Don't let Pseudomonas be your arch-nemesis: Updates in DFI

Nada El Faham, PharmD

Inpatient Clinical Pharmacist and former PGY2 ID Resident (2024-2025) at ANW

Allina Health

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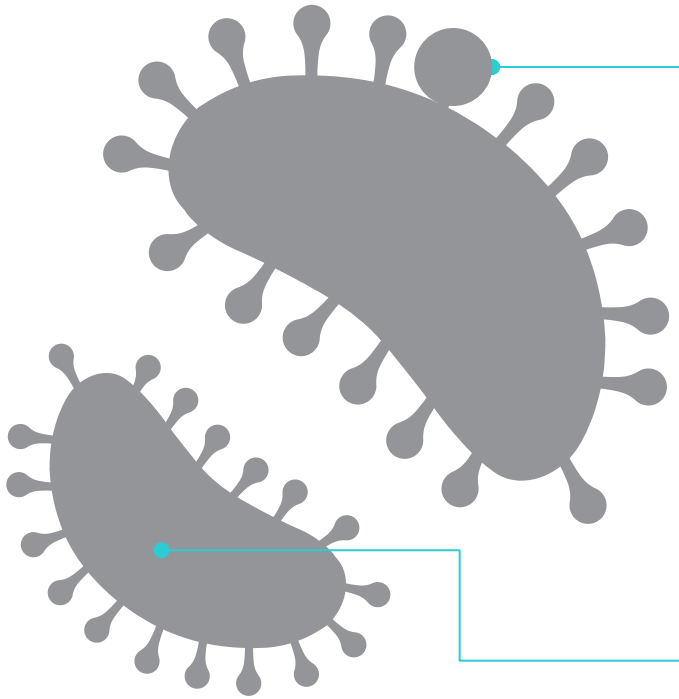
Abbreviations

- IWGDF: International Working Group on the Diabetic Foot
- IDSA: Infectious Diseases Society of America
- DFI: Diabetic Foot infection
- DFUI: Diabetic Foot Ulcer Infection

Objectives



01 Recognize IWGDF/IDSA guideline recommendations regarding empiric antibiotic therapy in DFIs

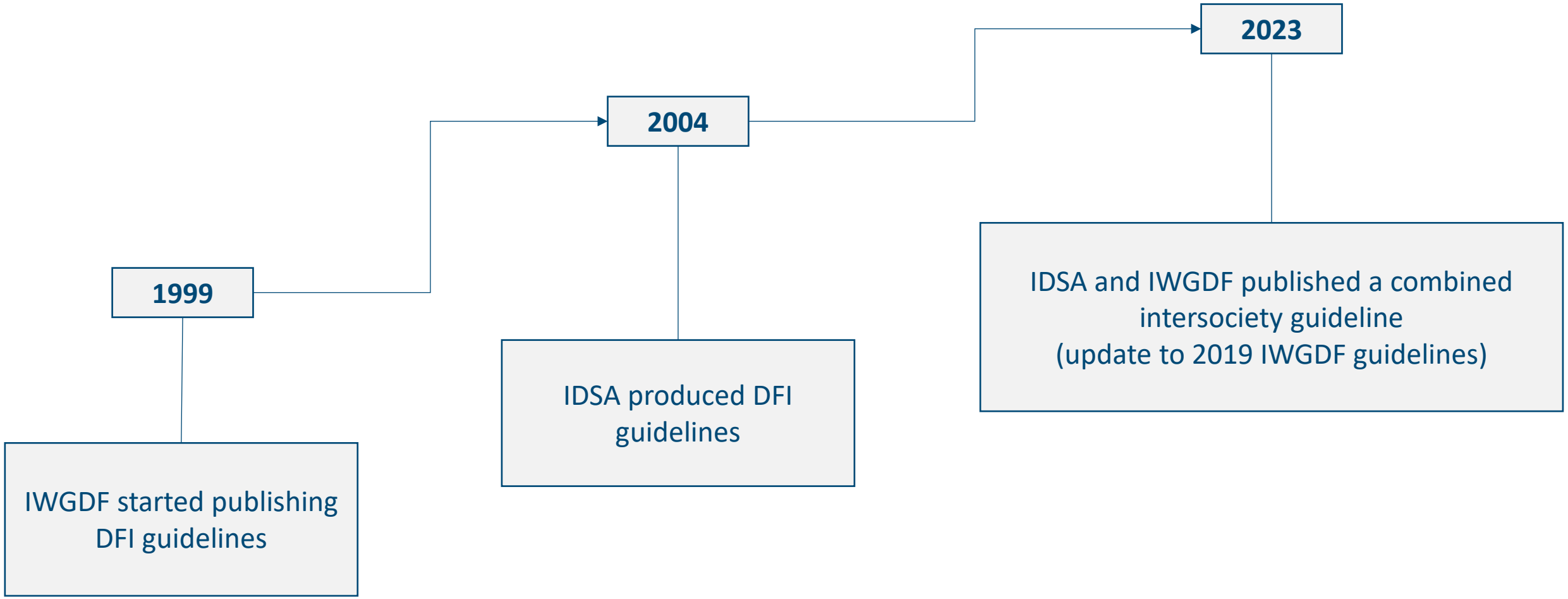
02 Identify risk factors and prevalence data for Pseudomonas involvement in DFIs

Diabetic Foot Infection (DFI): Background

- The International Diabetes Foundation has estimated ~535 million adults aged between 20 and 79 years living with diabetes in 2021 worldwide
- DFI remains the most frequent diabetes-related complication requiring hospitalization, and the most common precipitating event leading to lower extremity amputation

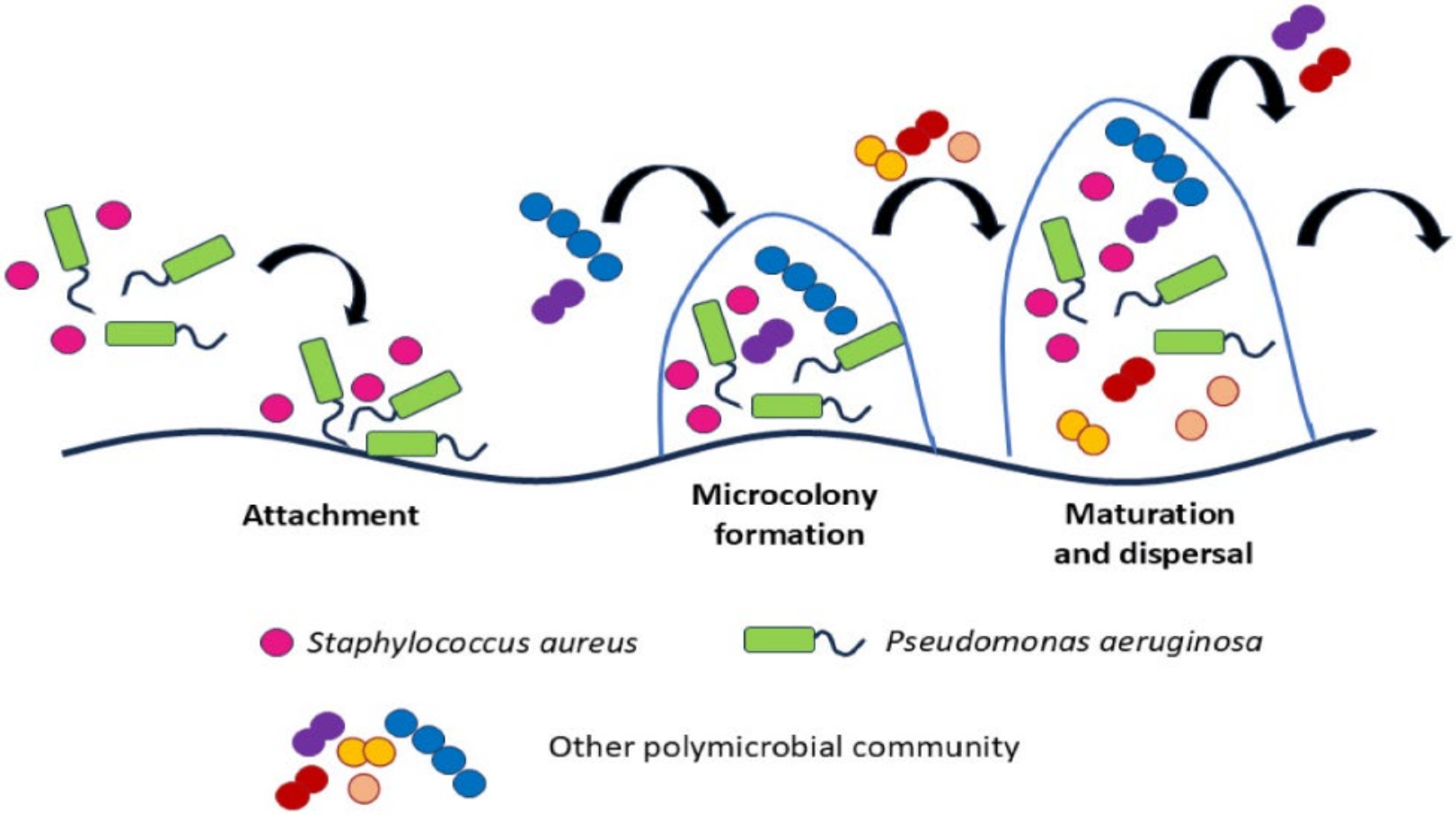
- Managing DFIs requires:
  - Careful diagnosis
  - Appropriate specimens for culture
  - Proper antimicrobial therapy selection
  - Determination of surgical interventions requirement

DFI Guidelines



https://www.idsociety.org/practice-guideline/diabetic-foot-infections/

Infection Process



https://doi.org/10.3390/amh70010009

Microbiologic Characteristics of DFIs

Initial wounds	Simpler microbiota predominantly Gram-positive cocci (*Staphylococcus* and *Streptococcus spp.*)
Chronic wounds	Polymicrobial with introduction of Gram-negative organisms (*Pseudomonas spp.*)
Deep wounds	Involvement of anaerobic organisms (predominantly *Bacteroides fragilis*)

https://pmc.ncbi.nlm.nih.gov/articles/PMC6912738/#sec3-jcm-08-01935

Empiric Antibiotics in DFI

Guidelines statement

"We strongly believe that for patients with a clinically uninfected ulcer, the potential harms (to the patient, the health care system, and society as a whole) of antibiotic therapy (adverse effects of antibiotic therapy, inconvenience to the patient, cost for the drug, and likelihood of driving antibiotic resistance) outweigh any theoretical (but unproven) benefits."

Empiric Pseudomonal Coverage in DFI

Per 2023 guidelines “Best Practice Statement”

- Do not empirically target against *Pseudomonas aeruginosa* in temperate climates

- Use empirical treatment of *Pseudomonas aeruginosa* if it has been isolated from cultures of the affected site within the previous few weeks, in a person with moderate or severe infection who resides in Asia or North Africa

Allina DFI Clinical Pathway

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DFI Classification

Allina DFI Clinical Pathway

Mild
At least two are present:
- Local swelling or induration
- Erythema >0.5 but <2cm around the wound
- Local tenderness or pain
- Local increased warmth
- Purulent or dishwater drainage/discharge

Moderate
Local infection with no systemic manifestations and involving:
- Erythema extending >2cm from the wound margin and/or
- Tissue deeper than skin and subcutaneous tissue (e.g., tendon, muscle, joint, and bone)

Severe
Local infection with the signs of SIRS, as manifested by two or more of the following:
- Temperature >38°C or <36°C
- Heart rate >90 beats/min
- Respiratory rate >20 breaths/min
- WBC >12,000 or <4,000

Empiric Pseudomonal Coverage in DFI

Per 2023 guidelines

Mild	No complicating features	GPC	Semisynthetic penicillinase-resistant penicillin (cloxacillin)
			1st generation cephalosporin (cephalexin)
	ß-lactam allergy or intolerance	GPC	Clindamycin; fluoroquinolone (levo/moxi-floxacin); trimethoprim-sulfamethoxazole; doxycycline
	Recent antibiotic exposure	GPC + GNR	ß-lactam- ß lactamase inhibitor1 (amoxicillin/clavulanate, ampicillin/sulbactam)
			Fluoroquinolone (levo/moxi-floxacin); trimethoprim-sulfamethoxazole
	High risk for MRSA	MRSA	Linezolid; trimethoprim-sulfamethoxazole; clindamycin; doxycycline, fluoroquinolone (levofloxacin, moxifloxacin)

https://www.idsociety.org/practice-guideline/diabetic-foot-infections/

Empiric Pseudomonal Coverage in DFI

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Per 2023 guidelines

Moderate or severe[d]	No complicating features	GPC ± GNR	ß-lactam- ß lactamase inhibitor1 (amoxicillin/clavulanate, ampicillin/sulbactam)
			2nd, 3rd generation cephalosporine (cefuroxime, cefotaxime, ceftriaxone)
	Recent antibiotics	GPC ± GNR	ß-lactam- ß lactamase inhibitor2 (ticarcillin/clavulanate, piperacillin/tazobactam)
			2nd, 3rd generation cephalosporine (cefuroxime, cefotaxime, ceftriaxone) group 1 carbapenem (ertapenem); (depends on prior therapy; seek advice)
	Macerated ulcer or warm climate	GNR, including *Pseudomonas* sp.	ß-lactam- ß lactamase inhibitor2 (ticarcillin/clavulanate, piperacillin/tazobactam) semisynthetic penicillinase-resistant penicillin (cloxacillin) + ceftazidime or ciprofloxacin group 2 carbapenem (mero/imi-penem)
	Ischaemic limb/necrosis/gas forming	GPC ± GNR ± strict anaerobes	ß-lactam- ß lactamase inhibitor1 (amoxicillin/clavulanate, ampicillin/sulbactam) or ß-lactam- ß lactamase inhibitor2 (ticarcillin/clavulanate, piperacillin/tazobactam)
			Group 1 (ertapenem) or 2 (mero/imi-penem) carbapenem

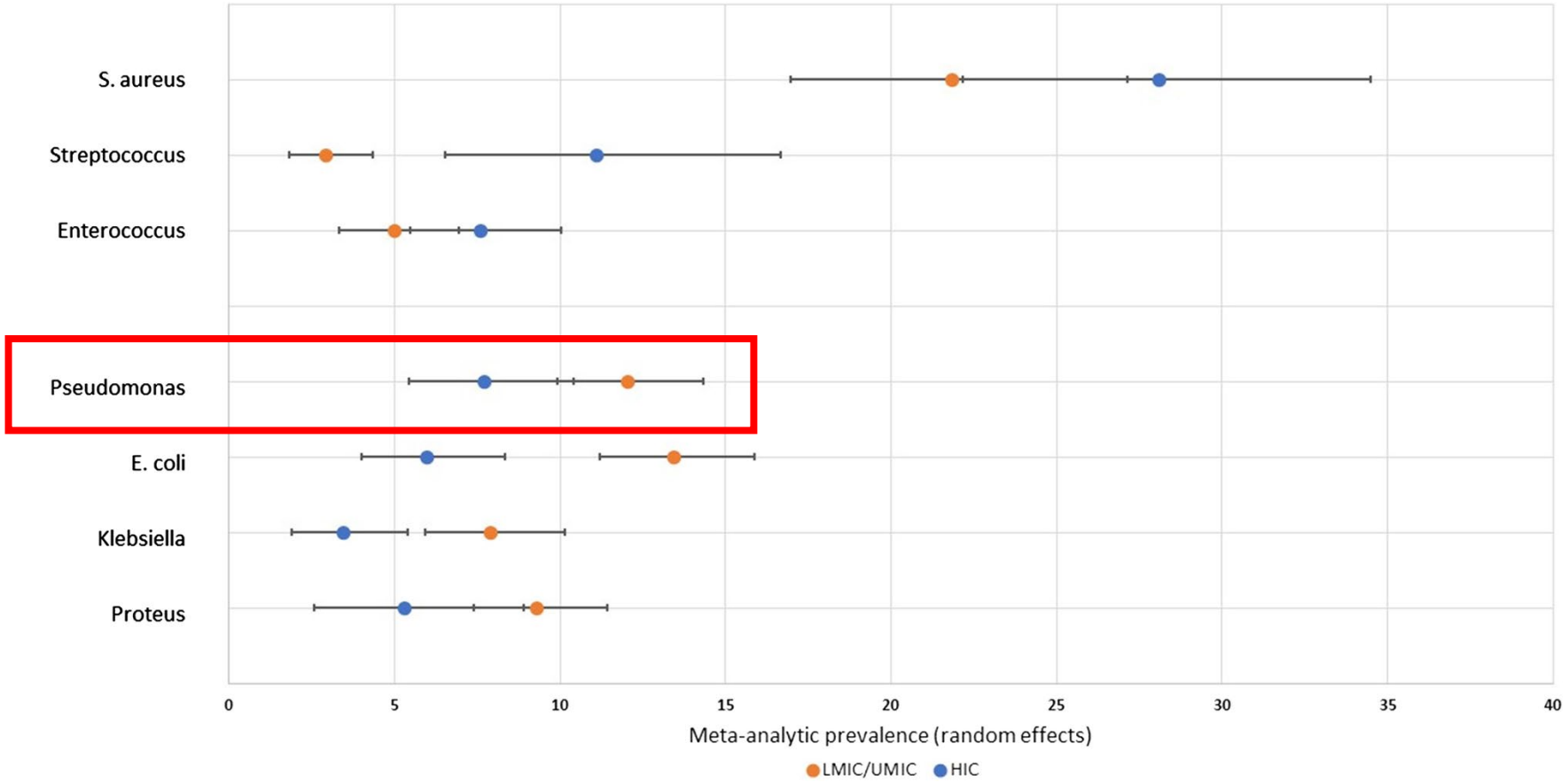
Empiric Pseudomonal Coverage in DFI

- *Pseudomonas spp.* are less commonly isolated in studies from North America and Europe, but are more prevalent in studies from (sub)tropical climates.

doi: 10.1186/s12879-021-06516-7

The Microbiology of DFI: A Meta-Analysis

The meta-analytic prevalence of the bacteria most frequently identified by aerobic culture in high-income (HIC) or upper-middle and lower-middle income countries (U/LMIC)



doi: 10.1186/s12879-021-06516-7

A Systematic Review of Antibiotic Use in DFUI

Included 16 studies

Locations varied, covering the continents of:

- Europe
- America
- Africa
- Asia
- Australia

https://doi.org/10.3947/ic.2021.0144

A Systematic Review of Antibiotic Use in DFUI

Microbiological profile of individual studies		
Authors	**Location**	**Most Frequent Pathogens**
Saltoglu et al, 2010 [18]	Turkey	CNS (24.2%), ***Pseudomonas aeruginosa* (20.9%)**, *Streptococcus spp.* (12.9%)
Xu et al, 2016 [28]	China	MSSA (24.5%), ESBL-positive pathogen (*E. coli, Klebsiella pneumoniae, Proteus mirabilis and Proteus vulgaris*) (9.17%), ***Pseudomonas aeruginosa* (7.8%)**
Patil et al, 2016 [29]	India	*S. aureus* (56.9%), *E. coli* (32.7%), ***Pseudomonas aeruginosa* (29.3%)**

CNS, Coagulase negative Staphylococcus; MSSA, methicillin-susceptible Staphylococcus aureus; MRSA, methicillin-resistant Staphylococcus aureus; ESBL: Extended Spectrum β-Lactamase.

https://doi.org/10.3947/ic.2021.0144

Prevalence of *Pseudomonas aeruginosa* in DFI

- The substantial differences in the microbiological profile in Western countries compared to Asian countries may be due to several factors, including:
  - Cultural
  - Geographic
  - Climatic factors
  - Methods of obtaining and analyzing specimens
  - Differences in the amount and type of antibiotics used

Within Asia

Pseudomonas aeruginosa

Is the most frequent DFI pathogen

https://doi.org/10.3947/ic.2021.0144

Empiric Pseudomonal Coverage in DFI

Research conducted by Harkless et al.

Piperacillin-tazobactam (pip/tazo) vs. ampicillin-sulbactam (amp/sulb)

- Statistically equivalent clinical efficacy in patients with moderate to severe DFI in the test of cure visit ($P = 0.124$)
- Similar results were shown on days 4 and 7, and at the end of treatment

https://doi.org/10.3947/ic.2021.0144

Empiric Pseudomonal Coverage in DFI

Research conducted by Patil et al.

Ceftriaxone (CRO) vs. levofloxacin + metronidazole (LVX + MDZ)

- Both the inpatient group receiving CRO and the outpatient group receiving the combination of LVX + MDZ were similar in efficacy (*P* >0.05)

https://doi.org/10.3947/ic.2021.0144

Antipseudomonal Antibiotics in DFI: A Practical Perspective From a Community Hospital

321-bed community hospital in the metropolitan Seattle region

Reviewed 100 patients

Represented 67% of total admitted patients with DFI in a 2-year period

67% with recurrent infection

Only 4 had *Pseudomonas spp.*

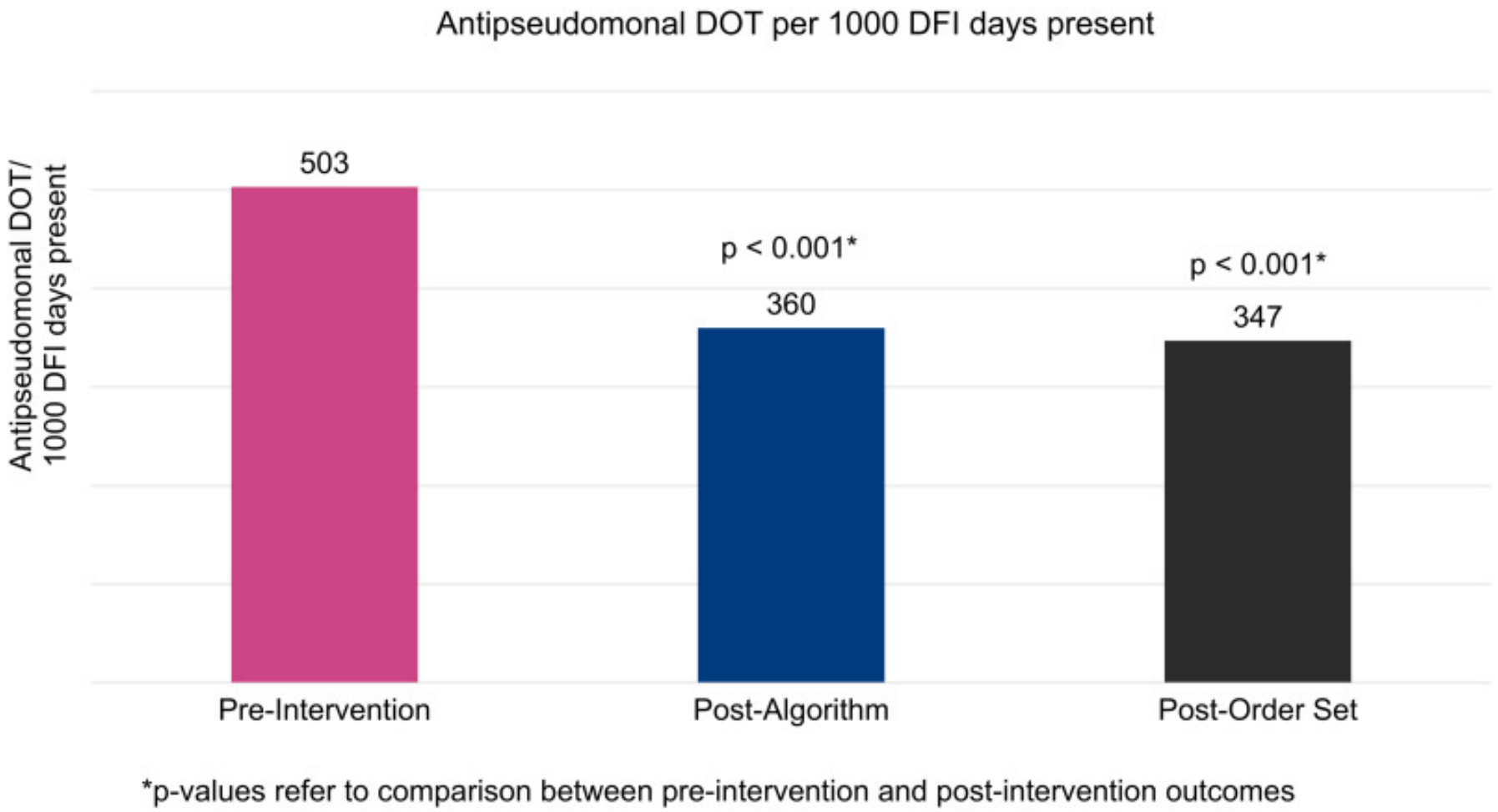
Discordant rates of antipseudomonal coverage (91%)

When compared with isolation in culture (5%)

https://doi.org/10.1093/ofid/ofae258

Healing Soles

Retrospective, observational, quasi-experimental study (2025)



doi: 10.1017/ash.2025.59. PMID: 40160223

Healing Soles

Retrospective, observational, quasi-experimental study (2025)

	Empiric antipseudomonal antibiotic use	Amputation within 30-days	30-day mortality
Pre-implementation	85.7%	48.6%	4.3%
Post-algorithm implementation	72.8% (*P* =0.06)	30% (*P* =0.024)	2.8% (*P* =0.65)
Post-order set implementation	68.5% (*P* = 0.01)	41.4% (*P*= 0.39)	1.4% (*P* =0.31)

doi: 10.1017/ash.2025.59. PMID: 40160223

Definitive DFI Antibiotic Selection

- Due to the complexity and polymicrobial nature of DFI, definitive treatment should especially be based on principles of antibiotic stewardship:
  - Infection source control with surgery, if possible
  - Narrowest spectrum
  - Shortest duration
  - Fewest adverse effects
  - Least expensive route
  - Switching to targeted (preferably oral) agents based on the cultured pathogens

Summary

- Empiric *Pseudomonas aeruginosa* coverage could be justified in:
  - Prior isolation from the same wound/site within recent weeks
  - Warm climate/non-temperate regions (Asia and North Africa)
  - Foot ulcer exposed to water or moist environments (macerated ulcers)
  - Severe infections
  - Locally elevated prevalence of *Pseudomonas aeruginosa* in DFIs

Future Directions

Areas with potential further development:

- To what extent can the currently recommended durations of antibiotic treatment be reduced?
- What is the place of new antibiotics in the management of DFIs?
- Is there a definition for and practical clinical use of the concept of chronic biofilm infection?
- What is the potential of the topical administration of antimicrobials to limit the use of systemic antibiotics in DFIs?

Question #1a

65-year-old male with type 2 diabetes, peripheral neuropathy, foot ulcer present for 1 week, moderate erythema (3 cm), no systemic signs, no prior cultures, no water exposure, lives in northern US (temperate climate).

Would you recommend empiric anti-pseudomonal coverage?

- Yes
- No

Question #1b

Same patient but lives in a tropical climate, wound macerated from food soaking in pond water, and prior isolation of *Pseudomonas spp.*

Would you recommend empiric anti-pseudomonal coverage?

- ○ Yes
- ○ No

Question #2

Your institutional antibiogram shows *Pseudomonas* represents 7% of all DFI isolates. How would this influence your empiric therapy decisions?

A. Include empiric *Pseudomonas* coverage for all moderate/severe DFIs
B. Reserve coverage only for patients with prior *Pseudomonas* or water exposure
C. Never cover empirically
D. Only cover if osteomyelitis is suspected

Question #3

Which empiric regimen do you prefer when *Pseudomonas* coverage is warranted for a DFI?

A. Piperacillin-tazobactam
B. Cefepime ± metronidazole
C. Meropenem
D. Ceftazidime
E. Other

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Thank you!

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