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Review

Perspectives on antibiotic management of diabetic foot osteomyelitis: A scoping review on routes of administration

Narimane Meddas [a,b], Benoit Gachet [c], Arthur Piraux [d], Eric Senneville [c], Laura M. Drudi [e,f], Magali Brousseau-Foley [b,g], Virginie Blanchette [a,b,*]

[a] VITAM: Sustainable Health Research Centre, Centre Intégré de santé et de Services Sociaux de la Capitale-Nationale, QC, Canada
[b] Department of Human Kinetics and Podiatric Medicine, Université du Québec à Trois Rivières, QC, Canada
[c] Gustave Dron Hospital, Department of Infectious Diseases, Tourcoing, France
[d] Univ Angers, POPS, SFR ICAT, F-49000 Angers, France
[e] Division of Vascular Surgery, Centre Hospitalier de l'Université de Montréal, Montreal, Quebec, Canada
[f] Innovation Hub, Centre de Recherche du Centre Hospitalier de l'Université de Montréal, Montreal, Quebec, Canada
[g] Centre Intégré Universitaire de santé et de service Sociaux de la Mauricie et du Centre-du-Québec affilié à l'Université de Montréal, Groupe de Médecine Familiale Universitaire de Trois-Rivières, QC, Canada

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ABSTRACT

Diabetic foot ulcers can progress to diabetic foot osteomyelitis (DFO). Intravenous (IV) antibiotics are traditionally the standard treatment for DFO, but it might reduce quality of life, increase adverse events and costs. Our objective was to examine the potential advantages and disadvantages of antibiotic administration routes for DFO to support a future patient decision aid tool. We conducted a scoping review using the Joanna Briggs Institute methodological framework to map evidence on antibiotic administration routes for DFO using the quintuple aim for quality of care. Records from databases, reference lists, and grey literature were deduplication in EndNote, screened in Rayyan, and assessed independently by two interdisciplinary reviewers. Of 6814, 25 studies were included, all quantitative and mainly retrospective observational (76 %). The majority (68 %) included adult patients with diabetic foot infection or DFO. Oral and IV antibiotics demonstrated comparable clinical outcomes across studies. Data on patient-reported outcomes and experience, team management, equity factors, and standardized definitions of clinical endpoints were largely scarce across studies. Current data suggest that oral antibiotic therapy may be a safe and effective alternative to IV therapy in selected patients with DFO, though substantial evidence gaps remain beyond infection management.

1. Introduction

Diabetes-related foot complications including foot ulcers and amputation are associated with reduced quality of life, and high morbidity and mortality rates [1–3]. Up to 34 % of people with diabetes will develop a foot ulcer during their lifetime [4]. It has been reported that 50 % of foot ulcers progress to diabetic foot infection (DFI). Data demonstrated that at least 20 % of people with a DFI require hospitalization and between 15–20 % of them will need an amputation [5,6]. DFI can spread from the overlying soft tissue, to cortical bone and medullary cavity, and leads to diabetic foot osteomyelitis (DFO) [7], whose prevalence vary from 10 % to 68 % depending on DFIs presentation [8]. DFO is one of the most challenging components of foot ulcer management considering the complexity of both diagnostic and therapeutic interventions, and its high relapse rate [9], one of the main causes of non-traumatic amputation, and has a 5-year mortality rate of 50 % [10].

Prompt and timely clinical diagnosis with microbiological and imaging evaluations of DFO leads to optimal management including antibiotic therapy and local wound care [11,12]. According to the International guidelines, antibiotic therapy for DFI is administered intravenously and orally [12], though intravenous (IV) administration is often preferred, especially for DFO, based on the accepted belief that IV therapy is inherently superior to oral therapy [13]. Recent studies indicate that, under certain conditions, particularly in care settings

* Corresponding author at: Département des sciences de l'activité Physique, 3351 Boul. Des Forges, Trois-Rivières, Québec G8Z 4M3, Canada.
E-mail addresses: narimane.meddas@uqtr.ca (N. Meddas), gachet.benoit@outlook.com (B. Gachet), arthur.piraux@univ-angers.fr (A. Piraux), senneric670@gmail.com (E. Senneville), laura.drudi.med@ssss.gouv.qc.ca (L.M. Drudi), Magali.Brousseau-Foley@uqtr.ca (M. Brousseau-Foley), Virginie.Blanchette@uqtr.ca (V. Blanchette).

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where the patient's life or limb is not threatened and the diabetic foot infection is mild to moderate, targeted oral antibiotics can be as safe and effective as intravenous antibiotics for treating diabetic foot osteomyelitis, with the choice of route largely depending on clinical presentation and care context [13–17]. Therefore, there may be advantages (benefits) and disadvantages (risks) to using oral antibiotic therapy in DFI rather than IV antibiotic therapy. Recent studies have demonstrated that oral antibiotic therapy is as effective as intravenous (IV) therapy for most bone and joint infections, with oral regimens being easier to administer and particularly practical for individuals in remote or resource-limited settings where access to IV therapy, equipment, or qualified nursing staff may be restricted. The choice between oral and IV administration extends beyond clinical efficacy, as it also impacts patient and care team experience, healthcare efficiency, and equity of access; for example, oral therapy can facilitate outpatient management, reduce the need for prolonged hospitalization and invasive procedures, and aligns with the goals of the "Quintuple Aim" framework for quality of care [13,17,18]. In contrast, IV antibiotic therapy is associated with more risks, inconveniences, longer hospital stay, and higher costs than oral therapy, as venous catheter infection may account for around 6 % of bloodstream infections [13,18]. As well, long-term use of catheters for prolonged antibiotic therapy can also favor the emergence of multi-resistant bacteria [19]. It was reported that around 95 % of the total cost of IV therapy arises from the administration procedure [18]. Therefore, this may influence negatively the "Quintuple aim." Moreover, a recent systematic review showed that oral antibiotic therapy was safer and more satisfying for people with diabetes and suggests that guidelines needed to adapt accordingly to help change clinical practice to reflect new evidence, as it can overcome ingrained preconceptions about oral versus IV antibiotic therapy [17]. Hence, the route of administration concerns all dimensions of quality of care and should not limited to effectiveness alone.

Yet, despite studies indicating that: 1) oral antibiotic therapy was not inferior to IV antibiotic therapy [14] and 2) no significant difference in cure rate of DFO based on the route of antibiotic therapy [20], a knowledge gap remains in the literature about the choice of route for antibiotic therapy in DFI, and about the clear criteria for selecting patient profiles (i.e. DFU classification, peripheral arterial disease status, etc.), to guide this choice with the patient. Clear, timely and coherent communication between the various medical disciplines and with patients remains a challenge in most healthcare systems [11,21]. This leads to fragmented care, less satisfactory management, and poorer clinical outcomes. From the patient's perspective, a successful DFI treatment pathway should prioritize coordination of care and meaningful outcomes focused on their goals, preferences and experience [22]. Therefore, we aim to map the evidence on antibiotic therapy for DFO in patients with DFU, with or without lower extremity amputation (LEA). It focuses on oral antibiotic therapy compared with intravenous antibiotic therapy as the standard treatment. Outcomes are examined in relation to the quintuple aim of quality of care, namely health outcomes, patient experience, efficiency, provider experience, and equity [23] (Appendix 1). This will enable our team to identify advantages, disadvantages, risks, and benefits of antibiotic therapy for DFO according to the route of administration, as well as identifying gaps in knowledge to aid decision-making with the patient beyond informed consent and clinical guidelines.

2. Methods

2.1. Study design

We conducted a scoping review guided by the Johanna Brigg Institute (JBI) Evidence Synthesis Manual, which provides a comprehensive framework for conducting this methodological design [24]. It is based on the method initially suggested by Arksey and O'Malley and improved successively by Levac and Peters *et al.* [24–26]. Our review used the Preferred Reporting Items for Systematic reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) reporting guidelines [27] (Appendix 2).

This project is interdisciplinary including podiatrist, infectious disease specialist, family physician, pharmacist, vascular surgeon, and microbiologist. Our protocol was developed in accordance with the IWGDF and IDSA infection chapter (2023) [12]. The protocol is registered with Open Science Framework.

Step 1: Identifying Research Questions and Definitions

We have adopted the PICO format i.e. population, intervention, comparator, outcomes [28], to define our main research question:

What is the scientific evidence related to the outcomes (O) of oral antibiotic therapy (I) for patient with diabetic foot osteomyelitis (P) compared to intravenous antibiotic therapy (C)?

Specific research questions are in Appendix 3.

Step 2: Search Strategy

This project includes two data sources. First, data was collected from a systemic search on the databases MEDLINE, CINAHL, Cochrane Library and Scopus. The search strategy was developed by the principal reviewer (NM), reviewed by an institutional librarian (Université du Québec à Trois-Rivières) and approved by the team. The search strategy combined key indexed words such as medical subject heading (MeSH) terms in MEDLINE or their equivalents in other databases, using Boolean operators, truncation and building blocks. It also included a free word search in Scopus. This strategy was adapted for other databases (Appendix 4). Reference lists and citations of included studies were also manually searched. The second source of data was grey literature which was identified using Google Scholar as well as specific websites (Appendix 5) by the principal reviewer (NM). The search strategy was developed using keywords to retrieve literature written in English and French, between 2000 and January 30th, 2025. The search period was limited to these years as this field is rapidly evolving (i.e. treatment options, emergence of multi-resistant strains, etc.) and the latest IWGDF/IDSA recommendations were updated in 2023.

Step 3: Study selection and screening criteria

Studies were selected independently by two reviewers (NM and BG) based on the PICO question, and inclusion and exclusion criteria (Table 1). The selection process was carried out in two stages: titles and abstracts selection, and then full text review. A meeting was scheduled between the reviewers, after a pilot screening of 200 titles and abstracts, to validate and refine the screening methods with an understanding of the selection process if necessary and then approved by the team. References were managed using EndNote 21 (2023, Clarivate, USA) for duplicate removal [29] and Rayyan (Rayyan Systems, Inc, USA) [30] for studies selection. Discrepancies between reviewers were resolved with a third reviewer (VB).

Step 4: Data Extraction

A Microsoft Excel spreadsheet was developed by the principal reviewer (NM) and validated by the team was used for data extraction which included PICO elements, authors, year of publication, study location, study type, objectives, relevant results related to specific research questions (e.g., health complications, patient satisfaction, quality and accessibility of care, recurrence of infection, safest and least expensive therapy, patient involvement in antibiotic therapy choice, DFI interprofessional management, etc.). Given the methodological design, the extraction process was refined as the review progressed [24].

Step 5: Collating, Summarizing and Reporting Results

The PRISMA flowchart described the selection process [27]. Data from included studies were organized in descriptive tables specific to PICO research questions. We analyzed data in terms of advantages, disadvantages, risks, and benefits of antibiotic therapy route of administration for DFO and reported results in a narrative synthesis.

3. Results

A total of 6814 records were identified from the databases and 121

Table 1
Inclusion and exclusion criteria including definition of concepts.

Criteria elements	Inclusion criteria	Exclusion criteria
Population	Individual with DFO[a], with or without a LEA[b].	Individual with another type of osteomyelitis not related to diabetic feet.
Intervention/ Comparison	Any oral and/or IV antibiotic therapy present in the IWGDF/ IDSA infection guidelines as standard treatment for DFI and/or DFO [12].	Any other therapy such as topical antibiotics or amputation.
Outcomes	Results pertaining to or describing data on the management of DFO in relation to antibiotic therapy routes of administration, including the experience of patients and healthcare professionals, accessibility of care, costs, equity.	NA
Settings	Any clinical setting including primary care clinics, emergency department, rehabilitation center, community resources, home care.	Experimental *in vitro* settings/ studies
Study design	Primary data.	Protocols, abstracts of conferences or meetings, systematic reviews, *meta*-analysis, *meta*-synthesis, and umbrella studies.
Language	English/French.	We don't exclude articles on language, but they are found in other languages and we're not able to interpret them, so we may exclude them.

DFI: Diabetic Foot Infection; DFO: Diabetic Foot Osteomyelitis; IDSA: Infectious Diseases Society of America; IWGDF: International Working Group on the Diabetic Foot; LEA: Lower Extremity Amputation; NA: none applicable.

[a] DFO is defined as bone infection, including infection of cortical bone with or without marrow involvement localized under the malleoli [12].

[b] LEA is defined as a surgery to remove part of a lower limb, whether in the leg, foot or toe, and always involves the removal of a bone [73].

from the grey literature. After removing duplicates and analyzing titles and abstracts, 91 studies were eligible for full-text analysis. Manual searching of reference lists and citation tracking produced no additional results. Finally, 25 studies were included (Fig. 1).

3.1. Characteristics of the included studies

All included studies (n = 25) were quantitative. Nineteen studies were retrospective (76 %) [14,15,31–47] and two were prospective (4 %) [48,49]. There were cohort studies [14,15,31–40,42–44,46,48], descriptive studies [41,45,50] and a case series [49]. Three studies were randomized controlled trials (RCTs) (12 %) [51–53], and one was a pilot clinical trial non randomised [47]. Eight studies were published between 2001 and 2008 (32 %) [31–34,48,49,51,52] and seventeen studies between 2014 and 2025 (68 %) [14,15,35–47,50,53], including 5 studies in 2024 [14,44–46,50]. The studies were conducted across 13 countries, most frequently in the United States (n = 7; 28 %) [14,15,33,36,43,51,52], followed by France (n = 3;12 %) [34,44,48], the United Kingdom (n = 3; 12 % including England) [37,45,47], Spain (n = 2; 8 %) [41,50], and Australia (n = 2; 8 %) [46,49]. Other studies came from Germany [31], Canada [32], Hungary [53], Iraq [35], Switzerland [38], Turkey [40], Italy [42] and Israel [39] (Table2).

3.2. Population and clinical presentation

The patients included in the studies were predominantly over 50 years old, with a predominance of males. Factors related to equity were scarce in most studies (Table 2), except for sex and age. However, four studies reported ethnicity [36,39,43,51], two reported low-income by homelessness [15] and uninsured or underinsured situation [43], and one study reported patients' level of education and social status [50]. Nine studies (36 %) focused on patients with DFO [14,15,32,34,37,43–45,48], with DFI in six studies (24 %) [31,35,41,50–52], with DFI and DFO in two studies (8 %) [38,53], and eight studies (32 %) included a mixed population with DFO, DFI, bone and joint infection and other types of infection [33,36,39,40,42,46,47,49].

Regarding comorbidities, nephropathy [14,31,33,34,38,40,41,43,44,46,50], peripheral arterial disease [15,32,33,37,40,41,43,44,50,51][and peripheral neuropathy [31,40,41,44,50] were the most reported, while Charcot foot [14,44] and retinopathy [44,50] were rarely reported. For the risk factors, smoking was reported in six studies [14,15,31,41,43,44], obesity in two studies [14,43] and alcohol in one study [31]. Eight studies reported the presence of previous DFU [35,36,40–42,44,50,53] and five studies reported one or more episodes of previous DFO [32,39,45,47,48] (Table 3). In patients who underwent LEA before the study, most reported cases involving minor LEA localized to the forefoot (i.e. hallux, toes and metatarsals) [14,15,31,34,37–39] Finally, the clinical presentation of DFI was generally reported as moderate to severe [15,35,41,53], with some cases of chronic or post-surgical infection [36,40,46,51]. In most studies, DFIs were evaluated according to unreported clinical criteria. Three studies [31,32,48] and two [50,53] used respectively the Wagner (score of 3–4) and PEDIS (grade 2 to 4) classification for foot ulcers. Four studies used the IDSA classification for infection, two of which classified infections as moderate to severe [15,41], one as mild to moderate [35] and one as mild soft tissue, moderate, and severe [38].

3.3. Context and approach of care

Most studies did not clearly indicate the care environment or the urban/rural location of patients. Studies were most often described as multicenter [31,36,37,40,45,49,51–53] or hospital-based [14,15,34,38,41–43,46), with a few conducted in specialized outpatient units [33,43,50], diabetic foot clinics [32,47,48] or orthopedic consultation clinics [35,39]. The tertiary care was mentioned in three studies [32,33,46], and community care in one study [33]. One study reported that continuing care in the community was provided to patients by a state-funded home nursing service [32]. Only two studies specified the distribution of care sites, one indicating that 10.9 % of patients were treated in intensive care, 72.7 % in general hospitals and 16.4 % of outpatients [49], and the other study indicating that patients were admitted to the emergency department, clinic and urgent care unit [15]. About patient location, only two studies provided partial data: one reported that 68 % of participants were living in the community prior to treatment [33], and another noted homelessness rates of 5 % and 12 % [15,43]. Similarly, only one study reported that 54 % of patients had been seen in a diabetic foot clinic prior to diagnosis [34], suggesting prior access to structured care pathways. Overall, these findings highlight a significant gap in reporting on care environments and patient backgrounds, limiting our understanding of the influence of healthcare access and context on treatment decisions and outcomes in DFI/DFO.

The context of care varied across studies. IV treatment was most often administered during hospitalization [31,33,36,37,39–41,43,44,46,53]. In contrast, oral antibiotics were frequently prescribed on an outpatient basis, including after hospital discharge or minor amputations [32,38,48,50]. Many studies also reported transitions between IV and oral treatment, indicating the use of sequential treatment strategies [34,52]. Home-care models, such as ambulatory parenteral antibiotic therapy (OPAT) or self-administered IV regimens, were mentioned in two studies [43,46].

Multidisciplinary management, including podiatrists, infectiologists,

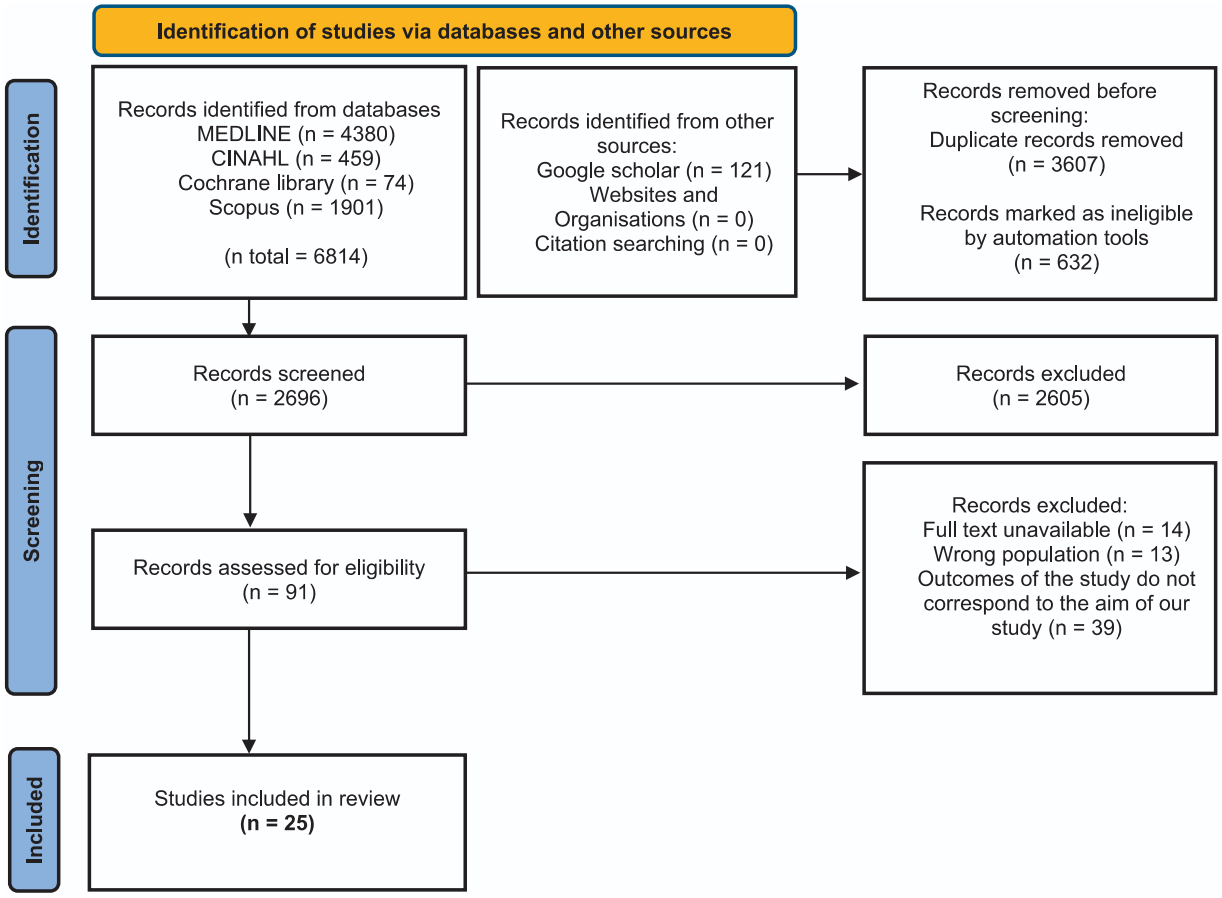

Fig. 1. Adapted PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram of the scoping review process [27].

vascular and orthopedic surgeons and diabetologists, was stated in many studies, but rarely detailed [14,31,32,34,35,37–39,41,43–48,51,53]. Of the included studies, the majority did not explicitly report which healthcare professional assessed patients first or who initiated antibiotic treatment, except for five studies which reported that the type and route of treatment was made by the infectious diseases section [14,31,32,41] and a multidisciplinary discussion [44]. This lack of detail limits our understanding of the initial clinical decision-making and care pathways in the management of DFI/DFO. The role of the patients and their care partners within the team was not reported. There were also no data in terms of team-related experience such as satisfaction or coordination of care.

The patient-related experience was largely unreported, except for 3 studies that reported patient involvement in the choice of treatment [15,44,47] and one study evaluated patient adherence to treatment [50]. There were no data on satisfaction or care environment experience for patients.

3.4. *Profile of oral and IV antibiotic therapy and outcomes*

Eleven studies described the use of IV treatment for DFO [37,39,43,44], DFI [31,41,53] and non-diabetic feet [33,36,40,46]. Five studies compared oral vs. IV treatment for DFI/DFO, including two for post-amputation residual osteomyelitis [14,15,35,42,51]. Four studies reported the use of oral treatment alone for DFI/DFO [32,38,48,50]. Two studies reported the switch from IV to oral treatment for DFI/DFO [34,52]. Finally, two studies reported combined or no use of oral and/or IV therapy for DFO and severe infections [45,49], and one study compared IV therapy vs antibiotic eluting bone void filer [47]. The type of antibiotic, route of administration and comparator varied across studies (Table 4). Most of the studies had no comparator (n = 15; 60 %).

The oral antibiotic regimens included rifampicin combinations [34,48], amoxicillin-clavulanate [32,38,52], linezolid [49], and other agents such as clindamycin or fluoroquinolones [35,42,45,50,51]. These antibiotics mainly target Gram-positive organisms, in particular *Staphylococcus aureus* (including Methicillin-Resistant *Staphylococcus aureus* (MRSA), *Enterococcus faecalis*) and, in some cases, Gram-negative bacilli (*Pseudomonas aeruginosa*, *Enterobacter cloacae*). Rifampicin was often combined with other agents to enhance activity against biofilm-forming staphylococci [48]. For IV antibiotic regimens, these included glycopeptides (e.g. teicoplanin, vancomycin, dalbavancin) [41,44], lipopeptides (daptomycin) [33], beta-lactams (ertapenem, ceftaroline) [36,39], oxazolidinones (linezolid) [49], fluroquinolones (moxifloxacin) [52], broad-spectrum agents such as tigecycline [31], and other antibiotic combinations [35,40,43,45,46,51,53]. These agents target gram-positive bacteria, particularly MRSA, and Gram-negative bacilli in polymicrobial infections. Empirical IV treatment was often adapted according to the results of bone cultures. Reports of antibiotic resistance after treatment were rare, only one study documented the presence of MRSA [34] and one used daptomycin when glycopeptides failed [33].

For the health outcomes, clinical resolution of the infection is the most reported primary outcome, except for nine studies that considered microbiological results in clinical success [15,33,38,40,41,47,51–53]. Clinical success was comparable between oral and IV therapy. Success rates were often similar or slightly superior in oral therapy groups (Table 4). Oral therapy was associated with fewer adverse events (e.g., gastro-intestinal symptoms, creatine phosphokinase elevation) [14,46], and potentially lower cost due to fewer hospitalizations and no IV access [46,49]. The infection recurrence rates were generally low

Table 2
Overview of the included studies (n = 25).

First author	Year of publication	Study location	Study design	Aim
Senneville et al. [48]	2001	France	Prospective cohort study	Evaluate the efficacy and tolerability of oral rifampicin–ofloxacin combination for treating with pedal DFO reliably documented by the culture of a surgical bone biopsy
Lipsky et al. [51]	2004	USA	RCT (open-label, multicenter)	Compare the efficacy and safety of IV and oral formulations of linezolid with those of aminopenicillin/beta-lactamase inhibitors for the treatment DFI
Rayner et al. [49]	2004	Australia	Prospective descriptive study (case series)	Evaluate the clinical efficacy and safety of linezolid in patients with osteomyelitis treated under a compassionate use program
Stengel et al. [31]	2005	Germany	Retrospective cohort study	Efficacy of IV fosfomycin as a second-line treatment for limb-threatening for DFI
Embil et al. [32]	2006	Canada	Retrospective cohort study	Evaluate the efficacy of oral antimicrobial therapy, with or without limited debridement, in diabetic patients with DFO treated in specialized clinics
Holtom et al. [33]	2007	USA	Retrospective cohort study	Evaluate the efficacy of daptomycin in the treatment of osteomyelitis of the foot or ankle, particularly in patients who have failed previous antibiotic treatments
Lipsky et al. [52]	2007	USA	RCT (Double-blind, multicenter)	Evaluate the clinical efficacy of moxifloxacin (IV → oral) compared with the combination piperacillin-tazobactam IV + amoxicillin-clavulanate oral in patients with DFI
Senneville et al. [34]	2008	France	Retrospective cohort study	Identify criteria predictive of remission in nonsurgical treatment of DFO
Lauf et al. [53]	2014	Hungary	RCT (Phase 3 randomized double-blind controlled trial)	Determine the safety and efficacy of once daily tigecycline compared with ertapenem ± vancomycin for the treatment of moderate DFI with and without DFO
Aliakbar et al. [35]	2019	Iraq	Retrospective cohort study	Evaluate the effectiveness of surgical wound care combined with systemic antibiotic treatment in mild and moderate DFI
Johnson et al. [36]	2019	USA	Retrospective cohort study	Assess clinical outcomes of patients with gram-positive osteomyelitis treated with ceftaroline fosamil in routine care settings
Bond et al. [37]	2019	England	Retrospective cohort study	Determine clinical outcomes of DFO treated with IV antibiotics
Gariani et al. [38]	2019	Switzerland	Retrospective cohort study	Assess the efficacy of oral amoxicillin-clavulanate for treating DFI, particularly for DFO
Feldman et al. [39]	2021	Israel	Retrospective cohort study	Compare the outcome of primary nonoperative antibiotic treatment versus digital amputation in patients with diabetes-related chronic digital osteomyelitis
Sipahi et al. [40]	2021	Turkey	Retrospective cohort study	Compare the efficacy of daptomycin and teicoplanin in the treatment of osteomyelitis, focusing on infection healing and treatment failure
Gill et al. [15]	2022	USA	Retrospective cohort study	Compare treatment failure rates between oral and intravenous antibiotic therapy for residual osteomyelitis after diabetic foot amputation
Navarro-Jiménez et al. [41]	2022	Spain	Retrospective, descriptive study	Describe the clinical experience with dalbavancin in the treatment of DFI in a multidisciplinary unit of a second level hospital
Melis et al. [42]	2022	Italy	Retrospective cohort study	Compare the outcomes of IV and oral antibiotic treatment in patients with bacterial osteomyelitis
Schechter et al. [43]	2023	USA	Retrospective cohort study	Describe Outpatient Parenteral Antibiotic Therapy (OPAT) treatment characteristics, adverse events, and outcomes among patients with DFO
Sanz-Corbalán et al. [50]	2024	Spain	Cross-sectional descriptive study	Assess the adherence to oral antibiotic treatment in outpatients with DFI (soft tissue versus. osteomyelitis)
Boucher et al. [44]	2024	France	Retrospective cohort study	Describe the efficacy and safety of dalbavancin in treating patients with DFO confirmed by bone culture
Uddin et al. [45]	2024	United Kingdom	Retrospective descriptive study	Explore the variation in systemic antibiotic treatment for DFO in clinical practice by NHS multidisciplinary foot team across England and Wales
Kipp et al. [14]	2024	USA	Retrospective cohort study	Evaluate treatment success in patients treated with oral versus IV antibiotics for residual DFO after amputation
Brand et al. [46]	2024	Australia	Retrospective cohort study	Describe patient demographics, diagnosis, microbiology and outcomes of patients treated by H-OPAT and S-OPAT within the Sunshine Coast Hospital and Health Service, Australia
Venkateswaran et al. [47]	2025	United Kingdom	Retrospective non-randomized, pilot study	Compare the efficacy and safety of systemic antibiotics versus antibiotic eluting bone void filler (AEBF) in treating pedal osteomyelitis

Abbreviations and symbols:
DFI: Diabetic Foot Infection; DFO: Diabetic Foot Osteomyelitis; IV: Intravenous; NHS: National Health Service; OPAT: Outpatient Parenteral Antibiotic Therapy; H-OPAT: Healthcare-Administered OPAT; S-OPAT: Self-Administered OPAT; RCT: Randomised Controlled Trials.
→: switch; +: with; ±: with or without adjunctive vancomycin

[32–34,44,48], except in five studies reporting higher recurrence rates, including two studies for the IV regimen [47,53], one study for oral regimen [38], and two studies with no significant difference between the two regimens [14,45]. Antibiotic resistance was poorly quantified, only one study reported the presence of MRSA and coagulase-negative staphylococci isolated from a bone sample [34]. Twelve studies reported amputation rates after treatment, seven studies reported LEA [31,32,34,39,41,45,47], four studies reported major amputations [31,39,44,47], and four studies did not specify the type of amputation [14,35,43,52]. Mortality was low across studies. When specified, deaths were predominantly unrelated to DFI/DFO or antibiotic treatment, often attributed to other comorbidities or unrelated clinical events such as infective endocarditis or causes occurring long after the follow-up period. [37,40,44,47–49,51–53].

Equity data regarding the route of administration was rarely reported as secondary outcome. Two studies reported that the oral route was more accessible and easier to administer [14,41]. None of the included studies used a standardized Core Outcome Set (COS), which limits to reporting outcomes across studies.

3.5. Co-interventions

In all included studies, oral and IV therapies were often initiated with co-interventions. Surgical procedures such as debridement were frequently reported [31–33,35–37,40,44,47,49,51–53]. Many studies also mentioned drainage [34–36,44,49,52], minor amputations [35,41,44,49,52], vascular care [31,32,41,47,52], and wound care [43,53]. However, few studies clearly indicated whether co-interventions accompanied antibiotic therapy [14,15,39,42,45,46], in these cases, it was often difficult to know whether the observed results

Table 3
Data from PROGRESS + factors framework for equity [74].

Authors, Year	P	R	O	G	R	E	S1	S2	+	Details *plus* (+) factors
Senneville et al., 2001 (48)									Age	Previous DFO
Lipsky et al., 2004 (51)									Age	PAD
Rayner et al., 2004 (49)									Age	/
Stengel et al., 2005, (31)									Age	Neuropathy, renal disease, smoking, alcohol
Embil et al., 2006 (32)									Age	PAD, previous DFO
Holtom et al., 2007 (33)									Age	Renal disease
Lipsky et al., 2007 (52)									Age	/
Senneville et al., 2008 (34)									Age	Renal disease

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Table 3 (*continued*)

Lauf et al., 2014 (53)				■					Age	Previous DFU
Aliakbar et al., 2019 (35)				■					Age	Previous DFU
Johnson et al., 2019 (36)		■		■					Age	PAD, Previous DFU
Bond et al., 2019 (37)				■					Age	PAD
Gariani et al., 2019 (38)				■					Age	Renal disease
Feldman et al., 2021 (39)		■		■					Age	Previous DFO
Sipahi et al., 2021 (40)				■					Age	Neuropathy, PAD, renal disease, previous DFU
Gill et al., 2022 (15)	■								Age, homelessness	PAD, smoking
Navarro-Jiménez et al., 2022 (41)				■					Age	Neuropathy, PAD, renal disease, smoking, previous DFU

(*continued on next page*)

Table 3 (*continued*)

Melis et al., 2022 (42)									Age	Previous DFU
Schechter et al., 2023 (43)									Age, homelessness	PAD, renal disease, smoking, obesity
Sanz-Corbalán et al., 2024 (50)									Age	Neuropathy, PAD, retinopathy, renal disease, previous DFU
Boucher et al., 2024 (44)									Age	Neuropathy, PAD, Charcot foot, retinopathy, renal disease, smoking, previous DFU
Uddin et al., 2024 (45)									Age	Previous DFO
Kipp et al., 2024 (14)									Age	Charcot foot, renal disease,
										smoking, obesity
Brand et al., 2024 (46)									Age	Renal disease
Venkateswaran et al., 2025 (47)									Age	Previous DFO

Abbreviations and symbols:
P: Place of residence; R: Race or ethnicity; O: Occupation; G: Gender or sex; R: Religion; E: Education level; S: Socioeconomic status; S: Social capital; +: other personal or contextual factors that can also contribute to health disparities.
DFU: Diabetic Foot Ulcer; DFO: Diabetic Foot Osteomyelitis; PAD: Peripheral Arterial Disease.

Table 4
Summary of the type of antibiotic, route of administration and comparator.

Authors, Year	Route of administration	Antibiotic*	Comparator*
Senneville et al., 2001 [48]	Oral	Oral rifampicin + ofloxacin (IV allowed initially in some patients)	None
Lipsky et al., 2004 [51][a]	Oral versus IV	Linezolid (oral or IV) *	Ampicillin-sulbactam IV
Rayner et al., 2004 [49]	Oral + IV or mixed combination	Linezolid (oral or IV) used in patients with resistant infections or intolerance to standard therapies	None
Stengel et al., 2005, [31]	IV	IV fosfomycin ± other antibiotics for severe DFI	None
Embil et al., 2006 [32]	Oral	Oral antimicrobial therapy ± short initial IV course	None
Holtom et al., 2007 [33]	IV	IV daptomycin ± concomitant antibiotics for Gram-positive foot/ankle osteomyelitis	None
Lipsky et al., 2007 [52]	IV switch to oral	Moxifloxacin (IV → oral)	Piperacillin–tazobactam IV → Amoxicillin–clavulanate oral
Senneville et al., 2008 [34]	IV switch to oral	Patients received IV antibiotics → oral antibiotics and local wound care for the nonsurgical treatment of DFO	None
Lauf et al., 2014 [53]	IV	Tigecycline IV	Ertapenem 1 g IV once daily ± adjunctive IV vancomycin
Aliakbar ete al., 2019 [35][b]	Oral versus IV	Oral* only, mild DFI	IV + oral*, moderate DFI with/without osteomyelitis
Johnson et al., 2019 [36]	IV	IV ceftaroline fosamil administered as monotherapy or with adjunctive antibiotics for gram-positive osteomyelitis	None
Bond et al., 2019 [37]	IV	IV antibiotics tailored individually based on microbiological culture for DFO	None
Gariani et al., 2019 [38]	Oral	Oral amoxicillin-clavulanate for treating diabetic foot infection	None
Feldman et al., 2021 [39]	IV	Nonoperative treatment with intravenous antibiotics (amoxicillin-clavulanate ± switch based on culture or clinical judgment)	None
Sipahi et al., 2021 [40]	IV	Daptomycine IV	Teicoplanine IV
Gill et al., 2022 [15][c]	Oral versus IV	Oral (antibiotic not mentioned)	IV (antibiotic not mentioned)
Navarro-Jiménez et al., 2022 [41]	IV	IV dalbavancin	None
Melis et al., 2022 [42][d]	Oral versus IV	Oral doxycycline/fluoroquinolones/ Cotrimoxazole	Amoxicillin/clavulanic acid/ fluoroquinolones/ linezolid IV ± oral
Schechter et al., 2023 [43]	IV	IV outpatient parenteral antibiotics (e.g., vancomycin, daptomycin, beta-lactams) for DFO	None
Sanz-Corbalán et al., 2024 [50]	Oral	Oral antibiotic treatment for diabetic foot infection (osteomyelitis and soft tissue infection)	None
Boucher et al., 2024 [44]	IV	IV dalbavancin as salvage therapy for DFO	None
Uddin et al., 2024 [45]	Oral + IV or mixed combination	Systemic antibiotic regimens (oral and/or IV) used to treat diabetic foot osteomyelitis in routine clinical settings across England and Wales	None
Kipp et al., 2024 [14][e]	Oral versus IV	Oral (antibiotic not mentioned)	IV (antibiotic not mentioned)
Brand et al., 2024 [46]	IV	Home nursing–administered OPAT (H-OPAT)	Self-administered OPAT (S-OPAT)
Venkateswaran et al., 2025 [47]	IV versus antibiotic eluting bone void filler	Systemic antibiotic therapy	Antibiotic eluting bone void filler (AEBF) for treating pedal osteomyelitis

Abbreviations and symbols:
DFI: Diabetic Foot Infection; DFO: Diabetic Foot Osteomyelitis; IV: Intravenous; OPAT: Outpatient Parenteral Antibiotic Therapy; H-OPAT: Healthcare-Administered OPAT; S-OPAT: Self-Administered OPAT.
→: switch; +: with; ±: with or without adjunctive vancomycin
*Statistically significant results ($p < 0.05$) or defined by the study as superior.
[a] : There was no statistically significant difference between treatment groups in the overall clinical cure rate, but only in the analysis by primary diagnosis (95 % CI, 1.9–25.2; $p = 0.018$).
[b] : Oral clindamycin and metronidazole have higher success rates in patients with mild DFI, and IV lincomycin and oral metronidazole show a higher cure rate in patients with moderate DFI with or without DFO.
[c] : No statistical significance when comparing treatment failure in patients receiving oral versus IV antibiotics ($p = 0,28$).
[d] : No significant difference in complete cure between oral and IV treatment ($p = 0.666$).
[e] : No statistical significance of failure rates between antibiotic routes for the treatment of residual osteomyelitis, thus concluding that oral antibiotics are not inferior to the IV route ($p = 0.2766$).

could be attributed to antibiotics alone or to unreported co-treatments. This lack of standardization in reporting limits the ability to identify the effect of antibiotic regimens and complicates comparisons between studies.

4. Discussion

We reviewed literature for antibiotic management of DFO in relation to route of administration (oral or IV) in patients with foot ulcers. Our aim was to retrieve data to aid decision-making with the patient beyond informed consent and clinical guidelines, within an interdisciplinary approach. However, as the data provided very little information on the impact of discussions within the team including an infectious disease specialist, this potential factor influencing the use of oral antibiotics was not evaluated.

Our results highlighted substantial heterogeneity in the reporting of patient characteristics, clinical presentation of the infection, treatment regimens and outcomes in studies evaluating oral vs. IV antibiotic therapy for DFO. Although clinical efficacy is generally similar between routes of administration, particularly in selected patients, significant knowledge gaps remain in the patient profile and team approach for the management, equity and standardization of outcome reporting. Our results demonstrate that studies, including RCTs focussed primarily on clinical outcomes, without considering other dimensions of quality of

care [23]. Our review also demonstrated the diversity and complexity of therapeutic approaches to DFI/DFO and the lack of reporting co-interventions for optimal cares. We analysed our results from three perspectives: 1) antibiotic therapy; 2) patient-centred and holistic care; and 3) the equity lens.

4.1. Antibiotic therapy for diabetic foot infection and osteomyelitis

The review confirmed the frequent use of IV antibiotic therapy in DFI/DFO management. However, most included studies focused on mild to moderate infections, not severe cases. This pattern should be interpreted cautiously considering recent IWGDF/IDSA guidelines [12], which support oral therapy for mild to moderate DFI and propose structured clinical scenarios (c.f. IWGDF Infection chapter recommendations 16, table 5) and evidence-based regimens (recommendation 12a) to guide antibiotic selection according to infection severity and patient context [12].

Despite the lack of data, many authors have suggested that the efficacy of oral antibiotic therapy is comparable to that of IV antibiotic therapy [32,38,48,50]. Indeed, studies of oral vs. IV antibiotic therapy in patients with or without amputation episodes have revealed no statistically significant differences, with similar success rates and advantages in terms of cost, ease of access and reduced hospitalization in the oral group [14,15,35,42,51]. These results are in line with those of other studies investigating oral antibiotic therapy of non-diabetic foot osteomyelitis [54,55]. Also, the OVIVA trial of non-diabetic bone and joint infections demonstrated the non-inferiority of early use of oral therapy over prolonged IV therapy and showed fewer catheter-related complications and shorter hospitalization in the oral group [56].

Many studies describe a sequential approach, initial IV followed by oral antibiotics once stabilized, as safe and effective [57,58]. Still, evidence remains limited to define which patients could safely start directly on oral therapy.

Oral therapy may particularly benefit patients with limited access to care, financial barriers, or homelessness, even though adherence to oral therapies remains very low in this population, limiting their effectiveness [59]. According to the IWGDF/IDSA guidelines, eligibility for oral antibiotics should be based not only on clinical criteria (such as infection severity and gastrointestinal absorption), but also on patient preferences and the context of care, ideally through team-based decision-making including patient, yet these aspects remain underexplored in the literature [12]. Specifically, oral therapy is appropriate when the diabetic foot infection (DFI) is mild to moderate, in patients who are reasonably selected according to their profile (e.g., microbiological results, no threat to life or limb), who are clinically and hemodynamically stable, able to tolerate and absorb oral antibiotics, and have no psychosocial or other reason to prefer IV treatment [16,17].Caution is required in the presence of peripheral arterial disease (PAD), as reduces blood perfusion, which may limit the efficacy of oral antibiotics, and justify use of the IV route [43,60].

In the management of DFO that is not threatening to the limb or life, with mild to moderate infection and without peripheral arterial disease or severity factors, the choice between oral and intravenous antibiotic therapy remains open, with both options considered effective in many cases [14,15,61]. Many recent studies, including two conducted in referral centers, show that oral antibiotic therapy is not inferior to intravenous administration for the treatment of residual osteomyelitis after amputation in diabetic patients, with similar success rates and no significant differences in relapse or complication rates [14,61].

Moreover, oral antibiotic therapy offers practical advantages such as reduced hospital stay duration, fewer catheter-related complications, and better patient satisfaction [14,15]. Despite the importance of this decision, there are no specific data on patient preferences or their involvement in choosing the route of administration for DFO. Shared decision-making (SDM), essential when different valid options exist, is underused in DFO management [15,61]. Integrating SDM could align treatments with patient needs, improving adherence by accounting for access, tolerance, and social factors. SDM improves the patient experience by taking into account their values and preferences, and promotes equity by reducing inequalities in access and participation, particularly among patients in context of vulnerability and/or marginalized population [61,62]. While SDM is a core component of patient-centered care, no study has evaluated its use specifically in DFO, highlighting the need for future research in this area [61].

4.2. Patient-centered and holistic care

Our results demonstrated a significant lack of data regarding patient-centered care and holistic approach regarding route of administration in context of DFI/DFO. The literature focuses mainly on clinical efficacy, practice variability and treatment optimization, without assessing patient satisfaction, quality of life or involvement in therapeutic decisions, even though these dimensions are essential for improving adherence and clinical outcomes [45,63]. The OVIVA trial demonstrated shorter hospital stays and fewer complications in patients treated orally and this is therefore associated with better quality of life. Yet, the patient satisfaction was not explicitly assessed [56]. When it comes to DFI/DFO management, the absence of such data highlighted a missed opportunity to engage/empower the patient into their treatment and enhance quality of care [64]. One study suggested that it would be important to develop strategies to help patients to think about their values and ensure that their preferences are in line with these, by developing decision-support tools, for example [65]. The integration of patients in decision-making on antibiotic administration is based on their empowerment, the quality of interactions with healthcare professionals and the perceived control over their care pathway; these factors are associated with increased participation in the decision-making process on antibiotic therapy, underlining the importance of strategies aimed at improving the active involvement of patients to optimize the appropriateness of prescriptions and quality of care [62]. Given the biomedical nature of infection management and its potentially fatal effects, a paradigm shift is needed to include patients beyond informed consent.

4.3. Equity lens

Despite the significant impact of DFO for patients and society [66], major gaps persist in addressing health equity and access to care within the current literature. Across the 25 studies reviewed, none focus on social determinants of health or plan analysis according to factors such as socioeconomic status, geographic location, ethnicity, or educational level. However, the literature underlines that these social determinants of health play a decisive role in the risk and prognosis of diabetic foot complications. People living in precarious conditions or with limited access to healthcare are at greater risk of complications, particularly amputation. It is therefore essential to integrate analysis of these social factors into the management and prevention of DFU, to reduce health inequalities and improve outcomes for the most vulnerable populations [67]. This lack of equity-oriented reporting is particularly concerning given that patients with diabetic foot complications often come from populations in context of vulnerability, those with lower income, limited mobility, or reduced access to specialized care [66,68]. Most studies described outpatient or home-based care models, but none examined whether such strategies were equally available, or if access was shaped by insurance status, urban, rural or remote location, or support systems. Ambulatory and home care offer many advantages, including improved patient and family satisfaction, reduced healthcare costs, and clinical outcomes comparable to those of traditional hospitalization. These models optimize patients' quality of life while reducing healthcare costs [69].

The potential of oral antibiotics to improve accessibility, by avoiding hospitalization or complex infusion infrastructure was demonstrated [38]. This may be done in real-world settings, based on clinical

judgment and informed by evidence-based medicine, but the fact remains that lack of knowledge remains about the patient's choice, preference, involvement and their impact on quality of care as well as DFI/DFO resolution. Equity in health care is closely linked to patient choice, as providing more equity-oriented care increases patients comfort and confidence, which in turn improves health outcomes and quality of care [70]. The absence of data on the populations benefiting from these regimens limits the capacity to assess whether these alternatives reduce or exacerbate health disparities. Similarly, while some studies mention treatment success in uninsured or underinsured populations [43], they do not explore how systemic barriers affect initiation, adherence, or follow-up.

Finally, this review revealed that most studies were conducted in high-income countries, with little representation from low- and middle-income settings, despite the global burden of diabetes and diabetic foot complications. This geographic imbalance further limits the generalizability of current findings.

5. Strengths and limitations

This scoping review offers a comprehensive synthesis of antibiotic strategies for DFI/DFO, with a specific focus on the route of administration. It is strengthened by a structured methodology, an extraction grid aligned with quality-of-care dimensions, and the inclusion of diverse study designs.

However, important limitations remain. Notably, 19 out of the 25 included studies were observational in design, which introduces a significant risk of selection, confounding, information and measurement bias and causal inferences are inappropriate. This predominance of observational studies restricts the ability to draw definitive conclusions about the comparative effectiveness and patient-centered outcomes of oral versus intravenous antibiotic therapies. Those studies are particularly prone to failing to adequately account for confounding variables (e.g., presence of peripheral vascular disease or smoking status), to the heterogeneity of co-interventions (e.g., use of offloading, patient education, surgical debridement), to not fully capturing the spectrum of disease severity (e.g., from mild to severe infections, or to comparing cases with similar clinical presentations), and to having insufficient follow-up periods to accurately assess long-term outcomes [71]. Because most available evidence comes from observational studies that lead to weak or conditional clinical recommendations [12], there is a critical need for more high-quality randomized controlled trials to reduce bias, strengthen causal inference, and provide a more reliable basis for clinical decision-making [72].

The heterogeneity across studies limits comparability, and most focused solely on clinical outcomes, with little attention to patient preferences or equity-related factors. Data from low- and middle-income countries were lacking, and outcome measures were rarely standardized. The limited reporting of co-interventions and care contexts also restricts interpretability. These gaps underscore the need for more holistic, equity-informed, and patient-centered research in DFO management.

6. Implication for care and research

This scoping review sheds light on essential aspects of DFO management that go beyond existing international guidelines, offering a complementary lens to strengthen clinical practices. While clinicians often follow exemplary recommendations to avoid deviation from standards, emerging data suggest promising directions that merit further exploration. The application of SDM in antibiotic therapy, in general, demonstrated benefits in terms of satisfaction, adherence, and fairness, supporting its integration to improve the patient experience [61,62]. The findings support a more patient-centered, equity-oriented approach, emphasizing the need to integrate shared decision-making into therapeutic choices. Furthermore, future research should address critical gaps by including: (1) a clear and consistent definition and classification of DFI/DFO; (2) standardized reporting of co-interventions and care contexts; (3) patient-reported outcomes and patient experience measures; and (4) core outcome sets (COS) encompassing not only infection resolution but also long-term functional recovery and quality of life. These dimensions are essential to capture the full impact of treatment and to guide the development of clinical decision-support tools rooted in real-world complexity. To support this effort, we propose a comparative summary of oral versus IV antibiotic therapy as a basis for developing patient-centered tools (Appendix 6).

The literature reports a predominance of retrospective cohort studies, with few randomized controlled trials. This lack of data contributes to the current variability in practices and prevents the optimization of care.

7. Conclusion

This scoping review mapped the current evidence on the antibiotic management of DFO/DFI. Oral therapy appears to be a feasible alternative to intravenous treatment in selected patients, but the overall quality of evidence remains limited. Key gaps persist regarding patient-centered outcomes, equity, and care delivery models. Future research should aim to strengthen clinical evidence through standardized outcome measures and integrate patient experience and accessibility considerations to support more effective and equitable care.

CRediT authorship contribution statement

Narimane Meddas: Writing – original draft, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Benoit Gachet:** Writing – review & editing, Data curation, Conceptualization. **Arthur Piraux:** Writing – review & editing, Methodology, Conceptualization. **Eric Senneville:** Writing – review & editing, Methodology, Conceptualization. **Laura M. Drudi:** Writing – review & editing, Methodology. **Magali Brousseau-Foley:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Conceptualization. **Virginie Blanchette:** Writing – review & editing, Visualization, Validation, Supervision, Project administration, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no financial or personal relashionsip to this project. The project is funded by the War amp.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2025.113035.

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