https://www.bradspellberg.com/oral-antibiotics

Treating Osteomyelitis with oral ABx

Study or Subgroup	Oral Events	Oral Total	IV Events	IV Total	Weight	Risk Difference M-H, Random, 95% CI	Year
Greenberg 1987	7	14	11	16	1.2%	-0.19 [-0.53, 0.16]	1987
Mader 1990	11	14	10	12	1.7%	-0.05 [-0.35, 0.25]	1990
Gentry 1990	24	31	22	28	3.3%	-0.01 [-0.22, 0.20]	1990
Gentry 1991	14	19	12	14	2.1%	-0.12 [-0.39, 0.15]	1991
Gomis 1999	11	16	8	16	1.3%	0.19 [-0.15, 0.52]	1999
Schrenzel 2004	18	22	11	17	1.9%	0.17 [-0.11, 0.45]	2004
Euba 2009	17	21	21	27	2.8%	0.03 [-0.20, 0.26]	2009
Li 2019	457	527	450	527	85.6%	0.01 [-0.03, 0.06]	2019
Total (95% CI)		**664**		**657**	**100.0%**	**0.01 [-0.03, 0.05]**	
Total events	559		545				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 4.74$, df = 7 (P = 0.69); $I^2 = 0\%$

Test for overall effect: Z = 0.61 (P = 0.54)



Wald-Dickler, N., Holtom, P. D., Phillips, M. C., Centor, R. M., Lee, R. A., Baden, R., & Spellberg, B. (2022). Oral Is the New IV. Challenging Decades of Blood and Bone Infection Dogma: A Systematic Review. *The American journal of medicine*, *135*(3), 369–379.e1. https://doi.org/10.1016/j.amjmed.2021.10.007

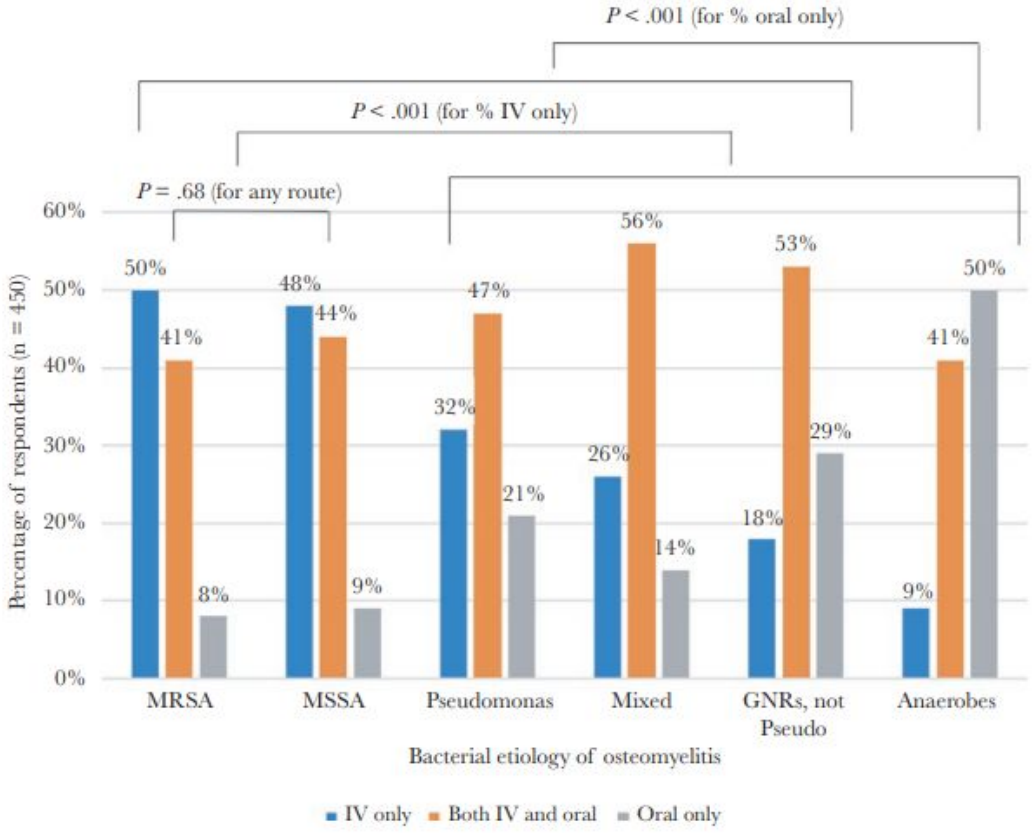
Treating Osteomyelitis with oral ABx

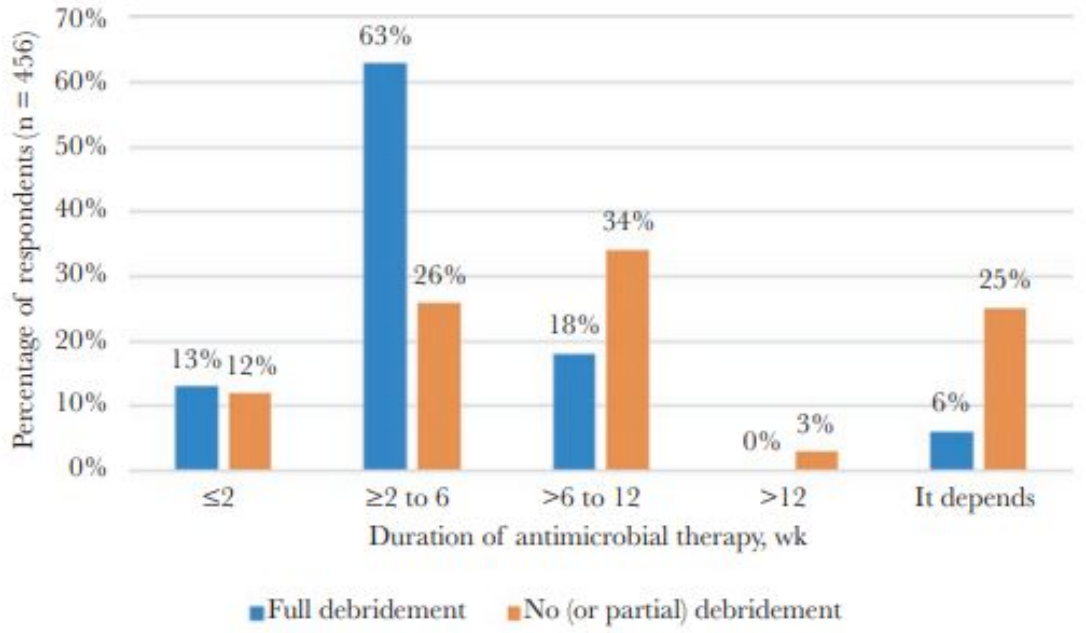
Drug	Dose	Comment/References
Ciprofloxacin	500-750 mg BID	Higher dose for *Pseudomonas*[38–40,50,545–551,555,556]
Levofloxacin	750 mg once daily	Levofloxacin dosing based on [53,476,587]; L-enantiomer of ofloxacin, the latter of which was widely studied for osteomyelitis[48,553,554,557,559]
TMP-SMX	7.5-10 TMP mg/kg/d divided twice or thrice daily (e.g., 2 DS tablets twice daily for a 70 kg adult)	Most studies used 7.5-10 mg/kg/d,[44,50,569,571,574]; 2 studies[568,573] used 4-6 mg/kg/d, with lower cure rates in one of them[568]
Clindamycin	600 mg TID; 900 TID or 600 QID for larger patients	450 mg QID may be used but was not favored in published studies[564,565,588]
Linezolid	600 mg BID	Standard dosing,[49,561,562,574] monitor for reversible hematotoxicity after 2 weeks, and irreversible neurotoxicity after 4 weeks
Tedizolid	200 mg once daily	115 patients total described, success rates ranging from 77% to 100% across small case series[589] 44 total patients, 17 patients with hard-ware associated infection, 13 with osteomyelitis, 5 with PJI, 2 with "other"; median treatment 12 weeks; 4 patients failed therapy (11%), 19 others were given continued antibiotic suppression due to retention of device[590]
Amoxicillin/ Clavulanate	500 mg TID or 875 mg BID	Specifically for DFO[48–50]
Rifampin	600 mg once daily	Doses studied include 600 once per day.[44,53,470,558,569] 900 mg once daily[476,559] or 600 mg BID,[477,574] unclear if efficacy or toxicity differs 300 mg doses less desirable due to lower AUC levels and less convenience for patients[25,26]
Fosfomycin*	4 to 16 g per day	Various doses studied with formulations available outside the US, not studied with the sachet powder formulation in the US[575–577]
Cephalexin or cefadroxil	Cephalexin 1.5-2 g per day in adults; 150 mg/kg/d in children; Cefadroxil 50 mg/kg/d in children	Only 2 studies in adults[430,431] and 2 in children[57,591] reported doses used

***There are no published data for the treatment of osteomyelitis with the sachet powder oral formulation of fosfomycin available in the US**
Clinical studies have also reported use of doxycycline or minocycline,[17,54,257,258] however the doses used in these studies were not described.

Table 5. Summary of Oral Antibiotic Doses Used in Published Studies for Osteomyelitis
Spellberg B, Aggrey G, Brennan MB, et al. Use of Novel Strategies to Develop Guidelines for Management of Pyogenic Osteomyelitis in Adults: A WikiGuidelines Group Consensus Statement. JAMA Netw Open. 2022;5(5):e2211321. doi:10.1001/jamanetworkopen.2022.11321

Sacral Osteomyelitis – what are we doing?





Kaka, Anjum S et al. "Diagnosis and Management of Osteomyelitis Associated With Stage 4 Pressure Ulcers: Report of a Query to the Emerging Infections Network of the Infectious Diseases Society of America." *Open forum infectious*

Sacral Osteomyelitis

Figure S1: Failure rate during follow-up

Figure S2-1: according to immediate or delayed effective antibiotic treatment during follow-up

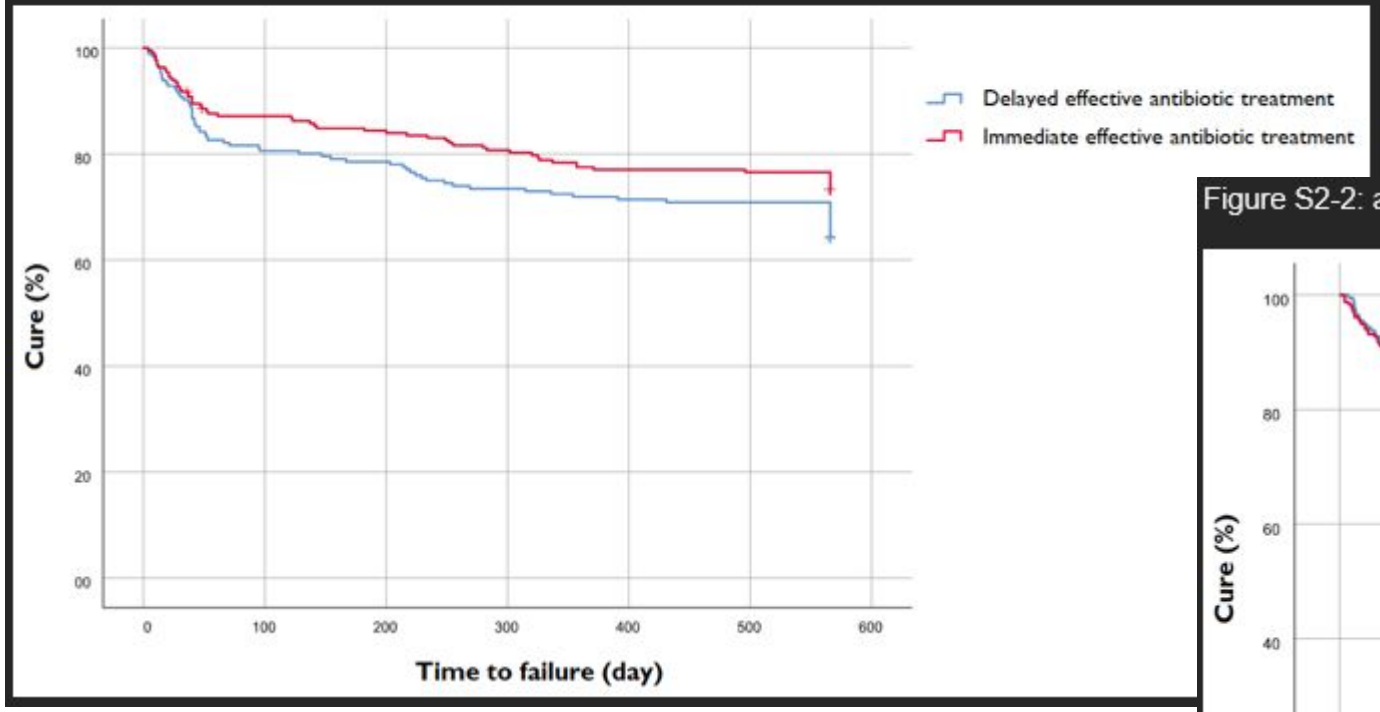
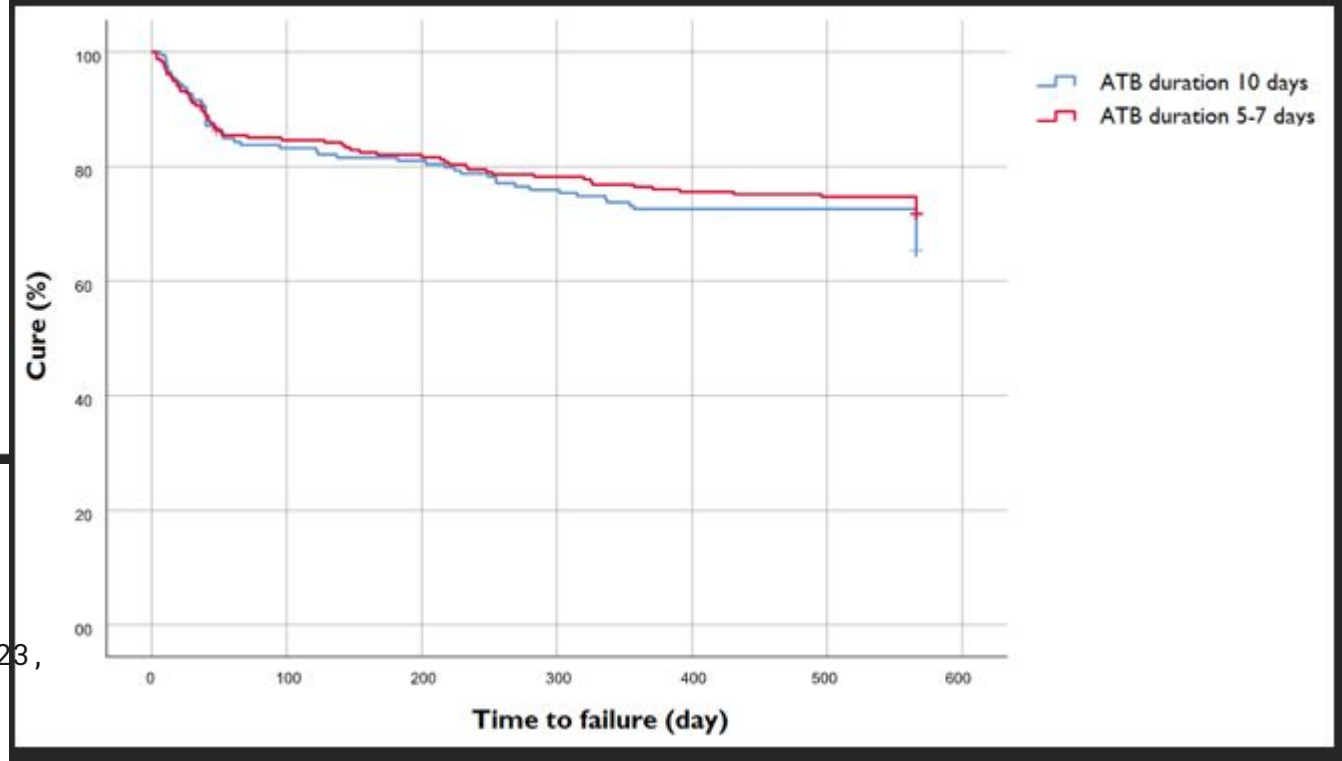


Figure S2-2: according to antibiotic treatment duration during follow-up



Dinh, Aurélien et al. “Short Antibiotic Treatment Duration for Osteomyelitis Complicating Pressure Ulcers: A Quasi-experimental Study.” *Open forum infectious diseases* vol. 10,3 ofad088. 16 Feb. 2023, doi:10.1093/ofid/ofad088

Sacral Osteomyelitis

- Goals are wound care and potential closure for chronic wounds
- Exposed bone does not mean infected bone
- No data found to support long antibiotic durations for sacral pressure ulcers with underlying osteomyelitis

- If chronic, treat the soft tissue as needed
- If acute, treat for standard osteomyelitis duration
- If debrided and flapped, consider truncated (5-7 day) treatment

Rifampin?

- Mixed data
- Large VA study, Wilson et al.
  - Rifampin reduced combined amputation/mortality endpoint (OR 0.65)
  - Small number of patients (130 of 6174 enrolled)
  - Larger proportion had Staph aureus compared to total population
- Dose 600mg daily, ~10mg/kg noninferior to 20mg/kg for Staph, Arvieux et al
- Pending studies with cool names, both for prosthetic joint infection
  - ROADMAP
  - RiCOTTA

Long acting lipoglycopeptides

- Oritavancin:
  - Weekly dosing
- Dalbavancin
  - Also weekly, 1-2 doses used in osteomyelitis

Cain, Alexander R et al. “Effectiveness of Dalbavancin Compared With Standard of Care for the Treatment of Osteomyelitis: A Real-world Analysis.” *Open forum infectious diseases* vol. 9,2 ofab589. 18 Dec. 2021, doi:10.1093/ofid/ofab589

Mark Redell, Miguel Sierra-Hoffman, Maha Assi, Markian Bochan, David Chansolme, Anurag Gandhi, Kathleen Sheridan, Ivan Soosaipillai, Thomas Walsh, Jill Massey, The CHROME Study, a Real-world Experience of Single- and Multiple-Dose Oritavancin for Treatment of Gram-Positive Infections, *Open Forum Infectious Diseases*, Volume 6, Issue 11, November 2019, ofz479, https://doi.org/10.1093/ofid/ofz479

Van Hise, N.W., Petrak, R.M., Shah, K. *et al.* Oritavancin Versus Daptomycin for Osteomyelitis Treatment After Surgical Debridement. *Infect Dis Ther* **13**, 535–547 (2024). https://doi.org/10.1007/s40121-024-00925-2

Questions?

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