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المجتمع الالتهاب الرئوي المكتسبات idsa المبادئ التوجيهية

Circulation. 2015;132:1435-1486 Published: 15 September 2015 Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications *AHA published a correction to the original 2015 guideline. See the August 22, 2016 correction. Larry M. Baddour, Walter R. Wilson, Arnold S. Bayer, Vance G. Fowler, Imad M. Tleyjeh, Michael J. Rybak, Bruno Barsic, Peter B. Lockhart, Michael H. Gewitz, Matthew E. Levison, Ann F. Bolger, James M. Steckelberg, Robert S. Baltimore, Anne M. Fink, Patrick O'Gara, and Kathryn A. Taubert Infective endocarditis is a potentially lethal disease that has undergone major changes in both host and pathogen. The epidemiology of infective endocarditis has become more complex with today's myriad healthcare-associated factors that predispose to infection. Moreover, changes in pathogen prevalence, in particular a more common staphylococcal origin, have affected outcomes, which have not improved despite medical and surgical advances. Methods and Results This statement updates the 2005 iteration, both of which were developed by the American Heart Association under the auspices of the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease of the Young. It includes an evidence-based system for diagnostic and treatment recommendations used by the American College of Cardiology and the American Heart Association for treatment recommendations. Conclusions Infective endocarditis is a complex disease, and patients with this disease generally require management by a team of physicians and allied health providers with a variety of areas of expertise. The recommendations provided in this document are intended to assist in the management of this uncommon but potentially deadly infection. The clinical variability and complexity in infective endocarditis, however, dictate that these recommendations be used to support and not supplant decisions in individual patient management. For information on the recommendations of this guideline, please see the AHA Scientific Statement. Listed below is a summary of 2022, 2023 and 2024 highlights for IDSA guidelines as well as guidelines endorsed by IDSA. Authors Category Primary study JournalArchives of internal medicine Year 2009 Links Pubmed, DOI BACKGROUND: الالتهاب الرئوي المجتمع المكتسبة (CAP) هي السبب الرئيسي لمعدلات الاعتلال والوفيات في جميع أنحاء العالم. المبادئ التوجيهية الممارسة السريرية لعلاج CAP التجريبية، وضعت بشكل مشترك من قبل جمعية الأمراض المعدية الأمريكية (IDSA) وجمعية الصدر الأمريكية (ATS)، لا تزال مثيرة للجدل وغير متسق. فما قمنا بتقييم تأثير العلاج التوجيهي-متطابقة على البقاء في المستشفى والنتائج الأخرى باستخدام قاعدة بيانات كبيرة بما في ذلك البالغين المعالجة ل CAP [illegible] Dec 13, 2012 Authors Category Primary study JournalInternal medicine journal Year 2004 Links Pubmed, DOI على الرغم من أن المبادئ التوجيهية الدعوة إلى هذه العناصر بسهولة، وقادر على الاستفادة، والرعاية التي يتلقاها المرضى الذين يعانون من السياسة الزراعية المشتركة لا تزال غير متجانسة. في هذا التقرير، تم بنجاح، وضعت على استخدام الحاسوب القائم على مساعد لصنع القرار، واختبارها، وتحسين تطبيق المبادئ التوجيهية المعروفة (CAP). المبادئ التوجيهية لأفضل الممارسات تحديد العناصر الأساسية للرعاية. فإنها أن يمكن تحسين معاملة المرضى الذين يعانون من الالتهاب الرئوي المجتمع. This translation has been produced by an automated softw van Asten, Zulfiqarali G Abbas, Geneve Allison, Javier Aragón-Sánchez, John M Embil, Lawrence A Lavery, Majdi Alhasan, Orhan Oz, Ilker Uçkay, Vilma Urbančič-Rovan, Zhang-Rong Xu, Edgar J G Peters The International Working Group on the Diabetic Foot (IWGDF) has published evidence-based guidelines on the management and prevention of diabetes-related foot diseases since 1999. The present guideline is an update of the 2019 IWGDF guideline on the diagnosis and management of foot infections in persons with diabetes mellitus. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework was used for the development of this guideline. This was structured around identifying clinically relevant questions in the P(A)ICO format, determining patient-important outcomes, systematically reviewing the evidence, assessing the certainty of the evidence, and finally moving from evidence to the recommendation. This guideline was developed for healthcare professionals involved in diabetes-related foot care to inform clinical care around patient-important outcomes. Two systematic reviews from 2019 were updated to inform this guideline, and a total of 149 studies (62 new) meeting inclusion criteria were identified from the updated search and incorporated in this guideline. Updated recommendations are derived from these systematic reviews, and best practice statements made where evidence was not available. Evidence was weighed in light of benefits and harms to arrive at a recommendation. The certainty of the evidence for some recommendations was modified in this update with a more refined application of the GRADE framework centred around patient important outcomes. This is highlighted in the rationale section of this update. A note is also made where the newly identified evidence did not alter the strength or certainty of evidence for previous recommendations. The recommendations presented here continue to cover various aspects of diagnosing soft tissue and bone infections, including the classification scheme for diagnosing infection and its severity. Guidance on how to collect microbiological samples, and how to process them to identify causative pathogens, is also outlined. Finally, we present the approach to treating foot infections in persons with diabetes, including selecting appropriate empiric and definitive antimicrobial therapy for soft tissue and bone infections; when and how to approach surgical treatment; and which adjunctive treatments may or may not affect the infectious outcomes of diabetes-related foot problems. We believe that following these recommendations will help healthcare professionals provide better care for persons with diabetes and foot infections, prevent the number of foot and limb amputations, and reduce the patient and healthcare burden of diabetes-related foot disease. Recommendation 1 a. Diagnose a soft tissue diabetes-related infection clinically based on the presence of local or systemic signs and symptoms of inflammation. (Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) recommendation: Strong; Certainty of evidence: Low) b. Asses the severity of any Diabetes-related foot infection (DFI) using the International Working Group on the Diabetic Foot (IWGDF)/Infectious Diseases Society of America (IDSA) classification scheme. (Strong; Low). Recommendation 2 a. Consider hospitalising all persons with diabetes and a foot infection who have either a severe foot infection as classified by the IWGDF/IDSA classification or a moderate infection which is associated with key relevant morbidities. (Conditional; Low). Recommendation 3 a. Assess inflammatory serum biomarkers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), or procalcitonin (PCT) in a person with diabetes and a possible infected foot ulcer for whom the clinical examination is diagnostically equivocal or uninterpretable. (Best Practice Statement). Recommendation 4 a. For diagnosing diabetes-related foot soft-tissue infection, we suggest not using foot temperature (however measured) or quantitative microbial analysis. (Conditional; Low). Recommendation 5 a. In a person with suspected soft tissue DFI, consider a sample for culture to determine the causative microorganisms, preferably by aseptically collecting a tissue specimen (by curettage or biopsy) from the wound. (Conditional; Moderate). Recommendation 6 a. Use conventional, rather than molecular, microbiology techniques for the first-line identification of pathogens from soft tissue or bone samples in a patient with a DFI. (Strong; Moderate). Recommendation 7 a. In a person with diabetes, consider using a combination of probe-to-bone test, plain X-rays, and ESR, or CRP, or PCT as the initial studies to diagnose osteomyelitis of the foot. (Conditional; Low). Recommendation 8 a. Perform magnetic resonance imaging (MRI) when the diagnosis of diabetes-related osteomyelitis of the foot remains in doubt despite clinical, plain X-rays and laboratory findings. (Strong; Moderate). Recommendation 9 a. Consider using positron emission tomography (PET), leucocyte scintigraphy, or single photon emission computed tomography (SPECT) as an alternative to MRI for the diagnosis of diabetes-related osteomyelitis of the foot. (Conditional; Low). Recommendation 10 a. In a person with diabetes for whom there is a suspicion of osteomyelitis of the foot (before or after treatment), bone (rather than soft tissue) samples should be obtained for culture, either intraoperatively or percutaneously. (Conditional; Moderate). Recommendation 11 a. Do not treat clinically uninfected foot ulcers with systemic or local antibiotic therapy when the goal is to reduce the risk of new infection or to promote ulcer healing. Best Practice Statement. Recommendation 12 a. Use any of the systemic antibiotic regimens that have been shown to be effective in published randomised controlled trials at standard (usual) dosing to treat a person with diabetes and a soft tissue infection of the foot. (Strong; High). b, Administer antibiotic therapy to a patient with a skin or soft tissue diabetic foot infection for a duration of 1–2 weeks. (Strong; High). c. Consider continuing treatment, perhaps for up to 3–4 weeks, if the infection is improving but is extensive and is resolving slower than expected or if the patient has severe peripheral artery disease (PAD). (Conditional, Low). d. If evidence of infection has not resolved after 4 weeks of apparently appropriate therapy, re-evaluate the patient, and reconsider the need for further diagnostic studies or alternative treatments. (Strong; Low). Recommendation 13 a. Select an antibiotic agent for treating a DFI based on the likely or proven causative pathogen(s) and their antibiotic susceptibilities; the clinical severity of the infection; published evidence of the efficacy of the agent for infections of the diabetes-related foot; the risk of adverse events including collateral damage to the commensal flora; the likelihood of drug interactions; agent availability and costs. Best Practice Statement. Recommendation 14 a. Target aerobic gram-positive pathogens only (beta-haemolytic streptococci and Staphylococcus aureus including methicillin-resistant strains if indicated) for people with a mild DFI, who have not recently received antibiotic therapy, and who reside in North America or Western Europe. Best Practice Statement. Recommendation 15 a. Do not empirically target antibiotic therapy against Pseudomonas aeruginosa in cases of DFI in temperate climates, but use empirical treatment of P. 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. Best Practice Statement. Recommendation 16 a. Consider a duration of up to 3 weeks of antibiotic therapy after minor amputation for diabetes-related osteomyelitis of the foot and positive bone margin culture and 6 weeks for diabetes-related foot osteomyelitis without bone resection or amputation. (Conditional; Low). Recommendation 17 a. Use the outcome at a minimum follow-up duration of 6 months after the end of the antibiotic therapy to diagnose remission of diabetes-related osteomyelitis of the foot. Best Practice Statement. Recommendation 18 a. The urgent surgical consultation should be obtained in cases of severe infection or moderate DFI complicated by extensive gangrene, necrotising infection, signs suggesting deep (below the fascia) abscess, compartment syndrome, or severe lower limb ischaemia. Best Practice Recommendation. Recommendation 19 a. Consider performing early (within 24–48 h) surgery combined with antibiotics for moderate and severe DFIs to remove the infected and necrotic tissue. (Conditional; Low). Recommendation 20 a. In people with diabetes, PAD and a foot ulcer or gangrene with infection involving any portion of the foot obtain an urgent consultation by a surgical specialist as well as a vascular specialist in order to determine the indications and timings of a drainage and/or revascularisation procedure. Best Practice Statement. Recommendation 21 a. Consider performing surgical resection of infected bone combined with systemic antibiotics in a person with diabetes-related osteomyelitis of the foot. (Conditional; Low). Recommendation 22 a. Consider antibiotic treatment without surgery in case of (i) forefoot osteomyelitis without an immediate need for incision and drainage to control infection, (ii) without PAD, and (iii) without exposed bone. (Conditional; Low). Recommendation 23 a. We suggest not using the following treatments to address DFIs: (a) adjunctive granulocyte colony-stimulating factor (G-CSF) treatment or (b) topical antiseptics, silver preparations, honey, bacteriophage therapy, or negative-pressure wound therapy (with or without instillation). (Conditional; Low). Recommendation 24 a. We suggest not using topical (sponge, cream, and cement) antibiotics in combination with systemic antibiotics for treating either soft-tissue infections or osteomyelitis of the foot in patients with diabetes. (Conditional; Low). Recommendation 25 a. We suggest not using Hyperbaric oxygen (HBO) therapy or topical oxygen therapy as an adjunctive treatment for the sole indication of treating a DFI. (Conditional; Low). Note: the available data did not allow making a recommendation on the use of rifampicin for the treatment of diabetes-related osteomyelitis of the foot. The prevalence of diabetes continues to increase globally and the International Diabetes Foundation has estimated that 537 million adults aged between 20 and 79 years worldwide were living with diabetes in 2021.1 This situation leads to a rising incidence of foot complications, including infections.1 DFIs are associated with substantial morbidities, requiring frequent healthcare provider visits, daily wound care, antimicrobial therapy, surgical procedures, and high healthcare costs.2 Of particular importance, DFIs remain the most frequent diabetes-related complications requiring hospitalisation and the most common precipitating events leading to lower extremity amputation.3,4 Outcomes in patients presenting with an infected diabetes-related foot ulcer (DFU) are suboptimal in one large prospective study, at the end of 1 year, the ulcer had healed in only 46% (and it later recurred in 10% of these), while 15% had died and 17% required a lower extremity amputation.5 Managing DFIs requires careful attention to properly diagnose the condition, obtain appropriate specimens for culture, thoughtfully select antimicrobial therapy, quickly determine when surgical interventions are required, and provide any needed additional wound and overall patient care. A systematic, evidence-based approach to managing DFIs likely improves outcomes, specifically the resolution of difficult cases of infection, and helps avoid complications, such as life-threatening infections and limb loss. This is best delivered by interdisciplinary teams, which should include among the membership, whenever possible, infectious diseases or clinical/medical microbiology specialist.6 This team should also attempt to ensure optimal local wound care (e.g., cleansing and debridement), pressure off-loading, peripheral vascular assessment (with revascularisation if needed), and metabolic (particularly glycaemic) control. For these aspects, the reader is referred to the other chapters of the IWGDF guideline on the management of diabetes-related foot ulcers in this special issue.7–9 If these aspects are not adequately addressed, and the focus is only on infection, the chance of treatment failure is greatly increased. Several guidelines are available to assist clinicians in managing DFIs. The IDSA produced a guideline in 2004, which was updated in 2012.10,11 A panel of experts convened by IWGDF has published widely used guideline documents quadrennially since 2004.12 The present 2023 edition of the IWGDF guidelines on the management of DFI updates the content of the 2019 edition on the diagnosis and treatment of DFIs and is part of the aforementioned guidelines.13 The IWGDF and IDSA have now agreed to provide a combined intersociety guideline on the diagnosis and treatment of DFIs; as a result, the expert panel involved in the creation of the new guideline document included for the first time members from both IWGDF and IDSA working on a single document. Infections of the skin and soft tissues of the foot in a person with diabetes most often follow a break in the protective skin envelope. The most common such break is a DFU, which usually involves at least the epidermis and part of the dermis. This complication most often occurs in those with peripheral neuropathy, and frequently those with PAD.14 Infection follows the colonisation of the wound by a complex microbiological flora. Wound colonisation by bacteria is a constant phenomenon, defined by the presence of bacteria on the wound surface but without evidence of invasion of the host tissues. Wound infection is a pathological state caused by the invasion and multiplication of microorganisms in host tissues that induce an inflammatory response, usually followed by tissue damage. Since all wounds are colonised (often with potentially pathogenic microorganisms), wound infection cannot be defined using only the results of wound cultures. Instead, DFIs are defined clinically based on the presence of manifestations of an inflammatory process involving a foot wound located below the malleoli. In persons with diabetes-related foot complications, signs and symptoms of inflammation may, however, be masked by the presence of peripheral neuropathy, PAD, or immune dysfunction. A patient with diabetes-related complications may need to undergo lower extremity amputation to control infection or develop multiorgan failure without local clinical signs that define a DFI, but this is highly uncommon. Although rarely the primary cause of foot ulcers, the presence of PAD increases the risk of an ulcer becoming infected4,15–17 and adversely affects the outcome of infection.4,18,19 Because the combination of infection with PAD is associated with a markedly increased risk of poor healing and amputation, clinicians should evaluate the state of wound perfusion and the potential need for a revascularisation procedure as soon as possible in all patients with a DFI.7 Factors that predispose to foot infection include having a wound that is deep, long-standing, recurrent, or of traumatic aetiology; the presence of diabetes-related immunological perturbations, particularly neutrophil dysfunction; and having concomitant chronic renal failure.16,18–23 Although examined in only a few studies, a history of chronic hyperglycaemia may predispose to DFIs, and the presence of hyperglycaemia at presentation may suggest a rapidly progressive or destructive (necrotising) infection.24,25 While most DFIs are relatively superficial at presentation, microorganisms can spread contiguously to subcutaneous tissues, including fascia, tendons, muscles, joints, and bones. The anatomy of the foot, which is divided into several separate but intercommunicating compartments, fosters the proximal spread of infection.26 The inflammatory response induced by infection may cause compartmental pressure to exceed capillary pressure, leading to ischaemic tissue necrosis in the affected compartment and thereby progressive infection.27,28 The tendons within the compartments facilitate the proximal spread of infection, which usually moves from higher to lower pressure areas. Bacterial virulence factors may also play a role in these complex infections.29,30 Systemic symptoms (e.g., feverishness or chills), marked leucocytosis, or major metabolic disturbances are uncommon in patients with a DFI, but their presence denotes a more severe, potentially limb-threatening (or even life-threatening) infection.4,31,32 If not quickly diagnosed and properly treated, DFIs tend to progress, sometimes rapidly.33 Thus, an experienced medical specialist (or team) with experience in infectious diseases should evaluate a patient with a severe DFI within 24 h34 Accumulations of purulent secretions, especially if under pressure or associated with necrosis, require prompt (usually within 24 h) surgical decompression and drainage. Although bone and/or joint resection (preferably using a conservative approach, with limited resection and avoiding amputation, if possible) may be required for successfully treating osteomyelitis, it is usually an infection of the soft tissues that requires urgent antimicrobial therapy and surgical intervention. This document aims to provide a comprehensive, evidence-based overview of guidelines for the diagnosis and treatment of foot infections in people with diabetes. These are intended to be of practical use for treating clinicians based on all available scientific evidence. The GRADE framework was used for developing this guideline.35 This is structured around identifying key clinical questions in the Population, Assessment, Comparison, Outcome and patient/population, intervention, comparison, outcomes format, determining patient-important outcomes, presenting the evidence, assessing the certainty of the evidence, and finally moving from evidence to the recommendation. The IWGDF editorial board appointed a multidisciplinary working group of independent experts (the authors of this guideline) to update the previously published 2019 guidelines. In addition, three members were delegated by the IDSA to join the committee. The key clinical questions were developed by revising the 2019 guideline PICOs and refining each component to reflect clinical relevance. Guidance is aimed at clinicians and other healthcare professionals involved in the diagnosis and management of DFIs. Patient important outcomes were generated and then classified based on their importance for decision-making. Outcomes defined by Jeffcoate et al were also used as a reference guide.36 All members voted on the outcomes, and those identified by consensus as "critically important" were included. The editorial board reviewed and approved the final set of P(A)ICOs through a consultation process with external experts from various geographical regions and the IDSA. The committee members then systematically reviewed the literature to address the set of pre-specified P(A)ICOs. The two updated IWGDF systematic reviews supporting this guideline have been completed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, which will be published separately.37 The updated protocols are available from PROSPERO (CRD42022324795, CRD42022324812).38,39 After careful weighing of the summary of judgments, the same teams of two members of the working group determined the direction, strength, and wording of the recommendation(s) for the specific clinical question. Recommendations aimed to be clear, specific, and unambiguous on what was recommended, for which persons, and under what circumstances. Recommendations were rated as 'for' or 'against' the particular intervention or 'either the intervention or the comparison', and the strength of each recommendation as 'strong' or 'conditional'. The certainty of evidence, rated as 'high', 'moderate', 'low' or 'very low' based on the critical outcome(s) reviewed for the question in accordance with GRADE, as explained above, was added to the strength of the recommendation. Summary of judgements tables and recommendations for each question were extensively discussed in online meetings of the working group. After discussion, a voting procedure was used for each recommendation to grade the direction of the recommendation as 'for' or 'against' the particular intervention (or 'either the intervention or the comparison'), and the strength of each recommendation as 'strong' or 'conditional'. A quorum of 60% of members was needed to be present for a discussion and vote to go ahead and a majority vote of those present was needed for final decisions on each recommendation. The outcomes of the voting are provided in the summary of judgement tables in the supplemental information of the guideline documents. Based on the summary of judgement tables, the rationales for the recommendations were written by the same team of two assessors of the working groups. These rationales are narrative (systematic) descriptions of how the working group came to the direction and strength of the recommendation and summarises the research evidence for the items in the summary of judgement tables.35,40 In addition, expert opinion, and aspects relevant to communicating to the reader regarding the intervention or recommendation can be added to these rationales. Finally, all recommendations, with their rationales, were collated into a consultation (draft) guideline manuscript that was reviewed by the same international external experts and persons with lived experience who reviewed the clinical questions and outcomes, as well as by the IWGDF Editorial Board. The working group then collated, reviewed and discussed all feedback on the consultation manuscript and revised accordingly to produce the final guidelines. In the publication "Standards for the development and methodology of the 2023 IWGDF guideline", the details of the methodology for the development of this guideline are described.41. See Figure 1 for a synthesising overview of the overall diagnosis and management of patients with DFIs, including diabetes-related osteomyelitis of the foot. 5.1.Diagnosis 5.1.1 Clinical QuestionCan the International Working Group of the Diabetic Foot/IDSA (IWGDF/IDSA) classification system for foot infections in persons with diabetes predict the outcome of such an infection? Recommendation 1: a. Diagnosis of a soft tissue diabetes-related infection clinically based on the presence of local or systemic signs and symptoms of inflammation. (Strong; Low) b. Assess the severity of any DFI using the IWGDF/IDSA classification scheme. (Strong; Low). RationaleThe clinician seeing a patient with diabetes and a foot ulcer should always assess for the presence of an infection and, if present, classify the infection's severity.42,43 Experts have proposed many classification schemes for DFU, many of which only include the presence or absence of "infection".9 Previous prospective and retrospective studies have validated all or part of the IWGDF/IDSA DFI classification as part of a larger diabetes-related foot classification system (PEDIS) (see Table 1).4,15 Other classifications for severe infection, for example, National Early Warning Score44,45 or quick sequential organ failure assessment,46 were developed for the identification or prediction of outcomes in patients with sepsis. However, there are no data to support changing from using the systemic inflammatory response syndrome (SIRS) that is part of the IWGDF/IDSA classification to any other classification for DFIs. Two commonly used classifications for DFUs, Wound, Ischaemia, and foot Infection, and Site, Ischaemia, Neuropathy, Bacterial Infection, and Depth, which use the IWGDF/IDSA classification for the infection component, have been validated with patient data.47,48 Importantly, in the current guideline, we define a DFI based on the presence of evidence of (a) inflammation of any part of the foot, not just of an ulcer, or (b) findings of SIRS. Because of the important diagnostic, therapeutic, and prognostic implications of osteomyelitis, we separated it out by indicating the presence of bone infection with "(O)" after the grade number (3 or 4) (see Table 1). We did not use the term osteitis, which would be an infection of the cortical bone only, without the involvement of the medulla. Although the pathogens enter the bone through contiguous spread from an ulcer to the cortex and not by haematological spread to the medulla, it is difficult to distinguish the cortical bone infection from medullary bone infection clinically by imaging or histology. Also, we think that the two entities do not require separate therapeutic interventions. Therefore, we decided to use the term osteomyelitis for both disease entities. In our systematic review on the diagnosis of foot infection in persons with diabetes, 49 new studies with a high risk of bias were identified that examined the outcomes of interest.50–54 The main questions addressed concerned whether there should be modifications of the current IDSA/IWGDF classification by combining the moderate and severe categories and considering risk categories according to soft tissue infections or osteomyelitis. Insufficient quality of evidence led us to not consider either laboratory risk indicators for necrotising fasciitis or SIRS as reliable tools for predicting lower extremity amputation, mortality, or other health outcomes.52,53 In the absence of additional validation studies, and moderate certainty attributed to the risk of bias, we elected not to alter the IDSA/IWGDF classification, as shown in Table 1. Defining the infection of the foot in persons with diabetes is of utmost importance, given the possible negative consequences of missing this diagnosis. Additionally, distinguishing infected from non-infected wounds may help avoid the unnecessary use of antibiotics in the absence of infection. Although based on low quality of evidence given the major impact, the use of the IWGDF/IDSA classification may have on outcome and antibiotic use in persons with DFIs, we made a strong recommendation. Recommendation 2: a. Consider hospitalising all persons with diabetes and a foot infection who have either a severe foot infection as classified by the IWGDF/IDSA classification or a moderate infection which is associated with key relevant morbidities. (Conditional; Low). RationaleRegarding the decision to hospitalise a patient with a DFI, the IWGDF/IDSA infection classification system facilitates risk stratification to inform this decision.4 Hospitalisation is an expensive and finite resource and may subject the patient to major inconvenience and potential nosocomial risks. But while many patients with a DFI do not need to be hospitalised, some certainly should be. The consideration should be given to hospitalise all persons with a severe foot infection to ensure timely and effective management, as well as those with a moderate infection associated with key relevant co-morbidities, in particular, PAD (see details in Table 2). This is due to a higher risk of poor outcomes in these cases, especially amputation or death.4,16,17,19 Of note, the presence of osteomyelitis does not necessarily require hospitalisation, since many of these patients are clinically stable and can be treated with oral antibiotic agents. Hospitalisation may be preferable (at least initially) in those patients who require intravenous antibiotic therapy, have substantial associated soft tissue infection, require special diagnostic testing, or require urgent surgical treatment. Fortunately, almost all patients with a mild infection, and many with a moderate infection but without any key relevant morbidities, can be treated in an ambulatory setting. The availability of home parenteral antibiotic programs in some countries is another site-dependent factor that influences the need for hospitalisation. Most published studies of DFIs have enrolled hospitalised patients, but over the past 2 decades, several have reported good results with outpatient treatment.51–53 Therefore, it is of utmost importance to correctly assess the infection severity as the patient management significantly differs from oral antibiotic treatments to complex combinations of surgery and parenteral broad-spectrum antibiotic regimens. Given the low certainty of the evidence, with inconsistency between studies, and the fact that differences in patient characteristics as well as health care policies between countries will influence the decision to hospitalise, we made a conditional recommendation. Recommendation 3: a. Assess inflammatory serum biomarkers such as CRP, ESR, or PCT in a person with diabetes and a possible infected foot ulcer for whom the clinical examination is diagnostically equivocal or uninterpretable. (Best Practice Statement). RationaleSerum tests for inflammatory biomarkers such as white blood cell (WBC) count, ESR, CRP, and PCT are widely available, easily obtained, and most, except PCT, are relatively inexpensive. A few studies have investigated other inflammatory markers for their role in diagnosing or following DFIs, but they were small and of low quality.11 Most available studies assessed the value of these inflammatory biomarkers by comparing them with the results of IDSA/IWGDF criteria for infection.4,54 Unfortunately, the severity of infection in patients included in the available studies was not always clearly defined, which may account for interstudy differences in findings. In addition, many studies do not specify if enroled patients were recently treated with antibiotic therapy, which could affect results.55 Of particular note is the WBC level, as it is used as part of the IDSA/IWGDF criteria for classifying infection as severe/grade 4. The available studies56–61 found little correlation of WBC with infection severity, with about half of the patients diagnosed with a DFI having a normal WBC.60,61 In most studies, ESR values have been higher in patients with an infected DFU compared with a noninfected DFU.56,57 ESR values can be affected by various co-morbidities (e.g., anaemia and azotaemia) and may not be elevated in acute infections due to the relatively slow response of this inflammatory biomarker. A highly elevated ESR (≥70 mm/h) has a sensitivity, specificity, and AUC for the diagnosis of DFO of 81%, 80%, and 0.84, respectively.62 Compared with ESR, CRP levels tend to rise more quickly with infection and fall more quickly with the resolution of infection. Serum values of CRP have consistently been found to be significantly higher in infected than noninfected DFUs and in patients with noninfected DFU than in those with no foot ulcer, with levels increasing significantly with the severity of infection.62,63 Compared to WBC and ESR, CRP has shown higher diagnostic accuracy for grade 2 (infected) DFU.63 Studies of serum PCT levels have also found that levels were significantly higher in infected DFU than noninfected DFU, but there was little correlation between the values and the infection severity.54,57,58,64,65 The highly variable cut-off values used make it difficult to interpret the results reported in studies that have investigated these inflammatory markers. Due to their limited specificity and sensitivity, not exceeding 0.85, when used as sole diagnostic tools, inflammatory biomarkers should be used when uncertainty persists after clinical assessment. We make a Best Practice Statement about the use of ESR, CRP, or PCT due to the potential harms related to potential over or underdiagnosing DFI, with low certainty of evidence based on studies of low quality, with inconsistency about the results and heterogeneity in cut-off values. Recommendation 4: a. For diagnosing diabetes-related foot soft-tissue infection, we suggest not using foot temperature (however measured) or quantitative microbial analysis. (Conditional; Low). RationaleWhile various imaging tests are widely used for diagnosing bone infection (see below), there are few data on their usefulness for soft-tissue infections. Other diagnostic tests studied for assessing DFI include photographic foot imaging and infrared thermography. Several studies with these instruments have examined their value in predicting the occurrence of foot ulcerations. Overall, employing either infrared or digital thermography does not appear to provide substantial help in diagnosing infection or predicting the clinical outcome in patients with a DFU seen in the hospital setting.66–69 While infrared imaging likely causes no harm, its use is limited by low availability. Some advocate using the presence of high numbers of bacteria on culture (usually defined as ≥105 colony-forming units per gram of tissue) as a basis for differentiating infected from uninfected DFUs.70,71 However, there is no convincing data (from studies using either conventional culture or molecular methods) supporting this concept.72 In published studies that assessed the validity of clinical signs for the diagnosis of DFI using microbial analysis as a referent test, the criteria used to define infection varied among the authors, and even between studies conducted by the same team. In some microbial analysis studies, patients receiving antibiotics at the time of the wound sampling (which may suppress bacterial growth and cause diminished organism counts) were included, while others failed to provide information on this important confounding issue. Of note, these methods for measuring what is sometimes called "wound bioburden" are time-consuming and relatively expensive. Furthermore, neither quantitative classical culture nor molecular quantitative techniques are currently available to most clinicians in their daily care of patients. Our recommendation against these diagnostic methods is based on the limited data to support the use of these time- and resource-consuming techniques, which are frequently unavailable, and may lead to overdiagnosing (and unnecessarily treating) IDFU. The recommendation is conditional based on low certainty of evidence. 5.1.2 Clinical questionIn a person with diabetes and infection of the foot, which test(s) can best identify the causative pathogen(s), and result in tailored use of antibiotics? Recommendation 5: a. In a person with suspected soft tissue DFI, consider a sample for culture to determine the causative microorganisms, preferably by aseptically collecting a tissue specimen (by curettage or biopsy) from the wound. (Conditional; Moderate). RationaleIn the great majority of cases, obtaining a specimen (after cleansing and debridement and trying to avoid contamination) for culture from a DFI provides useful information on the causative pathogen(s) and their antibiotic susceptibility, allowing appropriate selection of antibiotic therapy. In cases of an acute, non-severe DFI in a patient who has not recently received antibiotic therapy and has no other risk factors for unusual or antibiotic-resistant pathogens (e.g., based on specific exposures or previous culture results), selecting empiric therapy without culture may be reasonable. In other situations, despite superficial swabs being easier to perform, we advise collecting a soft tissue specimen on the basis of two systematic reviews73,74 (with low-quality evidence), one small prospective study75 and one well-designed prospective study,76 which reported higher sensitivity and specificity of tissue specimens for culture results than superficial swabs. Collecting a tissue specimen may require slightly more training and pose a slight risk of discomfort or bleeding, but we believe the benefits clearly outweigh this minimal risk of harm. The evidence informing which method of specimen collection to use is limited by the absence of a definitive criterion standard for defining the ulcer infection. Repeating cultures may be useful for a patient who is not responding to apparently appropriate therapy, but this may result in isolating antibiotic-resistant strains likely to be contaminants rather than pathogens. A key caveat is that the accuracy of culture results depends on the quality of the information provided between clinical and microbiology staff throughout the sample pathway, from collecting, to transporting, to processing and reporting. Clinicians should provide key clinical details associated with the patient and the sample, and clinical microbiology services should provide adequate comprehensive and clear reporting of the isolated organisms and their susceptibility profiles. For persons presenting in a low-income limited resource setting without ready access to culture or follow-up care, performing a Gram-stained smear of material from a DFI could be a relatively easy and inexpensive way to visualise the class of the likely causative pathogens, thus helping direct empiric therapy.77 The recommendation is conditional with a moderate certainty of evidence based on clinical studies with varying quality, including one large prospective study. Recommendation 6: a. Use conventional, rather than molecular, microbiology techniques for the first-line identification of pathogens from soft tissue or bone samples in a patient with a DFI (Strong; Moderate). RationaleMolecular microbiology techniques have demonstrated that the flora in most DFIs is more diverse and abundant than that revealed using conventional culture methods.78–82 Our systematic review identified 4 recent single-centre prospective studies that compared the results of different non-culture (molecular microbiological) methods to those of conventional culture.49,83–86 These studies addressed this question in both skin and soft-tissue infections and osteomyelitis of the foot. They consistently found an agreement of more than 0.70 between molecular microbiology and conventional culture methods regarding the most clinically relevant pathogens identified, except for anaerobes, which are more frequently identified by non-culture techniques.82 The studies also confirmed that non-culture techniques, especially metagenomic next-generation sequencing (mNGS) (NGS), identify more bacteria from tissue samples, including bone, than conventional cultures.83–86 Currently, the use of mNGS techniques does not lead to a shorter time until pathogen identification, but this might change with the deployment of newer techniques. These techniques may help choose the empirical antibiotic therapy and reduce the risk of inappropriate treatment (i.e., failing to cover bacteria involved, including multiresistant ones). On the other hand, as molecular microbiology techniques are currently unable to distinguish dead from living bacterial cells, there are concerns that they may lead to the unjustified use of broad-spectrum antibiotics. The studies that addressed molecular microbiology for either STI or DFO included relatively few subjects, were at high risk of bias, and did not provide information on the value of the findings for guidance on clinical management. Specifically, we do not know which of the many bacterial genera identified using molecular methods contribute to the clinical state of infection or require targeted antibiotic therapy. Overall, we acknowledge the essential role of molecular microbiology techniques in the understanding of the pathophysiology of DFIs, and that these are promising techniques for application in clinical practice in the future. We do not, however, recommend their use in daily practice, given the unclear significance of positive results, absence of demonstrated impact on antibiotic treatment, high costs, and limited availability. This is a strong recommendation against the use of non-culture techniques, based on a moderate certainty of evidence from prospective studies with a high risk of bias, the relative high costs and the lack of information to what extent these techniques will influence clinical management. Thus, for now, clinicians should continue to request conventional cultures of specimens to determine the identity of causative microorganisms and their antibiotic sensitivities. 5.1.3 Clinical questionIn a person with diabetes and suspected bone or joint infection of the foot, which tests have the best correlation with BonE BiOPsy (BeBoP) results for diagnosing diabetes-related osteomyelitis, including residual/postoperative osteomyelitis)? Recommendation 7: a. In a person with diabetes, consider using a combination of probe-to-bone test, plain X-rays, and ESR, or CRP, or PCT as the initial studies to diagnose osteomyelitis of the foot. Conditional; Low. RationaleThe diagnosis of osteomyelitis in the foot of a person with diabetes may be difficult partly because of a lack of a universally accepted definition or criterion standard, and partly related to low levels of inter-test agreement among commonly used diagnostic tests.87 Osteomyelitis may be present underlying any foot wound, especially those that have been present for many weeks or that are wide, deep, located over a bony prominence, showing visible bone, or accompanied by an erythematous, swollen ("sausage") toe.88 Diagnosis of bone infection of the foot is of paramount importance, given that its presence greatly increases the risk of minor and major amputations. The investigation of diabetes-related foot wounds suspected of having bone infection usually includes a physical examination and a conventional radiograph, while some blood biomarkers might be of interest; these issues are discussed below. An accurate diagnosis of DFO is essential to initiate appropriate therapy and to avoid unjustified prolonged antibiotic treatment and surgery in patients who do not have a DFO. Probe-to-bone testAmong clinical examinations of the foot, the PTB test is the most useful, but the performing clinician's technique and experience, the location of ulcer, and its aetiology may affect the test reliability.89,90 A systematic review of the PTB test found that for detecting DFO, the sensitivity was 0.87 and specificity 0.83.91 Overall, in diagnosing DFO, the PTB test suggests the diagnosis if it is positive in a high-risk patient and helps rule it out if it is negative in a low-risk patient. The procedure is easy to learn and perform, requiring only a sterile blunt metal probe (gently inserted into the wound, with a positive test defined by feeling a hard, gritty structure), is inexpensive and essentially harmless, but interobserver agreement is only moderate.92 Of note, if clinicians are not skilled in this test, they should not rely on its results as it may have been performed incorrectly, resulting in incorrect results. Plain X-rayAny patient with a possible bone infection should initially have plain X-rays of the foot. Interpreted by an experienced reader, characteristic findings of bone infection (see Table 3) are highly suggestive of osteomyelitis, but similar abnormal findings can be caused by Charcot osteoarthropathy and other disorders. As plain X-rays are relatively inexpensive, widely available, and cause minimal harm, we recommend them as part of the routine assessment of patients presenting with a DFI. This imaging exam provides useful information, especially about the status of the underlying osteoarticular tissues, the presence of gas in deep tissues, and the presence of any radio-opaque foreign body. In addition, the image can be used as a reference against which to compare new images if the patient presents with another foot problem. Because plain X-rays are insensitive to acute osteomyelitis, it is often useful to repeat a normal examination in 2–3 weeks when the suspicion of osteomyelitis is still high.93 A retrospective study of patients with histologically proven DFO found that after adjusting for confounders, inflammatory biomarkers, and plain X-rays were actually more useful than MRI.94 Because interpretation of plain X-rays can be difficult (even for an experienced reader) when non-infectious changes (especially those related to neuro-osteoarthropathy) are present, advanced imaging techniques or even bone culture may ultimately be needed to confirm or exclude osteomyelitis in the foot. Serum biomarkersIn a systematic published in 2019, it was found that ESR ≥70 mm/hr had a sensitivity, specificity, and AUC of 0.81, 0.8 and 0.84, respectively, while the value of PCT could not be assessed due to paucity of the data.62 A more recent systematic review and meta-analysis published in 2022 found that PCT had the highest diagnostic test accuracy when compared to that of ESR, WBC and ESR with sensitivity, specificity, and AUC of 0.85, 0.67 and 0.844 at a cut-off value of 0.33 ng/mL.63,95 Given the lack of inter-operator variability, the use of either ESR, CRP, or PCT as a sole biomarker for the detection of DFO in a patient with soft tissue DFI is not appropriate, but their use in combination with other diagnostic tests may be useful. A large-scale retrospective single-centre study with high risk of bias that used the results of culture and/or histology of bone samples as a reference standard found that ESR >60 mm/hr plus CRP ≥80 mg/L had a high positive predictive value, but a modest negative predictive value, for the diagnosis of DFO.96 In another study, the combination of elevated ESR (>43 mm/h) with a positive PTB test showed a high correlation with having positive bone culture and/or histology results.97 Overall, neither plain x-ray, inflammatory biomarkers (ESR, CRP and PCT) nor probe-to-bone tests can one their own solely and reliably rule in or rule out the diagnosis of DFO. When diagnostic doubt persists after the clinical assessment and review of plain X-rays of the foot, we recommend testing for ESR, CRP, or PCT. However, this recommendation is conditional because of the risk of over- or under-diagnosis of bone infection, based on a low quality of evidence with inconsistency in the data on diagnostic accuracy results. Recommendation 8: a. Perform MRI when the diagnosis of diabetes-related osteomyelitis of the foot remains in doubt despite clinical, plain X-rays and laboratory findings. (Strong; Moderate). Recommendation 9: a. Consider using PET, leucocyte scintigraphy, or SPECT as an alternative to MRI for the diagnosis of diabetes-related osteomyelitis of the foot. (Conditional; Low). RationaleDepending on the patient setting, advanced imaging for diagnosing osteomyelitis is not needed in many patients. When needed, MRI has been the most commonly ordered advanced imaging technique to diagnose DFO, with moderate costs (but about 10 times higher than that of plain X-rays) and wide availability in high-income countries. Besides being used as a (very sensitive) diagnostic tool, MRI gives a good overview of the anatomy of soft tissues as well as bones and joints, which can be of aid for detecting pre-operatively any purulent collections or the extent of bone involvement. Among advanced imaging techniques, MRI has been the most studied, is associated with lower costs than some other advanced imaging techniques, and gives an overview of the presence and extent of both soft tissue and bone infections in the foot.98,99 It is important to note that the presence of reactive bone marrow oedema from non-infectious pathologies, such as trauma, previous foot surgery or Charcot neuroarthropathy, lowers its specificity and positive predictive value.100,101 In selected patients with possible neuro-osteoarthropathy, newer techniques such as MR angiography, dynamic contrast-enhanced MRI or neurography may better distinguish Charcot arthropathy from osteomyelitis.102–105 The accuracy of MRI findings can be improved by using the results of a second read by an expert musculoskeletal radiologist.107 Another finding likely to augment the sensitivity of MRI for the diagnosis of DFO is the detection of an increased ratio of marrow region of interest (ROI)/joint fluid ROI on T2/Short Tau Inversion Recovery (STIR) sequences.106 A systematic review and meta-analysis that compared the diagnostic accuracy of imaging tests (plain X-rays, scintigraphy, MRI, SPECT and PET) for the diagnosis of DFO showed that 18F-fluorodeoxyglucose (FDG)–PET and 99mTc- exametazime Hexa Methyl Propylene Amine Oxime labelled WBC scintigraphy offer the highest specificity (0.92 for both).107 In patients with a contraindication to MRI, clinicians may choose other imaging techniques (e.g., FDG-PET/CT, HMPAO-labelled leucocyte scintigraphy or 99mTc labelled Ubiquicidin (UBI) SPECT/CT).107–112 Compared to nuclear (e.g., leukocyte) imaging, PET, especially combined with CT scan, offers high spatial resolution, precise anatomic localization, possibly higher sensitivity for chronic infection, easier performance, faster results, and low radiation exposure. Overall, the available studies that compared the diagnostic accuracy of MRI and nuclear imaging techniques in patients with a suspicion of DFO show conflicting results.105,106,109,113 MRI and FDG PET/CT have several advantages compared to other anatomical and functional imaging methods, including short acquisition time, high resolution, low radiation dose, and better tolerability.110 The availability and cost of these advanced imaging techniques may vary in different geographic locations, but they might be useful in situations when the diagnosis remains in doubt, and when there are limited options to obtain a BeBoP. For the diagnostic accuracy of advanced imaging in DFO, the overall certainty of the evidence is moderate because of serious inconsistency, imprecision, and indirectness of results in the included studies. Although the certainty of evidence was moderate, a strong recommendation is made regarding MRI use in DFO because of the high accuracy in results, especially regarding the information on both soft tissue and bone and joint structures. Despite the certainty of evidence being moderate, a conditional rather than a strong recommendation is made regarding SPECT/CT & PET/CT use in DFO because of the lack of accessibility and feasibility of this modality and the great resources and expertise required to implement this technique. Recommendation 10: a. In a person for whom there is suspicion of osteomyelitis of the foot (before or after treatment), consider obtaining bone (rather than soft tissue) samples for culture, either intraoperatively or percutaneously. (Conditional; Moderate). RationaleObtaining a bone specimen to diagnose osteomyelitis is the generally accepted criterion standard for diagnosing the infection, and the only definitive way to determine the causative pathogen(s). BonE BiOPsy is, however, usually not performed in most cases of suspected DFO due to the absence of a health care professional adequately trained to perform the procedure and/or the fear of possible adverse effects, especially fracture or induced infection of the bone.114 Published studies consistently report a low correlation between bone and non-bone culture results, most