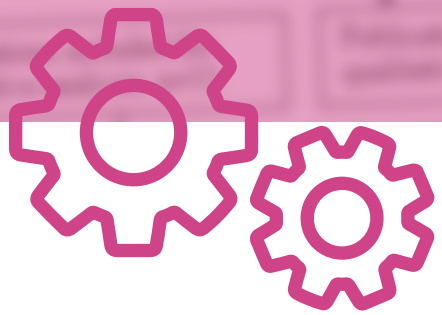
Standards for the development and methodology of the 2023 International Working Group on the Diabetic Foot Guidelines



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

IWGDF Guidelines

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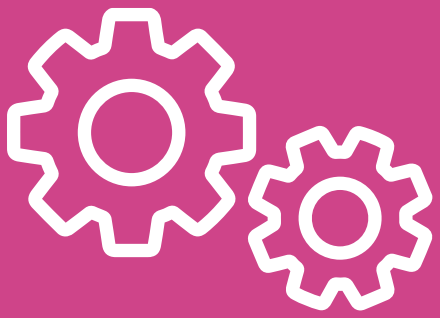

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ABSTRACT

Diabetes-related foot disease is a source of major patient burden and societal costs. Investing in evidence-based international guidelines on diabetes-related foot disease is important to reduce this burden and costs, provided the guidelines are focused on outcomes important to key stakeholders, evidence-based and properly implemented.

The International Working Group on the Diabetic Foot (IWGDF) has published and updated international guidelines since 1999. The 2023 updates were made using the Grading of Recommendations Assessment Development and Evaluation (GRADE) evidence-to-decision framework. This concerns formulating relevant clinical questions and important outcomes, conducting systematic reviews of the literature and meta-analyses where appropriate, completing summary of judgements tables, and writing recommendations that are specific, unambiguous and actionable, along with their transparent rationale.

We herein describe the development of the 2023 IWGDF Guidelines on the prevention and management of diabetes-related foot disease, which consists of seven chapters, each prepared by a separate working group of international experts. These chapters provide guidelines related to diabetes-related foot disease on: prevention; classification of diabetes-related foot ulcers; offloading; peripheral artery disease; infection; wound healing interventions; and active Charcot neuro-osteoarthropathy. Based on these seven guidelines, the IWGDF Editorial Board also produced a set of practical guidelines. Each guideline underwent extensive review by the members of the IWGDF Editorial Board as well as independent international experts in each field.

We believe that the adoption and implementation of the 2023 IWGDF guidelines by healthcare providers, public health agencies, and policymakers will improve the prevention and management of diabetes-related foot disease, and subsequently reduce the worldwide patient and societal burden this disease causes.

INTRODUCTION

The global prevalence of diabetes mellitus was 537 million in 2021 and is estimated to rise to 783 million by 2045; 75% of these people live in low- or middle-income countries (1). Diabetes-related foot disease is a source of major patient burden and societal costs. The frequency and severity of foot disease in persons with diabetes varies by region, largely due to differences in socio-economic conditions, cultural factors, and standards of and access to foot care (2). Foot ulcers are the most recognizable problem, with a yearly incidence of around 2%-4% in higher income (3), likely even higher in lower-income countries, and an estimated lifetime prevalence of 19-34% (4).

The most important factors underlying the development of foot ulcers are peripheral neuropathy, peripheral artery disease, foot deformities related to motor neuropathy, and minor foot trauma (4). These conspire to put the patient at risk for skin ulceration, making the foot susceptible to infection - an urgent medical problem. Only two-thirds of diabetes-related foot ulcers will eventually heal (5), and up to 28% may result in some form of lower extremity amputation (6). Every year, more than 1 million people with diabetes lose at least a part of their leg due to diabetes-related foot disease. This translates into the estimate that every 20 seconds a lower limb is lost to diabetes somewhere in the world (7).

Diabetes-related foot disease not only represents a personal tragedy for the affected patient, but it also affects that person's family and places a substantial financial burden on healthcare systems and society in general. In low-income countries, the cost of treating a complex diabetes-related foot ulcer can be equivalent to 5.7 years of annual income, potentially resulting in financial ruin for the patient and their family (8). Investing in evidence-based, internationally appropriate guidelines on diabetes-related foot disease is likely among the most cost-effective forms of healthcare expenditure, provided it is focused on outcomes important to key stakeholders and properly implemented (9).

INTERNATIONAL WORKING GROUP ON THE DIABETIC FOOT

The International Working Group on the Diabetic Foot (IWGDF; *www.iwgdfguidelines.org*), founded in 1996, consists of multidisciplinary experts involved in the care of patients with diabetes-related foot disease. The IWGDF aims to prevent the adverse effects of diabetes-related foot disease by developing and regularly updating international guidelines for use by all health care providers, public health agencies and policymakers involved in diabetes-related foot care. Developing and updating guidelines is managed by the IWGDF working groups. In 1999, the IWGDF published its first version of "International Consensus on the Diabetic Foot" and "Practical Guidelines on the Management and the Prevention of the Diabetic Foot". This publication has been translated into 26 languages, and more than 100,000 copies have been distributed globally. As healthcare systems and the prevalence of pathologies differ across regions in the world, the guidelines have to be adapted to local circumstances where applicable. These documents have been updated six times since then, in a 4-year cycle.

FROM CONSENSUS TO EVIDENCE-BASED GUIDELINES

While the core principles the IWGDF was founded on remain constant, the methodology by which the IWGDF guidelines have been developed has evolved over the past couple of decades. The initial guidelines, and each subsequent update, were developed by a consensus process and written by a panel of experts in the field. Systematic reviews were introduced in 2007 and formed the backbone of the guidelines' recommendations. Utilizing a multi-step review process, these guidelines were then revised by the IWGDF Editorial Board, followed by critical evaluation by global IWGDF representatives, culminating in an agreed-upon text. Finally, the IWGDF recruited representatives from over 100 countries around the world to help implement the recommended practices. In 2015, a new milestone was introduced to the IWGDF guideline development with the implementation of the GRADE framework to assess certainty of the evidence and formulate recommendations for clinical practice, based on both the available evidence and expert opinion. In 2019, we formulated clinical questions and relevant outcomes to guide the systematic review and writing of recommendations and introduced a definitions and criteria reference document for the most commonly used terms in diabetes-related foot disease (10).

THE 2023 UPDATE

For the 2023 IWGDF guidelines, the Editorial Board invited chairpersons being key investigators/clinicians in the field, with whom they selected international experts based on relevant specialty for the guideline and regional representation, to constitute seven multidisciplinary working groups, each tasked with producing a guideline on one of the following topics:

- Prevention of foot ulcers in persons with diabetes
- Classification of diabetes-related foot ulcers
- Diagnosis and treatment of foot infection in persons with diabetes
- Diagnosis and management of peripheral artery disease in persons with a foot ulcer and diabetes
- Offloading foot ulcers in persons with diabetes
- Interventions to enhance healing of foot ulcers in persons with diabetes
- Active Charcot neuro-osteoarthropathy

The first six guideline chapters are updates of the 2019 guideline on the topic, while the guideline on active Charcot neuro-osteoarthropathy is new for 2023. All can be found at *www.iwgdfguidelines.org*. As in earlier versions, the IWGDF Editorial Board produced a document titled "Practical Guidelines on the prevention and management of diabetes-related foot disease", based on these seven guidelines, intended as a brief outline of the essential parts of prevention and management of diabetes-related foot disease. We advise clinicians and other healthcare professionals to read the full guideline on each topic for the specific and detailed recommendations and the rationale underpinning them, as well as the associated systematic reviews for a detailed discussion of the evidence. In addition, this current

publication provides a more detailed description of the GRADE methodology followed and the process to develop the recommendations along with the rationale supporting them.

New in 2023, we took a more rigorous and strict approach by using the GRADE evidence-to-decision framework. Each member of the working groups was trained in guideline development through the International Guideline Development Credentialing & Certification Program (*www.inguide.org*) at the guideline panel member level (level 1) and at least two members of each working group at the guideline methodologist level (level 2). Each working group formulated clinical questions and defined important outcomes that were reviewed by an international panel of independent external experts (based on relevant specialty for the guideline and regional representation) and, for the first time, people with lived experience, as well as by the IWGDF Editorial Board. Summary of judgments were created based on a consideration of aspects that were important for determining the direction and the strength of the recommendation and included desirable and undesirable effects, resources required, for each of these the certainty of evidence, values, cost-effectiveness, equity, acceptability and feasibility.

Recommendations were thoroughly discussed within the working group, and reviewed again by the same external experts. New was a voting procedure, to improve transparency and clarity. The direction and strength were first voted on by each working group member, before the discussions started. Votes were repeated after discussion. The IWGDF Editorial Board members (the authors of this publication), a total of 69 working group members (including the Editorial Board members), and a total of 119 external experts and patient representatives from 63 countries and all continents were involved in the development of the 2023 IWGDF Guidelines.

The seven guidelines, the systematic reviews supporting them, the practical guidelines, this development and methodology document and the definitions and criteria document are all published as freely accessible articles online at *www.iwgdfguidelines.org*. We recommend that healthcare providers, public health agencies and policymakers use these guidelines as the basis for developing their own local (regional or national) guidelines, where the GRADE Adolopment approach can provide as framework for this.

METHODOLOGY USED FOR THE 2023 IWGDF SYSTEMATIC REVIEWS AND GUIDELINES

This section describes the various steps and methods set up by the IWGDF Editorial Board for use by the designated multidisciplinary working groups to develop guidelines for the prevention and management of diabetes-related foot disease. The aims were to produce high-quality systematic reviews to help inform each guideline, promote consistency among the guidelines developed, and ensure high-quality documents.

In the IWGDF guidelines, we have followed the GRADE evidence-to-decision framework. This is structured around developing clinical questions and relevant outcomes per question (in the PICO-format (Patient-Intervention-Comparison-Outcome)), conducting systematic searches and assessment of the available evidence, writing a summary of judgements, followed by developing recommendations and their rationale (11, 12). We will describe in detail the five key tasks in the development of the guidelines: i) establishing a diverse expert panel to develop the guideline, ii) defining key clinical questions and important outcomes , iii) performing systematic reviews and rigorous appraisals of all available evidence that address the clinical questions, iv) assessing key summary of judgements items for each clinical question and developing recommendations and their rationale based on these summaries of judgements, and v) consulting external stakeholders on each step.

1. Establishing a diverse expert panel to develop the guideline

First, a multidisciplinary working group of independent international experts for each of the seven guidelines was invited by the IWGDF Editorial Board to develop and author the guideline. International experts were defined as those having significant experience in practising or studying the topic of the guideline and have likely published on the topic. The working groups were comprised to ensure sufficient representation from different specialities (medical, science, professional practice) and different geographical regions in the world.

Each member of a guideline working group completed a declaration of interest for the guideline that they were involved in at the start of the guideline development process. These were published online at *www.iwgdfguidelines.org*. These declarations were monitored and kept up-to-date during guideline development as an item on the agenda of working group meetings.

2. Defining key clinical questions and important outcomes

Each working group started the guideline writing process by formulating the clinical questions they intended to address. This was to provide focus and structure to the setup of the evidence-based guidelines along the line of what a clinician or a patient would ask regarding the care provided in clinical practice to persons with diabetes-related foot disease. The questions generally involved diagnosis, prognosis, or treatment, and the members of the working group reached a consensus on the clinical questions they planned to address. The clinical questions were reviewed for their clinical relevance by the IWGDF Editorial Board and a panel of international external experts (including representatives of people with lived experience) from various geographical regions, to ensure global relevance to a wide

range of healthcare professionals and people with the disease so as to provide the most useful clinical information. These experts were selected by the working groups, under the guidance of the IWGDF Editorial Board. The final clinical questions were used for the systematic review and guidelines.

The clinical questions regarding interventions took the format of the "PICO", an acronym that at least includes the population (P) at risk (who are you studying?), the intervention (I) planned (what will you be doing?) and the outcome (O) of interest (what are the consequences of the intervention?). The C is for comparator or control and concerns the main alternative to the intervention considered, usual care, or nothing. The clinical questions regarding diagnosis or prognosis, take the format of the "PECO", which includes the population, exposure/assessment, comparator, and outcome.

Each working group devised specific outcomes following the GRADE process (13-15). Given the lack of a validated core outcome set for diabetes-related foot disease, the set of outcomes defined by the IWGDF-EWMA (16) was used as a guide to define the outcomes selected, and additionally expert opinion of the working group was used where such guidance did not exist. An extensive list of potential outcomes was rated on importance by the international external experts in the field (including the representatives with lived experience), with a score of 1 (not important), 2 (of some importance) or 3 (very important). Subsequently, each working group member independently rated these outcomes with a score ranging from 1 to 9, according to GRADE, and defined as 'not important for decision-making' (score 1-3.5), 'important but not critical for decision-making' (score 4-6.5), 'critically important for decision-making' (score 7-9) (17). Group means and medians were calculated, and discussed in a meeting with all working group members until a consensus was reached. Working groups were informed that critical outcomes, which have a larger effect on decision-making and recommendations, were the most important to address. As a last step, outcomes were matched with the interventions assessed as formulated in the clinical questions, with a maximum number of outcomes to be considered relevant per intervention, dependent on the question.

Following this multistep revision, the clinical questions and outcomes were finalized in February 2022.

3. Performing a systematic review (and meta-analysis)

Each working group undertook at least one systematic review of the medical literature that was designed to form the basis for the evidence-based guidelines. Each systematic review was prepared according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (18, 19) (*www.prisma-statement.org*). Each working group used the AMSTAR tool to check that they were addressing the most important aspects of their systematic review (*amstar.ca/Amstar_Checklist.php*). Systematic reviews were prospectively registered in the PROSPERO database for systematic reviews before the literature search started (*www.crd.york.ac.uk/prospero*).

The literature databases used for each systematic review were PubMed (via Medline), and either EMBASE (via Ovid SP), the Cochrane database, or both. Each working group devised a search string for each database. Individual working groups could consult a medical librarian to help in devising their search string. Study designs included in the systematic review on interventions were randomized controlled trials. Depending on the number of papers found with this higher-level study design, working groups could also include lower-level designs, e.g., non-randomized controlled trials, case-control studies, cohort

studies, (controlled) before-and-after studies, interrupted time series, prospective and retrospective non-controlled studies, cross-sectional studies and case series. Case reports were excluded from the systematic reviews. For diagnostic and prognostic questions, observational study designs were included. If systematic reviews (with meta-analysis) were identified, reference checking of the papers identified in that publication was performed to cross-check (and as such validate) our search results, but the systematic review itself was excluded. Literature in all languages was searched for and included.

Trial registries
The working groups searched two trial registries for ongoing studies: The World Health Organization International Clinical Trials Registry Platform (WHO-ICTRP) (*apps.who.int/trialsearch/default.aspx*) and the ClinicalTrials.gov registry (*www.clinicaltrials.gov*). A sensitive search string derived from the original search string for the systematic review was used to search for relevant studies in these trial databases.

Validation set
To ensure that the search string used for the systematic review was robust, working groups created a validation set of 10-20 known key publications from the last four years for each systematic review before performing the literature search. If any of the papers in the validation set was not identified in the literature search performed, the working group modified the search string.

Date of search
The literature search for all systematic reviews was conducted in March 2022. At the discretion of the working group the full search could be updated in November 2022. Any trial that was identified in a trial registry and was published before November 1, 2022, was also included.

Assessing retrieved publications from the search
Two members of each working group independently reviewed publications by title and abstract to assess their eligibility for inclusion in the analysis based on four criteria that were tailored to thre specific question at hand: population; study design; outcomes; and intervention or exposure/assessment. Publications were listed in the online application Rayyan (20) (*www.rayyan.ai*) to help in the eligibility assessment of publications. At their discretion, the working groups could calculate Cohen's kappa values to test for agreement between the two reviewers. The two reviewers discussed any disagreement on which publications to include and reached a consensus. If necessary, a 3rd member of the working group was involved to arbitrate. The same two reviewers independently assessed selected full-paper copies of included publications on the same four criteria for final eligibility. Reference lists of included papers were not tracked. Regarding the population of interest, if a mixed population was present in the studies retrieved, the minimum proportion of the population of interest in the sample, as defined by the working group (e.g. 80%), was used for eligibility.

To assess for possible publication bias or selective reporting of results, the working groups assessed studies identified by trial registries in the WHO and ClinicalTrial.gov databases using the methodology as outlined in the GRADE handbook (17). From relevant trials identified from these databases, related publications were searched for in the original literature search database, using the trial registration number of these relevant trials. If no publications were identified, the principal investigator of the trial was contacted and asked about the status of the trial and any possible results from the trial. Funnel plots were constructed where possible.

Data extraction

Data were extracted from each included publication that had a controlled study design and were summarized in an evidence table. This table included participant and study characteristics, characteristics of the intervention and control conditions, and primary and secondary outcomes. One of the reviewers of the original team of two extracted the data, while the other reviewer checked the table for content and presentation. All members of the working group discussed the data in the evidence tables.

Each working group created a PRISMA flow diagram showing the process of selection of papers for the qualitative analysis, and a risk of bias table presenting in detail the risk of bias per included publication.

Classifying study design and level of evidence

For each included publication, we used the Scottish Intercollegiate Grouping Network (SIGN) algorithm for classifying study design for questions of effectiveness (*www.sign.ac.uk/assets/study_design.pdf*). The same two reviewers that reviewed publications for eligibility independently assessed included publications with a controlled study design for methodological quality (i.e., risk of bias), using scoring sheets developed by the Dutch Cochrane Centre (*netherlands.cochrane.org/beoordelingsformulieren-en-andere-downloads*).

The two reviewers discussed any disagreement regarding the risk of bias and reached a consensus. The SIGN level of evidence was determined based on the risk of bias for each publication using the SIGN Grading System for Levels of Evidence (*www.sign.ac.uk/assets/sign_grading_system_1999_2012.pdf*) (21). Level 1 refers to randomized controlled trials and Level 2 refers to case-control, cohort, controlled before-and-after designs or interrupted time series. Risk of bias was scored for each study as: ++ (very low risk of bias); + (low risk of bias); or, – (high risk of bias).

Additionally, working groups assessed all publications with a controlled study design for quality of reporting using the 21-item scoring system for reports of clinical studies developed by the IWGDF in collaboration with EWMA (16). To prevent any conflict of interest, reviewers who were one of the authors of any study assessed for inclusion did not participate in the assessment, data extraction or discussion of publications of that study. They were involved in the working group discussions of the summary of judgements and recommendation to which that study contributed.

Rating of the certainty of evidence

The certainty of the evidence obtained through the systematic review was rated per PICO and for all outcomes related to that PICO. The certainty of evidence was rated as high, moderate, low, or very low, based on the assessment of the following items:

- Risk of bias (scored from the risk of bias assessment per paper)
- Inconsistency of results (i.e., true differences in the underlying treatment effect may be likely when there are widely differing estimates of the treatment effect [i.e. heterogeneity or variability in results] across studies)
- Imprecision (i.e., results are imprecise when studies include relatively few patients and few events and thus have a wide confidence interval (CI) around the estimate of the effect, providing uncertainty about the results)

- Indirectness (i.e., direct evidence consists of research that directly compares the interventions in which we are interested, delivered to the populations in which we are interested, and measures the prioritized outcomes important to patients)
- Publication bias (as could be obtained from the Clinical Trials search or from funnel plots, see above), where appropriate

The starting point in the certainty of the evidence rating when >1 level 1 study (RCT) was involved was "high". When only one RCT was available, the certainty rating started at moderate, as inconsistency could not be assessed. When no RCTs were available, so only observational controlled studies (level 2, i.e. cohort, case-control), certainty rating started at low. When only non-controlled studies were available, the certainty rating started at very low.

For each of these five above items that were scored as 'present', the certainty of the evidence rating was lowered by one level. For example: the certainty of the evidence could be reduced from "high" to "moderate" when the risk of bias in included studies was high, and further to "low" whe also imprecision was present. The certainty of the evidence could be raised based on the presence of a large effect size or evidence of a dose-response relationship (for observational studies only). For each of these two items that were scored as "present", the certainty of the evidence rating was raised by one. For example, the certainty of the evidence was raised from "low" to "moderate" when the effect size was large. Many of the older papers identified in the systematic reviews lacked data to calculate or assess for indirectness or imprecision. If so, we did not take these older papers for these certainty of evidence rating items into account.

Meta-analysis

A meta-analysis for the intervention-based systematic reviews was done when >1 RCT was available that included the same or a similar intervention, the same or a similar comparator, and the same outcome. Each assessable outcome for each clinical question was meta-analysed if appropriate, and we followed the methodology as outlined in the GRADE and Cochrane Handbooks (15, 17). The aim of the meta-analysis was to generate a pooled effect estimate. For dichotomous outcomes, all meta-analyses were performed using Mantel-Haenszel's statistical method and random effect models anticipating substantial heterogeneity. The results were reported as risk ratios and 95% confidence intervals. For continuous outcomes, meta-analyses were performed using the inverse variance method and random effect models anticipating substantial heterogeneity. The mean difference was reported as the effect measure, with 95% confidence intervals. For statistical analyses, two-tailed tests with alpha set at 0.05 were used. Heterogeneity was assessed using the Chi-squared test and the I^2 statistic and interpreted as low (0–49%), moderate (50–74%) or high (75–100%). A forest plot was made to visualize outcomes. Meta-analyses were conducted using RevMan 5, version 5.4 (The Cochrane Collaboration, Nordic Cochrane Centre, Copenhagen, Denmark). If no meta-analysis was done, the reason(s) for doing so were provided.

Summary of findings

At the discretion of each working group, a summary of findings tables was created for each clinical question in accordance with Cochrane and GRADE handbooks (15, 17). The summary of findings tables display the key information addressing each comparison, including the population, interventions, controls, and outcomes. For each outcome, the working group members added the number of studies, the number of participants, the relative effect, anticipated absolute effects (as determined by the GRADEPro online application), the certainty of evidence assessment (with explanations), and evidence statements in a controlled language based on effect size and certainty of evidence assessment using the GRADEPro online application summary of finding table templates (*www.gradepro.org*) (17). Thus, each summary of findings table summarises the entire process for each comparison. For comparisons that did not have controlled trials reporting any outcomes, findings were narratively summarised.

Conclusions and evidence statements

Finally, the two assessors per intervention group drew conclusions for each intervention based on the available evidence per outcome, formulated as evidence statements for the group of outcomes and accompanying assessment of the certainty of the evidence, according to Cochrane and GRADE (15, 17). The assessors rated the certainty of the evidence for each formulated evidence statement as "high", "moderate", "low" or "very low". GRADE defines "high" as "We are very confident that the true effect lies close to that of the estimate of the effect"; "moderate" as "We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different"; "low" as "Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect", and "very low" as "We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect" (17). All members of the working group participated in the discussion of these conclusions, reaching a consensus on the content and formulation of the conclusions.

The content of the statement was based on the evidence, with a focus on point estimates of effect, as advocated by GRADE, rather than statistical significance or 95% confidence intervals (15, 17). The wording for each evidence statement was in accordance with the methods described by GRADE. For an effect with a moderate certainty of evidence, the statement contains "likely results in …"; for an effect with low certainty of effect, the statement contains "may result in …"; for statements with a very low certainty of effect, the statement contains "(very) uncertain"; when the effect or effect size could not be estimated, no evidence statement was provided. All members of the working group discussed these evidence statements until a consensus was reached.

Systematic review of diagnostic procedures

We obtained specific methods for the systematic review of diagnostic studies from Brownrigg et al (22) and PRISMA guidelines (19), and we asked all groups systematically reviewing studies and writing guidelines on diagnostic procedures to follow the methods used in this study (22). Working groups assessed the methodological quality of included studies against parameters included in the QUADAS tool, a consensus quality assessment tool designed specifically for diagnostic accuracy studies (23). Reviewers extracted data and entered them in a QUADAS data extraction form and calculated positive and negative likelihood ratios' for each test in each study (24, 25).

Systematic review on prognosis
The methods used for the systematic review on prognostics in peripheral artery disease were the same as the ones used in the 2019 systematic review on this topic (26). To assess the methodological quality of included studies we used the QUIPS tool, designed specifically for prognostic studies (27, 28). To assess the risk of bias we used the QUIPS Risk of Bias Assessment Instrument for Prognostic Factor Studies.

Archiving and record keeping
For archiving of papers and recording of screening decisions and study scores, a full audit trail was kept, so that the process, procedures used and decisions made were transparent, including the literature search, selection process, votes for clinical questions, outcomes, and recommendations, and all assessments (e.g. risk of bias) and pdfs of full papers.

4. Assessing key summary of judgements items and writing the recommendations and their rationale

Summary of judgement tables
Based on the systematic review and meta-analyses (when available), the summary of findings tables (if applicable) and expert opinion, teams of two members of the working group drafted the summary of judgements tables for each clinical question following the GRADE Evidence-to-Decision domains tables. These summary of judgement tables are tables in which aspects of the intervention that are important to consider for developing and writing the recommendation, are assessed and described. The summary of judgement items assessed included desirable and undesirable effects, values, the certainty of evidence of effects, the balance of these effects, resources required, the certainty of evidence for these required resources, cost-effectiveness, equity, acceptability and feasibility. For each item, a judgement was made, the research evidence was summarised and additional considerations could be described. Definitions for these items can be found in the GRADE handbook (17) and at the end of the summary of judgements tables used in the guidelines.

Writing the recommendations and their rationale
After careful weighing of the summary of judgements, the same teams of two members of the working group drafted 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 was rated 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. Judgements for individual evidence-to-decision domains could change based on these discussion and arguments provided. 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 material of each guideline.

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 summarizes the research evidence for the items in the summary of judgement tables. (13, 14). In addition, expert opinion and aspects relevant to communicate to the reader regarding the intervention or recommendation could 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 it accordingly to produce the final guideline.

5. External review and feedback

The members of the IWGDF Editorial Board met online and in person on several occasions to thoroughly review each of the guideline chapters, which were then revised by the working groups based on this editorial review. The working groups then sent the guideline to the panel of independent international experts and people with lived experience for their critical review. The working group subsequently revised the document further based on these comments, after which the IWGDF Editorial Board did a final review of the recommendations and the rationale provided.

TIME INVESTMENT, EVALUATION AND UPDATING

The 2023 guideline development process for the seven guidelines developed took an estimated 10 years full-time working hour equivalent, involving working group and editorial board meetings, training, screening and assessment of the literature, completing tables, and writing and review of all documents. The 2023 process for guideline development will be evaluated a few months after publication of the guidelines within the IWGDF editorial board. Both the content, the process and methodology used will be evaluated and if needed, improvements or changes for the next round of guideline development will be defined. We will update each guideline and systematic review again in four years (2027).

CONCLUDING REMARKS

With the worldwide diabetes epidemic, it is now more imperative than ever that appropriate action be taken to ensure access to quality care for all people with diabetes, regardless of their age, geographic location, economic or social status. The IWGDF Guidelines on the prevention and management of diabetes-related foot disease are the result of a rather unique process that over 24 years has become more and more founded in a strong evidence base, with procedures to guarantee consistency, transparency and independency. The evidence base for how to help prevent and optimally manage diabetes-related foot disease is progressively growing, but it remains a challenge how to use this data to optimize outcomes in different healthcare systems, in countries with different resources and different cultures. The IWGDF hopes to see an increase in global awareness of diabetes-related foot disease and aims to stimulate this process of transforming global guidelines to local guidelines, leading to improved foot care throughout the world. Supported by limited published evidence of improved outcomes associated with using these IWGDF Guidelines (9, 29-33), we believe that implementation of the 2023 IWGDF Guidelines' recommendations will result in improved prevention and management of foot disease in people with diabetes and a subsequent worldwide reduction in the patient, the economic and societal burden caused by diabetes-related foot disease.

CONFLICT OF INTEREST

Production of the 2023 IWGDF Guidelines was supported by unrestricted grants from: Advanced Oxygen Therapy Inc., Essity, Mölnlycke, Reapplix, and Urgo Medical. These sponsors did not have any communication related to the systematic reviews of the literature or related to the guidelines with working group members during the writing of the guidelines, and have not seen any guideline or guideline-related document before publication.

Full conflict of interest statements of all authors can be found online at *www.iwgdfguidelines.org*.

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