University of Zurich[UZH]

The Balgrist

Antibiotic Therapy in Diabetic Foot Infections
IV vs PO, 2 Weeks vs 12 Weeks, What Should Be The Doses ?

Prof. Ílker Uçkay

Infeksiyoloji ve Kliniksel Araştırma Bölümü

Balgrist Ùniversite Hastanesi, Zürih

yes

no

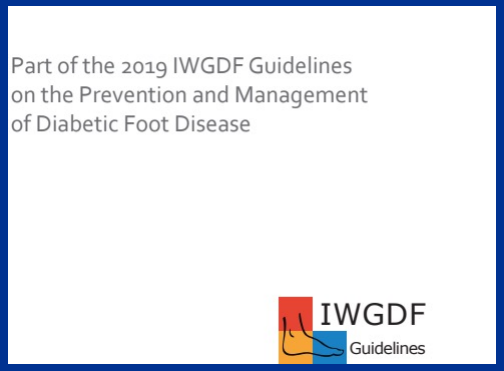
maybe

I Can Answer That!

reason number one

We ignore the «power» of (various) antibiotics in the diabetic foot

- *Lack of differences between (almost) all molecules (if no problem of resistance)*



IWGDF in press

ANTIBIOTICS AND BONE PENETRATION

Landersdorfer CB et al. *Clin Pharmacokinet* 2009;48:89-124

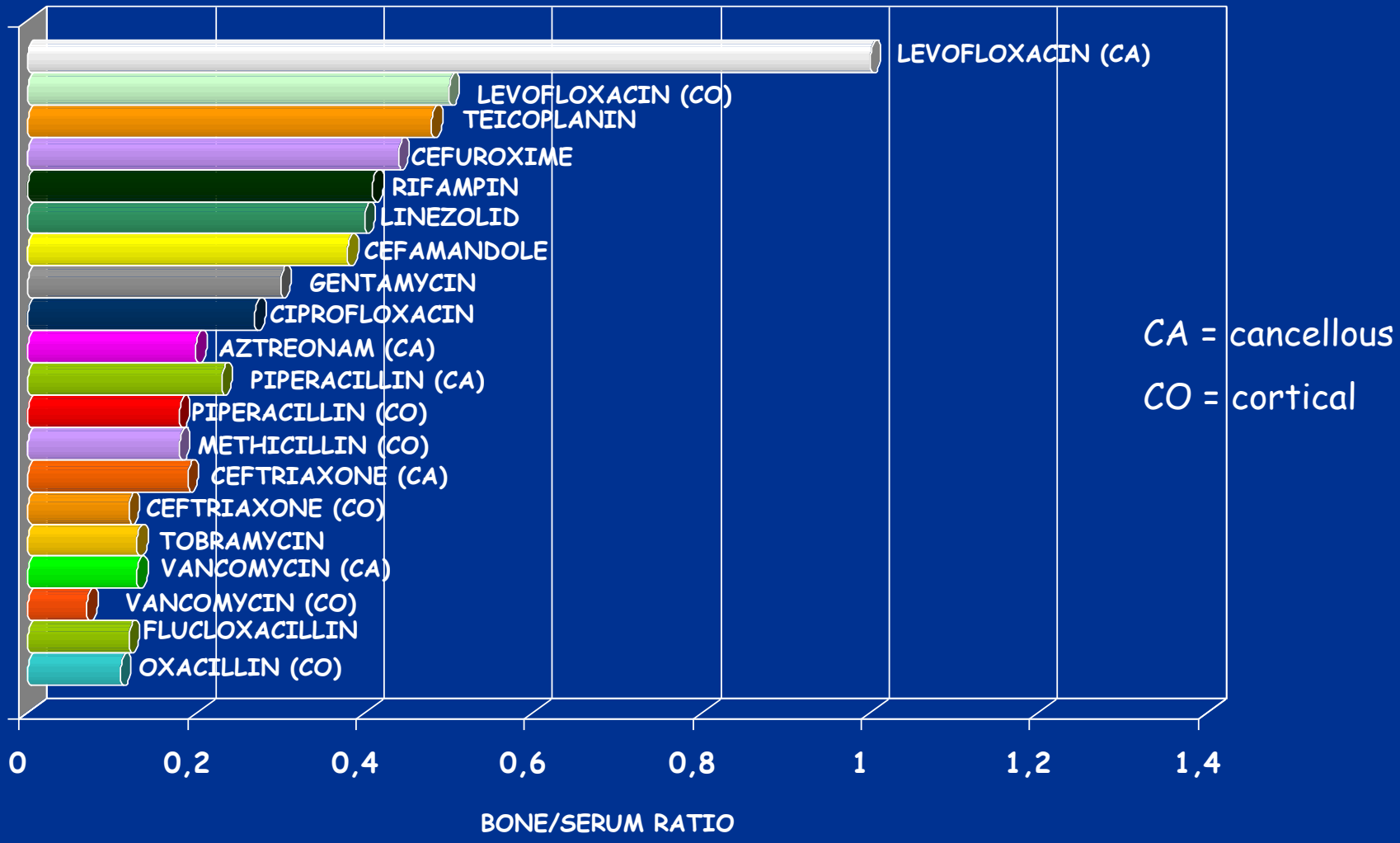


Table 7. Studies of Antibiotic Therapy for Diabetic Foot Infections Published Since 2004 (and Not Included in Previous Version of This Guideline)

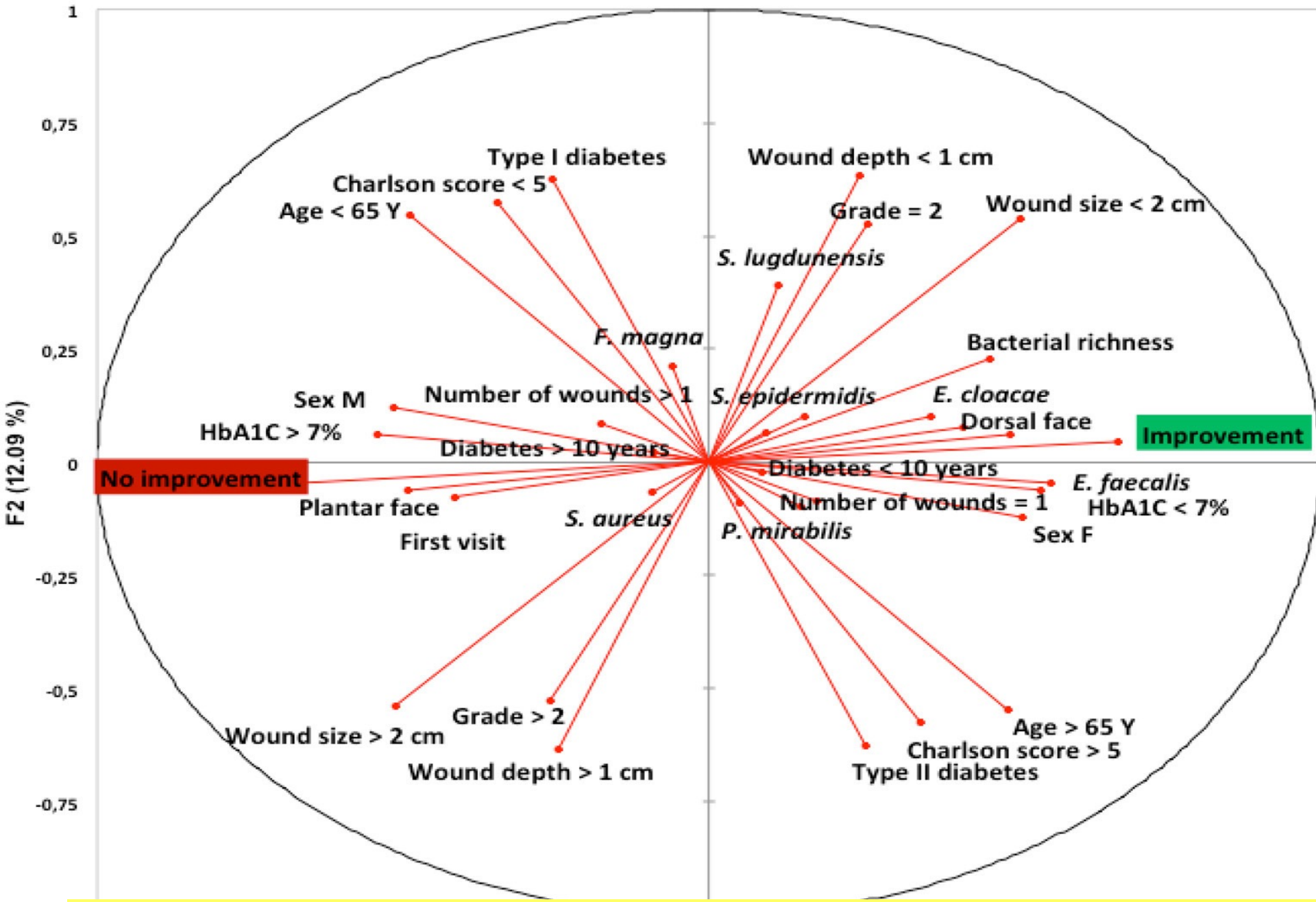
Antibiotic Agent(s) (Route)	Patients Treated, No.	Study Design	Patient Group	Type/Severity of Infection	Reference
Metronidazole + ceftriaxone vs ticarcillin/clavulanate (IV)	70	Prospective open label	H	Older men, Wagner grades 1–3	Clay 2004 [150]
Ceftobiprole vs vancomycin + ceftazidime (IV)	828	RCDBT DFI subgroup	H	cSSSI	Deresinski 2008 [147]
Piperacillin/tazobactam vs ampicillin/ sulbactam (IV)	314	Prospective open label	H	Moderate/severe infected DFU	Harkless 2005 [149]
Daptomycin vs vancomycin or Semisynthetic penicillin (IV)	133	RCSBT DFI subgroup	H	Gram + DFI	Lipsky 2005 [155]
Ertapenem vs piperacillin/ tazobactam (IV)	586	RCDBT	H	Moderate/severe DFI	Lipsky 2005 [120]
Moxifloxacin (IV to PO) vs piperacillin/tazobactam (IV) to amoxicillin/clavulanate (PO)	78	RCDBT DFI subgroup	H	cSSSI, including DFI (not classified)	Lipsky 2007 [148]
Pexiganan (topical) vs ofloxacin (PO)	835	2 RCDBTs	O	Mildly infected DFU	Lipsky 2008 [114]
Ceftriaxone vs fluoroquinolone (IV)	180	Prospective open label	H	"Severe limb-threatening" DFI	Lobmann 2004 [151]
Moxifloxacin vs amoxicillin/ clavulanate (IV to PO)	804	Prospective open label	H	cSSSI, including DFI	Vick-Fragoso 2009 [152]
Tigecycline vs ertapenem (IV)	944	RDBCT	H	Qualifying DFI± osteomyelitis	Clinicaltrials.gov 2010 [158]
Piperacillin/tazobactam vs imipenem/cilastatin (IV)	62	RCT open-label	H	Severe DFI, including osteomyelitis	Saltoglu 2010 [157]

IDSA 2012

We ignore if all retrieved pathogens should be treated

(especially in soft tissue infections)

- *If you insist, you might identify many co-pathogens*
- *Microbiology might change during treatment of (ischemic, ulcerated) DFIs*



Jneid et al. Frontiers in Cellular and Infection Microbiology 2018

55 diabetic foot infections, surgery 84%
2 microbiological assessments:
On admission, and 1 week later.

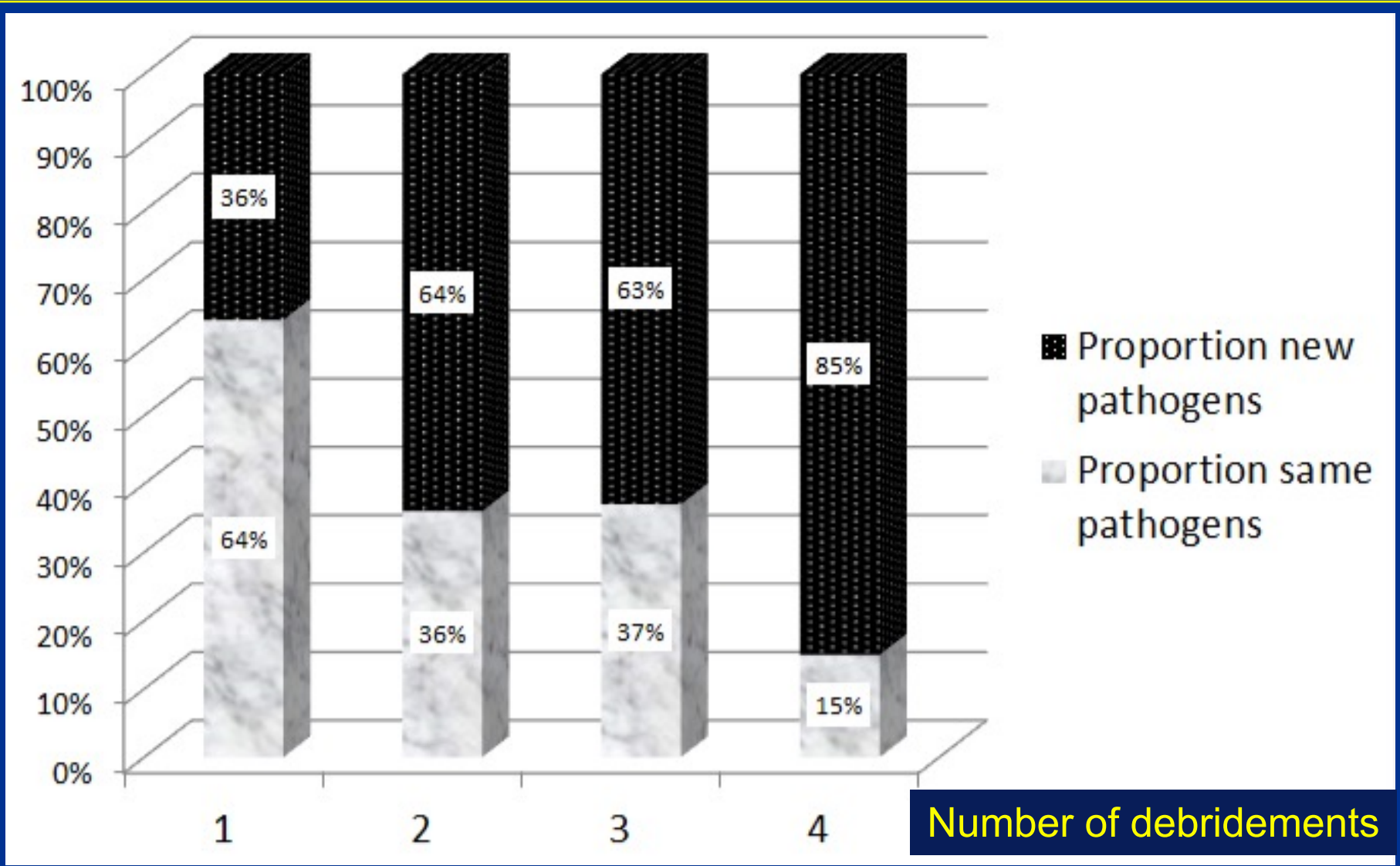
Table 1. First culture showing community acquired infections

Organisms isolated	Frequency (%) (n=55)
Klebsiella	14 (25.5)
E-coli	11 (20)
Enterococci	9 (16.4)
Proteus	4 (7.3)
Staphylococcus aureus	4 (7.3)
Enterobacter	3 (5.5)
Pseudomonas	1 (1.8)
Gram negative cocci	1 (1.8)
Non-fermenting gram neg bacilli	1 (1.8)
No growth	7 (12.7)

Table 3: Second culture showing hospital acquired infections.

Organism isolated	Frequency (%)
Pseudomonas	28 (50.9)
E. coli	8 (14.5)
Proteus	7 (12.7)
Gram positive cocci in pairs	4 (7.3)
Staphylococcus aureus	4 (7.3)
Non-fermenting gram negative bacilli	1 (1.8)
No growth	3 (5.5)

Proportions of « new infections »



DIABETICMedicine

DOI: 10.1111/j.1464-5491.2011.03528.x

Article: Clinical Practice

Does osteomyelitis in the feet of patients with diabetes really recur after surgical treatment? Natural history of a surgical series

J. Aragón-Sánchez[1], J.L. Lázaro-Martínez[2], C. Hernández-Herrero[3], N. Campillo-Vilorio[4], Y. Quintana-Marrero[1], E. García-Morales[2] and M.J. Hernández-Herrero[1]

[1]Diabetic Foot Unit, La Paloma Hospital, Las Palmas de Gran Canaria, [2]Diabetic Foot Unit, Complutense University Clinic, Madrid [3]Endocrinology Department. University Macarena Hospital, Seville, Spain and [4]Diabetic Foot Unit, Diabetology Department, Plaza de la Salud General Hospital, Dominican Republic

64 patients: median duration of follow-up was 101.8 weeks

- Recurrence 4.6%
- Re-ulceration 43.0%
- New osteomyelitis 16.9%

3

Infection is the tip of the iceberg, but competes with other important factors such as ischemia

Randomization In Clinical Trials

Diffficult over second-line or third line parameters of importance. Needs stratifications and multivariate adjustements

Diabetes Care Volume 37, March 2014

Antibiotics Versus Conservative Surgery for Treating Diabetic Foot Osteomyelitis: A Randomized Comparative Trial

José Luis Lázaro-Martínez,[1] Javier Aragón-Sánchez,[2] and Esther García-Morales[1]

RESULTS

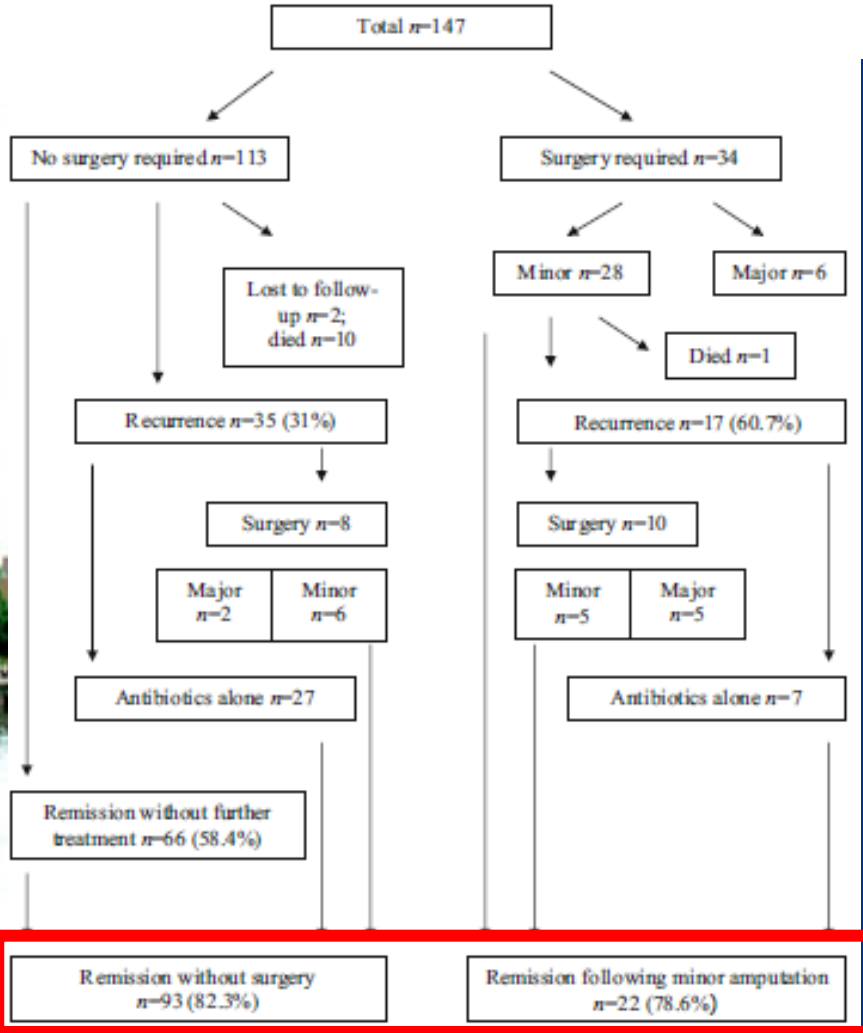
Eighteen patients (75%) achieved primary healing in the AG, and 19 (86.3%) in the SG ($P = 0.33$). The median time to healing was 7 weeks (quartile [Q] 1 to Q5, Q3–Q8) in the AG and 6 weeks (Q1–Q3, Q3–Q9) in the SG ($P = 0.72$). The conditions of four patients from the AG worsened (16.6%), and they underwent surgery. Three patients from the SG required reoperation. No difference was found between the two groups regarding minor amputations ($P = 0.336$).

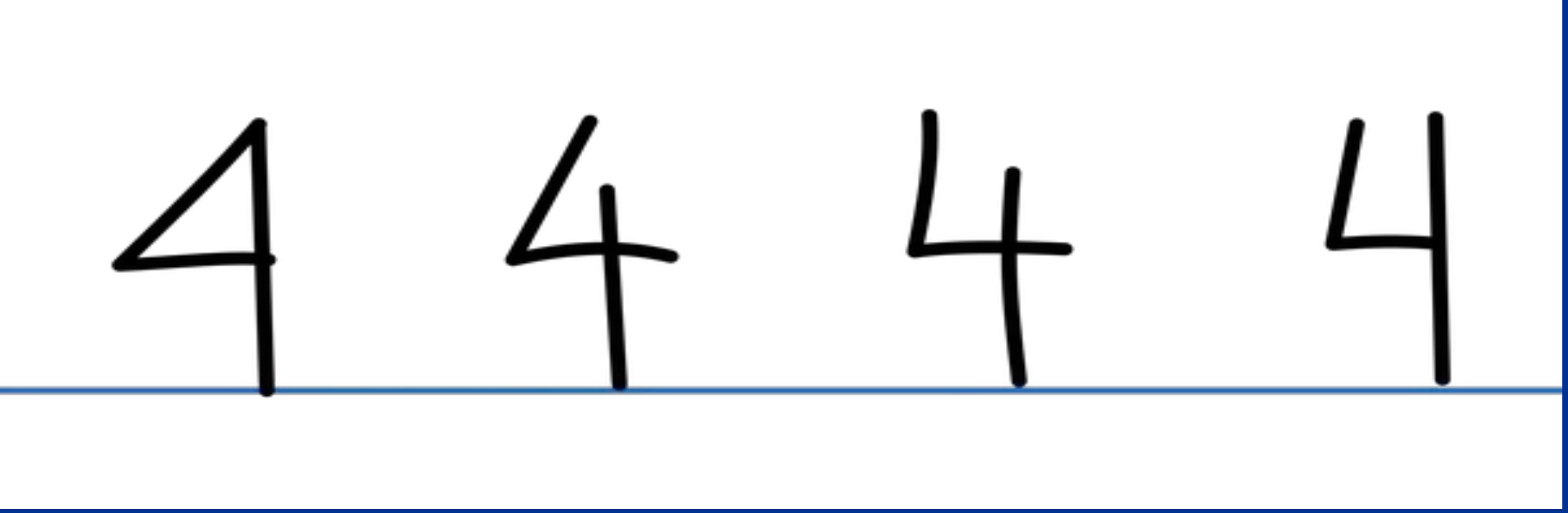
Diabetologia (2008) 51:962–967
DOI 10.1007/s00125-008-0976-1

ARTICLE

Primarily non-surgical management of osteomyelitis of the foot in diabetes

F. L. Game · W. J. Jeffcoate





For DFO, we rely on analogy, but ignore any differences between types of osteitis

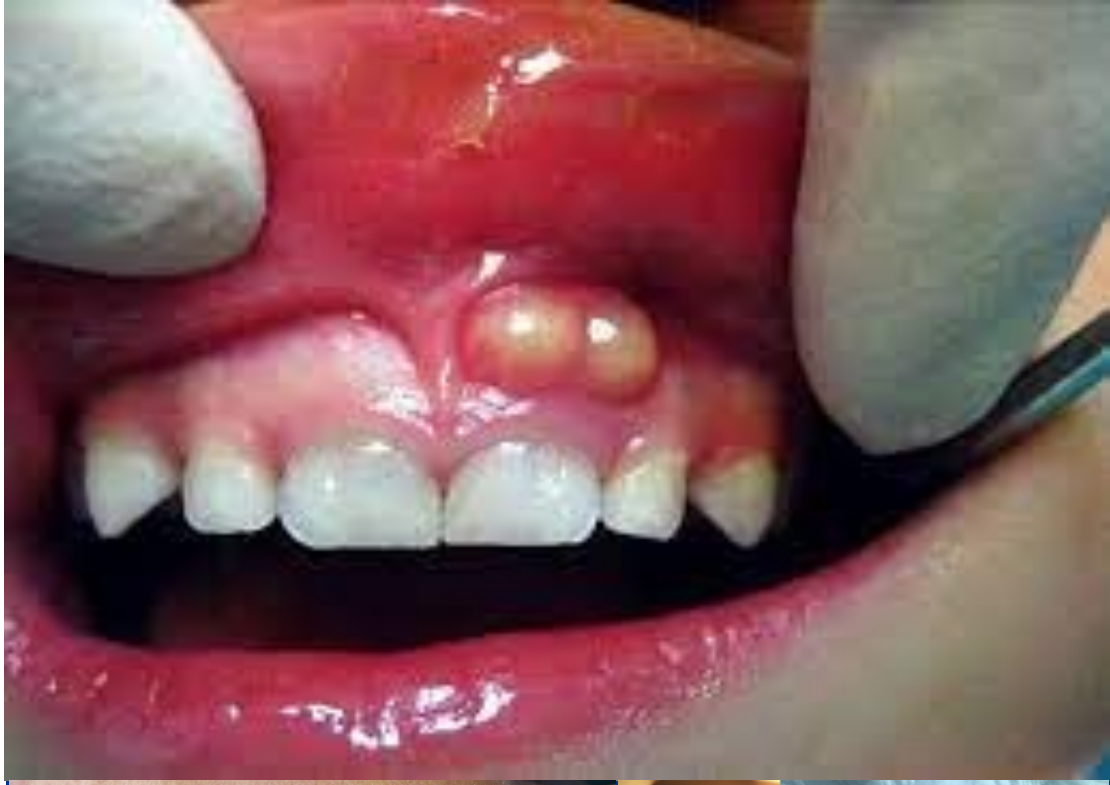
- *Should every bone infection be treated the same ?*
- *partial amputation? Size of osteitis? Sequesters?*
- *superficial bone contamination?*
- *if we use topical (local) antibiotic agents?*

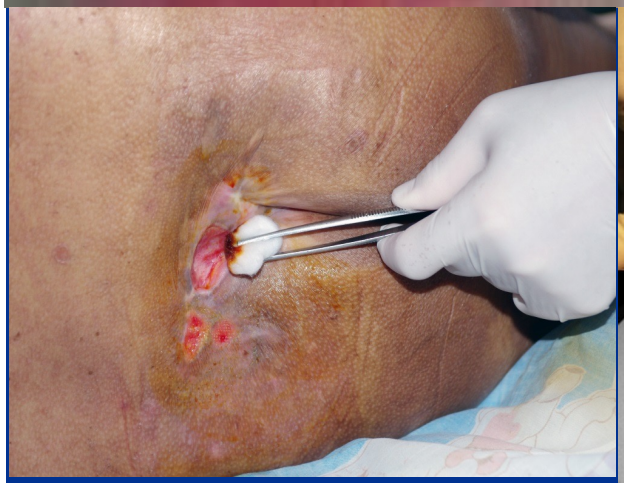
Prosthetic-joint infection
Coagulase-negative; staphylococci; *Staph aureus;* polymicrobial *Streptococcus* spp; gram-negative aerobic bacilli

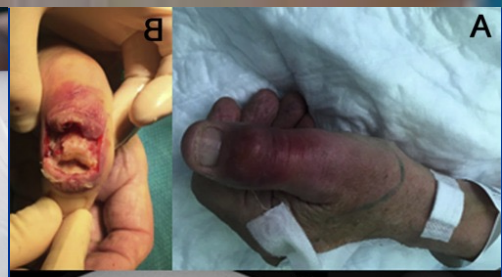
Vertebral osteomyelitis
Staph aureus; gram-negative aerobic bacilli; *Streptococcus* spp; *Mycobacterium tuberculosis*

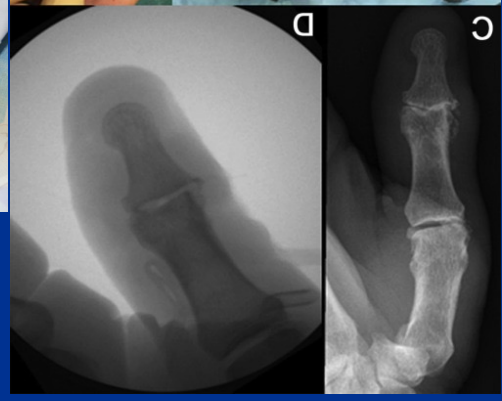
Post-traumatic infection
Staph aureus; polymicrobial gram-negative aerobic bacilli; anaerobes

Diabetic foot infection
Staph aureus; *Streptococcus* spp; *Enterococcus* spp; coagulase-negative staphylococci; gram-negative aerobic bacilli; anaerobes

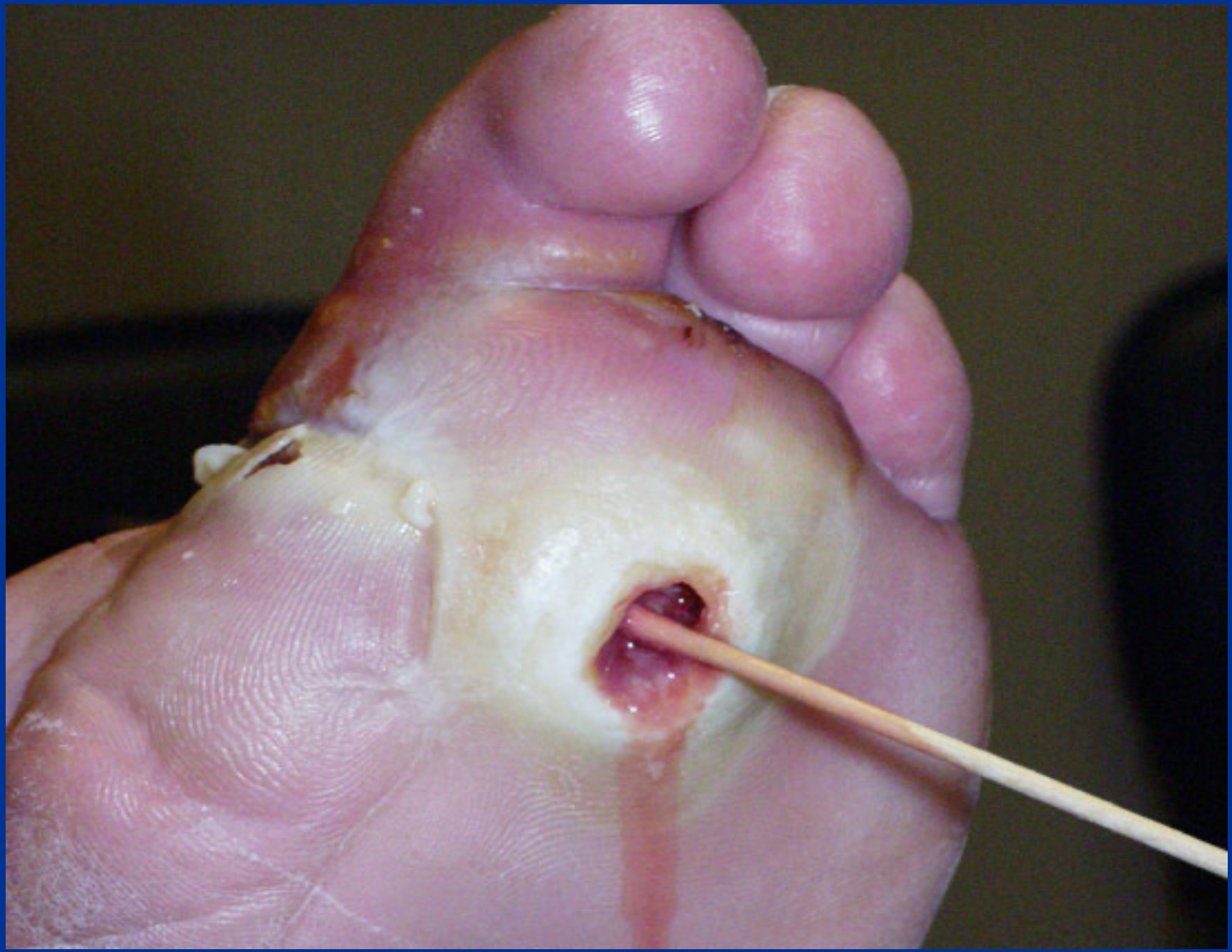


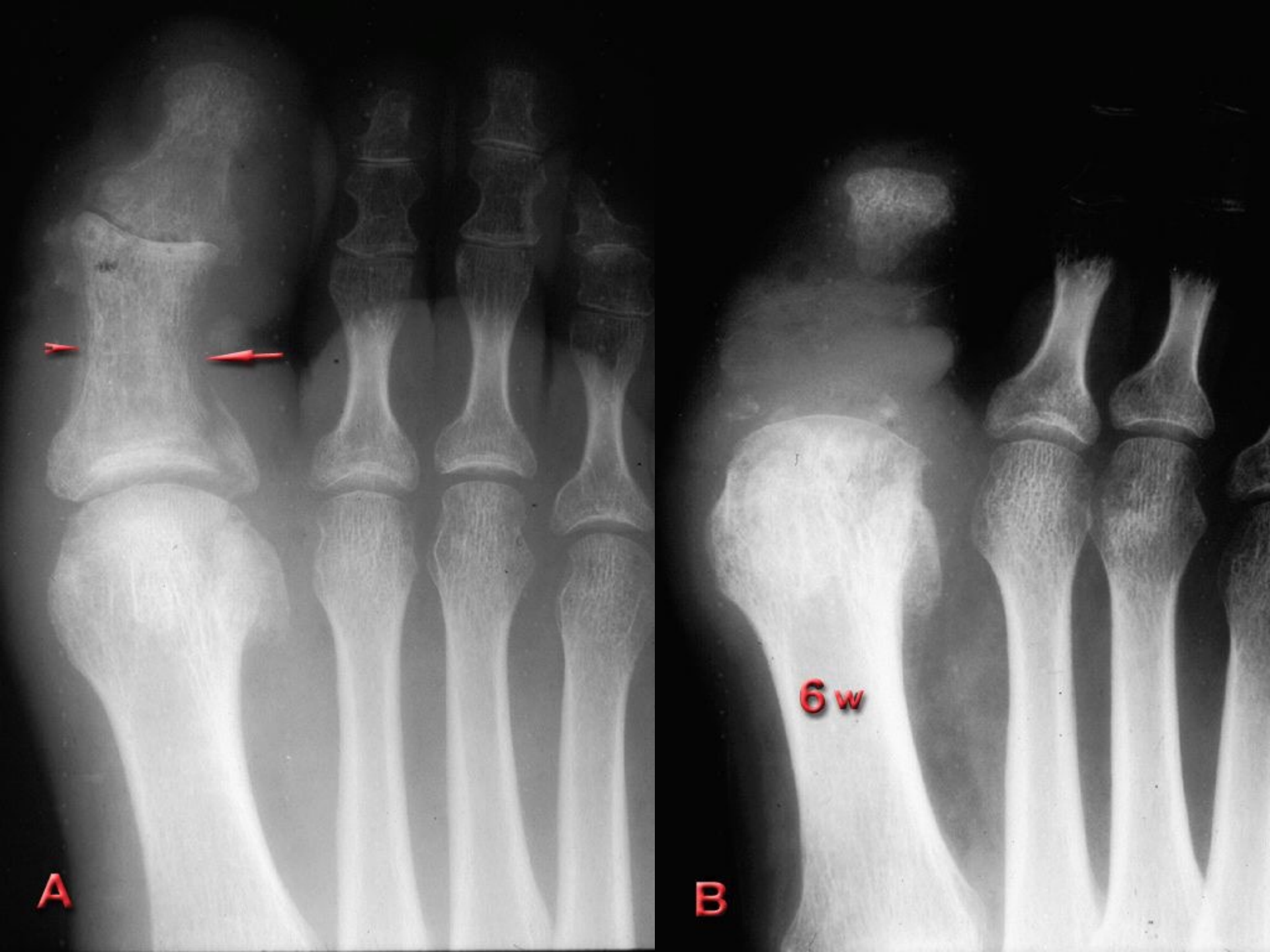






Lew et al, Lancet 2004

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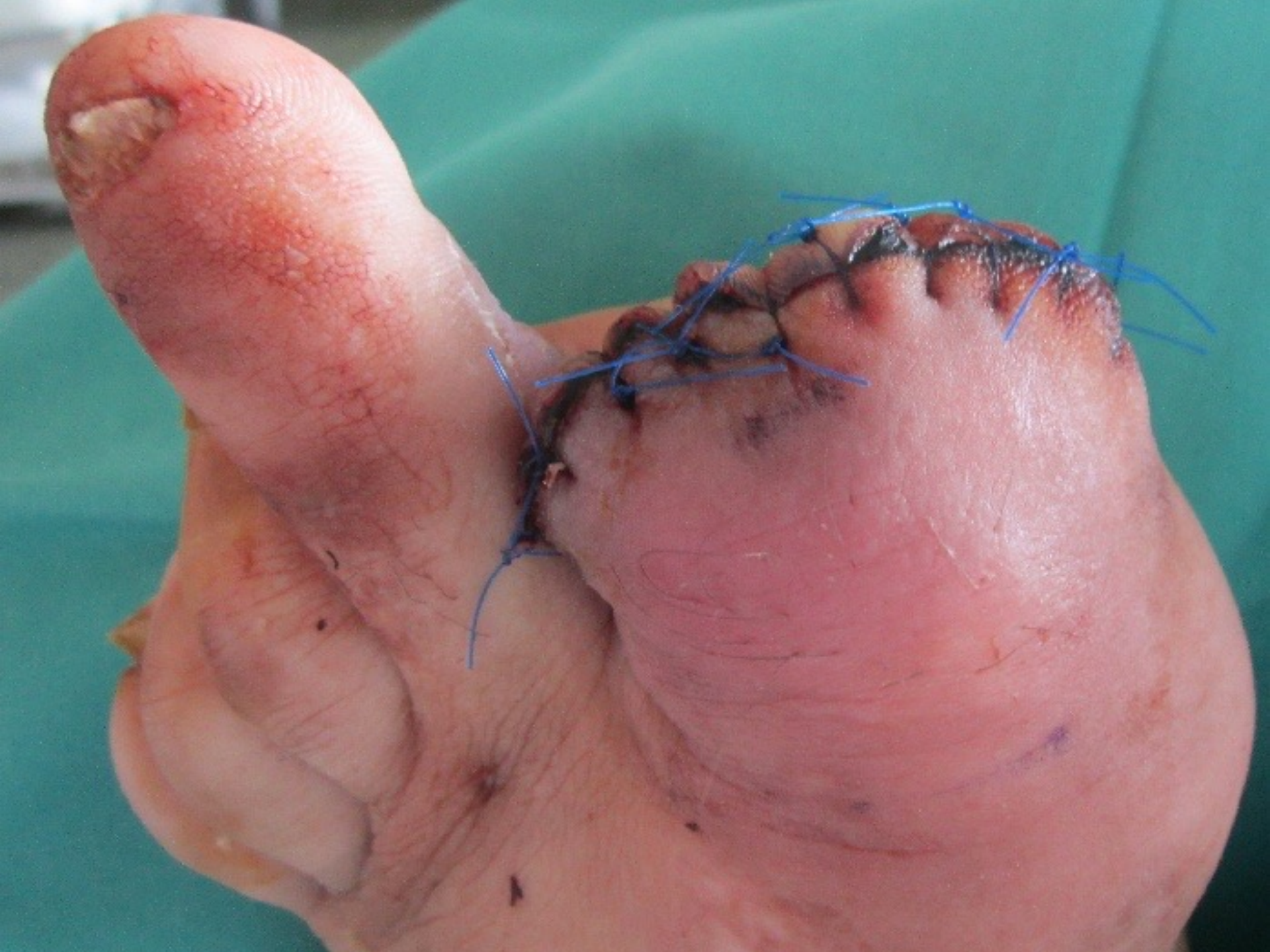


5

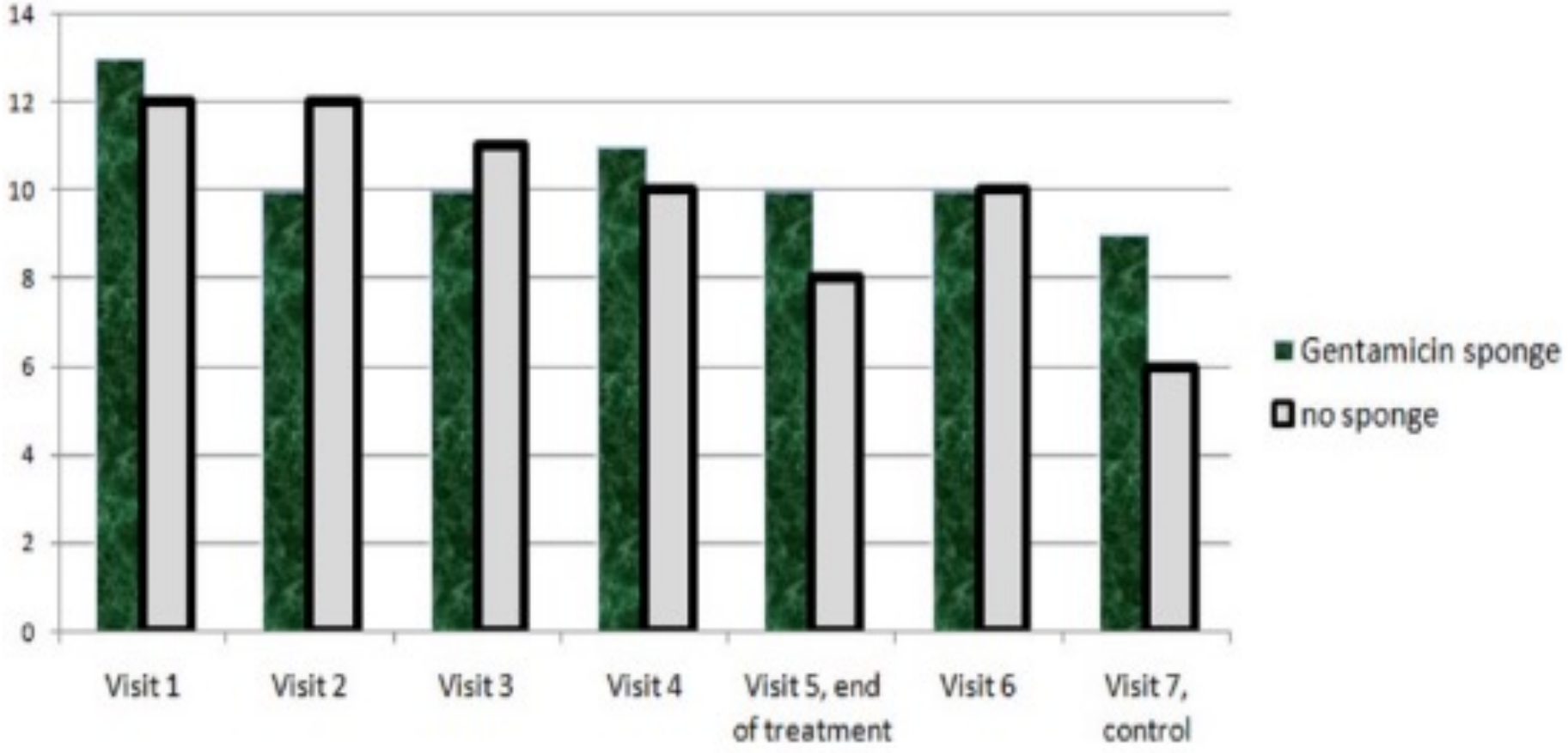
For Soft-Tissue DFIs, we ignore when to stop antibiotics

- *As long as there is visual redness ? Control CRP values ?*
- *Which proportion of ulcer-related mild ST-DFI can simply be debrided without systemic antibiotics (local antiseptics)?*

SAGE Open Medicine
Volume 6: 1–5

DOI: 10.1177/2050312118773950
journals.sagepub.com/home/smo
SAGE

A randomized controlled trial of the safety and efficacy of a topical gentamicin–collagen sponge in diabetic patients with a mild foot ulcer infection



OPEN

Annals of Surgery

DOI: 10.1097/SLA.0000000000005205

Moderate to Severe Soft Tissue Diabetic Foot Infections: A Randomized, Controlled, Pilot Trial of Post-Debridement Antibiotic Treatment for 10 versus 20 days

Truong-Thanh Pham, MD[1,2*], Karim Gariani, MD[3*], Jean-Christophe Richard, MD[2], Benjamin Kressmann, RN[1,2], François R. Jornayvaz, MD[3], Jacques Philippe, MD[3], Benjamin A. Lipsky, MD[1,4], İlker Uçkay, MD[1,2,5]

[*] *equal contribution as first authors*

Pilot study Geneva - (Surgical) soft tissue DFI

n = 66	10 days	*p - value*	20 days
Age (median)	70 years	0.16	73 years
PAD	63%	0.89	65%
S. aureus	34%	0.65	29%
Gram-negative	29%	0.65	23%
Polymicrobial	43%	0.94	42%
Debridemts. (med)	1	0.57	1
Remission	**77%**	**0.57**	**71%**
Adverse events	**40%**	**0.71**	**35%**
- serious AE	***17%***	***0.82***	***19%***
- antibiotic AE	***6%***	***0.31***	***13%***

Intention-to-Treat Population (similar to PP)

Importantly, 8 ST-DFIs in the short course arm and 5 cases in the long course arm recurred as DFO (8/35 **(22%)** vs 5/31 (16%); P = 0.53).

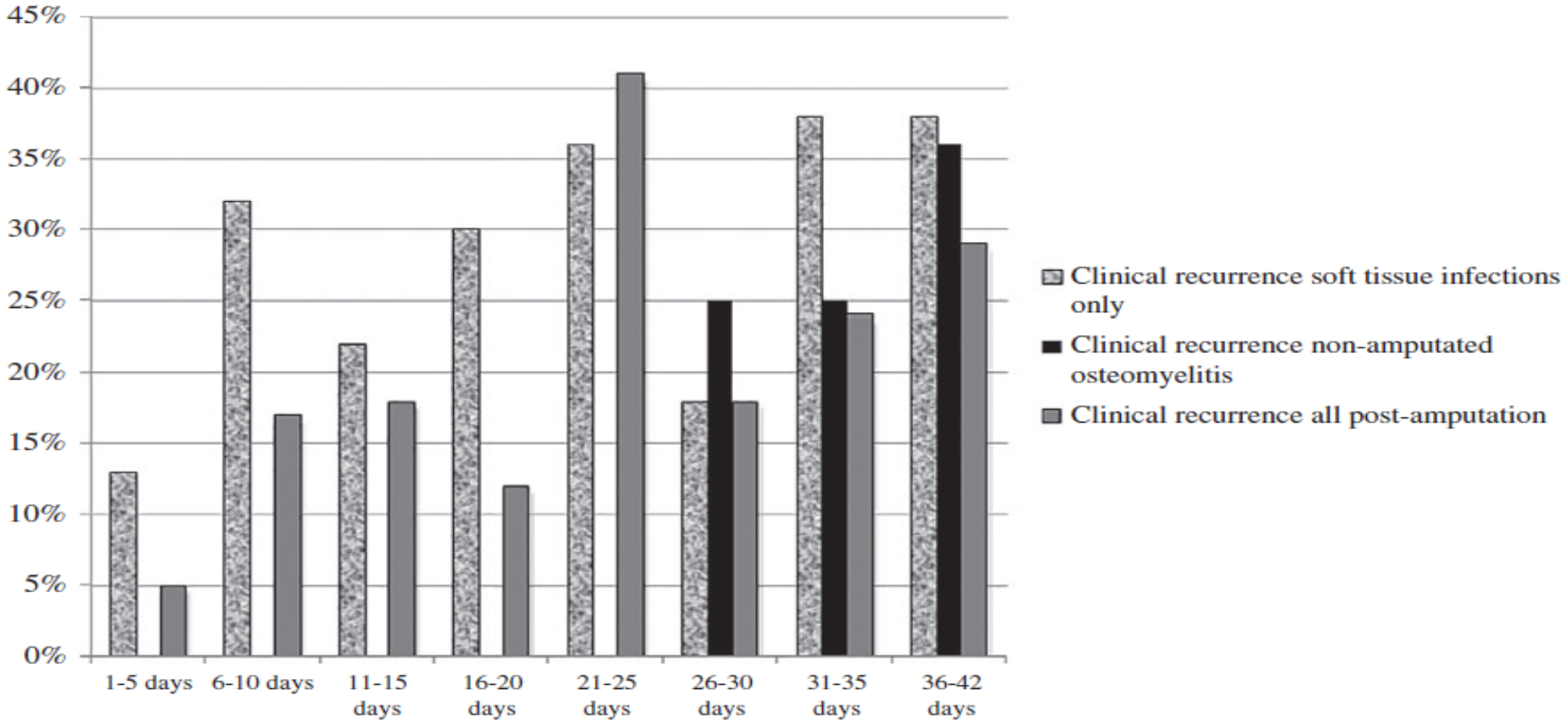
«Recurrence as DFO» 12 of 17 recurrences=70%.

Pham et al, Ann Surg 2022

ORIGINAL ARTICLE

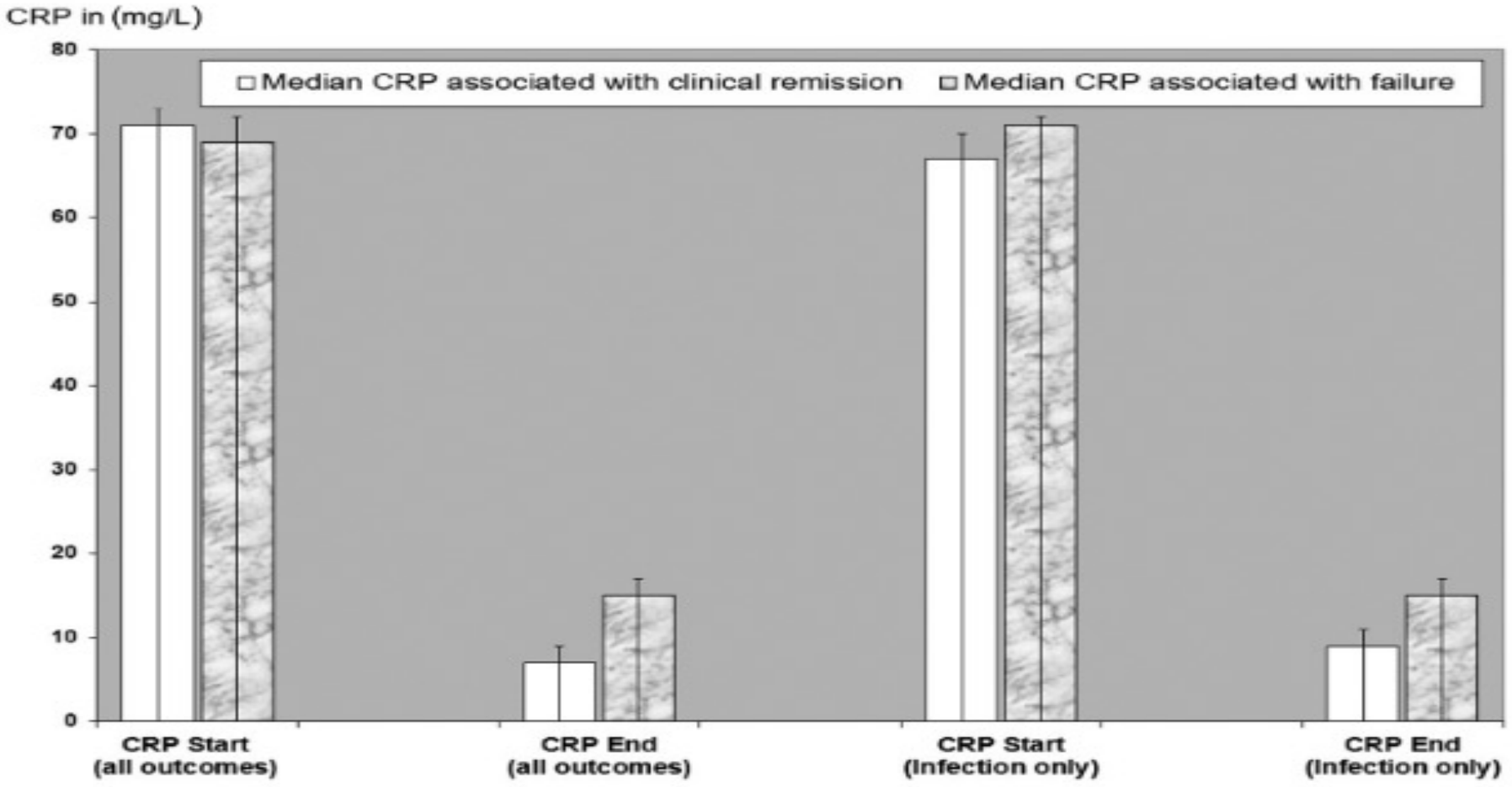
Remission in diabetic foot infections: Duration of antibiotic therapy and other possible associated factors

Karim Gariani MD[1,2] | Dan Lebowitz MD[1] | Elodie von Dach RN[3] | Benjamin Kressmann RN[1] | Benjamin A. Lipsky MD[1,4] | Ilker Uçkay MD[1,3]



Is routine measurement of the serum C-reactive protein level helpful during antibiotic therapy for diabetic foot infection?

Truong-Thanh Pham MD[1,2] | Oliver Wetzel MD[3] | Karim Gariani MD[4] | Benjamin Kressmann RN[1,2] | François R. Jornayvaz MD[4] | Benjamin A. Lipsky MD[1,5] | İlker Uçkay MD[1,2,6]




MEANING, MYSTERY AND MAGIC
OF THE NUMBER
6
SIX
Numerologist

Duration; always 6 weeks for DFO ?

Osteomyelitis

Daniel P Lew, Francis A Waldvogel

Lancet 2004; 364: 369–79

Services of Infectious Diseases and Medicine 2, Department of Internal Medicine, Geneva University Hospitals, Geneva, Switzerland (Prof D P Lew MD, Prof F A Waldvogel MD)

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Bone and joint infections are painful for patients and frustrating for both them and their doctors. The high success rates of antimicrobial therapy in most infectious diseases have not yet been achieved in bone and joint infections owing to the physiological and anatomical characteristics of bone. The key to successful management is early diagnosis, including bone sampling for microbiological and pathological examination to allow targeted and long-lasting antimicrobial therapy. The various types of osteomyelitis require differing medical and surgical therapeutic strategies. These types include, in order of decreasing frequency: osteomyelitis secondary to a contiguous focus of infection (after trauma, surgery, or insertion of a joint prosthesis); that secondary to vascular insufficiency (in diabetic foot infections); or that of haematogenous origin. Chronic osteomyelitis is associated with avascular necrosis of bone and formation of sequestrum (dead bone), and surgical debridement is necessary for cure in addition to antibiotic therapy. By contrast, acute osteomyelitis can respond to antibiotics alone. Generally, a multidisciplinary approach is required for success, involving expertise in orthopaedic surgery, infectious diseases, and plastic surgery, as well as vascular surgery, particularly for complex cases with soft-tissue loss.

Standart: 4 - 6 weeks

2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections[a]

Benjamin A. Lipsky,[1] Anthony R. Berendt,[2] Paul B. Cornia,[3] James C. Pile,[4] Edgar J. G. Peters,[5] David G. Armstrong,[6] H. Gunner Deery,[7] John M. Embil,[8] Warren S. Joseph,[9] Adolf W. Karchmer,[10] Michael S. Pinzur,[11] and Eric Senneville[12]

[1]Department of Medicine, University of Washington, Veterans Affairs Puget Sound Health Care System, Seattle; [2]Bone Infection Unit, Nuffield Orthopaedic Centre, Oxford University Hospitals NHS Trust, Oxford; [3]Department of Medicine, University of Washington, Veteran Affairs Puget Sound Health Care System, Seattle; [4]Divisions of Hospital Medicine and Infectious Diseases, MetroHealth Medical Center, Cleveland, Ohio; [5]Department of Internal Medicine, VU University Medical Center, Amsterdam, The Netherlands; [6]Southern Arizona Limb Salvage Alliance, Department of Surgery, University of Arizona, Tucson; [7]Northern Michigan Infectious Diseases, Petoskey; [8]Department of Medicine, University of Manitoba, Winnipeg, Canada; [9]Division of Podiatric Surgery, Department of Surgery, Roxborough Memorial Hospital, Philadelphia, Pennsylvania; [10]Department of Medicine, Division of Infectious Diseases, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts; [11]Department of Orthopaedic Surgery and Rehabilitation, Loyola University Medical Center, Maywood, Illinois; and [12]Department of Infectious Diseases, Dron Hospital, Tourcoing, France

DFO: 4 - 6 weeks

Cut-point 6 Wochen - retrospektiv

International Journal of Antimicrobial Agents 53 (2019) 246–260

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag

Review

Short- versus long-course antibiotics in osteomyelitis: A systematic review and meta-analysis

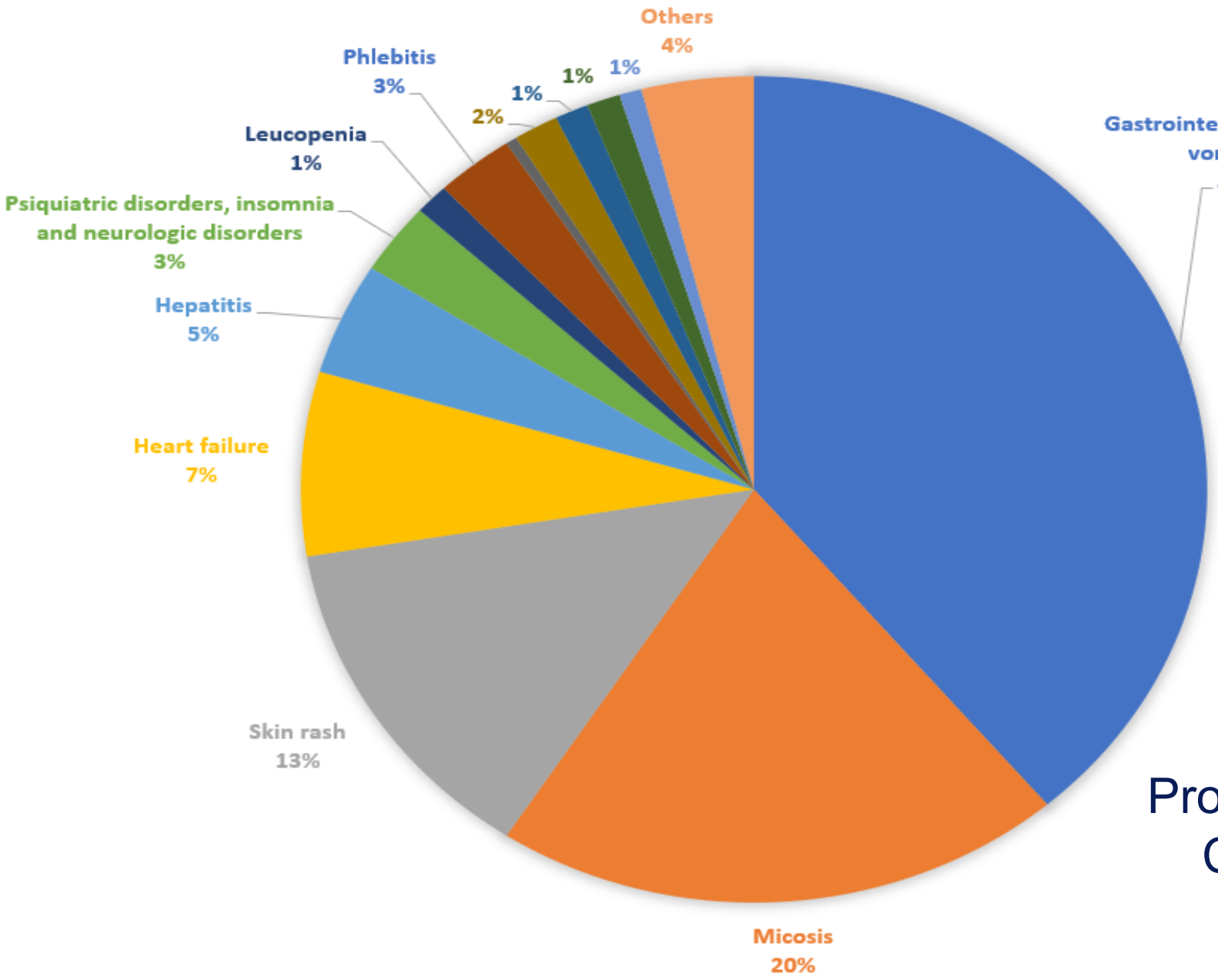
Chung-Yen Huang[a], Ronan W. Hsieh[b], Hung-Teng Yen[a], Tzu-Chun Hsu[c], Chun-Yu Chen[d,e,f],

In conclusion, it is safe and effective to treat acute osteomyelitis of childhood with a short course (2–3 weeks) of antibiotics. A short antibiotic course (<4–6 weeks) may be similarly effective in diabetic foot osteomyelitis and chronic osteomyelitis, although the supporting evidence is relatively insufficient. A long course (6 weeks) of antibiotics may still be preferred in vertebral osteomyelitis, especially in patients infected with *S. aureus*. However,

All antibiotic adverse events

Incidence	Author	Journal
18%	Prendki et al.	Eur J Clin Microbiol Infect Dis (2017)
29%	Schindler et al.	J Infect (2013)
14%	Uçkay et al.	(2017-2019)

ANTIBIOTIC-RELATED DVERSE EVENTS IN OSTEOARTICULAR INFECTIONS, N=250. BALGRIST UNIVERSITY HOSPITAL



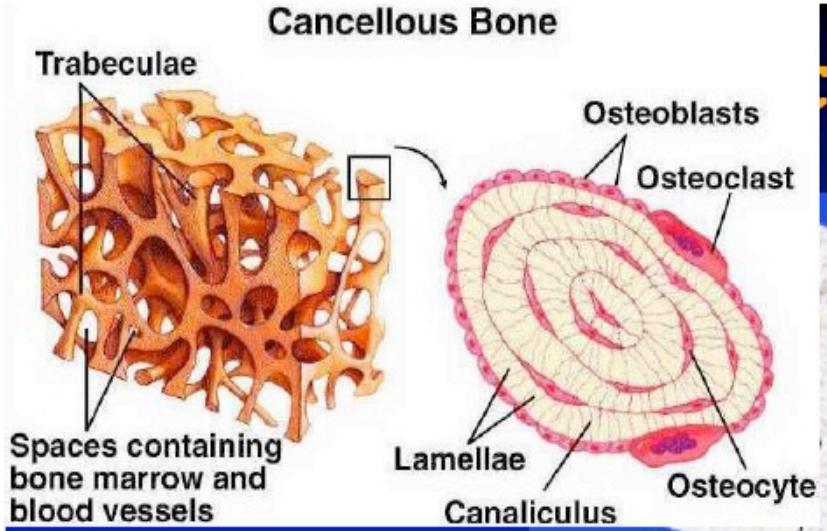
Prospective Cohort

DFI yes / no	AE_total 0	1	Total
0	1,386 88.00	189 12.00	1,575 100.00
1	676 91.72	61 8.28	737 100.00
Total	2,062 89.19	250 10.81	2,312 100.00

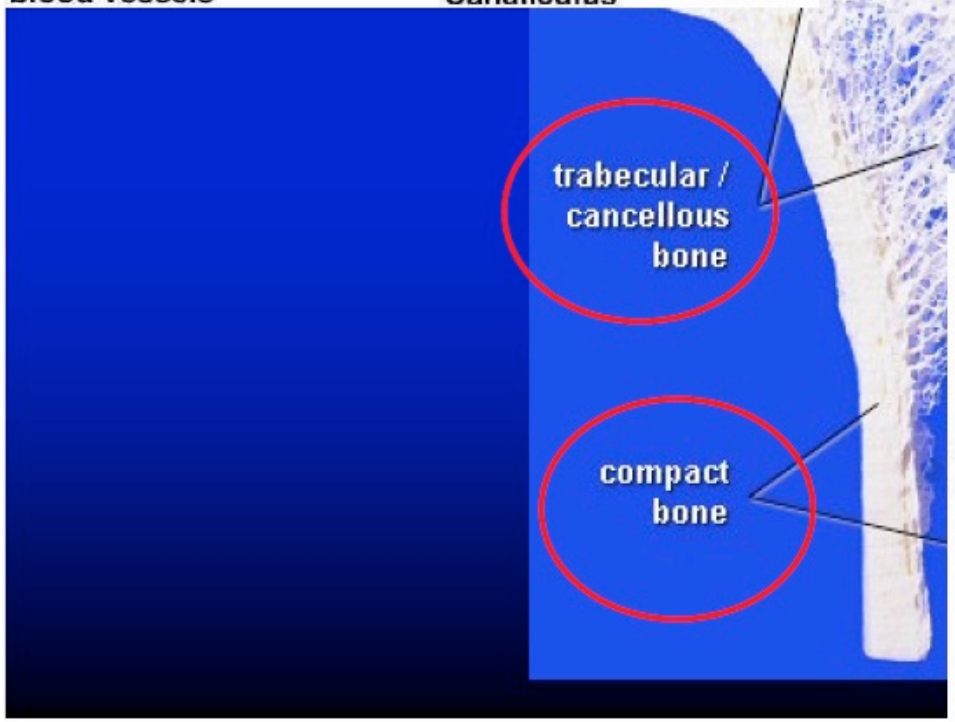
Pearson chi2(1) = 7.2167 Pr = 0.007

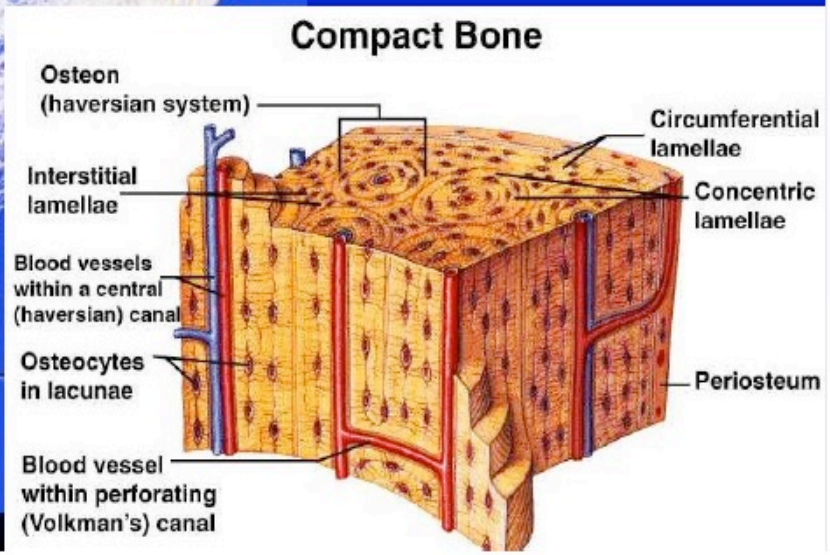
Fisher's exact = 0.008

Intravenous and dosing


Cancellous Bone
Trabeculae
Osteoblasts
Osteoclast
Spaces containing bone marrow and blood vessels
Lamellae
Canaliculus
Osteocyte


CONFORMAZIONE


trabecular / cancellous bone
compact bone


Compact Bone
Osteon (haversian system)
Circumferential lamellae
Interstitial lamellae
Concentric lamellae
Blood vessels within a central (haversian) canal
Osteocytes in lacunae
Periosteum
Blood vessel within perforating (Volkman's) canal

THE COCHRANE COLLABORATION®

Analysis 1.2. Comparison 1 Oral antibiotic versus parenteral antibiotic (AB), Outcome 2 Remission at least 12 months after the end of treatment.

Review: Antibiotics for treating chronic osteomyelitis in adults

Comparison: 1 Oral antibiotic versus parenteral antibiotic (AB)

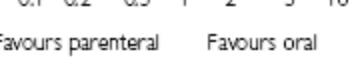
Outcome: 2 Remission at least 12 months after the end of treatment

Study or subgroup	Oral AB n/N	Parenteral AB n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Gentry 1990	24/31	22/28		48.5 %	0.99 [0.75, 1.29]
Gentry 1991	14/19	12/14		29.0 %	0.86 [0.61, 1.21]
Mader 1990	11/14	10/12		22.6 %	0.94 [0.65, 1.37]
Total (95% CI)	**64**	**54**		**100.0 %**	**0.94 [0.78, 1.13]**

Total events: 49 (Oral AB), 44 (Parenteral AB)

Heterogeneity: $Chi^2 = 0.38$, df = 2 (P = 0.83); $I^2 = 0.0\%$

Test for overall effect: Z = 0.66 (P = 0.51)



Conterno et al. Cochrane 2008

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Oral versus Intravenous Antibiotics for Bone and Joint Infection

H.-K. Li, I. Rombach, R. Zambellas, A.S. Walker, M.A. McNally, B.L. Atkins, B.A. Lipsky, H.C. Hughes, D. Bose, M. Kümin, C. Scarborough, P.C. Matthews, A.J. Brent, J. Lomas, R. Gundle, M. Rogers, A. Taylor, B. Angus, I. Byren, A.R. Berendt, S. Warren, F.E. Fitzgerald, D.J.F. Mack, S. Hopkins, J. Folb, H.E. Reynolds, E. Moore, J. Marshall, N. Jenkins, C.E. Moran, A.F. Woodhouse, S. Stafford, R.A. Seaton, C. Vallance, C.J. Hemsley, K. Bisnauthsing, J.A.T. Sandoe, I. Aggarwal, S.C. Ellis, D.J. Bunn, R.K. Sutherland, G. Barlow, C. Cooper, C. Geue, N. McMeekin, A.H. Briggs, P. Sendi, E. Khatamzas, T. Wangrangsimakul, T.H.N. Wong, L.K. Barrett, A. Alvand, C.F. Old, J. Bostock, J. Paul, G. Cooke, G.E. Thwaites, P. Bejon, and M. Scarborough, for the OVIVA Trial Collaborators*

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DOI: 10.1111/dom.13651

WILEY

BRIEF REPORT

Oral amoxicillin-clavulanate for treating diabetic foot infections

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Aim: To assess amoxicillin-clavulanate (AMC) for the oral therapy of diabetic foot infections (DFIs), especially for diabetic foot osteomyelitis (DFO).

Methods: We performed a retrospective cohort analysis among 794 DFI episodes, including 339 DFO cases.

Results: The median duration of antibiotic therapy after surgical debridement (including partial amputation) was 30 days (DFO, 30 days). Oral AMC was prescribed for a median of 20 days (interquartile range, 12-30 days). The median ratio of oral AMC among the entire antibiotic treatment was 0.9 (interquartile range, 0.7-1.0). After a median follow-up of 3.3 years, 178 DFIs (22%) overall recurred (DFO, 75; 22%). Overall, oral AMC led to 74% remission compared with 79% with other regimens (χ^2-test; $P = 0.15$). In multivariate analyses and stratified subgroup analyses, oral AMC resulted in similar clinical outcomes to other antimicrobial regimens, when used orally from the start, after an initial parenteral therapy, or when prescribed for DFO.

Conclusions: Oral AMC is a reasonable option when treating patients with DFIs and DFOs.

J. Bone Joint Infect., 7, 61–70, 2022
https://doi.org/10.5194/jbji-7-61-2022

JBJI
Journal of Bone and Joint Infection
Open Access

Short and oral antimicrobial therapy for diabetic foot infection: a narrative review of current knowledge

Steven M. Maurer[1], Zehra S. Hepp[1,2], Shawna McCallin[3], Felix W. A. Waibel[1], Federico C. Romero[5], Yılmaz Zorman[6], Benjamin A. Lipsky[7], and İlker Uçkay[4]

Editorial Commentary

Oral antibiotic therapy in diabetic foot osteomyelitis: one small step or a giant leap of faith?

Prashanth R. J. Vas[1], Maria Demetriou[2], Nikolaos Papanas[2]

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Provenance: This is an invited article commissioned by the Editorial Office, *Annals of Translational Medicine*.

Comment on: Li HK, Rombach I, Zambellas R, *et al.* Oral versus Intravenous Antibiotics for Bone and Joint Infection. N Engl J Med 2019;380:425-36.

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journal homepage: www.elsevier.com/locate/ijid

Review

Antibiotic penetration into bone and joints: An updated review

Abrar K. Thabit*, Dania F. Fatani, Maryam S. Bamakhrama, Ola A. Barnawi, Lana O. Basudan, Shahad F. Alhejaili

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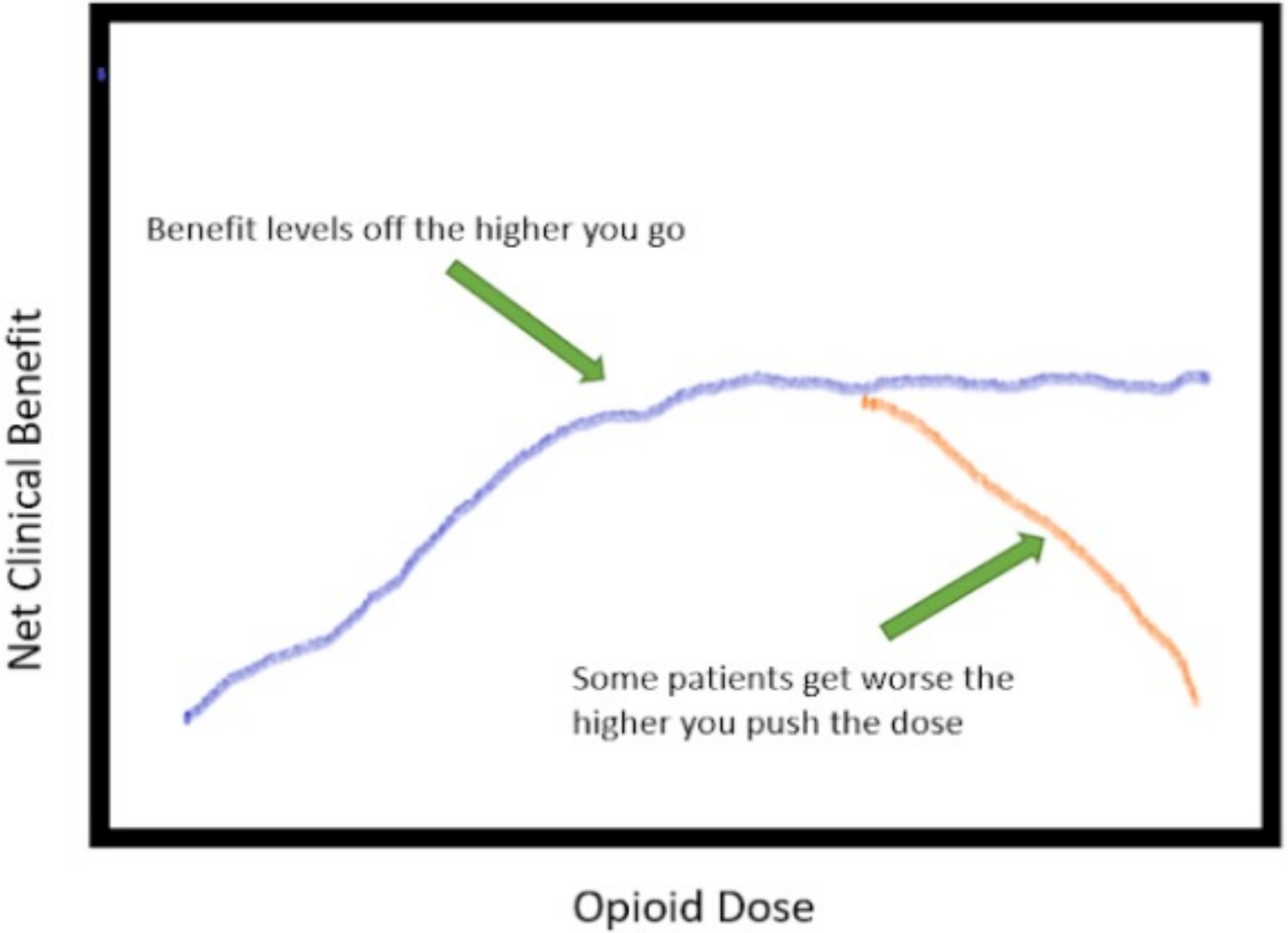
More than 30 antibiotics were evaluated

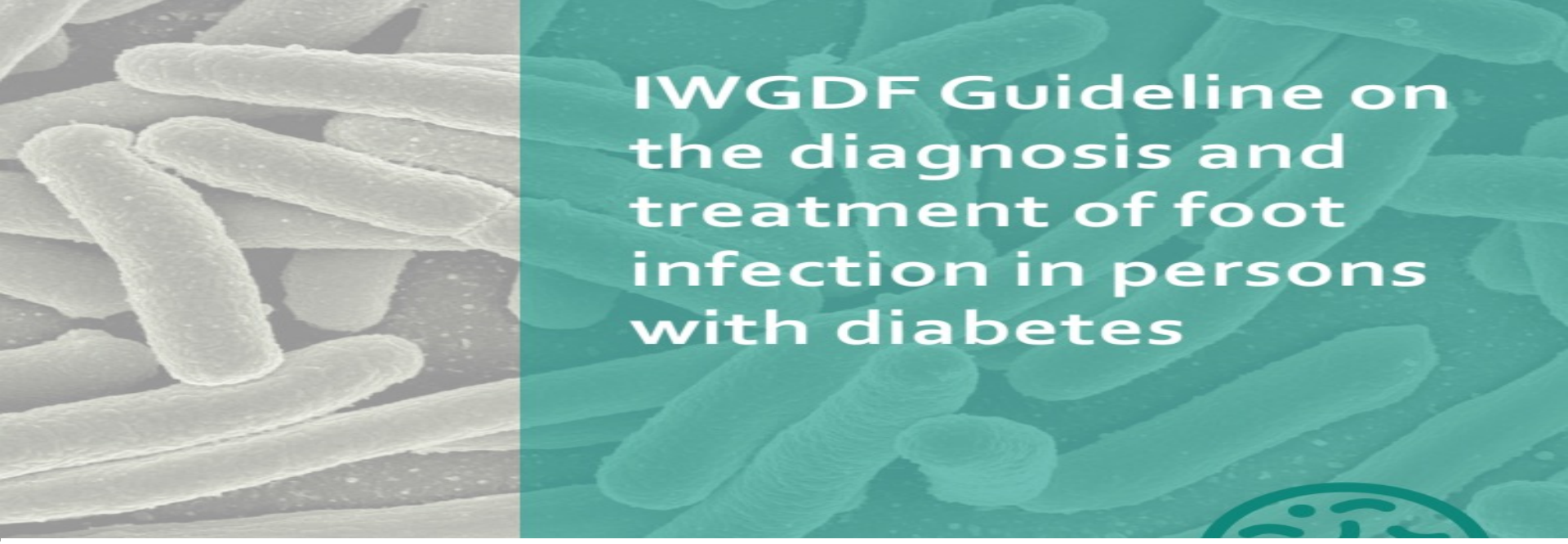
Overall, most antibiotics, including amoxicillin, tazobactam, cloxacillin, cephalosporins, carbapenems, aztreonam, aminoglycosides, quinolones, doxycycline, vancomycin, linezolid, daptomycin, clindamycin, co-trimoxazole, fosfomycin, rifampin, dalbavancin, oritavancin, showed good penetration into bone.

Few exceptions include penicillin and metronidazole

Antibiotics are not like pain killers




FOLLOW THE
GUIDELINES



SUPPLEMENT ARTICLE

WILEY

Guidelines on the diagnosis and treatment of foot infection in persons with diabetes (IWGDF 2019 update)

Benjamin A. Lipsky[1,2] | Éric Senneville[3] | Zulfiqarali G. Abbas[4] | Javier Aragón-Sánchez[5] | Mathew Diggle[6] | John M. Embil[7] | Shigeo Kono[8] | Lawrence A. Lavery[9] | Matthew Malone[10] | Suzanne A. van Asten[11] | Vilma Urbančič-Rovan[12] | Edgar J.G. Peters[13] on behalf of the International Working Group on the Diabetic Foot (IWGDF)

PICO

The PICO Principle assists you in organizing and focusing your question into a searchable query.

P

Participants / Population
Who are the relevant patients?

I

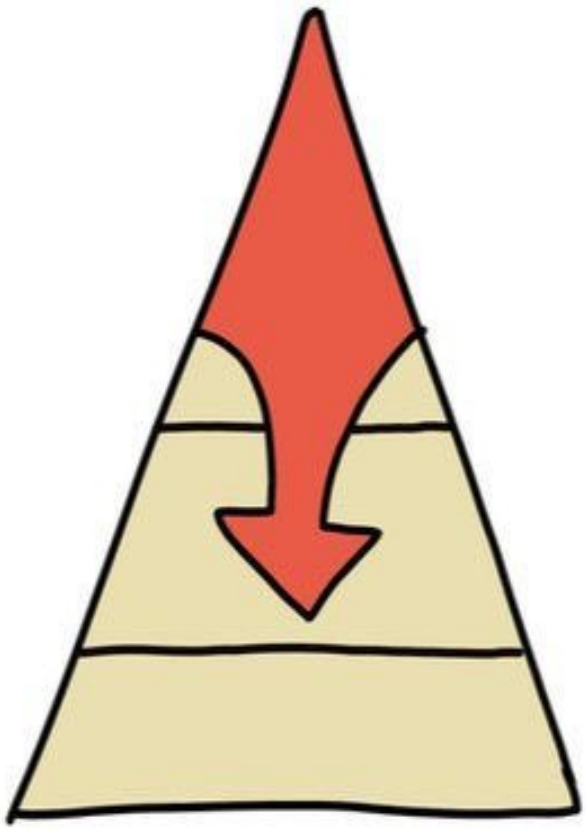
Intervention / Indication
What is the management strategy, diagnostic test or exposure that you are researching?

C

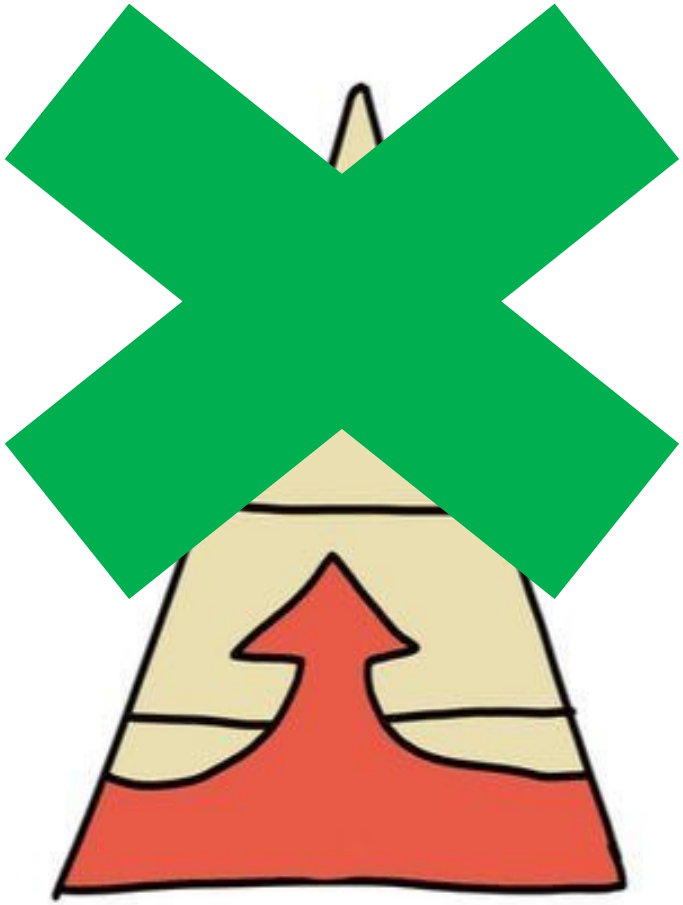
Comparator / Control
Is there a control or alternative management strategy, test, or exposure?

O

Outcome
What are the patient-relevant consequences?



top-down



buttom-up

Prospective non-inferior; 6 vs. 12 weeks

Six-Week Versus Twelve-Week Antibiotic Therapy for Nonsurgically Treated Diabetic Foot Osteomyelitis: A Multicenter Open-Label Controlled Randomized Study

Alina Tone,[1] Sophie Nguyen,[1] Fabrice Devemy,[2] Hélène Topolinski,[3] Michel Valette,[1] Marie Cazaubiel,[4] Armelle Fayard,[5] Éric Beltrand,[6] Christine Lemaire,[3] and Éric Senneville[1]

Diabetes Care 2015;38:302–307 | DOI: 10.2337/dc14-1514

Table 4—Clinical outcome of 40 diabetic patients with osteomyelitis of the foot treated nonsurgically according to the duration of antibiotic therapy

Patient outcome	6 weeks *n* = 20	12 weeks *n* = 20	*P*
Overall remission	12 (60)	14 (70)	0.50
Complete healing[a]	18 (90)	16 (80)	0.38
Time to complete healing (weeks ± SD)	13.1 ± 12.2	16.8 ± 17.4	0.44
Overall failure	8 (40)	6 (30)	0.50
Noncomplete healing	2 (10)	4 (20)	0.37
Relapsing osteomyelitis	2 (15)	3 (15)	1
Worsening radiological bone abnormalities	6 (30)	4 (20)	0.46
Bone resection	2 (10)	2 (10)	1
Spread of osteomyelitis to contiguous sites	4 (20)	2 (10)	0.37
Major amputation	2 (10)	2 (10)	1

Choice of systemic antibiotic agents

Treat a person with a diabetic foot infection with an antibiotic agent that has been shown to be effective in a published randomized controlled trial and is appropriate for the individual patient.

Some agents to consider include penicillins, cephalosporins, carbapenems, metronidazole (in combinationwith other antibiotic[s]), clindamycin, linezolid, daptomycin, quinolones, or vancomycin, but not tigecycline. (Strong; high)

IWDGF 2019

World guidelines are saying ….

Treat patients with a mild diabetic foot infection, and most with a moderate diabetic foot infection, with oral antibiotic therapy, either at presentation or when clearly improving with initial intravenous therapy. **(Weak; low)**

We suggest not using any currently available topical antimicrobial agent for treating a mild diabetic foot infection **(Weak; moderate)**

IWDGF 2019

2nd interim analysis, n = 237 (actually 360)

No significant differences between the groups

In multivariate logistic regression analysis, a short antibiotic duration did not influence overall failure rate (odds ratio 0.8, 95% confidence interval 0.4-1.7).

Results were still underpowered to fulfil non-inferiority (overall 17 difference points [90% confidence interval: 13% to 21%].

In terms of severe adverse events, short antibiotic regimens yielded as many adverse events than with a long course (4/110 vs. 4/127 adverse events; p=0.84).

Intravenous Treatment

Administer antibiotic therapy initially by the parenteral route to any patient with a severe diabetic foot infection.

Switch to oral therapy if the patient is clinically improving and has no contraindications to oral therapy and if there is an appropriate oral agent available. (Strong; low)

IWDGF 2019

World guidelines Soft Tissue Infections

Administer antibiotic therapy to a patient with a skin or soft tissue diabetic foot infection for a duration of 1 to 2 weeks. (Strong; high)

Consider continuing treatment, perhaps for up to 3 to 4 weeks, if the infection is improving but is extensive and is resolving slower than expected or if the patient has severe peripheral artery disease. (Weak; low)

IWDGF 2019

OXFORD ACADEMIC

Clinical Infectious Diseases

ACCEPTED MANUSCRIPT

Three versus six weeks of antibiotic therapy for diabetic foot osteomyelitis: A prospective, randomized, non-inferiority pilot trial

Karim Gariani, MD, Truong-Thanh Pham, MD, Benjamin Kressmann, RN, François R Jornayvaz, MD, Giacomo Gastaldi, MD, Dimitrios Stafylakis, MD, Jacques Philippe, MD, Benjamin A Lipsky, MD, İlker Uçkay, MD

Clinical Infectious Diseases, ciaa1758, https://doi.org/10.1093/cid/ciaa1758

Published: 26 November 2020 **Article history** ▾

Pilot study Geneva – (Surgical) diabetic foot osteitis

n = 93	3 Wochen	*p - value*	6 Wochen
Age (median)	70 years	0.23	65 years
PAD	61%	0.42	53%
- Angioplasty	9%	0.87	8%
S. aureus	48%	0.94	47%
Partial amputation	36%	0.97	37%
Hyperbaric oxygen	14%	0.61	10%
IV antibiotic (med.)	1 day	0.37	3 days
Remission	**84%**	**0.21**	**74%**
Adverse events	**37%**	**0.55**	**33%**
- antibiotic AE	***9%***	***0.44***	***14%***

2017-2019; not published yet;

Two-tailed difference: 8.5 percentage points 95%CI - 0.28 till + 0.06

Cluster-controlled Cox regression (remission)

***n* = 93**	**Univariate**	**Multivariate**
Angioplasty	1.4, 0.6-3.2	1.6, 0.8-3.2
S. aureus	1.1, 0.7-1.9	1.4, 0.8-2.4
Hyperbaric oxygen	1.1, 0.5-2.4	1.0, 0.3-2.9
IV antibiotic (med.)	1.0, 0.97-1.03	1.0, 0.98-1.05
3 wks (compared to 6 wks)	**1.0, 0.6-1.6**	**1.1, 0.6-1.7**
Number debridements	1.0, 0.8-1.2	n.d.
Partial amputation	0.7, 0.4-1.2	n.d.

Waibel *et al. Trials* (2020) 21:54
https://doi.org/10.1186/s13063-019-4006-z

Trials

STUDY PROTOCOL Open Access

Optimization of the antibiotic management of diabetic foot infections: protocol for two randomized controlled trials

Felix Waibel[1†], Martin Berli[1†], Sabrina Catanzaro[2], Kati Sairanen[2], Madlaina Schöni[1], Thomas Böni[1], Jan Burkhard[3], Dominique Holy[3], Tanja Huber[4], Maik Bertram[5], Karin Läubli[6], Dario Frustaci[2,7], Andrea Rosskopf[8], Sander Botter[7] and Ilker Uçkay[2,9*]

Trials ongoing in Zurich; target n = 440

	Residual infection post-amputation	Conservative therapy (with some debridement)
Soft tissue	1 vs. 4 days	10 vs. 20 days
Osteomyelitis	1 vs. 3 weeks	3 vs. 6 weeks

University of Zurich[UZH]

The Balgrist

Conclusions

DFI and DFO are multifacetted diseases, of which infection is only a part of the problem

The antibiotic regimens do not seem to influence much the mid- and longterm outcomes of chronic DFO, especially if surgery is performed

Several trials are under way regarding the minimal accepted duration

There seems to be room for reduction of antibiotic use (especially in standard cases), if there is willingness

Thank you very much for your attention

Swiss Working Group (2019)

Diabetic Foot Infection: Treatment

Issue	Action
4. Antibiotics 2	- Duration of treatment A. Soft tissue infection • Mild: 5-7 days or dependent on clinical course • Moderate: 7-14 days or dependent on clinical course • Severe: 12-20 days or dependent on clinical course B. Osteomyelitis • 4-6 weeks if no resection of infected bone • 2-6 weeks if residual infected (but viable) bone after resection • 0-1 week if no residual infected tissue after resection (eg postamputation)