

Stewardship: Shorter = Better

Diagnosis	Short (d)	Long (d)	Result	#RCT
CAP	3-5	5-14	Equal	12
Atypical CAP	1	3	Equal	1
VAP	8	15	Equal	2
cUTI/Pyelo	5 or 7	10 or 14	Equal	8*
Intra-abd	4	10	Equal	2
GNB Bacteremia	7	14	Equal	3**
Cellulitis/Wound/Abscess	5-6	10	Equal	4 [†]
Osteomyelitis	42	84	Equal	2
Osteo with Removed Implant	28	42	Equal	1
Debrided Diabetic Osteo	10-21	42-90	Equal	2 [‡]
Septic Arthritis	14	28	Equal	1
AECB & Sinusitis	≤5	≥7	Equal	>25
Neutropenic Fever	AFx72 h	+ANC>500	Equal	1
<i>P. vivax</i> Malaria	7	14	Equal	1

Total: 14 Diseases

64 RCTs

*1 RCT in males; **GNB bacteremia also in UTI/cIAI RCTs; †3 RCTs equal, 1 (low dose oral flucox)
[†]relapses 2° endpoint; ‡all patients debrided, in 1 study total bone resection (clean margins); refs at
<https://www.bradspellberg.com/shorter-is-better>

Refs „shorter is better“ (B.Spellberg)

Community Acquired Pneumonia: 12 RCTs (total N = 7,295 patients)

- Singh N, Rogers P, Atwood CW, Wagener MM, Yu VL. Short-course empiric antibiotic therapy for patients with pulmonary infiltrates in the intensive care unit. A proposed solution for indiscriminate antibiotic prescription. *Am J Respir Crit Care Med* 2000; 162(2 Pt 1): 505-11.
- Dunbar LM, Khashab MM, Kahn JB, Zadeikis N, Xiang JX, Tennenberg AM. Efficacy of 750-mg, 5-day levofloxacin in the treatment of community-acquired pneumonia caused by atypical pathogens. *Current medical research and opinion* 2004; 20(4): 555-63.
- Zhao X, Wu JF, Xiu QY, et al. A randomized controlled clinical trial of levofloxacin 750 mg versus 500 mg intravenous infusion in the treatment of community-acquired pneumonia. *Diagn Microbiol Infect Dis* 2014; 80(2): 141-7.
- Pakistan Multicentre Amoxicillin Short Course Therapy pneumonia study g. Clinical efficacy of 3 days versus 5 days of oral amoxicillin for treatment of childhood pneumonia: a multicentre double-blind trial. *Lancet* 2002; 360(9336): 835-41.
- Greenberg D, Givon-Lavi N, Sadaka Y, Ben-Shimol S, Bar-Ziv J, Dagan R. Short-course antibiotic treatment for community-acquired alveolar pneumonia in ambulatory children: a double-blind, randomized, placebo-controlled trial. *The Pediatric infectious disease journal* 2014; 33(2): 136-42.
- el Moussaoui R, de Borgie CA, van den Broek P, et al. Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: randomised, double blind study. *Bmj* 2006; 332(7554): 1355.
- Uranga A, Espana PP, Bilbao A, et al. Duration of Antibiotic Treatment in Community-Acquired Pneumonia: A Multicenter Randomized Clinical Trial. *JAMA internal medicine* 2016; 176(9): 1257-65.
- Dinh A, Davido B, Bouchand F, Duran C, Ropers J, Cremieux AC. Honey, I shrunk the antibiotic therapy. *Clin Infect Dis* 2018; 66(12):1981-2.
- Harris JA, Kolokathis A, Campbell M, Cassell GH, Hammerschlag MR. Safety and efficacy of azithromycin in the treatment of community-acquired pneumonia in children. *The Pediatric infectious disease journal* 1998; 17(10): 865-71.
- Ginsburg AS, Mvalo T, Nkwopara E. et al. Amoxicillin for 3 or 5 Days for Chest-Indrawing Pneumonia in Malawian Children. *NEJM*. 2020 383: 13-23.
- Pernica JM, Harman S, Kam AJ, et al. Short-Course Antimicrobial Therapy for Pediatric Community-Acquired Pneumonia. *JAMA Pediatrics*, 2021; DOI: 10.1001/jamapediatrics.2020.6735.
- Dinh A, Ropers J, Duran C, et al. Discontinuing β -lactam treatment after 3 days for patients with community-acquired pneumonia in non-critical care wards (PTC): a double-blind, randomised, placebo-controlled, non-inferiority trial. *Lancet*. 2021 397:1195-1203.

Atypical Community Acquired Pneumonia: 1 RCTs (total N = 100 patients)

- Schonwald S, Kuzman I, Oresković K, et al. Azithromycin: single 1.5 g dose in the treatment of patients with atypical pneumonia syndrome--a randomized study. *Infection* 1999; 22(3):198-202.

Refs „shorter is better“ (B.Spellberg)

Nosocomial/Ventilator Associated Pneumonia: 2 RCTs (total N = 626 patients)

- Chastre J, Wolff M, Fagon JY, et al. Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: a randomized trial. *JAMA : the journal of the American Medical Association* 2003; 290(19): 2588-98.
- Capellier G, Mockly H, Charpentier C, et al. Early-onset ventilator-associated pneumonia in adults randomized clinical trial: comparison of 8 versus 15 days of antibiotic treatment. *PLoS One* 2012; 7(8): e41290.

Complicated UTI/Pyelonephritis: 8 RCTs (total N = 1,614 patients)

- Jernelius H, Zbornik J, Bauer CA. One or three weeks' treatment of acute pyelonephritis? A double-blind comparison, using a fixed combination of pivampicillin plus pivmecillinam. *Acta Med Scand* 1988; 223(5): 469-77.
- de Gier R, Karperien A, Bouter K, et al. A sequential study of intravenous and oral Fleroxacin for 7 or 14 days in the treatment of complicated urinary tract infections. *Int J Antimicrob Agents* 1995; 6(1): 27-30.
- Talan DA, Stamm WE, Hooton TM, et al. Comparison of ciprofloxacin (7 days) and trimethoprim-sulfamethoxazole (14 days) for acute uncomplicated pyelonephritis pyelonephritis in women: a randomized trial. *JAMA : the journal of the American Medical Association* 2000; 283(12): 1583-90.
- Sandberg T, Skoog G, Hermansson AB, et al. Ciprofloxacin for 7 days versus 14 days in women with acute pyelonephritis: a randomised, open-label and double-blind, placebo-controlled, non-inferiority trial. *Lancet* 2012; 380(9840): 484-90.
- Peterson J, Kaul S, Khashab M, Fisher AC, Kahn JB. A double-blind, randomized comparison of levofloxacin 750 mg once-daily for five days with ciprofloxacin 400/500 mg twice-daily for 10 days for the treatment of complicated urinary tract infections and acute pyelonephritis. *Urology* 2008; 71(1): 17-22.
- Klausner HA, Brown P, Peterson J, et al. A trial of levofloxacin 750 mg once daily for 5 days versus ciprofloxacin 400 mg and/or 500 mg twice daily for 10 days in the treatment of acute pyelonephritis. *Current medical research and opinion* 2007; 23(11): 2637-45.
- Dinh A, Davido B, Etienne M, et al. Is 5 days of oral fluoroquinolone enough for acute uncomplicated pyelonephritis? The DTP randomized trial. *Eur J Clin Microbiol Infect Dis.* 2017; 36:1443-8.
- Drekonja DM, Trautner B, Amundson C, et al. Effect of 7 vs 14 Days of Antibiotic Therapy on Resolution of Symptoms Among Afebrile Men With Urinary Tract Infection: A Randomized Clinical Trial. *JAMA* 2021; 326(4):324-331.

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Complicated Intra-Abdominal Infections: 2 RCTs (total N = 766 patients)

- Sawyer RG, Claridge JA, Nathens AB, et al. Trial of short-course antimicrobial therapy for intraabdominal infection. *N Engl J Med* 2015; 372(21): 1996-2005.
- Montravers P, Tubach F, Lescot T, et al. Short-course antibiotic therapy for critically ill patients treated for postoperative intra-abdominal infection: the DURAPOP randomised clinical trial. *Intensive Care Med* 2018; 44(3):300-310.

GNB Bacteremia: 3 RCTs (total N = 1,186 patients; not including multiple cUTI/cIAI pts in above trials who were also bacteremic)

- Yahav D, Franceschini E, Koppel F, et al. Seven versus fourteen Days of Antibiotic Therapy for uncomplicated Gram-negative Bacteremia: a Non-inferiority Randomized Controlled Trial. *Clin Infect Dis* 2019 69:1091-8.
- von Dach E, Albrich WC, Brunel AS, et al. Effect of C-Reactive Protein-Guided Antibiotic Treatment Duration, 7-Day Treatment, or 14-Day Treatment on 30-Day Clinical Failure Rate in Patients With Uncomplicated Gram-Negative Bacteremia: A Randomized Clinical Trial. *JAMA*. 2020. 323:2160-9.
- Molina J, Montero-Matos E, Praena-Segovia J, et al. Seven versus 14-days course of antibiotics for the treatment of bloodstream infections by Enterobacterales. A randomized, controlled trial. *Clin Microbiol Infect*. 2021. ePub.

Acute Bacterial Skin and Skin Structure Infections: 4 RCTs (3 non-inferior, total N = 1,412 patients; 1 trial, N = 151 of low dose oral flucloxacillin which is poorly absorbed had excess relapses at 90 d)

- Hepburn MJ, Dooley DP, Skidmore PJ, Ellis MW, Starnes WF, Hasewinkle WC. Comparison of short-course (5 days) and standard (10 days) treatment for uncomplicated cellulitis. *Arch Intern Med* 2004; 164(15): 1669-74.
- Prokocimer P, De Anda C, Fang E, Mehra P, Das A. Tedizolid phosphate vs linezolid for treatment of acute bacterial skin and skin structure infections: the ESTABLISH-1 randomized trial. *JAMA : the journal of the American Medical Association* 2013; 309(6): 559-69.
- Moran GJ, Fang E, Corey GR, Das AF, De Anda C, Prokocimer P. Tedizolid for 6 days versus linezolid for 10 days for acute bacterial skin and skin-structure infections (ESTABLISH-2): a randomised, double-blind, phase 3, non-inferiority trial. *Lancet Infect Dis* 2014; 14(8): 696-705.
- Cranendonk et al. Antibiotic treatment for 6 days versus 12 days in patients with severe cellulitis: a multicentre randomised, double-blind, placebo-controlled, non-inferiority trial. *Clin Microbiol Infect* 2019; 26(5):606-612.

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Osteomyelitis Not Surgically Treated 6 vs. 12 weeks: 2 RCTs (total N = 391 patients)

- Bernard L, Dinh A, Ghout I, et al. Antibiotic treatment for 6 weeks versus 12 weeks in patients with pyogenic vertebral osteomyelitis: an open-label, non-inferiority, randomised, controlled trial. *Lancet* 2015. 385:875-82.
- Tone A, et al. Six-week versus twelve-week antibiotic therapy for nonsurgically treated diabetic foot osteomyelitis: a multicenter open-label controlled randomized study. *Diabetes Care* 2015;38:302-307.

Osteomyelitis with Removed Orthopedic Implant: 1 RCT (total N = 123 patients, including 39 pts with 2-stage exchanged PJI)

- Benkabouche M, Racloz G, Spechbach H, et al. Four versus six weeks of antibiotic therapy for osteoarticular infections after implant removal: a randomized trial. *J Antimicrobial Chemother* 2019. 74:2394-2399.

Diabetic Foot Osteomyelitis with Debridement or Total Bone Resection: 2 RCTs (total N = 130 patients)

- Lazaro-Martinez J, Aragon-Sanchez J, Garcia-Martinez E, et al. Antibiotics versus conservative surgery for treating diabetic foot osteomyelitis: a randomized comparative trial. *Diabetes Care* 2014;37:789-95.
- Gariani K, Pham T-T, Kressman B, et al. Three versus six weeks of antibiotic therapy for diabetic foot osteomyelitis: A prospective, randomized, non-inferiority pilot trial. *Clin Infect Dis* 2021. ePub.

Septic Arthritis: 1 RCTs (total N = 154 patients)

- Gjika E, et al. Two weeks versus four weeks of antibiotic therapy after surgical drainage for native joint bacterial arthritis: a prospective, randomised, non-inferiority trial. *Ann Rheum Dis* 2019; 78:1114–1121.

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Acute Exacerbation Chronic Bronchitis/COPD: >20 RCTs (total N = 10,698 patients)

- El Moussaoui R, Roede BM, Speelman P, Bresser P, Prins JM, Bossuyt PM. Short-course antibiotic treatment in acute exacerbations of chronic bronchitis and COPD: a meta-analysis of double-blind studies. *Thorax* 2008; 63(5):415-22.

Acute Bacterial Sinusitis: 6 RCTs (total N = 2,423 patients)

- Henry DC, Riffer E, Sokol WN, Chaudry NI, Swanson RN. Randomized double-blind study comparing 3- and 6-day regimens of azithromycin with a 10-day amoxicillin-clavulanate regimen for treatment of acute bacterial sinusitis. *Antimicrob Agents Chemother.* 2003;47(9):2770-2774.
- Ferguson BJ, Anon J, Poole MD, et al. Short treatment durations for acute bacterial rhinosinusitis: Five days of gemifloxacin versus 7 days of gemifloxacin. *Otolaryngol Head Neck Surg.* 2002;127(1):1-6.
- Sher LD, McAdoo MA, Bettis RB, Turner MA, Li NF, Pierce PF. A multicenter, randomized, investigator-blinded study of 5- and 10-day gatifloxacin versus 10-day amoxicillin/clavulanate in patients with acute bacterial sinusitis. *Clin Ther.* 2002;24(2):269-281.
- Roos K, Brunswig-Pitschner C, Kostrica R, et al. Efficacy and tolerability of once-daily therapy with telithromycin for 5 or 10 days for the treatment of acute maxillary sinusitis. *Chemotherapy.* 2002;48(2):100-108.
- Williams JW Jr, Holleman DR Jr, Samsa GP, Simel DL. Randomized controlled trial of 3 vs 10 days of trimethoprim/sulfamethoxazole for acute maxillary sinusitis. *JAMA.* 1995;273(13):1015-1021.
- Klapan I, Culig J, Oresković K, Matrapazovski M, Radosević S. Azithromycin versus amoxicillin/clavulanate in the treatment of acute sinusitis. *Am J Otolaryngol.* 1999;20(1):7-11.

Neutropenic Fever: 1 RCTs (total N = 157 patients)

- Aguilar-Guisado M, Espigado I, Martin-Pena A, et al. Optimisation of empirical antimicrobial therapy in patients with haematological malignancies and febrile neutropenia (How Long study): an open-label, randomised, controlled phase 4 trial. *Lancet Haematol* 2017; 4(12): e573-e83.

P. vivax Malaria: 1 RCTs (total N = 1,872 patients)

- Taylor W, et al. Short-course primaquine for the radical cure of Plasmodium vivax malaria: a multicentre, randomised, placebo-controlled non-inferiority trial. *Lancet* 2019; 394(10202):929-938.