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SUPPLEMENT ARTICLE

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Diabetic foot disease: "The Times They are A Changin' "

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Abstract

Diabetic foot disease greatly impacts both affected patients and society, but remains the "Cinderella" of diabetes-related complications. However, recent progress in research and guideline development have led to increased awareness of the problem and improved clinical outcomes. Thus, it is time for a shift in global perception of this increasingly prevalent problem. In this special issue, we present 7 up-to-date clinical guidelines and 10 systematic reviews developed by the International Working Group on the Diabetic Foot, together with 17 informative and stimulating related papers. These guidelines offer new recommendations on ulcer classification, diagnosis of infection severity, and vascular assessment, to assist in ulcer risk stratification, diagnosis and interdisciplinary communication. Key developments include providing guidance on methodological assessment of research papers; expanding the evidence base for ulcer treatment by the use of wound products and offloading treatment and suggestions for improving ulcer prevention through technological advances in patient monitoring of risk factors and footwear. The 17 invited papers discuss related topics ranging from stem cell research to patient psychology and describe the way forward in diabetic foot care. While there is much more to learn, the new knowledge of underlying pathways, advancements in diagnosis, treatment and prevention presented in this supplement should help improve outcomes and reduce the great and growing burden of diabetic foot disease.

KEYWORDS

clinical guidelines, diabetic foot, diagnosis, prevention, ulcer healing

Diabetic foot disease ranks 10th globally among diseases that pose the heaviest burden on patients and society.[1] During their lifetime, up to 30% of the people with diabetes will develop a foot ulcer,[2] and every 20 seconds someone in the world has an amputation of (part of) the leg because of diabetes.[3] Despite these grave statistics, foot disease is widely considered the "Cinderella" of diabetes-related complications, given the relatively limited attention it receives, both in clinical practice and research, compared to other complications of the disease. But, to quote Bob Dylan, "the times they are a-changin,"[4] interest in this common, costly, complex and challenging area of medicine has clearly been growing in recent decades. We who work in this field believe it is time for a shift in the perception on diabetic foot disease to a more positive one, as it looks like the prince has a footpath to his Cinderella. We hope you

Editorial for DMRR special issue on diabetic foot disease.

will "please heed the call"[4] and be stimulated and enlightened by the new information highlighted by this special issue in *Diabetes Metabolism in Research and Reviews* (DMRR).

The issue features seven guidelines, 10 systematic reviews and two other supporting documents from the International Working Group on the Diabetic Foot (IWGDF). Supplementing these documents are 17 invited papers on related, important and exciting topics. This wealth of knowledge is the result of close collaboration and tireless efforts by more than 100 dedicated experts worldwide from many different disciplines. The IWGDF started this unique initiative more than 20 years ago and the resulting guidelines, with translations into more than 25 languages (www.iwgdfguidelines.org), have had a major impact on diabetic foot care worldwide. Although the grim statistics on diabetic foot disease and its consequences can be depressing, the good news is that the number of lower extremity amputations among persons with diabetes has dropped substantially in the last decades, illustrating the progress made.[5,6]

Optimally managing diabetic foot disease has been a challenge to clinicians and researchers for many years, due to its complex multifactorial aetiology, lack of adequate tools to study the underlying pathology, and the need for developing closely interacting interdisciplinary teams. The 2019 IWGDF guidelines and systematic reviews include concrete and practical methods to better diagnose, treat and prevent diabetic foot disease, by employing a structured and comprehensive approach. The IWGDF guideline on ulcer classification helps guide a clinician to systematically evaluate a patient with a foot ulcer and facilitates interdisciplinary communication.[7] When the clinician diagnoses a foot ulcer as infected, the infection guidelines provide a clear, updated scheme on how to assess infection severity, thereby aiding clinical management.[8] If peripheral artery disease (PAD) is suspected, the PAD guideline provides a structure for further vascular assessment.[9] However, diagnosing PAD and assessing its severity is still a challenge and better techniques are needed.[10] These data on the wound, infection severity and vascular status are combined in the WIfI classification that predicts risk of amputation and potential benefit of a revascularization procedure.

Although we have seen major developments, restoring adequate blood flow to the foot in patients with distal and diffuse PAD remains a challenge.[11] Recent studies have provided a clearer understanding of the complex interaction of bone marrow, stem cells, growth factors and vascular repair.[12] Interestingly, the presence of neuropathy seems to affect the bone marrow of people with diabetes, resulting in poor stem cell mobilization.[12] The insights provided by these studies now need to be translated into clinical practice.

Several landmark studies have expanded the evidence base for foot ulcer treatment. These include reports that demonstrate an increased potential of specific wound products for healing neuroischemic and hard-to-heal diabetic foot ulcers.[13-15] Additionally, recent meta-analyses strengthen the recommendation for using non-removable offloading interventions for healing neuropathic plantar foot ulcers.[16] More complicated, as well as non-plantar, foot ulcers also require offloading, and the IWGDF offloading guideline contains new recommendations for these, summarized in a simple to use offloading diagram.[16]

There are fewer studies of prevention of foot ulcers than of their treatment, but a recent meta-analysis provides data on determining which patients are at highest risk.[17] The 2019 prevention guideline offers an updated risk stratification scheme to help tailor prevention to the individual patient,[18] but to improve outcomes we need further precision to get the right treatment to the right patient at the right time.[19] This is particularly true after a patient heals a foot ulcer, as 40% of foot ulcers may recur in 12 months.[2] Technological advances in patient monitoring for early recognition of foot problems, in tracking physical activity and better understanding its role in ulcer development, and in design of therapeutic footwear hold promise in helping to relieve the burden of disease in high-risk patients.[20-22]

Other achievements demonstrate that research and guidelines on diabetic foot disease are now drawing the attention they deserve. Highly ranked journals have published-quality studies over the last 2 years.[13,14] Of the papers in the previous special issue on the diabetic foot in *DMRR* in 2016 (Volume 32, Suppl. 1), seven ranked in the top 10 of most cited papers for this journal in that year. We now have a multidisciplinary guideline on how to conduct and assess research in this field, based on a 21-item checklist that can help to improve the quality of future research.[23] We have continued to improve the methodological approach to writing the IWGDF guidelines, which may act as an example for guideline development in other fields.[24] Finally, the IWGDF guidelines have a unique platform for presentation at the International Symposium on the Diabetic Foot (www.diabeticfoot.nl). This four-day global conference held once every 4 years is often called the "Olympic games" of the diabetic foot, attracting 1500 professionals from 100 different countries.

We hope this short discussion illustrates the enormous progress made and the increased exposure and awareness for this important complication of diabetes. While Cinderella has made it to the ball (Figure 1), we know that "the present now will later be past",[4] and call for continued efforts to expand our knowledge even further. The newly acquired knowledge should be implemented in daily practice to further reduce the patient and societal burden of diabetic foot disease and we are already at work on the 2023 IWGDF guidelines!

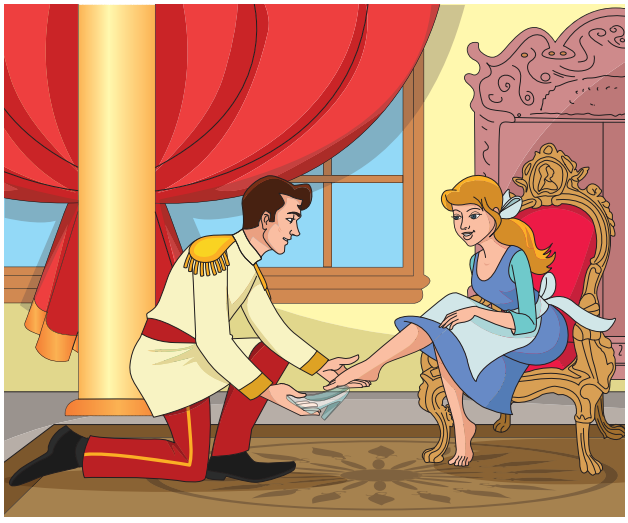

FIGURE 1 Finding the right shoe at the right time for the right person

AUTHOR CONTRIBUTIONS

S.A.B. drafted the manuscript. J.v.N., M.M.S., B.A.L. and N.A.C. critically reviewed and edited the manuscript. All authors have read and approved the final manuscript.

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