Guidelines on the classification of foot ulcers in people with diabetes

IWGDF 2023 update

Part of the 2023 IWGDF Guidelines on the prevention and management of diabetes-related foot disease

IWGDF Guidelines

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ABSTRACT

This publication represents a scheduled update of the 2019 guidelines of the International Working Group of the Diabetic Foot (IWGDF) addressing the use of systems to classify foot ulcers in people with diabetes in routine clinical practice. The guidelines are based on a systematic review of the available literature that identified 28 classifications addressed in 149 articles and, subsequently, expert opinion using the GRADE methodology. First, we have developed a list of classification systems considered as being potentially adequate for use in a clinical setting, through the summary of judgments for diagnostic tests, focusing on the usability, accuracy and reliability of each system to predict ulcer-related complications as well as use of resources. Second, we have determined, following group debate and consensus, which of them should be used in specific clinical scenarios. In conclusion of this process, in a person with diabetes and a foot ulcer we recommend:

1. for communication among healthcare professionals: to use the SINBAD (Site, Ischaemia, Bacterial infection, Area and Depth) classification (first option) or consider using WIfI (Wound, Ischaemia, foot Infection) system (alternative option, when the required equipment and level of expertise is available and it is considered feasible) and in each case the individual variables that compose the systems should be described rather than a total score;
2. for predicting the outcome of an ulcer in a specific individual: no existing system could be recommended;
3. for characterising a person with an infected ulcer: the use of the IDSA/IWGDF (first option) classification or consider using the WIfI system (alternative option, when the required equipment and level of expertise is available and it is considered as feasible);
4. for characterising a person with peripheral artery disease: consider using the WIfI system as a means to stratify healing likelihood and amputation risk;
5. for the audit of outcome(s) of populations: the use of the SINBAD score.

For all recommendations made using GRADE, the certainty of evidence was judged, at best, as being low. Nevertheless, based on rational application of current data this approach allowed the proposal of recommendations, which are likely to have clinical utility.

LIST OF RECOMMENDATIONS

1a. In a person with diabetes and a foot ulcer, use the SINBAD system for communication between healthcare professionals about the characteristics of an ulcer, and clearly state the presence or absence of each of the composing variables. (Strength of recommendation: Strong; Certainty of evidence: Low)

1b. In a person with diabetes and a foot ulcer, when resources exist in addition to an appropriate level of expertise and it is considered feasible, consider using the WIfI system for communication about the characteristics of an ulcer between healthcare professionals, but with characterisation of each of the composing variables. (Conditional; Low)

2. Do not use any of the currently available classification/scoring systems to offer an individual outcome prognosis for a person with diabetes and a foot ulcer. (Strong; Low)

3a. To classify a person with diabetes and an infected foot ulcer, use the IDSA/IWGDF (2015 version) system. (Strong; Low)

3b. To classify a person with diabetes and an infected foot ulcer, when resources exist in addition to an appropriate level of expertise and it is considered feasible, consider using the WIfI system. (Conditional; Low)

4. In a person with diabetes, peripheral artery disease and a foot ulcer, consider using the WIfI system as a means to stratify healing likelihood and amputation risk. (Conditional; Low)

5. Use the SINBAD system score for any regional/national/international audits, to allow comparisons between institutions on the outcomes of people with diabetes and a foot ulcer. (Strong; Low)

INTRODUCTION

It is estimated that diabetes affects 537 million people worldwide, 10.5% of the adult population, and the increase in prevalence is occurring at a faster rate in low- and middle-income countries (1). Up to one in three people with diabetes will develop a foot ulcer in their lifetime (2). The risk of developing a diabetes-related foot ulcer, and the factors associated with the development of complications (such as hospitalisation, lower extremity amputation, and mortality) may be patient-related, limb-related or ulcer-related. The impact of individual factors on the outcome of foot ulcers in people with diabetes will vary across communities and countries. For example, infection will more strongly influence the outcome in settings where antibiotics are not readily available, whereas ischaemia will have a greater impact in settings where peripheral artery disease is more prevalent. Of note, more than 80% of people with diabetes live in low- and middle-income countries, in which many diagnostic tools are not readily available and are not expected to become so in the near future (1).

A classification system may be defined as a descriptive tool that aims to divide patients into groups while not necessarily relating to the risk of adverse outcome(s), whereas a scoring system will attribute a scale by which the contribution of factors within the system is quantified and scores can be amalgamated to produce an overall (usually numerical) score with an increased score being associated with a higher risk of adverse outcome(s). In other words, classification systems tend to focus on discrimination (the ability to separate data/individuals into classes), while scoring systems tend to focus on calibration (a measure of the closeness of the estimated probability of a certain event to the underlying probability of the population under study) (3). With both types of tools, one can attempt to create more homogeneous groups of patients for which similar levels of care should be provided and also to standardize the modifiable factors that one should focus on to improve clinical outcomes. This does not mean that we should provide the same care to all patients within the same strata, but that the urgency and use of resources should be prioritised for those in most need. This approach does not invalidate clinical experience, knowledge, and the overall approach that we should provide for a person with an established diabetes-related foot ulcer but is designed to help us standardize communication among healthcare professionals and to facilitate more rational use of available resources (independently of their nature). On the other hand, the correct application of such systems is dependent on knowledge and experience of the required procedures to collect each of the variables that compose a system, and on how to apply the overall system.

Due to its frequency, complexity, and limited resources to treat diabetes-related foot ulcers, it is vital to accurately characterize them, understand their severity and to direct patients at most need to specialized care. To do so, healthcare providers should use the classification(s) that have evidence of their accuracy, reliability, and potential impact on clinical care.

In our systematic review (4), we found numerous proposed classification and scoring systems for foot ulcers in people with diabetes (n=28), and this suggests that none is ideal for routine use in populations worldwide. This also highlights the differing purposes of diabetes-related foot ulcer classification and scoring systems that can be used for: (a) communication among healthcare professionals (independent of the level of clinical care); (b) clinical prognostication of the outcome of an individual ulcer; (c) the

assessment of a person with infection; (d) the assessment of a person with peripheral artery disease; and (e) clinical audit of outcomes across units and populations.

The intended use of a classification or scoring system will influence its content. A system designed to assess the risk or prognosis for an individual with diabetes and an ulcer on their foot will necessarily require a certain level of detail. In contrast, a system seeking to compare outcomes between populations will need to minimise data input by busy clinicians and should have a less burdensome requirement for data collection and processing, if it is to be usable in clinical practice. While classifications used for communication among healthcare professionals should ideally be simple to memorise and use. This guideline aims to provide recommendations on the use of classifications of established foot ulcers in people with diabetes for the various purposes on behalf of the International Working Group of the Diabetic Foot (IWGDF).

WHAT'S NEW

We have made several changes to the recommendations included in this updated 2023 diabetes-related foot ulcer classification guideline when compared to the previous 2019 guideline (5). The main changes are the following:

- Used a systematic review instead of a critical review to support our recommendations;
- Used a more thorough GRADE methodology approach by grading effect sizes, grading certainty (quality) of evidence with 'very low' as an option, developing summary of findings tables and developing summary of judgement tables;
- Added new important outcomes, including hospitalization, health-related quality of life, diabetes-related foot ulcer and amputation free survival, and costs;
- Added the use of alternative options for communication between healthcare professionals and management of for complex cases (such as in the presence of infection or peripheral arterial disease) acknowledging the differences in access to equipment and detail needed according to the settings.

METHODS

In this guideline we have followed the key steps of the GRADE evidence-to-decision framework, including: i) establishing a diverse expert panel to develop the guideline, ii) defining key clinical questions and important outcomes in the PI/ECO-format (Patient-Intervention/Exposure-Comparison-Outcome), iii) performing systematic reviews and rigorous appraisals of all available evidence that address the questions, iv) assessing key summary of judgements items for each question, v) developing recommendations and their rationale based on these summary of judgements, and vi) consulting external stakeholders on each step (6, 7). The methodology for this guideline is summarised below; we refer those seeking a more detailed description on the methods for developing and writing these guidelines to the 'IWGDF Guidelines development and methodology' document (8).

First, a diverse multidisciplinary working group of independent international experts in developing, assessing, or disseminating classification or scoring systems for diabetes-related foot ulcers (the authors of this guideline) was invited by the IWGDF Editorial Board to develop and author this guideline. International experts were defined as those having significant experience in practising or studying classification or scoring systems to characterise diabetes-related foot ulcers and published on the topic in the previous four years. The working group comprised endocrinologists, internal medicine physicians, physiatrists, podiatrists and vascular surgeons from the United States of America, Europe, Asia and Australia.

Second, the working group devised important clinical questions and associated outcomes, building on the last version of the guideline, to be answered using the GRADE approach. The questions and outcomes were reviewed and prioritised with the help of nine external clinical experts and two persons with lived diabetes-related foot ulcer experience from various geographical regions, and the IWGDF Editorial Board. The aim was to ensure the questions and outcomes were of relevance to a wide range of healthcare professionals and people with the disease so as to provide the most useful clinical information on how to classify foot ulcers in people with diabetes. The working group classified the outcomes as critically important or important, aligning with international diabetes-related foot ulcer standards (9) or the expert opinion of the working group if definitions did not exist.

As stated in our systematic review (4), critically important outcomes were grouped and defined as

a. clinical outcomes
    - lower extremity amputation: resection of a segment of a limb through a bone or through a joint in the lower extremity,
    - wound healing: achieving intact skin, meaning complete epithelialization without any drainage of a previous foot ulcer site,
    - hospitalization: care in a hospital that requires admission as an inpatient and usually requires an overnight stay,
    - survival: the state or fact of continuing to be alive or exist,
    - health-related quality of life: a person's perceived physical and mental health,
b. post-baseline clinical outcomes
    - ulcer-free period: time that a person is alive and without a foot ulcer,
    - lower extremity amputation-free period: time that a person is alive and without amputation,
c. usability
    - facilitate referral and communication: the act of referring someone or something for consultation, review, or further action,
    - feasibility: the state or degree of being easily or conveniently done,
    - reliability: the extent that the instrument yields the same results over multiple trials,
    - audit: the ability to compare outcomes between institutions,
    - guide management/ interventions, and
d. use of resources: requirements of physical, personnel or financial costs.

The following outcomes were considered important but not critical and therefore not included: future infection, well-being, functionality/physical functioning, pain, acceptability, costs (direct/indirect) related to the implementation of the system, cost-effectiveness, and satisfaction/ patient preference.

Third, we systematically reviewed the literature and appraised all studies addressing the above agreed upon clinical questions (4). Due to the expected low number of validation studies per classification, along with high heterogeneity of the clinical settings, follow-up periods, and clinical outcome reporting and definition, the group decided not to perform a meta-analysis. Finally, we developed summary of findings tables, including evidence statements, for each assessable outcome for each question which we presented in full in the systematic review. The systematic review supporting this guideline is published separately (4).

Fourth, based on the systematic review, summary of findings tables and expert opinion, teams of two members of the working group developed summary of judgements tables for each question following GRADE (see supplemental information).

However, in comparison with the remaining guidelines developed by the IWGDF, this one is different in three main respects. First, we did not raise clinical questions relating to treatment/intervention, but prognostic questions, and this requires a major difference in the way that the clinical questions are formulated. Second, within the prognostic clinical questions, we focused on validity measures (namely, accuracy and reliability) creating a methodological approach between the diagnostic (discriminative properties) and prognostic (ability to estimate the likelihood of a specific event). Consequently, we have used the GRADE approach for diagnostic questions and respective "summary of judgments" (10). Third, although in our systematic review we have provided a summary of the available evidence and an evidence statement for each available classification and have therefore created a summary of judgments for each classification, we considered that it would not be beneficial to suggest recommendations for each of them. Instead, we have used this process to be able to recommend one classification as the first line and, whenever appropriate, a second line (alternative) classification to be used for each of the specified four clinical contexts. For one of the scenarios (assessment of a person with a foot ulcer and peripheral artery disease) we have determined that the "Peripheral Artery Disease" group should provide guidelines as to which system to recommend and so this was not addressed by our group (11). However, to provide readers with all the information about which classifications to use we have copied the information present on the "Peripheral Artery Disease" group guidelines.

The summary of judgments for diagnostic questions included the following items: problem priority, test accuracy, desirable effects, undesirable effects, the certainty of the evidence of test accuracy, the certainty of the evidence of the effects of the test, the certainty of the evidence of management's effect, certainty of the evidence of the link between the test result and management, the certainty of any effect on management, value, the balance of effects, resources required, the certainty of the evidence of required resources, cost-effectiveness, equity, acceptability to stakeholders and feasibility. All these items were assessed independently by two reviewers and then presented and discussed within the entire group.

The group determined that the diabetes-related foot ulcer problem has high priority, given the first step for our systematic review and creation of the guidelines was the selection of critical outcomes within

this field by the editorial board, experts, and patient representatives from several countries (further details in the acknowledgments section). For similar reasons, the group determined that there is probably no important uncertainty or variability in the way people value the main outcome(s).

The accuracy of each classification was based on the results of the systematic review, emphasising those studies in which direct comparison between classifications was conducted. The group considered direct improvement of care in any of the five clinical scenarios as desirable effects, and adverse events directly linked to the application of the classification as undesirable effects. For the certainty of test accuracy, the group used the information collected from the systematic review and mostly based their decision in the risk of bias of the retrieved studies, inconsistency of results, and indirectness and imprecision.

Most of the evidence found determined only the accuracy of classifications. Strong evidence that implementing the use of a specific classification in clinical practice could have a true impact on decision making, change a management plan and consequently the person's prognosis was lacking. Due to either lack of any evidence, or evidence that was limited to the availability of indirect evidence only, the certainty of the evidence of test's effects, management effect, or the link between test result and management were mainly based on expert opinion.

For the balance of effects, the group assessed all these items together and determined if, at this point, there was enough information in favour or against the use of each specific classification.

For the resources required, the group considered potential financial or human resources directly linked to the collection of the information required for each classification. As, however, there was no specific detail about these in the systematic review the available evidence was very low.

Taking into consideration the balance of effects and the resources required, the group reflected on the potential cost-effectiveness of each classification. However, we highlight that these outcomes were not considered as critically important and so were given less priority in our selection of the systems to recommend.

The group defined equity in this context as the ability of all people with diabetes and a foot ulcer (i.e. on a societal level) to have equitable access to the procedures required for the classification application.

Acceptability to stakeholders was based on expert opinion and consideration of whether there was balance in the classification between its completeness, simplicity, and objectivity.

Feasibility was determined based on the groups' experience and the ease of use of each classification.

After this entire process, having considered the available evidence, those systems that were considered to be unsuitable to be used in routine clinical practice were excluded from the list of systems that could be chosen as first or second line in each of the four specific scenarios. The reasons for recommending or not recommending a specific system are described in Appendix 1.

The summary of judgments for all the 28 systems are reported in Appendix 2 (Supplementary tables 1 to 28). In Table 1, we present the summary of judgments for each of the classifications that passed this first stage (6 of 28), meaning those we considered that, in face of the available evidence, could be

conditionally or strongly recommended: DIAFORA, Infectious Diseases Society of America (IDSA)/IWGDF, SINBAD, University of Texas Wound Classification System (UTWCS), (Meggitt-)Wagner and WIfI (Wound, Ischaemia, foot Infection).

All of these systems were considered to be accurate, to have moderate desirable effects, small to trivial undesirable effects, with a balance of effects that probably favours their use in clinical practice and is likely to be acceptable to stakeholders. The overall level of certainty of the evidence for the different aspects of the judgments made about these systems varied between very low and low.

Table 1: Summary of Judgments for the classifications considered as suitable for clinical use

Classification/ judgment	DIAFORA	IDSA/IWGDF	SINBAD	UTWCS	Wagner	WIfI
Problem priority	Yes	Yes	Yes	Yes	Yes	Yes
Test accuracy	Accurate	Accurate	Accurate	Accurate	Accurate	Accurate
Desirable effects	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Undesirable effects	Trivial	Small	Trivial	Trivial	Trivial	Trivial
Certainty of evidence of test accuracy	Low	Low	Low	Low	Low	Low
Certainty of evidence of test's effects	Very low	Very low	Very low	Very low	Low	Very low
Certainty of evidence of management's effect	Very low	Very low	Very low	Very low	Low	Very low
Certainty of the evidence of link between test result/management	Low	Low	Low	Low	Low	Low
Certainty of effects	Very low	Very low	Very low	Very low	Low	Very low
How much people value the main outcome	Probably no important uncertainty or variability	Probably no important uncertainty or variability	Probably no important uncertainty or variability	Probably no important uncertainty or variability	Probably no important uncertainty or variability	Probably no important uncertainty or variability
Balance of effects	Probably favors the intervention	Probably favors the intervention	Probably favors the intervention	Probably favors the intervention	Probably favors the intervention	Probably favors the intervention
Resources required	Negligible costs and savings	Moderate costs	Moderate savings	Moderate costs	Negligible costs and savings	Moderate savings
Certainty of evidence of required resources	Low	Low	Low	Low	Very low	Very low
Cost effectiveness	Does not favor either	Does not favor either	Probably favors the intervention	Does not favor either	Does not favor either	Probably favors the intervention
Equity	Probably no impact	Probably reduced	Probably increased	Probably reduced	Probably increased	Probably reduced
Acceptability (to stakeholders)	Probably yes	Probably yes	Probably yes	Probably yes	Probably yes	Probably yes
Feasibility	Probably yes	Probably yes	Yes	Probably yes	Yes	Probably no

Note: For each colour a stronger shade implies a stronger assessment, Green filling represents a positive judgment (this is, supporting the use of the system), Blue filling represents a neutral judgment (this is, a balance between supporting or not the use of the system), and Red filling represents a negative judgment (this is, not favouring the use of the system). IDSA/IWGDF: Infectious Diseases Society of America/ International Working Group on the Diabetic Foot; UTWCS: University of Texas Wound Classification System.

After careful weighing of the summary of judgements, the team proposed to the working group a direction, strength, certainty of evidence and wording of recommendation(s) and rationale to address the question concerned. Certainty of evidence was rated as 'high', 'moderate', 'low' or 'very low' based on the critical outcome(s) reviewed for the question in accordance with GRADE. Recommendations aimed to be clear, specific, and unambiguous on what was recommended, for which persons, and under what circumstances. Rationale for each recommendation was also provided and based on the summary of judgements tables (12, 13).

Fifth, summary of judgements tables and recommendations for each question were extensively discussed in online meetings with 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, and the strength of each recommendation as 'strong' or 'conditional'. A quorum of 60% of members were 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 supplementary material Appendix 2 and 3.

Finally, all recommendations, with the rationales, were collated into a consultation (draft) guideline manuscript that was reviewed by the same clinical experts and persons with lived experience who reviewed the clinical questions, as well as by members of 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 guideline manuscript.

MANAGEMENT OF CONFLICT OF INTERESTS

The classification guideline working group is committed to developing trustworthy clinical practice guidelines through transparency and full disclosure by those participating in the process of guideline development. In order to prevent a major Conflict of Interest (COI) members of the guideline group were not allowed to serve as an officer, board member, trustee, owner, or employee of a company directly or indirectly involved in the topic of this guideline. Before the first and last meeting of the guideline working group, members were asked to report any COI in writing. In addition, at the beginning of each meeting this question was also asked and if answered yes, the members were asked to submit a COI form. These COIs included income received from biomedical companies, device manufacturers, pharmaceutical companies, or other companies producing products related to the field. In addition, industry relationships had to be disclosed each time and these included: ownerships of stocks/options or bonds of a company; any consultancy, scientific advisory committee membership, or lecturer for a company, research grants, income from patents. These incomes could either be personal or obtained by an institution with which the member had a relationship. All disclosures were reviewed by the chair and secretary of the working groups, and these can be found at *www.iwgdfguidelines.org*. No company was involved in the development or review of the guideline. Nobody else involved in the guideline received any payment or remuneration of any costs, except for travel and accommodation expenses when meeting on-site.

RESULTS

Overall, 5 clinical questions, each with up to 13 (critically) important outcomes, were finalised and addressed by this guideline. The accompanying systematic review identified 149 eligible studies, assessing 28 different systems. Based on the systematic review and expert opinion of the group, 28 summary of judgements tables were completed (see supplementary material Appendix 2) with 7 recommendations developed that address the clinical questions and have in consideration the existence of different clinical settings.

Furthermore, to guarantee the accuracy of most of the systems recommended to characterise foot ulcers, specific training, skills, and experience will be required. These specific skills and training are not described in the studies performed and may differ between centres and countries. Any recommendations, therefore, should be read in the understanding that the person applying the different systems should be an appropriately trained healthcare professional who, according to their national or regional standards, has the knowledge, expertise, and skills necessary to manage people with a diabetes-related foot ulcer following the IWGDF practical guidelines (14).

RECOMMENDATIONS

FOR COMMUNICATION AMONG HEALTHCARE PROFESSIONALS

Clinical question: In a person with diabetes and a foot ulcer, which classification system(s) is/ are the best for communication among healthcare professionals and to optimise the process of referral?

Recommendation 1a: In a person with diabetes and a foot ulcer, use the SINBAD system for communication about the characteristics of an ulcer between healthcare professionals, and clearly stating the presence or absence of each of the composing variables. (Strength of recommendation: Strong; Certainty of evidence: Low)

Recommendation 1b: In a person with diabetes and a foot ulcer, when resources exist in addition to an appropriate level of expertise and it is considered feasible, consider using the WIfI system for communication about the characteristics of an ulcer between healthcare professionals, but with characterisation of each of the composing variables. (Conditional; Low)

Rationale: Standardising communication between healthcare professionals about the severity of a foot ulcer could greatly improve the quality of any triage process, referral, or follow-up for a person with a diabetes-related foot ulcer. For a classification system to be used by all healthcare professionals managing people with a diabetes-related foot ulcer to make an adequate referral and or triage a referral to them, it should be quick and simple to apply and preferably require no complex or expensive equipment. On the other hand, for it to be useful to the receiving professional, it should contain appropriate information to allow triage of patients to ensure timely review and this may require more detailed information in some settings. Such a classification system should also be confirmed to have a high interobserver reliability. Although most people with diabetes and a foot ulcer may benefit from referral to a multidisciplinary team without delay, factors necessitating urgent review should at least include the dimensions of the ulcer (area and depth), presence of infection, and ischaemia. Any classification system for use as a triage tool will therefore need to include these criteria without the need for measurements that require specialist equipment (e.g., toe pressures, transcutaneous oxygen pressure ($TcPO_2$)). However, in settings where this equipment is available and there is a suspicion or confirmation of the presence of peripheral artery disease, more detailed information is extremely relevant for the receiving professional.

For these recommendations, the group focused on the organizational aspects of the six selected systems, mainly on accuracy measures (retrieved from our systematic review (4)), feasibility, equity, resources, etc.

The SINBAD system grades Site, Ischemia, Neuropathy, Bacterial infection, Area, and Depth as either 0 or 1 point (see below), creating an easy-to-use scoring system that can achieve a maximum of 6 points (15), as described in Table 2

Table 2: SINBAD system

Category	Definition	Score
Site	Forefoot	0
	Midfoot and hindfoot	1
Ischemia	Pedal blood flow intact: at least one palpable pulse	0
	Clinical evidence of reduced pedal flow	1
Neuropathy	Protective sensation intact	0
	Protective sensation lost	1
Bacterial infection	None	0
	Present	1
Area Ulcer	Ulcer $<1 cm^2$	0
	Ulcer $\geq 1\ cm^2$	1
Depth	Ulcer confined to skin and subcutaneous tissue	0
	Ulcer reaching muscle, tendon or deeper	1
Total possible score		0 – 6

The SINBAD system is simple and quick to use, requires no specialist equipment beyond clinical examination alone, and contains the necessary information to allow for triage by a specialist team. It would therefore be feasible to employ this classification system in localities where such equipment, including non-invasive measures of perfusion, are not readily available, which is the case for most geographic settings where diabetes-related foot ulcers occur. If used for the purpose of communication among healthcare professionals, it is important to use the individual clinical descriptors and not merely the total score. This scoring system has been validated in 12 studies for several foot ulcer-related clinical outcomes (including healing, amputation, hospitalisation, death, etc.) with somewhat consistent results and also substantial to good reliability (4). Therefore, we consider the description of the presence or absence of the variables included in this system to be the minimum information to be shared for an adequate communication among healthcare professionals about the characteristics of a foot ulcer. For this purpose, we consider that the use of the final score is insufficient.

The classification proposed by Meggitt and modified by Wagner (16) is the oldest classification and grades wounds into pre- or post-ulcerative site (grade 0), superficial ulcer (grade 1), ulcer penetrating to tendon or joint capsule (grade 2), lesion involving deeper tissues (grade 3), forefoot gangrene (grade 4) and whole foot gangrene involving more than two thirds of the foot (grade 5). In our systematic review it was the system with the highest number of articles validating it (n=74) (4). Most of the articles, however, were considered to be at high risk of bias and some inconsistency was observed, along with a predominance of studies reporting association measures instead of accuracy measures. Also, our group considered this classification to have a poor clinical discrimination, as it does not include area, neuropathy, infection and peripheral artery disease individually. It is also rendered blunt by the major impact of gangrene in this classification.

The DIAFORA score includes four foot-related and four ulcer-related variables: neuropathy, foot deformity, arteriopathy, previous foot ulcer or lower extremity amputation; and presence of multiple ulcers, infection, gangrene and/or bone involvement, respectively. This system, like Wagner, also includes

gangrene (17), but no external validation or reliability assessment was conducted (4) and therefore we could not recommend it for this purpose.

The UTWCS system was used in 30 articles (most at high risk of bias, using stage or grade separately and reported mostly association measures), while the WIfI system was used in 13 (with five being conducted in the same institution and with a larger population including previously reported participants plus additional participants) (4). For both systems the certainty of evidence was considered to be low. The WIfI system uses a combination of scores for wound (based on depth of ulcer or extent of gangrene), ischaemia (based on ankle pressure, toe pressure or $TcPO_2$), and foot infection (based on IDSA/IWGDF criteria), detailed in Table 3, to provide a 1-year risk for amputation and 1-year benefit for revascularisation, both stratified as very low, low, moderate, or high (18). This has benefit over perfusion pressures alone by including associated wound and infection criteria to provide a more holistic wound overview in revascularisation decision-making. UTWCS (19) and WIfI (18) both require equipment and clinical expertise to conduct the ankle-brachial index (ABI) as a minimum, which reduces equity and feasibility. In addition, false positives may lead to more anxiety, and thus we do not support the use of such tests without proper training. On the other hand, those individuals with previous signs and symptoms may already have a recent ABI test result or may be followed in settings in which vascular examination is possible and feasible. Neither UTWCS nor WIfI included loss of protective sensation (for which it is important to recommend offloading) as a variable.

In comparison with the WIfI system, the UTWCS system has less detail and classifies DFUs using a bidimensional 4 × 4 matrix, according to depth (Grades 0, 1, 2, and 3) and presence of infection (Stage B), ischaemia (Stage C), or both (Stage D) (19). The original publication (19) described a combination of clinical signs and symptoms, plus one or more non-invasive criteria (transcutaneous oxygen measurements, ABI, or toe systolic pressure) to assess perfusion. In addition,-size (area) is not included in this classification.

For these reasons, when resources exist in addition to an appropriate level of expertise and it is considered feasible, we recommend healthcare professional to also consider the use of the WIfI system for communication about the characteristics of an ulcer (see Table 3), focusing on the description of the grade of each composing variable.

Table 3: WIfI system

Wound

Grade	DFU	Gangrene
0	No ulcer	No gangrene
	Clinical description: minor tissue loss. Salvageable with simple digital amputation (1 or 2 digits) or skin coverage.	
1	Small, shallow ulcer(s) on distal leg or foot; no exposed bone, unless limited to distal phalanx	No gangrene
	Clinical description: minor tissue loss. Salvageable with simple digital amputation (1 or 2 digits) or skin coverage.	
2	Deeper ulcer with exposed bone, joint or tendon; generally not involving the heel; shallow heel ulcer, without calcaneal involvement	Gangrenous changes limited to digits
	Clinical description: major tissue loss salvageable with multiple (≥ 3) digital amputations or standard TMA ± skin coverage.	
3	Extensive, deep ulcer involving forefoot and/or midfoot; deep, full thickness heel ulcer ± calcaneal involvement	Extensive gangrene involving forefoot and /or midfoot; full thickness heel necrosis ± calcaneal involvement
	Clinical description: extensive tissue loss salvageable only with a complex foot reconstruction or non-traditional TMA (Chopart or Lisfranc); flap coverage or complex wound management needed for large soft tissue defect	

Ischaemia

Grade	ABI	Ankle systolic pressure (mmHg)	TP, $TcPO_2$ (mmHg)
0	≥ 0.80	> 100	≥ 60
1	0.6 – 0.79	70 – 100	40 – 59
2	0.4 – 0.59	50 – 70	30 – 39
3	≤ 0.39	< 50	< 30

Foot Infection

Grade	Clinical manifestations
0	No symptoms or signs of infection Infection present, as defined by the presence of at least 2 of the following items: • Local swelling or induration • Erythema > 0.5 to ≤ 2 cm around the ulcer • Local tenderness or pain • Local warmth • Purulent discharge (thick, opaque to white, or sanguineous secretion)
1	Local infection involving only the skin and the subcutaneous tissue (without involvement of deeper tissues and without systemic signs as described below). Exclude other causes of an inflammatory response of the skin (e.g., trauma, gout, acute Charcot neuro-osteoarthropathy, fracture, thrombosis, venous stasis)
2	Local infection (as described above) with erythema >2 cm, or involving structures deeper than skin and subcutaneous tissues (e.g., abscess, osteomyelitis, septic arthritis, fasciitis), and No systemic inflammatory response signs (as described below)
3	Local infection (as described above) with the signs of SIRS, as manifested by two or more of the following: • Temperature > 38°C or < 36°C • Heart rate > 90 beats/min • Respiratory rate > 20 breaths/min or $PaCO_2$ < 32 mm Hg • White blood cell count > 12,000 or < 4000 cu/mm or 10% immature (band) forms

ABI: Ankle-Brachial Index; $PaCO_2$: Partial Pressure of Carbon Dioxide; SIRS: Systemic Inflammatory Response Syndrome; $TcPO_2$: Transcutaneous Partial Oxygen Pressure; TMA: Transmetatarsal Amputation; TP: Toe Pressure

FOR PREDICTING THE OUTCOME OF AN ULCER IN A SPECIFIC INDIVIDUAL

Clinical question: In a person with diabetes and a foot ulcer, which classification system(s) is/ are the best to assess the prognosis of an individual person with diabetes and a foot ulcer?

Recommendation 2: Do not use any of the currently available classification/scoring systems to offer an individual outcome prognosis for a person with diabetes and a foot ulcer. (Strong; Low)

Rationale: We can use systems in a clinical setting to stratify people by a similar probability of developing a certain event and to create more homogenous groups that should receive similar healthcare or to estimate the individual probability of a specific person with a certain number of characteristics. A good example of the latter is the Framingham Risk Score for cardiovascular disease (20). This model uses six different variables and estimates the individual's risk at 10 years of developing or dying of cardiovascular disease.

To be used as a prognostic tool, a classification system needs to be complex enough to provide individualised outcome prediction yet quick to use within a busy clinical service, ideally not requiring measurements in addition to those performed for routine clinical care. The classification also needs to

be widely validated for the population in which its use is proposed, as the dominant factors for poor outcomes in foot ulcers in people with diabetes vary worldwide due to differences in the population, the local context and available resources for clinical care. This validation should include how well the classification system predicts both ulcer healing and risk of amputation. However, we found insufficient reporting of accuracy measures of the classifications and, even when they were described, they had wide confidence intervals, due to high variability, small sample sizes and low event rates (eg. for major amputation).

For this purpose we considered that likelihood ratios (both positive and negative) would be the more informative accuracy measures, as they summarise (in this context) how many times it is more (or less) likely for patients to develop the clinical outcome of interest than not developing it when they are classified to be at high risk (or low risk, respectively), and are not affected by the outcomes' prevalence (in contrast to the predictive values) (21).

In the rare cases in which positive likelihood ratios were reported (4) they were below 5, while negative likelihood ratios were around 0.2-0.4, indicating only small changes in the pre- to post-test probability of the clinical outcomes of interest would occur (22). A classification or scoring system should also have good inter- and intra- observer reliability to provide consistency of prognostic outcomes and allow for monitoring of progress with any intervention. None of the systems evaluated met these criteria, and so further research may be required, to either appropriately validate an existing classification, or to develop a classification/ scoring system according to these criteria.

The quality of evidence for the prediction of foot ulcer-related outcomes is weak (4) and thus the applicability of the accuracy of a classification system in predicting individual patient outcomes is poor. This has led to our current strong recommendation against the use of any system for prediction of individual patient outcomes.

FOR CLASSIFYING A PERSON WITH AN INFECTED ULCER

Clinical question: In a person with diabetes and an infected foot ulcer, which classification system(s) is/ are the best to predict clinical and health resources outcomes?

Recommendation 3a: To classify a person with diabetes and an infected foot ulcer, use the IDSA/IWGDF system (2015 version) (Strong; Low)

Recommendation 3b: To classify a person with diabetes and an infected foot ulcer, when resources exist in addition to an appropriate level of expertise and it is considered feasible, consider using the WIfI system. (Conditional; Low)

Rationale: The IDSA/IWGDF classification consists of four grades diabetic foot infection (see Table 4). It was originally developed as part of the PEDIS classification for research purposes (23) and is used as a guideline for management, in particular to identify which patients require hospital admission. Although the components of each grade may be considered complex, and a previous study has shown only moderate reliability (4), the criteria are widely used.

Table 4: IDSA/IWGDF system

Clinical manifestations	Infection severity	PEDIS grade
Wound lacking purulence or any manifestations of inflammation	Uninfected	1
Presence of ≥ 2 manifestations of inflammation (purulence, or erythema, tenderness, warmth, or induration), but any cellulitis/erythema extends ≤ 2cm around the ulcer, and infection is limited to the skin or superficial subcutaneous tissues; no other local complications or systemic illness	Mild	2
Infection (as above) in a patient who is systemically well and metabolically stable but which has ≥ 1 of the following characteristics: cellulitis extending >2cm, lymphangitic streaking, spread beneath the superficial fascia, deep-tissue abscess, gangrene, and involvement of muscle, tendon, joint or bone	Moderate	3
Infection in a patient with systemic toxicity or metabolic instability (e.g. fever, chills, tachycardia, hypotension, confusion, vomiting, leucocytosis, acidosis, severe hyperglycaemia, or azotaemia)	Severe	4

In our systematic review, we found eight studies validating this system and, although most were at high risk of bias, they showed that an increase in the severity of the infection was associated with a lower incidence of ulcer healing, higher incidence of amputation, hospital admission(s) and having longer length of in-hospital stays (24).

In 2019, this classification underwent a modification during the process of developing the IWGDF guidelines (25). However, this updated version was derived from a study classified as being at high risk of bias (26) and so, at present, we cannot recommend its use.

Of note, whilst the IDSA/IWGDF is incorporated into WIfI (see Table 3), in situations where only infection is being assessed and equipment is not available to use WIfI, the IDSA/IWGDF infection classification can stand alone. On the other hand, in a case of suspected or confirmed infected ulcer complicated by ischaemia, meaning when in the presence of previously diagnosed peripheral artery disease or in a setting in which surgeons with vascular surgery expertise are available, the use of the WIfI classification could be considered.

The studies conducted to validate the UTWCS system have clearly shown that the concomitant presence of infection and peripheral artery disease in a person with diabetes and an ulcer has an incremental effect on the risk of poor clinical outcomes (such as non-healing, delay in healing, or amputation) as well as in costs (19, 27-36). For example, it is well known that oral antibiotic therapy is less effective in people with limited vascular supply. So, the group considered that, when resources and clinical expertise are available, vascular status should be ascertained.

As discussed for the first clinical scenario (communication between healthcare professionals), when comparing the WIfI with the UTWCS system we considered that the certainty of evidence is similar (low for both) (4), but the level of detail of the WIfI system and the direct link to clinical management

favors its use in comparison to UTWCS. In our opinion, the remaining classifications do not provide enough information to allow an accurate characterization of an infected foot ulcer.

We would like to emphasise that this recommendation is intended to classify the severity of infection in people with diabetes and an ulcer of the foot only, and not the severity of any lower limb infection overall. In addition, our focus was to base our recommendation on the available evidence of the accuracy of the systems to predict clinical outcomes and health resource use and not to direct health care professionals to clinical management decisions. We draw attention to this, as these differences may create disparities between our recommendations and the strength of these recommendations in comparison to the ones from the infection group (37).

FOR CLASSIFYING A PERSON WITH AN ULCER AND PERIPHERAL ARTERY DISEASE

Clinical question: In a person with diabetes, peripheral artery disease and a foot ulcer, which classification system(s) is/ are the best to predict clinical and health resources outcomes?

Recommendation 4: In a person with diabetes, peripheral artery disease and a foot ulcer, consider using the WIfI system as a means to stratify healing likelihood and amputation risk (Conditional; Low)

Rationale: Given that 1) there is a specific group to create recommendations on how to diagnose and treat peripheral artery disease in people with diabetes, 2) the importance of aligning the recommendations between groups within the IWGDF, and 3) the similarity of the population used (although the peripheral artery disease group included people with gangrene of the foot whereas our populations was restricted to ulcers of the foot alone) and the most important outcomes selected (prediction of healing and amputation), we have shared the results of our systematic review with the peripheral artery disease group and agreed that this group should make the recommendation on which system to use in this specific clinical context.

The peripheral artery disease working group has recommended the use of the WIfI classification to estimate the likelihood of healing and amputation (11). The choice of this system aligns with the classification working group's selection for the other purposes for which recommendations were made (see recommendation 2 and Table 3).

The peripheral artery disease working group applies this recommendation to both people with a foot ulcer or gangrene, focusing on tissue loss. By supporting the use of this system for both types of population we consider that it will also facilitate its implementation as, in people with diabetes and peripheral artery disease, gangrene without an open ulcer is often seen.

The peripheral artery disease working group also reinforces the importance of taking a relevant history for peripheral artery disease and examining the foot pulses, but also that pedal Doppler waveforms in combination with ankle brachial index (ABI) and toe brachial index (TBI) measurements are preferable as methods to diagnose peripheral artery disease in people with diabetes and with foot ulcers. For a population with suspected peripheral artery disease, we endorse the peripheral artery disease group's statements of the importance of access to these diagnostic procedures but highlight the need for the

clinical experts to perform them reliably and accurately. This method of grading ischaemia is included in the WIfI classification along with the ulcer depth and infection characterization, a system that is considered as relatively easy to apply and accurate when performed in settings where these resources are available.

FOR THE AUDIT OF OUTCOME(S) OF POPULATIONS

Clinical question: In a population of people with diabetes and foot ulcers and in which the purpose is to use for audit, which classification system(s) is/ are the best to predict clinical and health resources outcomes?

Recommendation 5: Use the SINBAD system for any regional/national/international audits to allow comparisons between institutions on the outcomes of people with diabetes and foot ulcers. (Strong; Low)

Rationale: The term "audit" refers to characterisation of all diabetes-related foot ulcers managed in a particular area or centre, to compare outcomes with a reference population or national standard and does not allude to the financial implications of care. Ideally, one classification system should be used internationally to allow comparisons of outcomes. In order to do this, such a classification system would need to accurately assess foot ulcer severity across the spectrum of aetiologies. Thus, healthcare systems where peripheral artery disease is a major contributor to nonhealing, and amputation can be compared with healthcare systems where infection is a major cause of amputation because of limited antibiotic availability. Further, the system should be simple to use, and require no specialist equipment, to allow the necessary clinical data to be collected routinely from all patients in all healthcare settings spanning the spectrum from low to high resource availability.

From the six pre-selected systems, only SINBAD and (Meggitt-)Wagner systems were considered to be clearly feasible. The Wagner classification, as stated previously, was the most frequently reported in the articles that we found in our systematic review (4). However, it is considered as having insufficient detail when compared with SINBAD.

Although none of the existing systems was designed, as far as we are aware, for audit, only the SINBAD score has actually been used for conducting a nationwide audit in the United Kingdom, within the National Diabetes Foot Care Audit (NDFA) of England and Wales. The 2021 annual report of the NDFA (38) reports the outcome of 76,310 people with diabetes with 108,450 ulcers at presentation and showed that a higher SINBAD score led to a lower chance of being alive and ulcer-free at 12 weeks and a higher chance of major amputation within 6 months. The group has determined that no other system should be suggested as an alternative option due to a lack of evidence of the remaining systems feasibility.

FURTHER CONSIDERATIONS / FUTURE RESEARCH / KEY CONTROVERSIES

This document represents the update of our 2019 recommendations on the classification of foot ulcers in people with diabetes (5). Rather than just including new evidence published since that time, in this round we have conducted a systematic as opposed to a critical review and we have used the full GRADE approach (39) for the evidence analysis and development of the recommendations. This led to a change in the certainty of evidence in several scenarios. In fact, for all recommendations the certainty of evidence was graded as low.

Another change was the proposal of first line and second line systems to be used for communication among professionals and for the management of infected foot ulcers, which we believe will lead to a more tailored use of these systems in the different contexts across the world. With this process we have developed six recommendations as well as including one from the "Peripheral Artery Disease" working group which is embedded in our document (11).

In our systematic review (4) we retrieved 149 articles that assessed 28 different systems used to characterize foot ulcers in people with diabetes. However, the current available evidence remains limited due to a lack of articles directly comparing existing systems, with small sample sizes being common; most studies being graded at high risk of bias, frequently reporting only association measures (without multivariable adjustment); and focusing largely on healing or amputation. All of these aspects should be considered before conducting the much-needed future research on this topic to support the use of existing systems, instead of creating new ones that tend to be merely derivative.

Due to the limitations in the available evidence, we were only able to recommend the use of six (21%) out of the 28 systems found (DIAFORA, IDSA/IWGDF, SINBAD, UTWCS, Wagner and WIfI). Moreover, when choosing the ones more indicated for specific scenarios, DIAFORA, UTWCS and Wagner were not selected to be applied for clinical use or audits.

The systems varied considerably in the number (ranging from 3 to more than 30) and type of variables included. Some require blood samples and biomarkers analysis, others specific equipment, while others only use readily available data. The population for its intended use also varied greatly, from infected diabetes-related foot ulcers to chronic wounds of any type. Some had a bi-dimensional structure, other require the use of an app to improve feasibility, others presented an easy to calculate score, and others are a linear grading system. All of this has an impact on complexity, detail, acceptability and feasibility. Some of the choices made by the group may be debatable, but were transparent, carefully discussed and agreed within this group, and the IWGDF editorial board. Questions will inevitably arise as there is much less information about the process to develop recommendations in the diagnostic and prognostic field than in areas that are about therapeutics or other interventions.

One of the debatable decisions is the use of the Summary of Judgments devised for diagnostic clinical questions when we were actually evaluating prognostic clinical questions. However, we believe that we should focus on the use of these systems to change clinical management and not just on their ability to predict the clinical course of any individual. This leads to the acknowledgement that several of the items

related to the assessment of the impact of implementing these systems in clinical practice had insufficient supporting evidence and were consequently graded mainly on expert opinion.

As expected, several members of the group had potential conflict of interest concerning some of the identified systems. By looking for experts in the field, it would be predictable that several of the members had any role in developing, validating, or discussing the existing classification systems. In such cases, those members that were authors or co-authors of an article developing a specific system were not able to score or grade any of the items in the risk of bias, summary of judgments, direction, or strength of recommendation in which such potential conflict of interest may have played a role. The group decided to not perform a meta-analysis, because we considered that the expected heterogeneity on the definition of outcomes, follow-up and clinical setting was too high to enable generation of a meaningful meta-analysis.

One of the scenarios for which we assign high priority for development is the potential for a classification to be used in the prognosis of clinical outcome in an individual. For this specific application we believe that a high level of detail would be required and that machine learning techniques (included in decision support systems) may be key. As an example, we have the models developed by Xie et al. (40), although their use may reduce equity, and further validation studies are required. Alternatively, there may be an option for refinement of existing systems. Also, SINBAD has not yet been assessed to improve stratification by including patient-related morbid factors such as the presence of end-stage renal failure or history of past amputation, and it is envisaged that such future determinations, potentially also combined with systemic validated biomarkers, may, at least at a group level, add clinical utility to such wound classification system alone in predicting foot ulcer outcomes.

As in the 2019 IWGDF classification guidelines, we continue to surmise that there may never be a single preferred foot ulcer classification system for people with diabetes, since the specification of any classification will depend heavily on its purpose and clinical setting. Furthermore, we stress the importance of assessing the impact of including the use of a system in clinical practice, such as that seen by the use of the SINBAD system within the UK-based NDFA, which has consistently found that faster referral to a specialist foot care service is associated with fewer severe ulcers and better 12 weeks outcomes (38). Consequently, being able to classify the severity of an ulcer easily and adequately and to communicate it quickly and in a standardized manner to the specialist foot care service is expected to have a positive impact on clinical outcomes.

CONCLUDING REMARKS

Classification of foot ulcers in people with diabetes is of paramount importance in daily practice. It aims to help in communication among healthcare professionals, assessment/ alignment of broad risk categories and choice of best treatment strategy, as well as audit of clinical outcomes across units and populations.

Based on evidence and consensus judgement using the GRADE methodology, this guideline recommends the use of SINBAD as the priority wound classification system to utilise in people with diabetes and a foot ulcer, for inter-professional communication (describing each composite variable), clinical audits (using the full score), but the use of other more specific assessment systems for infection (IDSA/IWGDF) and peripheral artery disease (WIfI) or when resources exist in addition to an appropriate level of expertise (WIfI).

We encourage clinicians to use the classifications described in this guideline. To do so, specific diagnostic tools are required, standardised definitions (41) should be used and training should be promoted.

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CONTRIBUTION OF AUTHORS

The guideline working group was chaired by FG and MM-S acted as scientific secretary. All members are well-recognised experts in the field with the aim to create an international, multidisciplinary expert guideline committee, including the disciplines endocrinology, internal medicine, physiatry, podiatry and vascular surgery from the United States of America, Europe, Asia and Australia. The working group consisted of eight members in total (the authors of this guideline). All members of the guideline working group were involved in the evidence-to-decision framework process, mostly working in teams (see Methods), from summarising the available evidence in the supporting systematic review (4) to writing the recommendations and rationales. MM-S wrote the draft guideline, and all co-authors reviewed the draft and provided feedback, in writing and during online meetings, during which the content was discussed. All authors reviewed the final draft guideline document and agreed with the content and presentation of the definitive document. All members of the working group undertook Level I GRADE training, and the chair and secretary undertook Level 2 Guideline Methodology training (InGuide program, McMaster University).

REFERENCES

(1) Federation ID. IDF Diabetes Atlas Tenth Edition. IDF Diabetes Atlas. 2021.

(2) Armstrong DG, Boulton AJ, Bus SA. Diabetic foot ulcers and their recurrence. New England Journal of Medicine. 2017;376(24):2367-75.

(3) Walsh CG, Sharman K, Hripcsak G. Beyond discrimination: a comparison of calibration methods and clinical usefulness of predictive models of readmission risk. Journal of biomedical informatics. 2017;76:9-18.

(4) Monteiro-Soares M, Hamilton EJ, Russell DA, Sirisawasdi G, Boyko EJ, Mills JL, et al. Classification of foot ulcers in people with diabetes: a systematic review. Diab Metab Res Rev. 2023;e3645.

(5) Monteiro-Soares M, Russell D, Boyko EJ, Jeffcoate W, Mills JL, Morbach S, et al. Guidelines on the classification of diabetic foot ulcers (IWGDF 2019). Diabetes/metabolism research and reviews. 2020;36:e3273.

(6) Alonso-Coello P, Schünemann HJ, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. bmj. 2016;353.

(7) Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. Bmj. 2008;336(7650):924-6.

(8) Bus SA, Van Netten JJ, Apelqvist J, Fitridge R, Game F, Monteiro-Soares M, et al. Standards for the development and methodology of the 2023 International Working Group on the Diabetic Foot guidelines. Diab Metab Res Rev. 2023;e3656.

(9) van Netten JJ, Bus SA, Apelqvist J, Lipsky BA, Hinchliffe RJ, Game F, et al. Definitions and criteria for diabetic foot disease. Diabetes/metabolism research and reviews. 2020;36:e3268.

(10) Schünemann HJ, Oxman AD, Brozek J, Glasziou P, Bossuyt P, Chang S, et al. GRADE: assessing the quality of evidence for diagnostic recommendations. BMJ Evidence-Based Medicine. 2008;13(6):162-3.

(11) Fitridge R, Chuter VH, Mills JL, Hinchliffe RJ, Azuma N, Behrendt C-A, et al. The intersocietal IWGDF, ESVS, SVS guidelines on peripheral artery disease in patients with diabetes mellitus and a foot ulcer. Diab Metab Res Rev. 2023.

(12) Alonso-Coello P, Oxman AD, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 2: Clinical practice guidelines. Bmj. 2016;353:i2089.

(13) Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. Bmj. 2008;336(7650):924-6.

(14) Schaper NC, Van Netten JJ, Apelqvist J, Bus SA, Fitridge R, Game F, et al. Practical guidelines on the prevention and management of diabetes-related foot disease. Diab Metab Res Rev. 2023;e3657.

(15) Ince P, Abbas ZG, Lutale JK, Basit A, Ali SM, Chohan F, et al. Use of the SINBAD classification system and score in comparing outcome of foot ulcer management on three continents. Diabetes care. 2008;31(5):964-7.

(16) Wagner F. A classification and treatment program for diabetic, neuropathic, and dysvascular foot problems. Instr Course Lect. 1979;28(1):143-65.

(17) Monteiro-Soares M, Dinis-Ribeiro M. A new diabetic foot risk assessment tool: DIAFORA. Diabetes/Metabolism Research and Reviews. 2016;32(4):429-35.

(18) Mills Sr JL, Conte MS, Armstrong DG, Pomposelli FB, Schanzer A, Sidawy AN, et al. The society for vascular surgery lower extremity threatened limb classification system: risk stratification based on wound, ischaemia, and foot infection (WIfI). Journal of vascular surgery. 2014;59(1):220-34. e2.

(19) Armstrong DG, Lavery LA, Harkless LB. Validation of a diabetic wound classification system: the contribution of depth, infection, and ischaemia to risk of amputation. Diabetes care. 1998;21(5):855-9.

(20) Kannel WB, McGee D, Gordon T. A general cardiovascular risk profile: the Framingham Study. The American journal of cardiology. 1976;38(1):46-51.

(21) Deeks JJ, Altman DG. Diagnostic tests 4: likelihood ratios. Bmj. 2004;329(7458):168-9.

(22) Jaeschke R, Guyatt GH, Sackett DL, Guyatt G, Bass E, Brill-Edwards P, et al. Users' guides to the medical literature: III. How to use an article about a diagnostic test B. What are the results and will they help me in caring for my patients? Jama. 1994;271(9):703-7.

(23) Schaper N. Diabetic foot ulcer classification system for research purposes: a progress report on criteria for including patients in research studies. Diabetes/Metabolism Research and Reviews. 2004;20(S1):S90-S5.

(24) Monteiro-Soares M, Hamilton EJ, Russell D, Srisawasdi G, Boyko EJ, Mills JL, et al. Classification of foot ulcers in people with diabetes: a systematic review. DMRR. 2023.

(25) Lipsky BA, Senneville É, Abbas ZG, Aragón-Sánchez J, Diggle M, Embil JM, et al. Guidelines on the diagnosis and treatment of foot infection in persons with diabetes (IWGDF 2019 update). Diabetes/metabolism research and reviews. 2020;36:e3280.

(26) Lavery LA, Ryan EC, Ahn J, Crisologo PA, Oz OK, La Fontaine J, et al. The infected diabetic foot: re-evaluating the Infectious Diseases Society of America diabetic foot infection classification. Clinical Infectious Diseases. 2020;70(8):1573-9.

(27) Ali S, Fareed A, Humail S, Basit A, Ahmedani M, Fawwad A, et al. The personal cost of diabetic foot disease in the developing world—a study from Pakistan. Diabetic medicine. 2008;25(10):1231-3.

(28) Ali SM, Basit A, Fawwad A, Ahmedani MY, Miyan Z, Malik RA. Presentation and outcome of diabetic foot at a tertiary care unit. Pak J Med Sci. 2008;24(5):651-6.

(29) Gul A, Basit A, Ali SM, Ahmadani MY, Miyan Z. Role of wound classification in predicting the outcome of diabetic foot ulcer. JPMA The Journal of the Pakistan Medical Association. 2006;56(10):444.

(30) Habacher W, Rakovac I, Görzer E, Haas W, Gfrerer RJ, Wach P, et al. A model to analyse costs and benefit of intensified diabetic foot care in Austria. Journal of evaluation in clinical practice. 2007;13(6):906-12.

(31) Leese GP, Soto-Pedre E, Schofield C. Independent observational analysis of ulcer outcomes for SINBAD and university of Texas ulcer scoring systems. Diabetes Care. 2021;44(2):326-31.

(32) Monami M, Longo R, Desideri CM, Masotti G, Marchionni N, Mannucci E. The diabetic person beyond a foot ulcer: healing, recurrence, and depressive symptoms. Journal of the American Podiatric Medical Association. 2008;98(2):130-6.

(33) Oyibo S, Jude E, Tarawneh I, Nguyen H, Armstrong D, Harkless L, et al. The effects of ulcer size and site, patient's age, sex and type and duration of diabetes on the outcome of diabetic foot ulcers. Diabetic Medicine. 2001;18(2):133-8.

(34) Parisi MCR, Zantut-Wittmann DE, Pavin EJ, Machado H, Nery M, Jeffcoate WJ. Comparison of three systems of classification in predicting the outcome of diabetic foot ulcers in a Brazilian population. European Journal of Endocrinology. 2008;159(4):417.

(35) Prompers L, Huijberts M, Schaper N, Apelqvist J, Bakker K, Edmonds M, et al. Resource utilisation and costs associated with the treatment of diabetic foot ulcers. Prospective data from the Eurodiale Study. Diabetologia. 2008;51(10):1826-34.

(36) Smith-Strøm H, Iversen MM, Igland J, Østbye T, Graue M, Skeie S, et al. Severity and duration of diabetic foot ulcer (DFU) before seeking care as predictors of healing time: a retrospective cohort study. PLoS One. 2017;12(5):e0177176.

(37) Senneville É, Albalawi Z, Van Asten SA, Abbas ZG, Allison G, Aragón-Sánchez J, et al. Guidelines on the diagnosis and treatment of foot infection in persons with diabetes (IWGDF/IDSA 2023). Diab Metab Res Rev. 2023;in press.

(38) (NDFA) NDFCA. NDFA Interval Review: July 2014-March 2021. *www.hqip.org.uk/wp-content/uploads/2022/05/REF240_NDFA-Rep_FINAL-v1.1-20220511.pdf*; 2022.

(39) Schünemann H, Brożek J, Guyatt G, Oxman A. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. The GRADE Working Group, 2013. Available from guidelinedevelopment org/handbook. 2019.

(40) Xie P, Li Y, Deng B, Du C, Rui S, Deng W, et al. An explainable machine learning model for predicting in-hospital amputation rate of patients with diabetic foot ulcer. International Wound Journal. 2022;19(4):910-8.

(41) Van Netten JJ, Bus SA, Apelqvist J, Chen P, Chuter VH, Fitridge R, et al. Definitions and criteria for diabetes-related foot disease (2023 update). Diab Metab Res Rev. 2023;e3654.

(42) Monteiro-Soares M, Martins-Mendes D, Vaz-Carneiro A, Dinis-Ribeiro M. Lower-limb amputation following foot ulcers in patients with diabetes: classification systems, external validation and comparative analysis. Diabetes/metabolism research and reviews. 2015;31(5):515-29.

(43) Rigor J, Martins-Mendes D, Monteiro-Soares M. Risk factors for mortality in patients with a diabetic foot ulcer: a cohort study. European Journal of Internal Medicine. 2020;71:107-10.

(44) Chetpet A, DikShit B, Phalgune D. Evaluating a Risk Score for Lower Extremity Amputation in Patients with Diabetic Foot Infections. Journal of Clinical & Diagnostic Research. 2018;12(10).

(45) Lavery LA, Armstrong DG, Murdoch DP, Peters EJ, Lipsky BA. Validation of the Infectious Diseases Society of America's diabetic foot infection classification system. Clinical infectious diseases. 2007;44(4):562-5.

(46) Pickwell K, Siersma V, Kars M, Apelqvist J, Bakker K, Edmonds M, et al. Predictors of lower-extremity amputation in patients with an infected diabetic foot ulcer. Diabetes care. 2015;38(5):852-7.

(47) Richard J-L, Sotto A, Jourdan N, Combescure C, Vannereau D, Rodier M, et al. Risk factors and healing impact of multidrug-resistant bacteria in diabetic foot ulcers. Diabetes & metabolism. 2008;34(4):363-9.

(48) Rubio JA, Jiménez S, Lázaro-Martínez JL. Mortality in patients with diabetic foot ulcers: Causes, risk factors, and their association with evolution and severity of ulcer. Journal of Clinical Medicine. 2020;9(9):3009.

(49) Ryan EC, Crisologo PA, Oz OK, La Fontaine J, Wukich DK, Lavery LA. Do SIRS Criteria Predict Clinical Outcomes in Diabetic Skin and Soft Tissue Infections? The Journal of Foot and Ankle Surgery. 2019;58(6):1055-7.

(50) Saltoglu N, Yemisen M, Ergonul O, Kadanali A, Karagoz G, Batirel A, et al. Predictors for limb loss among patient with diabetic foot infections: an observational retrospective multicentric study in Turkey. Clinical microbiology and infection. 2015;21(7):659-64.

(51) Seth A, Attri AK, Kataria H, Kochhar S, Seth SA, Gautam N. Clinical profile and outcome in patients of diabetic foot infection. International Journal of Applied and Basic Medical Research. 2019;9(1):14.

(52) Wukich DK, Hobizal KB, Brooks MM. Severity of diabetic foot infection and rate of limb salvage. Foot & ankle international. 2013;34(3):351-8.

(53) Bravo-Molina A, Linares-Palomino JP, Vera-Arroyo B, Salmerón-Febres LM, Ros-Díe E. Inter-observer agreement of the Wagner, University of Texas and PEDIS classification systems for the diabetic foot syndrome. Foot and Ankle Surgery. 2018;24(1):60-4.

(54) Alsabek MB, Abdul Aziz AR. Diabetic foot ulcer, the effect of resource-poor environments on healing time and direct cost: A cohort study during Syrian crisis. International Wound Journal. 2022;19(3):531-7.

(55) Chuan F, Tang K, Jiang P, Zhou B, He X. Reliability and validity of the perfusion, extent, depth, infection and sensation (PEDIS) classification system and score in patients with diabetic foot ulcer. PloS one. 2015;10(4):e0124739.

(56) Jeon BJ, Choi HJ, Kang JS, Tak MS, Park ES. Comparison of five systems of classification of diabetic foot ulcers and predictive factors for amputation. International wound journal. 2017;14(3):537-45.

(57) Camilleri A, Gatt A, Formosa C. Inter-rater reliability of four validated diabetic foot ulcer classification systems. Journal of Tissue Viability. 2020;29(4):284-90.

(58) Forsythe RO, Ozdemir BA, Chemla ES, Jones KG, Hinchliffe RJ. Interobserver reliability of three validated scoring systems in the assessment of diabetic foot ulcers. The International Journal of Lower Extremity Wounds. 2016;15(3):213-9.

(59) Jørgensen TS, Hellsten Y, Gottlieb H, Brorson S. Assessment of diabetic foot ulcers based on pictorial material: an interobserver study. Journal of Wound Care. 2020;29(11):658-63.

(60) Santema TB, Lenselink EA, Balm R, Ubbink DT. Comparing the Meggitt-Wagner and the University of Texas wound classification systems for diabetic foot ulcers: inter-observer analyses. International wound journal. 2016;13(6):1137-41.

(61) Bates-Jensen B. New pressure ulcer status tool. Decubitus. 1990;3(3):14-5.

(62) Arisandi D, Oe M, Roselyne Yotsu R, Matsumoto M, Ogai K, Nakagami G, et al. Evaluation of validity of the new diabetic foot ulcer assessment scale in Indonesia. Wound repair and regeneration. 2016;24(5):876-84.

(63) Oe M, Yotsu RR, Arisandi D, Sakai Y, Takehara K, Nakagami G, et al. Validity of DMIST for monitoring healing of diabetic foot ulcers. Wound Repair and Regeneration. 2020;28(4):539-46.

(64) Thomas DR, Rodeheaver GT, Bartolucci AA, Franz RA, Sussman C, Ferrell BA, et al. Pressure ulcer scale for healing: derivation and validation of the PUSH tool. The PUSH Task Force. Advances in wound care: the journal for prevention and healing. 1997;10(5):96-101.

(65) Margolis DJ, Allen-Taylor L, Hoffstad O, Berlin JA. Diabetic neuropathic foot ulcers: the association of wound size, wound duration, and wound grade on healing. Diabetes care. 2002;25(10):1835-9.

(66) Margolis DJ, Allen-Taylor L, Hoffstad O, Berlin JA. Diabetic neuropathic foot ulcers: predicting which ones will not heal. The American journal of medicine. 2003;115(8):627-31.

(67) Margolis DJ, Allen-Taylor L, Hoffstad O, Berlin JA. Diabetic neuropathic foot ulcers and amputation. Wound Repair and Regeneration. 2005;13(3):230-6.

(68) Van Battum P, Schaper N, Prompers L, Apelqvist J, Jude E, Piaggesi A, et al. Differences in minor amputation rate in diabetic foot disease throughout Europe are in part explained by differences in disease severity at presentation. Diabetic medicine. 2011;28(2):199-205.

(69) Gardner SE, Frantz RA, Troia C, Eastman S, MacDonald M, Buresh K, et al. A tool to assess clinical signs and symptoms of localized infection in chronic wounds: development and reliability. Ostomy/Wound Management. 2001;47(1):40-7.

(70) Younes NA, Albsoul AM. The DEPA scoring system and its correlation with the healing rate of diabetic foot ulcers. The Journal of foot and ankle surgery. 2004;43(4):209-13.

(71) Lee DW, Kwak SH, Kim JH, Choi HJ. Prediction of diabetic foot amputation using newly revised DIRECT coding system: Comparison of accuracy with that of five existing classification systems. International Wound Journal. 2022.

(72) Kumar S, Arava S, Pavan B, Kiran G, Chandan G, Kumar N. Diabetic ulcer severity score: clinical validation and outcome. International Surgery Journal. 2016;3(3):1606-10.

(73) Shashikala C, Nandini VK, Kagwad S. Validation of Diabetic Ulcer Severity Score (DUSS). 2017.

(74) Yang S, Gu Z, Lu C, Zhang T, Guo X, Xue G, et al. Neutrophil extracellular traps are markers of wound healing impairment in patients with diabetic foot ulcers treated in a multidisciplinary setting. Advances in wound care. 2020;9(1):16-27.

(75) Spanos K, Saleptsis V, Athanasoulas A, Karathanos C, Bargiota A, Chan P, et al. Factors associated with ulcer healing and quality of life in patients with diabetic foot ulcer. Angiology. 2017;68(3):242-50.

(76) Jun YJ, Shin D, Choi WJ, Hwang JH, Kim H, Kim TG, et al. A Mobile application for wound assessment and treatment: findings of a user trial. The International Journal of Lower Extremity Wounds. 2016;15(4):344-53.

(77) Jun D, Kwon Y, Bae J, Lee M, Kim J, Choi H, et al. Using DIRECT wound assessment to predict limb salvage and provide prognosis of diabetic foot ulcers. Journal of Wound Management and Research. 2021;17(1):9-18.

(78) Wong C-H, Khin L-W, Heng K-S, Tan K-C, Low C-O. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. Critical care medicine. 2004;32(7):1535-41.

(79) Sen P, Demirdal T. Predictive ability of LRINEC score in the prediction of limb loss and mortality in diabetic foot infection. Diagnostic Microbiology and Infectious Disease. 2021;100(1):115323.

(80) Chaudhary N, Huda F, Roshan R, Basu S, Rajput D, Singh SK. Lower Limb Amputation Rates in Patients With Diabetes and an Infected Foot Ulcer: A Prospective Observational Study. Wound Management & Prevention. 2021;67(7):22-30.

(81) Amadou C, Carlier A, Amouyal C, Bourron O, Aubert C, Couture T, et al. Five-year mortality in patients with diabetic foot ulcer during 2009–2010 was lower than expected. Diabetes & Metabolism. 2020;46(3):230-5.

(82) Treece K, Macfarlane R, Pound N, Game F, Jeffcoate W. Validation of a system of foot ulcer classification in diabetes mellitus. Diabetic medicine. 2004;21(9):987-91.

(83) Chipchase S, Treece K, Pound N, Game F, Jeffcoate W. Heel ulcers don't heal in diabetes. Or do they? Diabetic medicine. 2005;22(9):1258-62.

(84) Ince P, Kendrick D, Game F, Jeffcoate W. The association between baseline characteristics and the outcome of foot lesions in a UK population with diabetes. Diabetic Medicine. 2007;24(9):977-81.

(85) Martínez-De Jesús FR. A checklist system to score healing progress of diabetic foot ulcers. The international journal of lower extremity wounds. 2010;9(2):74-83.

(86) Huang Y, Xie T, Cao Y, Wu M, Yu L, Lu S, et al. Comparison of two classification systems in predicting the outcome of diabetic foot ulcers: the W agner grade and the S aint E lian W ound score systems. Wound Repair and Regeneration. 2015;23(3):379-85.

(87) Carro GV, Saurral R, Carlucci E, Gette F, Llanos MdlÁ, Amato PS. A comparison between diabetic foot classifications WIfI, Saint Elian, and Texas: description of wounds and clinical outcomes. The International Journal of Lower Extremity Wounds. 2022;21(2):120-30.

(88) NIȚĂ G, GHERASIM A, NIȚĂ O, POPA AD, ARHIRE LI, MIHALACHE L, et al. Factors influencing length of hospital stay in patients with diabetic foot ulcers. Romanian JouRnal of medical PRactice. 2021;16(2):77.

(89) Leese G, Schofield C, McMurray B, Libby G, Golden J, MacAlpine R, et al. Scottish foot ulcer risk score predicts foot ulcer healing in a regional specialist foot clinic. Diabetes care. 2007;30(8):2064-9.

(90) Tardivo JP, Baptista MS, Correa JA, Adami F, Pinhal MAS. Development of the tardivo algorithm to predict amputation risk of diabetic foot. PLoS One. 2015;10(8):e0135707.

(91) Pertama D, Suryadhi N, Yeasa I. Validitas skor tardivo untuk memprediksi terjadinya amputasi pada kaki diabetes di Rsup Sanglash. Medicina. 2018;49(1):33-7.

(92) Van Acker K, De Block C, Abrams P, Bouten A, De Leeuw I, Droste J, et al. The choice of diabetic foot ulcer classification in relation to the final outcome. Wounds. 2002;14:16-25.

(93) Fife CE, Horn SD, Smout RJ, Barrett RS, Thomson B. A predictive model for diabetic foot ulcer outcome: the wound healing index. Advances in Wound Care. 2016;5(7):279-87.