Guidelines on offloading foot ulcers in persons 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

Offloading mechanical tissue stress is arguably the most important of multiple interventions needed to heal diabetes-related foot ulcers. This is the 2023 International Working Group on the Diabetic Foot (IWGDF) evidence-based guideline on offloading interventions to promote healing of foot ulcers in persons with diabetes. It serves as an update of the 2019 IWGDF guideline.

We followed the GRADE approach by devising clinical questions and important outcomes in the PICO (Patient-Intervention-Control-Outcome) format, undertaking a systematic review and meta-analyses, developing summary of judgements tables and writing recommendations and rationales for each question. Each recommendation is based on the evidence found in the systematic review, expert opinion where evidence was not available, and a careful weighing of GRADE summary of judgement items including desirable and undesirable effects, certainty of evidence, patient values, resources required, cost effectiveness, equity, feasibility and acceptability.

For healing a neuropathic plantar forefoot or midfoot ulcer in a person with diabetes, use a non-removable knee-high offloading device as the first-choice offloading intervention. If contraindications or patient intolerance to non-removable offloading exist, consider using a removable knee-high or ankle-high offloading device as the second-choice offloading intervention. If no offloading devices are available, consider using appropriately fitting footwear combined with felted foam as the third-choice offloading intervention. If such non-surgical offloading treatment fails to heal a plantar forefoot ulcer, consider an Achilles tendon lengthening, metatarsal head resection, joint arthroplasty, or metatarsal osteotomy. For healing a neuropathic plantar or apex lesser digit ulcer secondary to flexbile toe deformity, use digital flexor tendon tenotomy. For healing rearfoot, non-plantar or ulcers complicated with infection or ischaemia, further recommendations have been outlined. All recommendations have been summarized in an offloading clinical pathway to help facilitate implementation of this guideline into clinical practice.

These offloading guideline recommendations should help healthcare professionals provide the best care and outcomes for persons with diabetes-related foot ulcers and reduce the person's risk of infection, hospitalisation and amputation.

LIST OF RECOMMENDATIONS

1a. In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer, use a non-removable knee-high offloading device as the first choice of offloading treatment to promote healing of the ulcer. (GRADE recommendation: Strong; Certainty of evidence: Moderate)

1b. In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer for which a non-removable knee-high offloading device is to be used, choose either a total contact cast or non-removable knee-high walker based upon local resources and the person's individual factors and acceptability. (Conditional; Moderate)

2. In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer for whom a non-removable knee-high offloading device is contraindicated or not tolerated, consider using either a removable knee-high or ankle-high offloading device as the second choice of offloading treatment to promote healing of the ulcer, and encourage the person to use the device during all weight-bearing activities. (Conditional; Low)

3. In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer, do not use, and educate the person not to use conventional footwear or standard therapeutic footwear over an offloading device, to promote healing of the ulcer. (Strong; Low)

4. In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer for which offloading devices are not available, consider using felted foam in combination with appropriately fitting footwear as the third choice of offloading treatment to promote healing of the ulcer. (Conditional; Very Low)

5a. In a person with diabetes and a neuropathic plantar metatarsal head ulcer for which non-surgical offloading treatment fails, consider using Achilles tendon lengthening in combination with an offloading device to promote and sustain healing of the ulcer. (Conditional; Moderate)

5b. In a person with diabetes and a neuropathic plantar metatarsal head ulcer for which non-surgical offloading treatment fails, consider using metatarsal head resection in combination with an offloading device to promote and sustain healing of the ulcer. (Conditional; Low)

5c. In a person with diabetes and a neuropathic hallux ulcer for which non-surgical offloading treatment fails, consider using joint arthroplasty in combination with an offloading device to promote and sustain healing of the ulcer. (Conditional; Low)

5d. In a person with diabetes and a neuropathic plantar ulcer on metatarsal heads 2-5 for which non-surgical offloading treatment fails, consider using a metatarsal osteotomy in combination with an offloading device to promote and sustain healing of the ulcer. (Conditional; Very low)

6. In a person with diabetes and a neuropathic plantar or apex ulcer on digits 2-5, secondary to a flexible toe deformity, use a digital flexor tenotomy to promote and sustain healing of the ulcer. (Strong; Moderate)

7. In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer with either mild infection or mild ischaemia, consider using a non-removable knee-high offloading device to promote healing of the ulcer. (Conditional; Low)

8. In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer with both mild infection and mild ischaemia, or with either moderate infection or moderate ischaemia, consider using a removable offloading device to promote healing of the ulcer. (Conditional; Low)
9. In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer with both moderate infection and moderate ischaemia, or with either severe infection or severe ischaemia, primarily address the infection and/or ischaemia, and use a removable offloading intervention over no offloading based on the person's individual factors, to promote healing of the ulcer. (Strong; Very low)
10. In a person with diabetes and a neuropathic plantar rearfoot ulcer, consider using a non-removable knee-high offloading device over a removable offloading device to promote healing of the ulcer. (Conditional; Very low)
11. In a person with diabetes and a non-plantar foot ulcer, use a removable offloading device, footwear modifications, toe spacers, orthoses, or digital flexor tenotomy, depending on the type and location of the foot ulcer, to promote healing of the ulcer. (Strong; Very low)
12. In a person with diabetes and a foot ulcer for which a knee-high or ankle-high offloading device is used, consider also using a shoe lift on the contralateral limb to improve the person's comfort and balance while walking in the device. (Conditional; Very low)

INTRODUCTION

Diabetes-related foot ulceration (DFU) is a leading cause of global disability, mortality and healthcare cost burdens (1-5). DFUs annually affect around 20 million people worldwide (2, 4), and without appropriate care, these foot ulcers can lead to infection, hospitalisation, amputation and death (1-5). Thus, healing of DFU is of paramount global importance (1-5).

The most common cause of DFU is high mechanical tissue stress on the foot of a person with diabetes and a loss of protective sensation (2, 6-8). Loss of protective sensation results from peripheral neuropathy and affects around half of all people with diabetes (2, 3, 9). Mechanical tissue stress is composed of plantar pressures and shear accumulated during repetitive cycles of weight-bearing activity (2, 6-8). Peripheral neuropathy can also lead to further changes in gait, foot deformity and soft tissue, all of which can further elevate mechanical tissue stress (7, 8, 10). Once a DFU forms, healing is chronically delayed if the area is not effectively offloaded (2, 6, 11).

Multiple interventions are typically required to effectively heal a DFU, including local wound management, management of any infection and peripheral artery disease, and offloading (12, 13). For this, a collaborative team approach is needed from different specialities, as well as an engaged and empowered patient (13). The first three of those interventions are covered in other parts of the International Working Group of the Diabetic Foot (IWGDF) Guidelines (13-16). In people with neuropathic DFUs, offloading has been found to be arguably the most important of these interventions for effective healing (11-13, 17, 18). There is a long-standing clinical tradition of using different offloading devices, footwear, surgery, and other offloading interventions to heal DFUs (6, 19-22). Previous IWGDF Guidelines have shown that sufficient evidence is available to support the use of non-removable knee-high offloading devices to heal plantar forefoot ulcers, over all other offloading interventions (11, 13, 19). It also identified that more high-quality studies are needed to confirm the promising effects of other offloading interventions to heal DFUs, in order to better inform practitioners about effective treatments (11, 19).

Over the past four years, a number of new trials have been performed in the area of offloading that add to the evidence base for treating people with DFU (23-29). Ulcer healing is still recognised as the key critically important outcome for people with DFU. However, other outcomes of importance to people with DFU are receiving more attention and also require careful consideration when developing recommendations in new offloading guidelines, such as effects on plantar pressure, weight-bearing activity, adherence, adverse effects, quality of life, and costs.

This new 2023 guideline aims to update the previous 2019 IWGDF guideline on offloading DFUs by following the best practice GRADE approach for guideline development to consider all new evidence and important outcomes so as to provide contemporary evidence-based international recommendations and rationale for offloading DFUs (19). This guideline is part of a series of new 2023 IWGDF guidelines including those on ulcer classification, peripheral artery disease, infection, wound healing, prevention, and Charcot foot (14-16, 30-32).

WHAT'S NEW

We have made several changes in this updated 2023 offloading guideline when compared to the previous 2019 offloading guideline. The main changes are the following:

- Used a more thorough GRADE methodological approach to the guideline and the systematic review supporting it, by performing meta-analyses, 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 clinical questions on the topics of ankle-high offloading devices, plantar digital foot ulcers, combination of interventions, educational and psychological interventions, and offloading for the contralateral limb.
- Added new important outcomes, including sustained healing, balance and the specific adverse effects/events of new lesions, falls, infections and amputations.
- Removable knee-high and ankle-high offloading devices are now grouped into one recommendation for second-choice offloading device treatment, rather than separate recommendations for second and third-choice treatment, respectively, effectively upgrading ankle-high offloading devices. This is based on added evidence in the last 4 years and the more thorough GRADE approach used.
- Added four new recommendations for specific surgical offloading interventions rather than grouping surgical interventions into one recommendation.
- Added a new recommendation on offloading for the contralateral limb.
- Updated the strength of recommendation in two recommendations and the certainty of evidence in nine recommendations based on using the more thorough GRADE approach.

METHODS

In this guideline we have followed the key steps of the GRADE evidence-to-decision approach, including: i) establishing a diverse expert panel to develop the guideline, ii) defining key clinical questions and important outcomes in the PICO-format (Patient-Intervention-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 (33, 34). 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 (35).

First, a multidisciplinary working group of independent international experts in offloading DFU (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 clinical practice and/or studying offloading DFU and published on the topic in the previous four years. The working group comprised members from exercise and human movement science, orthopaedic surgery, podiatry, prosthetics and orthotics, endocrinology, and rehabilitation science disciplines from Europe, North America, 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 six external clinical experts and two persons with lived DFU 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 patients so as to provide the most useful clinical information on offloading interventions to treat foot ulcers in people with diabetes. The working group classified the outcomes as critically important or important, aligning with international DFU standards (12, 36) or the expert opinion of the working group if standards did not exist.

Third, we systematically reviewed the literature and appraised all studies addressing the above agreed upon clinical questions. Each assessable outcome for each question was meta-analysed if appropriate, and had effect sizes and certainty of evidence (CoE) assessed using the Cochrane and GRADE Handbooks. 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 (11).

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 online supplemental information). The summary of judgement items assessed included desirable and undesirable effects, balance of effects, CoE, values, costs, cost-effectiveness, equity, acceptability and feasibility. Definitions for these items can be found in the summary of judgements table in the online supplemental information. After careful weighing up of the summary of judgements, the team proposed to the working group a direction, strength, CoE and wording of recommendation(s) and

rationale to address the question concerned. CoE 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 (33, 34).

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 online supplemental information.

Finally, all recommendations, with their rationales, were collated into a consultation (draft) guideline manuscript that was reviewed by the same clinical experts and persons with lived DFU 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.

CONFLICT OF INTEREST STATEMENT

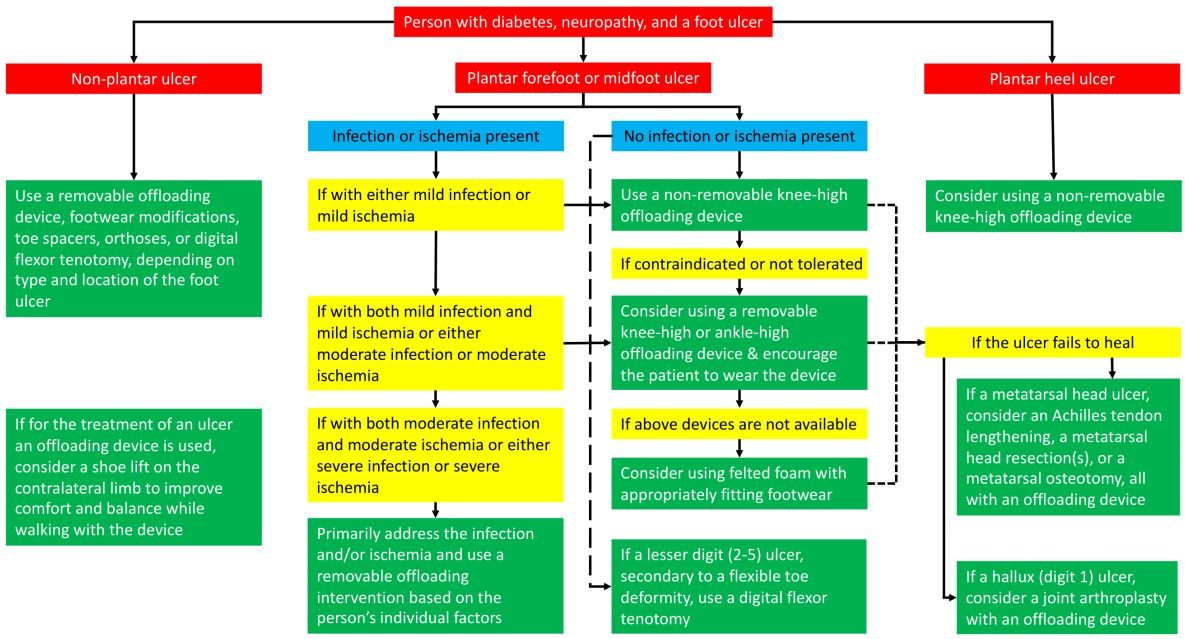
The offloading guideline working group is committed to developing trustworthy clinical practice guidelines through transparency and full disclosure by those participating in the process of guideline development. In order to prevent a major Conflict of Interest (COI) members of the guideline group were 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 involved in the guideline development received any payment or remuneration of any costs, except for travel and accommodation expenses when meeting in-person.

RESULTS

Overall, 14 clinical questions, each with up to 13 (critically) important outcomes, were finalised and addressed by this guideline. The accompanying systematic review identified 194 eligible studies, performed 35 meta-analyses and developed 17 summary of findings tables with 128 evidence statements to collectively address these questions (11). Based on the systematic review and expert opinion of the group, 20 summary of judgements tables were completed (see supplemental information) with 16 recommendations developed that addressed the clinical questions. A clinical pathway, using a diagrammatic overview and incorporating all 16 recommendations, summarises the recommended approach to offloading treatment to heal a DFU (Figure 1).

Note, different offloading interventions are mentioned in this guideline and they are discussed according to the following categories: offloading devices, footwear, other offloading techniques, and surgical offloading techniques. We refer readers to the glossary at the end of this guideline for the definitions and descriptions of each of these offloading interventions and categories. Furthermore, many of the offloading devices and interventions recommended require specific training, skills, and experience to apply properly. The specific skills and training are not described in the studies performed and may differ between centres and countries. We suggest that the person applying the offloading should be a properly trained healthcare professional who according to their national or regional standards has the knowledge, expertise, and skills necessary to treat DFU.

Figure 1: Flow diagram on the recommended offloading treatment for a person with diabetes and a foot ulcer



RECOMMENDATIONS

OFFLOADING DEVICES

Clinical question 1: In a person with diabetes and a plantar forefoot or midfoot ulcer, should non-removable offloading devices be used over removable offloading devices?

Recommendation 1a: In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer, use a non-removable knee-high offloading device as the first choice of offloading treatment to promote healing of the ulcer. (GRADE recommendation: Strong; CoE: Moderate)

Rationale: Non-removable knee-high offloading devices are devices that extend up the leg to a level just below the knee and cannot be readily removed by the patient, such as total contact casts (TCCs) and non-removable walkers (see Glossary for definitions). They should also incorporate a foot-device interface that helps reduce peak pressure at the ulcer location. For TCCs, foot-device interfaces are typically accommodated within the TCC method via the hand-moulding of the TCC to the shape of the plantar surface to redistribute pressure over the foot. For walkers, the foot-device interfaces typically consists of prefabricated (which may be of a modifiable modular design) or custom insoles. Additionally, felted foam may be added around the perimeter of the ulcer as part of the foot-device interface in order to further reduce pressure and promote healing of the ulcer. Lastly, we suggest persons use a walking aid if stability is compromised by wearing the device and risk of falling is high.

Our systematic review and meta-analyses identified 10 randomised controlled trials (RCTs) and 6 other controlled studies, with 4 non-controlled studies also adding relevant evidence for this question (11). We judged the overall desirable effects (benefits) to be moderate, based on our meta-analysis finding non-removable knee-high devices likely cause moderate increases in the critical outcome of proportions of ulcers healed compared to removable offloading devices (risk ratio (RR) 1.24, 95% CI 1.09-1.41; Moderate CoE) and may also cause moderate decreases in infections (RR 0.58, 0.34-0.99; Low CoE) and amputations (RR 0.53, 0.19-1.50; Very low CoE). Whereas we judged the overall undesirable effects (harms) to be small, we found non-removable knee-high devices may also cause moderate increases in new lesions compared to removable devices (RR 1.77, 0.89-3.54; Low CoE), small decreases in patient satisfaction (mean difference (MD) 0.21 lower on 10-point scale, 1.47 lower to 1.05 higher; Very low CoE) and little-to-no difference for falls (RR NA; Very low CoE). However, the evidence was very uncertain for falls as one other controlled study also noted two persons using bilateral TCCs discontinued use because of falls. Therefore, we judged the balance of effects clearly favours non-removable offloading devices over removable offloading devices, based on a moderate CoE for our critical outcome of ulcers healed.

Findings for other important surrogate outcomes for ulcers healed, such as adherence, activity and plantar pressure, provide potential rationale for this improved ulcers healed rate. The principal advantage of non-removable devices over removable offloading devices is enforced adherence, with our meta-analysis finding non-removable devices may cause large decreases in non-adherence (RR 0.07, 0.01-0.79; Very low CoE). Additionally, another review found some evidence that a reduction in weight-bearing activity may benefit ulcer healing (37), with our meta-analysis finding non-removable versus removable devices may cause small decreases in weight-bearing activity (MD 671 less daily steps, 95%

CI 1,680 less to 338 more; Very low CoE). Finally, plantar pressure reductions are well-known to be associated with improved healing, with our meta-analysis finding non-removable versus removable devices may cause small increases in plantar pressure (MD 39 kPa higher, 95% CI 7 less to 84 more; Very low CoE). However, we note that in our meta-analysis, we compared TCCs to removable knee-high walkers that can be made non-removable, and thus, in our judgement plantar pressure reductions in reality should be similar between non-removable and removable walkers (11). Therefore, in our judgement, non-removable compared to removable offloading devices result in similar plantar pressure reductions, small reductions in weight-bearing activity and large increases in adherence and hence heal more ulcers.

In terms of costs of initial treatment, our systematic review found non-removable compared to removable devices may cause small increases in initial treatment costs (MD €14.60 higher, 95% CI 7.68 lower to 136.88 higher; Very low CoE). However, conversely in terms of cost-effectiveness over the full duration of treatment, our systematic review found non-removable versus removable devices may be moderately more cost-effective (MD NA; N=2; n=2,053; Low CoE).

Additionally, although a lack of evidence was identified, our expert opinion judgement is that health equity is likely reduced with the use of non-removable devices compared to removable devices due to implementation of such interventions likely being limited in some low-, and middle-income countries by patients' ability to pay for them and access to healthcare professionals with the skills and resources to provide the interventions. Thus, based on this and multiple published surveys showing low use of non-removable offloading devices in clinical practice, and in particular TCCs (20, 22, 38, 39), we judged using non-removable offloading devices to be probably not equitable or acceptable to many patients and clinicians (20, 21). However, we judged implementation of such non-removable offloading as probably feasible, in the context of comparing to other removable devices, as most removable knee-high devices could readily be converted to a non-removable format using cast tape, straps or other methods.

In summary, based on our judgements that non-removable compared to removable devices should produce moderate desirable effects and small undesirable effects, and with moderate certainty of supporting evidence for critical outcomes, we consider the balance of effects strongly favour non-removable offloading devices. Furthermore, our judgements were that there should only be a small increase in initial costs for the resources required for non-removable devices, but over the treatment duration non-removable devices should be moderately more cost-effective and feasible to implement. However, in terms of the impact on health equity and acceptability, our judgements were removable devices may be favoured. Thus, after weighing up all important summary of judgement items we consider a strong recommendation in favour of non-removable offloading devices is justified and based on moderate CoE. However, in cases where the plantar ulcer is on the lesser digits and secondary to flexible toe deformity present, we refer to recommendation 6.

Clinical question 2: In a person with diabetes and a plantar forefoot or midfoot ulcer, should a total contact cast be used over another non-removable knee-high offloading device?

Recommendation 1b: In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer for which a non-removable knee-high offloading device is to be used, choose either a total contact cast or

non-removable knee-high walker based upon local resources and the person's individual factors and acceptability. (Conditional; Moderate)

Rationale: When choosing a non-removable knee-high offloading device, two modalities are generally used, a TCC or a prefabricated removable walker that is rendered non-removable. Both are used in clinical practice, which justifies the question regarding which is more effective and preferred for offloading plantar forefoot and midfoot DFUs.

Our systematic review and meta-analyses identified 5 RCTs and 1 other controlled study, with 6 non-controlled studies also adding relevant evidence for this question (11). We judged the overall desirable effects to be small, based on our meta-analysis finding TCCs likely make little-to-no difference compared to non-removable knee-high walkers in proportions of ulcers healed (RR 1.05, 95% CI: 0.92-1.19; Moderate CoE), infections (RR 1.00, 0.07-14.90; Low CoE) and amputations (RR 1.05, 0.07-15.68; Low CoE). Whereas we judged the overall undesirable effects to be small, TCCs may also cause small increases in plantar pressure compared to non-removable walkers (MD 39 kPa more; 95% CI: 5-73; Low CoE), large increases in new lesions (i.e. abrasions, ulcers; RR 2.04, 95% CI: 0.70-5.96; Low CoE), moderate increases in falls but the evidence is very uncertain (RR 1.47, 95% CI: 0.16-13.18; Very low CoE), and small decreases in patient satisfaction (MD -1.60 lower on 10-point scale, 2.91-0.29 lower; Low CoE). Therefore, we judged the balance of effects did not favour either TCCs or non-removable walkers, based on a moderate CoE for our critical outcome of ulcers healed.

In terms of initial costs, our meta-analysis found TCCs and non-removable walkers may cause little-to-no difference in initial costs (MD €0.77 lower, €11.62 lower to €10.09 higher; Very low CoE), but that TCCs were likely to be moderately less cost-effective over the treatment duration than non-removable walkers (MD €564.79 higher, 781.57-348.01 higher; Moderate CoE), with the results of one health technology assessment that could not be pooled also pointing in that direction (40). An additional consideration that has been reported in the literature which may impact provider preference between the two types of devices is application time. TCCs were found to take longer to apply and remove than a non-removable knee-high walker (MD 13 minutes longer, $p<0.001$; MD 4.8 minutes longer, $p<0.0001$, respectively) (41, 42).

Additionally, based on our expert opinion only as no evidence existed, we judged equity to probably be reduced with TCCs compared to non-removable walkers as they are likely to only be available to those willing to pay for ongoing TCC materials, have access to clinicians with the skills and resources to provide TCCs and may require more consultations than non-removable walkers. For similar reasons to those in Recommendation 1, we judged TCCs were probably less acceptable compared to non-removable walkers based on multiple published surveys finding they are not commonly used in clinical practice. Finally, we judged TCCs were probably not as feasible to implement as non-removable walkers for similar above cost, resource and skill reasons.

In summary, many of the important outcomes favour non-removable walkers, but TCC show slightly better effect sizes for some of the critically important outcomes (i.e. ulcers healed and amputation). Based on our judgements that TCCs compared to removable devices may produce small desirable effects and small undesirable effects, and with moderate certainty of supporting evidence for critical outcomes, we consider the balance of effects does not favour one device over the other. We have

therefore made a conditional recommendation that healthcare professionals may choose to use either a TCC or non-removable knee-high walker for people with a neuropathic plantar forefoot or midfoot ulcer and the certainty of the evidence is moderate. The choice between a TCC or non-removable knee-high walker should ultimately be dependent upon the resources available, technician skills, patient preferences, and the appropriateness of the device to fit the level of any foot deformity present (i.e. using a TCC with a severely deformed foot).

Clinical question 3: In a person with diabetes and a plantar forefoot or midfoot ulcer, should removable knee-high offloading devices be used over removable ankle-high offloading devices?

Recommendation 2: In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer for whom a non-removable knee-high offloading device is contraindicated or not tolerated, consider using either a removable knee-high or ankle-high offloading device as the second choice of offloading treatment to promote healing of the ulcer, and encourage the person to wear the device during all weight-bearing activities. (Conditional; Low)

Rationale: There are circumstances when a non-removable knee-high offloading device is contraindicated (e.g. heavily exudating wound or moderate infection) or not acceptable to the person with a plantar forefoot or midfoot ulcer. This can include when the person declines to wear the device or the person's circumstances do not support its use, such as unable to use the device as part of the person's job. A removable knee-high or ankle-high offloading device may be a solution to overcome these issues, such as removable knee-high walker or healing sandal, respectively (see Glossary for definitions) (11). Again, when using a removable offloading device an appropriate foot-device interface should be used and a walking aid should also be considered (see Recommendation 1 for details).

Our systematic review and meta-analyses identified 4 RCTs and 2 other controlled studies, with 7 non-controlled studies adding relevant evidence for this question (11). We judged the overall desirable effects to be small, based on our meta-analysis finding removable knee-high compared to removable ankle-high offloading devices may cause little-to-no difference in proportions of ulcers healed (RR 1.00, 95% CI 0.86-1.16; Low CoE) and infections (RR 1.00, 0.51-1.94; Low CoE), but small decreases in plantar pressure (MD 42 kPa lower, 95% CI 68-12 lower; Low CoE) and new lesions (RR 0.87, 0.42-1.82; Very low CoE), and moderate decreases in weight-bearing activity (MD 969 daily steps, 95% CI 2,004 lower to 67 higher; Very low CoE). Whereas, we also judged the overall undesirable effects to be small, finding removable knee-high may also cause small decreases in patient satisfaction compared to ankle-high devices (MD -0.6 lower on 10-point scale, 1.8 lower to 0.7 higher, Very low CoE), and moderate increases in non-adherence (RR 1.66, 95% CI 1.10-2.52; Low CoE), falls (RR 2.00, 95% CI 0.13-30.34; Very low CoE) and amputations (RR 1.96, 95% CI 0.52-7.34; Very low CoE), but the evidence is very uncertain. Therefore, we judged the balance of effects did not favour either removable knee-high or removable ankle-high offloading devices, based on a low CoE for our critical outcome of ulcers healed.

Interestingly, the evidence to support either the use of knee-high or ankle high devices for other important surrogate outcomes for ulcers healed, including plantar pressure reduction, weight bearing activity, and adherence, is inconsistent. Our meta-analysis indicates that knee-high devices reduce more plantar pressure and weight-bearing activity, but also reduce adherence compared to ankle-high devices.

The lower levels of adherence could explain why the mechanistic effects of a reduction in plantar pressure and weight bearing activity observed in knee-high devices does not lead to an improvement in ulcer healing rates. If people with a plantar forefoot or midfoot ulcers can be encouraged to wear a knee-high device, then given the observed reduction in plantar pressure and activity this may translate into better ulcer healing rates compared to an ankle-high device.

One RCT (11) found one-off material costs for knee-high devices were higher than for ankle-high devices (MD NA; US$150-200 v $25-75; p=NR; Very low CoE). However, one large cost-effectiveness analysis (40), using evidence from several trials and expert opinion, found knee-high devices to be more cost-effective than removable ankle-high devices (MD NA; $1,629 v $1,934; p=NR; Low CoE). However, the variety of different types of devices included in the intervention and comparator groups increases the uncertainty around the cost effectiveness of individual devices.

Additionally, based on our expert opinion only as no evidence existed, we judged there would probably be no impact on equity as there is a balance between costs and cost-effectiveness between removable knee-high and ankle-high devices, they are likely similarly available in low-, middle- and high-income countries and the clinical skills to apply both devices is also similar. However, we judged knee-high devices were probably less acceptable over ankle-high devices due to the slightly lower participant satisfaction or acceptability of knee-high devices and multiple published surveys of clinical practice suggested the healthcare professional's acceptability to using removable knee-high devices is also slightly lower than ankle-high devices (20, 21). Finally, we judged removable knee-high devices were probably as feasible to implement as removable ankle-high devices based on our expert opinion.

In summary, based on our judgements that removable knee-high devices compared to removable ankle-high devices may produce small desirable effects and small undesirable effects, and with low certainty of supporting evidence for critical outcomes, we consider the balance of effects does not favour one device over the other. We have therefore made a conditional recommendation that healthcare professionals should use a person-centred approach to prescribing either a knee-high or ankle-high offloading device, taking into consideration offloading capacity and adherence levels to wearing the device. A device with less pressure reduction worn more regularly may be equally or more effective at healing a plantar forefoot or midfoot ulcer than a device with high levels of pressure reduction worn less frequently. Thus, people should be educated on the benefit of adherence to using a removable offloading device during all weight-bearing activity to improve the effectiveness of the device to heal their ulcer.

Please note, this means in contrast to the 2019 IWGDF guideline, removable knee-high and ankle-high offloading devices are now grouped into one recommendation for second-choice of offloading treatment, rather than separate recommendations for second and third-choice treatment, respectively, as in 2019. Effectively that means an upgrade for ankle-high offloading devices to second-choice of offloading treatment, and is based on the current available evidence as well as on analysis and interpretation using the more thorough GRADE approach.

Clinical question 4: In a person with diabetes and a plantar forefoot or midfoot ulcer, should removable above ankle-high offloading devices be used over removable below ankle-high offloading devices?

Recommendation: No recommendation made.

Rationale: Ankle-high offloading devices can range in height from above the ankle such as ankle-high walkers, to below the ankle such as postoperative healing shoes, and all are used in clinical practice for treating plantar forefoot and midfoot DFU (see Glossary for further definitions and examples).

We considered there was insufficient evidence to answer this question, based on our systematic review finding of no controlled studies that compared above ankle-high to below-ankle-high devices for the critical outcome of ulcers healed and most other important outcomes, such as weight-bearing activity, adherence, new lesions, falls, infections, amputations or costs. Furthermore, as ankle-high offloading has already been incorporated in an earlier recommendation, we considered there was limited priority to develop a specific recommendation on types of ankle-high offloading to address this specific question if it were to be based mainly on expert opinion.

Otherwise, there was some evidence from repeated measures studies on other important outcomes of plantar pressure, quality of life and balance. Studies compared a variety of different above ankle-high cast walkers to below ankle-high offloading devices which made specific comparisons challenging. Three repeated measures studies (11), found little-to-no difference in plantar pressure reduction between the two different height devices. One of these studies also found removable above ankle-high compared to below ankle-high devices may make little-to-no effect on balance. There is evidence from one repeated measures study (11) though, that found removable above ankle-high compared to below ankle-high devices may increase patient comfort. However, all the current research is limited to repeated measures studies in surrogate populations for people with DFU. Thus, a larger evidence base is needed on this clinical question in particular regarding the critical outcome of ulcers healed, before any recommendation can be made.

FOOTWEAR

Clinical question 5: In a person with diabetes and a plantar forefoot or midfoot ulcer, should footwear be used over offloading devices?

Recommendation 3: In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer, do not use, and educate the person not to use conventional footwear or standard therapeutic footwear over an offloading device, to promote healing of the ulcer. (Strong; Low)

Rationale: Conventional footwear is off-the-shelf footwear that does not have any intended therapeutic effect; whereas standard therapeutic footwear is off-the-shelf footwear with some intended therapeutic effect, such as extra-depth footwear, but is not custom-made footwear (see Glossary for more detail).

Unlike with offloading devices, all controlled studies that investigated conventional or standard therapeutic footwear did so as the comparator/control to another offloading intervention, such as an offloading device. Therefore, for our systematic review and meta-analysis we compared offloading device interventions to therapeutic footwear controls and have used this evidence to inform this clinical question.

Our systematic review and meta-analyses identified 5 RCTs for this question, with 5 non-controlled studies adding relevant evidence (11). We judged the overall desirable effects to be small for therapeutic footwear, based on our meta-analysis finding offloading devices may increase new lesions compared to therapeutic footwear (RR 1.60, 0.07-37.75; Very low CoE). Whereas, we judged the overall undesirable effects to be large for therapeutic footwear, finding offloading devices may moderately increase the proportions of ulcers healed compared to therapeutic footwear (RR 1.39, 95% CI 0.89-2.18; Low CoE), plus non-removable knee-high offloading devices had larger effects again on ulcers healed compared to therapeutic footwear (RR 1.98, 95% CI 0.99-3.93). Further, offloading devices may cause large decreases in plantar pressure (MD 239 kPa lower, 317-160 lower; Low CoE), infections (RR 0.15, 0.03-0.79; Low CoE) and amputations (RR 0.18, 0.01-3.56; Very low CoE) compared to therapeutic footwear, and little-to-no difference in patient satisfaction (MD 2.8 of 100mm VAS lower, 10.6 lower to 4.9 higher; Very low CoE). Therefore, we judged the balance of effects to strongly favour offloading devices over therapeutic footwear based on a low CoE for our critical outcome of ulcers healed.

We found offloading devices may cause small increases in material costs compared to therapeutic footwear ($20 vs $7; Very low CoE), but one large cost-effectiveness analysis (40), found offloading devices compared to therapeutic footwear likely causes large increases in cost-effectiveness (MD NA; $877 v $1934; Moderate CoE).

Additionally, based on our expert opinion only as no evidence existed, we judged therapeutic footwear would probably increase health equity compared to offloading devices as footwear is more likely to be available and cheaper in low-income countries. Further, we considered therapeutic footwear would be probably acceptable and feasible in most places.

In summary, based on our judgements that therapeutic footwear compared to offloading devices may produce small desirable effects but large undesirable effects, and with low certainty of supporting evidence for critical outcomes, we consider the balance of effects does not favour therapeutic footwear and instead favours offloading devices. Thus, we

we have made a strong recommendation against the use of conventional or standard therapeutic footwear for treating plantar forefoot or midfoot DFUs in preference of a wide range of options for offloading devices, when these are available. This recommendation is based on low CoE.

OTHER OFFLOADING INTERVENTIONS

Clinical question 6: In a person with diabetes and a plantar forefoot or midfoot ulcer, should any other non-surgical offloading intervention be used over another non-surgical offloading intervention?

Recommendation 4: In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer for which offloading devices are not available, consider using felted foam in combination with appropriately fitting footwear as the third choice of offloading treatment to promote healing of the ulcer. (Conditional; Very Low)

Rationale: Other offloading interventions are defined as any intervention undertaken with the intention of relieving mechanical stress from a specific region of the foot, that is not an offloading device, footwear, or surgical procedure. Despite many practice surveys reporting high use of other offloading interventions, such as felted foam and wheelchairs (21, 22), there has been limited evidence to support other offloading interventions to heal DFUs (11). Our systematic review identified 3 RCTs and 2 other controlled studies, with 5 non-controlled studies adding relevant evidence for this question (11). The other offloading intervention with most controlled studies was felted foam, however wheelchairs, botulinum toxin injections, gait retraining and foam wound dressings also had controlled studies (11). We note no controlled studies were identified for offloading interventions such as bedrest, crutches, callus debridement, foot-related exercises, or knee scooters.

Felted foam was the only intervention defined as an other offloading intervention for which our systematic review found any potentially favourable evidence on the critical outcome of healed ulcers. Our systematic review found wheelchairs were not favoured over wheelchairs in combination with removable offloading devices as they may cause moderate decreases in the proportions of ulcers healed (RR 0.77, 0.59-1.00; Low CoE) and large increases in amputations (RR 12.24, 95% CI 0.69 to 216.92; Very low CoE). Further, whilst our systematic review found gait retraining, botulinum toxin injections, and foam wound dressings may reduce plantar pressure based on (very) low CoE, we considered plantar pressure evidence alone was not sufficient to justify completing summary of judgements or recommendations. Therefore, we only performed summary of judgements for this clinical question on felted foam, and specifically the use of felted foam in combination with a removable ankle-high offloading device compared to the removable ankle-high offloading device alone.

Our systematic review and meta-analyses identified 2 RCTs and one other controlled study on felted foam (11). We judged the desirable effects for felted foam with removable ankle-high offloading device intervention compared to the device alone to be small, based on our systematic review finding little-to-no difference in the proportions of ulcers healed (RR 0.97, 0.82-1.19; Very low CoE), but moderate decreases in plantar pressure outcomes (MD 98 kPa lower, 151-45 lower; Very low CoE). Furthermore, we judged the undesirable effects to be trivial, finding the intervention may result in little-to-no difference in new lesions (RR 1.00, 0.07-14.85; Very low COE) and infections (RR 1.07, 0.41-2.77; Very low CoE). Therefore, we judged the balance of effects probably favours the felted foam with a removable ankle-high offloading device intervention over the device alone, however, based on very low CoE. We also note the systematic review found whether the felted foam is applied to the foot or the device may make little-to-no difference.

In terms of the other important judgements for this felted foam intervention, there was no evidence identified in our systematic review for resources required, cost-effectiveness or health equity. However, based on our expert opinion, we judged the additional resources required for the use of felted foam to be negligible. While felted foam is an additional cost and requires frequent replacement (at least weekly), from an offloading treatment perspective we judged that felted foam is inexpensive to purchase, in low-, middle- and high-income countries, and requires little additional skill to apply. For the same reasons, we judged health equity to be probably increased. Multiple published surveys of offloading practices around the world show the use of felted foam to be high in many countries (21,

22). Therefore, we also considered felted foam to have a positive impact on acceptability and feasibility to implement.

Unfortunately, as identified in clinical questions 1-5, offloading devices are not always feasible to use in all parts of the world due to lack of availability, whereas felted foam and footwear are typically available everywhere. Therefore, we also considered whether felted foam with appropriately fitting footwear may also be an acceptable option for offloading DFU when no offloading devices are available. Whilst our systematic review identified no evidence, based on our expert opinion we considered that felted foam used with appropriately fitting footwear compared to footwear alone may promote healing of the ulcer in a similar mechanistic manner to how felted foam used in combination with ankle-high offloading devices may promote healing over the use of the device alone. We define appropriately fitting footwear as footwear that provides sufficient room for the patients' foot shape and the additional felted foam. Thus, this recommendation would enable some form of offloading treatment for people with a plantar forefoot or midfoot DFU when offloading devices as recommended in Recommendation 1 to 3 are not available. However, we stress that this would be a last resort non-surgical offloading option and that felted foam should not be used as a single treatment modality.

In summary, we consider a conditional recommendation in favour of the intervention of felted foam in combination with a removable ankle-high device compared to a removable ankle-high device alone is justified, based on a probably favourable balance of effects, resources required, equity, acceptability and feasibility. This conditional recommendation is based on very low CoE, and thus, not all patients will be best served by this recommendation, so there is a need to carefully consider the patients circumstances, preferences and values when considering implementing this recommendation. However, because ankle-high offloading devices already have a conditional recommendation as a second-choice offloading treatment (see Recommendation 2), and based on the evidence probably favouring the added use of felted foam for this clinical question, we have incorporated the felted foam consideration under the foot-device interface consideration as outlined in Recommendations 1 and 2. For this Recommendation 4 though, and based on our expert opinion, we have recommended to consider only when offloading devices are not available, that felted foam may be used in combination with appropriately fitting footwear, as a third choice of non-surgical offloading treatment to promote healing of the ulcer.

SURGICAL OFFLOADING INTERVENTIONS

Clinical question 7: In a person with diabetes and a plantar forefoot or midfoot ulcer, should any surgical offloading intervention be used over other offloading interventions?

Recommendation 5a: In a person with diabetes and a neuropathic plantar metatarsal head ulcer for which non-surgical offloading treatment fails, consider using Achilles tendon lengthening in combination with an offloading device to promote and sustain healing of the ulcer. (Conditional; Moderate)

Recommendation 5b: In a person with diabetes and a neuropathic plantar metatarsal head ulcer for which non-surgical offloading treatment fails, consider using metatarsal head resection in combination with an offloading device to promote and sustain healing of the ulcer. (Conditional; Low)

Recommendation 5c: In a person with diabetes and a neuropathic hallux ulcer for which non-surgical offloading treatment fails, consider using joint arthroplasty in combination with an offloading device to promote and sustain healing of the ulcer. (Conditional; Low)

Recommendation 5d: In a person with diabetes and a neuropathic plantar ulcer on metatarsal heads 2-5 for which non-surgical offloading treatment fails, consider using a metatarsal osteotomy in combination with an offloading device to promote and sustain healing of the ulcer. (Conditional; Very low)

Rationale: Surgical offloading interventions have been traditionally used for plantar forefoot and midfoot DFU that are considered hard-to-heal with non-surgical offloading interventions (11). These surgical interventions change the structure and function of the foot and therefore provide a more permanent offloading solution for areas of elevated mechanical tissue stress, even when the patient is not adherent to using an offloading device. However, surgical offloading also potentially comes with increased risk of complications (11).

Regarding Achilles tendon lengthening, we identified 2 RCTs and 5 non-controlled studies (11). We judged the overall desirable effects to be moderate, based on systematic review finding Achilles tendon lengthening in combination with a TCC likely causes small increases in the proportion of ulcers healed compared to a TCC alone (RR 1.10, 0.96-1.27; Moderate CoE), and may cause large increases in sustained healing once healed (RR 3.41, 1.42-8.18, Moderate CoE), large decreases in forefoot plantar pressure (MD 218 kPa lower, 410-26 lower; Low CoE), moderate decreases in new lesions (RR 0.71, 0.22-2.28; Very low CoE) and large decreases in amputations (RR 0.35, 0.01-8.38; Very low CoE). Whereas we judged the overall undesirable effects as moderate, with large increases in new rearfoot ulcers (RR 9.56, 0.54-170.46; Moderate CoE), falls (RR 5.31, 0.27-106.46; Low CoE) and infections (RR 3.19, 0.13-75.43; Low CoE). Thus, we judged our balance of effects probably favours Achilles tendon lengthening in combination with TCC over TCCs alone only if non-surgical offloading treatment has already failed.

For resources required, cost-effectiveness, equity, acceptability and feasibility, our systematic review identified no supporting evidence and hence our judgments were based on expert opinion. We judged the resources required as moderate, as the Achilles tendon lengthening intervention requires additional resources such as operating theatres, skilled surgeons, hardware, post-operative care, etc. Conversely, we judged cost-effectiveness probably favours the intervention, based on a moderate desirable effect outweighing the initial moderate resources required. We judged the impact of health equity as probably reduced as the Achilles tendon lengthening intervention is unlikely to be available everywhere in the world, is probably not acceptable to some patients and healthcare professionals, except if non-surgical offloading interventions consistently fail, and the feasibility of Achilles tendon lengthening may vary based on the local resources available.

In summary, we consider a conditional recommendation in favour of the Achilles tendon lengthening in combination with an offloading device compared to an offloading device alone is justified when non-surgical offloading interventions have failed based on moderate desirable effects and despite moderate undesirable effects. If non-surgical treatment has already failed, the balance of effects at that point may favour the surgical intervention. We judged the CoE for this recommendation to be moderate based on

finding that the critical outcomes of ulcers healed and sustained healing have moderate certainty of supporting evidence.

Regarding metatarsal head (MTH) resection, we identified one RCT, 2 other controlled studies and 7 non-controlled studies. We judged the desirable effects to be moderate, based on our meta-analysis finding MTH resection in combination with offloading devices compared to offloading devices alone may cause moderate increases in proportion of ulcers healed (RR 1.33, 1.12-1.58; Low CoE) and sustained healing (RR 1.21, 1.09-1.35; Low CoE), moderate decreases in infections (RR 0.55, 0.25-1.19; Very low CoE) and amputations (RR 0.68, 0.28-1.66; Very low CoE), and large decreases in plantar pressure (MD 511 kPa lower, 607-415 lower; Very low CoE). We judged the undesirable effects to be small, based on moderate increases in new transfer lesions (RR 1.50, 0.46-4.86; Very low CoE) and large decreases in weight-bearing activity (MD 2.2 lower on 4-point scale, 3.2-1.2 lower; Low CoE). Although some persons may experience improved wound healing in association with a reduction in activity, excessively large reductions are likely to yield declines in individuals' general health. We also emphasize that the indication for MTH resection may include management of infection, such as osteomyelitis or joint infection, as well as surgical offloading of a prominent metatarsal head. This makes the comparison to conservative treatment difficult as the magnitude of the undesirable effect may also vary due to the joint in question. It is expected that there is a higher risk of undesirable effects in the first metatarsal phalangeal joint than in the second to fifth metatarsals. Overall, we judged our balance of effects probably favours MTH resection in combination with an offloading device over a device alone.

We found MTH resection may also cause moderate decreases in quality of life during healing (MD 1.2 lower on 4-point discomfort scale, 2.1-0.3 lower; Low CoE) but moderate increases in quality of life after healing (MD 2.5 higher on 10-point global satisfaction scale, 0.4-4.6 higher; Low CoE), and small increases in cost-effectiveness, but evidence is very uncertain. Based primarily on expert opinion, we considered equity and acceptability to be probably reduced, and the and the feasibility of the intervention may vary based on the local resources available.

In summary, we consider a conditional recommendation in favour of the MTH resection in combination with an offloading device or footwear when non-surgical offloading interventions have failed, and the CoE for this recommendation as low.

As both Achilles tendon lengthening and MTH resection have a conditional recommendation in favor of the intervention to treat a neuropathic plantar MTH ulcer, the question arises as to when to perform one over the other. Based on our expert opinion, Achilles tendon lengthening is indicated in the case of someone with such an ulcer and an equinus position of the foot. When osteomyelitis of the metatarsal head or infection in the metatarsophalangeal (MTP) joint is identified, as proven by either Magnetic Resonance Imaging (MRI) or the ulcer permitting a probe to reach the bone or joint (15), MTH resection or joint arthroplasty should be considered. In the case of previous MTH resection or osteotomies and a transfer ulcer to another metatarsal head, we suggest either an Achilles tendon lengthening alone, or in combination with an MTH resection when infection or osteomyelitis is identified.

Regarding joint arthroplasty, we identified 2 controlled studies and 4 non-controlled studies. We judged the desirable effects to be moderate, based on our meta-analysis finding metatarsal-phalangeal joint

arthroplasty in combination with a non-removable offloading device may cause a small increase in proportion of ulcers healed over devices alone (RR 1.07, 0.89-1.28; Low CoE) and sustained healing (RR 1.19, 0.67-2.12; Low CoE), and large decreases in amputations (RR 0.48, 0.05-4.85; Very low CoE). Whereas, we judged the undesirable effects to be small, based on little-to-no differences for infections (RR 0.95, 0.44-2.05; Low CoE) and new lesions (RR NA; Very low CoE), but the evidence is very uncertain as zero new lesions were reported when in our expert opinion we would expect some new lesions and other outcomes such as falls weren't reported. Thus, we judged the balance of effects probably favours joint arthroplasty in combination with a non-removable offloading device over a device alone if non-surgical offloading treatment fails. We also emphasize that the indication for joint arthroplasty is for a hallux ulcer with limited range of motion of the first metatarsal-phalangeal joint. In case of other deformities with a hallux ulcer, joint arthroplasty may not be indicated. Otherwise, we consider based on only expert opinion the costs to be moderate, equity probably reduced, low acceptability and the feasibility of the intervention may vary based on the local resources available.

In summary, we consider a conditional recommendation in favour of the metatarsal-phalangeal joint arthroplasty in combination with a non-removable offloading device when non-surgical offloading interventions have failed, and the CoE for this recommendation as low based on the low CoE for the critical outcomes of ulcers healed and sustained healing.

Regarding metatarsal osteotomy, we identified one controlled study and 5 non-controlled studies. We judged the desirable effects to be moderate, based on our meta-analysis finding metatarsal osteotomy in combination with a non-removable offloading device may cause shorter time-to-healing (RR NA; 51.3 vs 159.3 days time-to-healing; p=0.004; Low CoE), large decreases in amputations (RR 0.17, 0.02-1.24; Very low CoE), and moderate decreases in plantar pressure (MD 136 kPa lower, 144-128 lower; Very low CoE) over non-surgical care (11). Whereas, we judged the undesirable effects to be small, based on our systematic review finding little-to-no difference for sustained healing, and very uncertain effects on infections and new lesions, based on only non-controlled studies. We therefore judged the desirable effects as moderate and the undesirable effect as small, and thus a balance of effects probably in favour of the metatarsal osteotomy. Furthermore, we considered the costs as moderate, equity and acceptability probably reduced, and the feasibility of the intervention may vary based on the local resources available.

In summary, we consider a conditional recommendation in favour of the metatarsal osteotomy over conservative care, and the CoE for this recommendation as low based on the low CoE for the critical outcomes of ulcers healed. However, we highlight this conditional recommendation is limited to metatarsals 2-5. This is due in our expert opinion to the increased risk of undesirable effects when performing the osteotomy on the first ray. Additionally, in case of infection in the distal part of the metatarsals or in the MTP joint, consider using a MTH resection instead (recommendation 5b). Otherwise please refer to the comments in Recommendation 5b regarding the combined use of the Achilles tendon lengthening combined with MTP joint resection or metatarsal osteotomy.

We decided not to put forward a recommendation for the use of joint arthrodesis, based on the limited available evidence. The only controlled study regarding joint arthrodesis in combination with offloading devices compared to offloading devices alone is based on a population of people with Charcot midfoot

deformity and DFUs and that study found little-to-no difference in healing (43). That paper is included in the guideline on the Charcot foot (32), and hence, we have considered a recommendation was not justified.

Overall, there is some evidence to support surgical offloading in combination with offloading devices over offloading devices alone to improve ulcers healed and time-to-healing of plantar forefoot or midfoot DFU that prove to be hard-to-heal with non-surgical treatment, and much more evidence for sustained healing. However, the number of controlled studies for each surgical intervention is still low, the quality of these studies is generally low and the comparator is often not a gold standard treatment, and therefore we consider the CoE for most of the above recommendations to be low. For these and other reasons, we rate the strength of these recommendations as conditional, and recommend these interventions only when non-surgical offloading treatment fails in healing the foot ulcer. We also highlight that surgical offloading is contraindicated when severe ischaemia is present.

Recommendation 6: In a person with diabetes and a neuropathic plantar or apex ulcer on digits 2-5, secondary to a flexible toe deformity, use a digital flexor tenotomy to promote and sustain healing of the ulcer. (Strong; Moderate)

Rationale: A tenotomy of the flexor tendon of digits of the foot has been used to treat plantar or apex ulcers on flexible claw or hammer toe deformities. The recommendation for a digital flexor tenotomy procedure is limited to digits 2-5, based on our expert opinion that ulcers on the first toe are instead likely caused by other deformities or by limited joint motion, which are conditions that may contribute to the non-healing of the ulcer if a digital flexor tenotomy would be performed on the first toe.

Our systematic review identified 1 RCT and 13 non-controlled studies (11). We judged the desirable effects to be moderate, based on our systematic review finding digital flexor tenotomies in combination with removable ankle-high offloading devices likely causes large increases in proportion of ulcers healed (RR 2.43, 1.05-5.59; Moderate CoE) and sustained healing (RR 2.52, 0.70-9.01; Moderate CoE), and may cause large decreases in infections (RR 0.33, 0.02-7.14; Low CoE) and plantar pressure at the ulcer site (MD 398 kPa lower, 524-28 lower; Low CoE) in comparison to devices alone. The non-controlled studies also showed an overall healing rate of 97% in a mean 29.5 days (44) for digital flexor tenotomy which further supported the intervention findings in the RCT. Whereas, we judged the undesirable effects to be small, based on our systematic review finding of zero transfer lesions in the RCT, but that digital flexor tenotomy caused small increases in transfer lesions in most non-controlled studies (23), and little-to-no difference in balance and amputations again based on zero events. We also found digital flexor tenotomies in combination with ankle-high devices may cause small increases in patient satisfaction compared to devices alone (7.7 vs 3.9 on 10cm VAS scale; p=NR; Very low CoE). Therefore, with moderate desirable and small undesirable effects, we judged the balance of effects to be in favour of the digital flexor tenotomy in combination with ankle-high offloading devices over devices alone.

Furthermore, based on our expert opinion, we judged any additional resources and costs required to be negligible to small, as the tenotomy is a relatively straightforward procedure that can be performed in an outpatient clinic. As such, it is a surgery that requires little additional resources, and may be cost-effective based on our findings on balance of effects in favour of digital flexor tenotomy and our

judgement that initial costs would be small. We furthermore judged equity to be probably increased based on our expert opinion that tenotomies have negligible to small additionally required costs, require little extra surgical skill and are readily available around the world. We also judged tenotomies to be probably acceptable to most people for the above reasons and feasible to implement.

In summary, we previously considered digital flexor tenotomy to be a promising intervention for people with hammertoes and recalcitrant lesser digital ulcers that failed non-surgical treatment. However, based on the outcomes from a recent RCT (23), we now consider a strong recommendation in favour of digital flexor tenotomy as a first line of treatment is justified for neuropathic plantar or apex ulcer on digits 2-5, secondary to a flexible toe deformity. This is based on the clear balance of effects in favour of tenotomies over conservative care, and the CoE for this recommendation is graded as moderate based on the moderate CoE for the critical outcomes of ulcers healed and sustained healing. However, when digital flexor tenotomies are not available, we refer to the offloading device recommendations for plantar ulcers (Recommendations 1-4) or non-plantar ulcers (Recommendation 9) for treating a neuropathic plantar or apex ulcer on digits 2-5.

OTHER ULCERS

Clinical question 8: In a person with diabetes and a plantar forefoot or midfoot ulcer complicated by infection or ischaemia, should any one offloading intervention be used over another offloading intervention?

Recommendation 7a: In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer with either mild infection or mild ischaemia, consider using a non-removable knee-high offloading device to promote healing of the ulcer. (Conditional; Low)

Recommendation 7b: In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer with both mild infection and mild ischaemia, or with either moderate infection or moderate ischaemia, consider using a removable offloading device to promote healing of the ulcer. (Conditional; Low)

Recommendation 7c: In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer with both moderate infection and moderate ischaemia, or with either severe infection or severe ischaemia, primarily address the infection and/or ischaemia, and use a removable offloading intervention over no offloading based on the person's individual factors to promote healing of the ulcer. (Strong; Very low)

Rationale: Many plantar ulcers seen in clinical practice are not purely neuropathic, but have some level of infection and/or ischaemia present. Due to the neuropathic origin and mechanical stress that often caused and continues to affect these ulcers, these infected and ischaemic ulcers still require some form of offloading treatment. However, healthcare professionals should be more cautious about what kind of offloading treatment to use if ulcers are complicated by infection or ischaemia. Although greater caution is warranted in selecting an appropriate means to offload the mechanical stress in these more complicated ulcers, the same arguments and indications for recommendations 1 to 6 are generally

applicable. Here, we will only report some specific aspects about the offloading treatment at different levels of infection and ischaemia, with data from our systematic review included.

Our systematic review identified one controlled study, supported by 3 non-controlled studies, that found non-removable knee-high devices versus removable devices may cause large increases in proportion of infected ulcers healed (adjusted OR 2.53, 1.19-5.35; Low CoE) (11). In our expert opinion, we consider such an outcome is likely in all plantar forefoot or midfoot DFUs complicated by either mild infection or mild ischaemia, or mild-to-moderate amounts of exudate (11). The improved healing is likely to be associated with increased levels of adherence for non-removable versus removable devices. It is possible that if removable devices were worn more frequently, there would be similar levels of healing between the devices. Furthermore, in our expert opinion, the presence of mild infection or mild ischaemia should not affect the resources required, cost-effectiveness, equity, acceptability and feasibility considerations for non-removable versus removable offloading devices as outlined in the rationale for Recommendations 1 and we refer the reader to those judgements. We do stress that when the ulcer is infected or ischaemic, it should be monitored more regularly via at least weekly visits to a healthcare professional, to enable the device to be removed and the ulcer and any infection checked. However, clearly more research is needed to investigate the use of non-removable knee-high devices compared to removable devices for healing a plantar forefoot or midfoot DFU complicated by either mild infection or mild ischaemia.

Non-removable offloading should not be used when both mild infection and mild ischaemia, moderate infection or ischaemia, or heavy exudate is present and these conditions require frequent inspection or wound care, potentially daily (11). Removable offloading devices can be considered for healing these ulcers, and we recommend any removable offloading device as per Recommendation 2, although note that one controlled study found removable knee-high devices may cause moderate increases in ulcers healed in people with infection compared to removable ankle-high devices (26). However, if the ulcer does not require daily inspection or wound care, but only removal of the device with certain indications (e.g. fever present) or otherwise at weekly clinic visits, a knee-high removable device may be rendered non-removable to promote adherence and efficacy. This should only be provided as long as the circumferential wrapping or other closure technique used can be removed and applied at any time, by a homecare professional or a trained partner.

If a neuropathic plantar forefoot or midfoot ulcer is complicated by both moderate infection and moderate ischaemia, or by severe infection or severe ischaemia, then the infection or ischaemia treatment should be planned first before determining the appropriate offloading intervention. This may mean the person remain fully non-weight-bearing during a period that the infection or ischaemia treatment prohibits the use of offloading. However, in cases where a person will be weight-bearing prior to resolution of the infection or severe ischaemia, the best offloading option that will work in conjunction with infection and/or ischaemia interventions should be implemented. As no evidence exists for offloading these severe infection or ischaemic complications, in our expert opinion, the choice of removable offloading intervention needs to consider a patient's individual factors, such as, their function, ambulatory status, and activity level. When the infection and ischaemia status improve, the recommendations for mild to moderate infection or ischaemia apply (Recommendations 7a and 7b), or, when the infection or ischaemia are resolved, the recommendations for non-complicated foot ulcers

apply (Recommendations 1- 6). Again, further research is needed to investigate the efficacy of offloading devices to heal these plantar DFU complicated by moderate-to-severe infection or ischaemia.

In summary, based on the lack of evidence for desirable and undesirable effects, patient preferences and costs, the strength of recommendations 7a-7b are conditional. However, we have made a strong recommendation for 7c based on our expert opinion that offloading compared to no offloading in these situations should provide a clear balance of effects in favour of offloading. The overall CoE for recommendations 7a-7b is low based on the limited controlled studies and very low for 7c that is only based on expert option that these plantar ulcers still require offloading for healing (11).

Clinical question 9: In a person with diabetes and a plantar digital ulcer, should any one offloading intervention be used over another offloading intervention?

Recommendation: No recommendation.

Rationale: We considered this question was not different enough from already existing questions 1 through 8 to assess the literature, write summary of judgements and write a specific recommendation for this question. Thus, we refer to earlier Recommendations 1 through 6 already addressing this question.

Clinical question 10: In a person with diabetes and a plantar rearfoot ulcer, should any one offloading intervention be used over another offloading intervention?

Recommendation 8: In a person with diabetes and a neuropathic plantar rearfoot ulcer, consider using a non-removable knee-high offloading device over a removable offloading device to promote healing of the ulcer. (Conditional; Very low)

Rationale: Neuropathic plantar rearfoot ulcers are less prevalent than forefoot ulcers (45), but are considered more of a challenge to offload and heal (11). However, there is little evidence available on offloading interventions to treat plantar rearfoot ulcers (11), and when studies were available, they did not specifically report outcomes for the subgroup of plantar rearfoot ulcers, such as in one large RCT, where 28% of rearfoot DFU were on the plantar surface (46).

Our systematic review and meta-analysis identified 1 RCT, 1 controlled study, and 5 non-controlled studies for this question (11). We judged the desirable effects to be moderate, based on our meta-analysis finding non-removable knee-high devices may cause large increases in plantar rearfoot ulcers healed compared to removable devices (RR 5.00, 0.30-83.69; Very low CoE), shorter time-to-ulcer healing (MD NA; 69 vs 107 days), and little-to-no difference in rearfoot plantar pressure (MD 20 kPa lower, 70 lower to 111 higher; Very low CoE), but the evidence is very uncertain. There was no data on other outcomes and thus we are reliant on our expert opinion judgement that undesirable effects may be small based on the evidence in Recommendation 1. Therefore, with moderate desirable and small undesirable effects, we judged the balance of effects to probably favour non-removable over removable offloading devices for plantar rearfoot ulcers, but based on a very low CoE for our critical outcome of ulcers healed. We do not intend to make a recommendation around the specific choice of non-

removable device (e.g. TCC or non-removable walker) to offload plantar rearfoot DFUs as there is insufficient evidence to support one over the other.

If a non-removable device is contraindicated, our meta-analysis found removable knee-high versus ankle-high offloading devices may cause large increases in proportions ulcers healed (RR 5.60, 0.87-36.22; Very low CoE), and small decreases in rearfoot plantar pressure (MD 36 kPa lower, 69-4 lower; Very low CoE), but the evidence is very uncertain. There were no data on the other important outcomes, such as weight-bearing activity, adherence, new lesions, falls, infections, quality of life, costs, cost-effectiveness, or balance for using offloading interventions to treat plantar rearfoot DFUs. We did not provide expert opinion on those outcomes, as we lack sufficient experience with treating rearfoot ulcers in people with diabetes, being uncommon in clinical practice. For resources required, equity, acceptability and feasibility, considerations for non-removable versus removable offloading devices should be similar regardless of the site of ulceration and have been discussed under clinical question 1. There is no data on the cost effectiveness of different offloading devices to heal plantar rearfoot DFUs.

In summary, the balance of effects probably favours non-removable over removable offloading devices for plantar rearfoot ulcers, with the CoE for this recommendation being very low based on the very low CoE for the critical outcome of ulcers healed. Therefore, we make a conditional recommendation in favour of non-removable offloading devices based on a very low CoE.

Clinical question 11: In a person with diabetes and a non-plantar foot ulcer, should any one offloading intervention be used over another offloading intervention?

Recommendation 9: In a person with diabetes and a non-plantar foot ulcer, use a removable offloading device, footwear modifications, toe spacers, orthoses, or digial flexor tenotomy, depending on the type and location of the foot ulcer, to promote healing of the ulcer. (Strong; Very low)

Rationale: Non-plantar foot ulcers also require offloading, when pressure or friction on that region of the foot is a likely cause of the ulcer, such as from tightly fitting footwear or rubbing between toes. Overall, our systematic review identified no controlled studies reporting outcomes addressing this question on how to offload non-plantar foot ulcers, despite these ulcers being prevalent and needing relief from mechanical stress (11, 45). Our systematic review did identify 2 RCTs and 1 other controlled trial that reported baseline non-plantar DFU characteristics, but they did not report outcomes for this question (11). One of the RCTs, a large high-quality RCT compared a custom-made fiberglass heel cast in addition to usual care ("usual care was not standardised") with usual care in patients that mostly (72%) had non-plantar rearfoot DFUs (the other 28% had plantar rearfoot ulcers), but did not subgroup the outcomes for non-plantar rearfoot DFUs (46). The study found no differences in proportion ulcers healed, adverse events or patient preferences, but did find the heel cast had higher overall costs.

Therefore, until new evidence becomes available, our recommendation is based entirely on expert opinion. Our expert opinion is to choose the best modality based on the principle that it prevents any tissue stress or contact with the ulcer and is an appropriate fit for the rest of the foot so as not to produce new lesions. A number of different interventions can be used to reduce pressure on a non-plantar ulcer, depending on the type and location of the ulcer. For example, appropriately fitting footwear or footwear modifications can reduce pressure on ulcers on the foot margins and dorsal foot,

toe spacers can reduce pressure on interdigital ulcers and specific ankle-foot orthoses may reduce pressure on ulcers on the back of the rearfoot or medial/lateral foot when lying in bed. Furthermore, a digital flexor tenotomy may be used to reduce pressure on and promote healing of dorsal ulcers on deformed toes (23, 47).

Further research is needed to investigate offloading interventions for healing a non-plantar foot ulcer. Due to the paucity of data, we rate the CoE for this recommendation as very low. However, we consider this a strong recommendation, based on our opinion that the use of these offloading interventions compared with using no offloading intervention would promote DFU healing, reduce tissue stress and be of preference to the patient, and that should outweigh any undesirable effects of the intervention.

GENERAL QUESTIONS

Clinical question 12: In a person with diabetes and a foot ulcer, should a combination of offloading interventions be used over a single offloading intervention?

Recommendation: No recommendation.

Rationale: In the multidisciplinary treatment of DFUs, typically a combination of multiple treatments are provided at once for improved effect on ulcer healing, for example offloading, wound dressings, debridement, revascularisation or antibiotics for infection (13). In a similar manner, a combination of offloading treatments to improve the effect on DFU healing may be provided, and justifies the question whether such combined offloading interventions should be used over a single offloading intervention to heal DFUs.

Our systematic review identified that nearly all studies primarily investigating surgical offloading interventions (e.g. Achilles tendon lengthening, digital flexor tenotomies, etc.) or other offloading interventions (e.g. felted foam, wheelchairs) did so in combination with an offloading device or footwear, and compared outcomes to a single intervention control (11). In contrast, our systematic review identified no studies that primarily investigated offloading devices or footwear, in combination with another offloading intervention.

Therefore, all the available evidence on the effect of a combination of interventions has already been considered in earlier clinical questions and recommendations made and we refrain from making a specific recommendation on this clinical question. We refer the reader to clinical questions 6, 7a-f and 11 for the combination of either a surgical or other offloading intervention in combination with an offloading device or footwear for the recommendations on combination interventions.

Clinical question 13: In a person with diabetes and a foot ulcer, should educational or psychological interventions along with an offloading intervention be used over an offloading intervention alone?

Recommendation: No recommendation.

Rationale: Our systematic review did not identify any studies investigating educational or psychological interventions for the purpose of enhancing the use of an offloading intervention (11). Furthermore, we considered there is insufficient expert opinion to be able to make any appropriately-informed judgements on the balance of effects of educational or psychological interventions along with an offloading intervention. Therefore, we were unable to make a specific recommendation to address this question. However, despite this lack of evidence, we consider this question is an important one. We encourage clinical researchers to conduct studies that investigate educational or psychological interventions intended to improve outcomes of offloading interventions, especially since educational and psychological interventions have shown promise in other areas of diabetes and diabetes-related foot disease, such as for self-care and footwear adherence for ulcer prevention (48-52).

Clinical question 14: In a person with diabetes and a foot ulcer, should an offloading intervention for the contralateral limb along with an offloading intervention for the ipsilateral limb be used over only an offloading intervention for the ipsilateral limb?

Recommendation 10: In a person with diabetes and a foot ulcer for which a knee-high or ankle-high offloading device is used, consider also using a shoe lift on the contralateral limb to improve the person's comfort and balance with walking in the device. (Conditional; Very low)

Rationale: People with a DFU who are provided with a knee-high or ankle-high offloading device may experience discomfort or issues with postural balance or gait stability when the thickness of the device's sole produces a leg-length discrepancy. For these cases, a contralateral lift may be indicated to reduce this leg-length discrepancy and improve gait. Furthermore, consideration should be given to using a walking aid if stability is compromised by wearing the device and risk of falling is high.

Our systematic review identified only 1 repeated measures study addressing this question and it investigated a contralateral shoe lift with an ipsilateral removable offloading device intervention versus the same ipsilateral offloading device alone (11). We judged the desirable effects for the intervention to be small based on little-to-no differences in plantar forefoot pressure found for removable knee-high device in combination with a contralateral shoe lift compared to the device alone (MD 1 kPa lower, 17 lower to 20 higher; Very low CoE) and removable ankle-high device in combination with a contralateral shoe lift compared to the device alone (MD 6 kPa lower, 10 lower to 22 higher; Very low CoE). However, moderate increases in perceived comfort (MD 2.2 higher, 0.1-4.3 higher; Very low CoE) and small improvements in balance were found in the groups with the removable device in combination with the contralateral shoe lift compared to the device alone. Additionally, we judged the undesirable effects to be trivial. Based on our expert opinion, we considered the additional costs of such an intervention to be negligible, the intervention would probably have no impact on equity, and would probably be acceptable and feasible. Thus, we considered a conditional recommendation in favour of such a contralateral shoe lift was justified based on the balance of effects favouring the contralateral shoe life, and a CoE for this recommendation of very low.

KEY CONSIDERATIONS FOR FUTURE RESEARCH

1. In the large number of studies conducted on the efficacy of non-removable offloading devices (TCC or non-removable walkers), many different versions, types and methods of devices and casts have been used. These different versions of devices, and the skills of the technician or healthcare professional to apply them, may potentially lead to different outcomes and varied costs as indicated in our systematic review. However, more trials are still needed comparing these different versions, types and methods of non-removable offloading devices with each other, so that more informed clinical decisions can be made in future on which are most effective to treat DFU and different DFU types.
2. Likewise, there are many different removable offloading devices, including knee-high devices and ankle-high offloading devices such as ankle-high walkers, forefoot offloading shoes, cast shoes, healing sandals, post-operative healing shoes, custom-made temporary shoes, etc. These removable devices can be prefabricated or custom-made, extend to the knee, just above-ankle or below-ankle, and incorporate different mechanical features and also may lead to different outcomes. Again more trials are needed to compare these different versions, types and methods of removable offloading devices with each other, so that more informed clinical decisions can be made in future on which are most effective to treat DFU and different DFU types. Note, this need for more trials also includes the comparison between knee-high and ankle-high removable devices since both are included as the recommended treatment in Recommendation 2.
3. Many RCTs on offloading interventions do not directly measure the degree to which the mechanical tissue stress on the ulcer has been changed by the offloading intervention. Such measurements improve our understanding of the role of offloading in healing, as do several other outcomes. While we acknowledge based on the above evidence provided that more high-quality RCTs on the primary outcome of ulcer healing are needed, the focus can be strengthened by measuring the factors impacting on the mechanical tissue stress levels that lead to different healing outcomes, such as plantar pressure, shear stress, weight-bearing activity (including steps and standing duration), and adherence to using offloading interventions or a combined plantar tissue stress measure (53, 54). If such combined plantar tissue stress measures are able to detect objective thresholds for effective healing, this may enable the development of future smart offloading treatments designed to meet such threshold targets (53, 55).
4. In developing the recommendations for this guideline, we have made an overall judgement that a reduction in weight bearing activity is beneficial to ulcer healing based on one other review (37) and our expert opinion. We acknowledge that in making this judgement we still do not fully appreciate if reducing weight-bearing activity is a desirable or undesirable effect on different DFU and health outcomes. Thus, we recommend more research is done to determine the effect that weight-bearing activity in combination with offloading interventions has on important outcomes, such as healing ulcers, adverse events, quality of life, and general health outcomes. An ideal offloading intervention would adequately offload a foot ulcer for effective healing while allowing the person to maintain or even increase activity levels to contribute to an improvement in overall general cardiovascular health and quality of life.
5. Offloading studies have focused almost exclusively on the treatment of non-complicated neuropathic plantar forefoot ulcers. Little data are still available on the value of offloading in healing

plantar foot ulcers complicated by infection or ischaemia, rearfoot ulcers, or non-plantar ulcers, even though these ulcers together are now arguably more common than purely neuropathic plantar forefoot and midfoot ulcers. Whilst promisingly there have been some new trials investigating offloading interventions in these more complicated DFU populations since 2019 (26, 27, 29), still comparatively little research has been done in these DFU sub-populations. Again, we stress that properly designed studies on offloading ulcers other than the non-complicated neuropathic plantar forefoot or midfoot ulcer are urgently needed.

6. Adherence to an intervention is crucial in healing foot ulcers. It is consistently reported that those who do not adhere to an offloading intervention present with worse healing outcomes. A stronger focus is required, both in research and in clinical practice, on the objective measurement and improvement of offloading treatment adherence, and understanding people's thoughts, views, emotions and practices around adhering to using offloading devices to treat foot ulcers (56, 57).
7. Surgical offloading has primarily been used to heal foot ulcers in selected patients, typically where non-surgical offloading interventions have failed. The evidence for several surgical interventions is mostly based on only a few older controlled studies. More high-quality RCTs on surgical offloading procedures in comparison to first-choice offloading devices are still required to determine the effectiveness of surgical interventions on the healing of both non-complicated and complicated foot ulcers. For digital flexor tenotomy, a recent RCT has added to the evidence base for this intervention (23), affecting the strength and CoE, and providing an example of what impact well-controlled studies can have in this area.
8. Information on undesirable effects (such as new lesions, falls, infections, amputations), quality of life and costs, equity, acceptability, and feasibility is critical in clinical decision making on offloading treatment. By incorporating the GRADE methodology and multiple meta-analyses pooling these outcomes, the 2023 guidelines are much more considerate of these outcomes than prior iterations in the analysis of the literature on offloading interventions. Still most RCTs are underpowered for these important outcomes. When trials report these outcomes using the same definitions there is the possibility of pooling data in meta-analyses as we have been able to do in our systematic review to better address these outcomes in the overall judgement. We recommend future trials continue to ensure they collect these outcomes based on standard definitions as recommended by Jeffcoate et al. and van Netten et al (12, 36) and on the summary of judgements tables as provided by GRADE.
9. Costs and cost-effectiveness have also received little attention in offloading studies, despite the fact that reimbursement through insured care is more and more dependent on proven cost-effectiveness. Very few additional cost studies have been performed since our previous guidelines in 2019 (58), so more attention is still warranted in view of the continuing pressure on healthcare cost containment.
10. Most interventions discussed are investigated in studies from high-income countries with relatively temperate climates. Whilst promisingly there have been some trials investigating offloading interventions in low and middle-income countries and countries with tropical climates published since 2019 (59-61), there is still a need for more specific guidance on approaches to ulcer healing in lower-income countries where climate and/or resources may be a factor in choice of offloading device, adherence to wearing the device and its efficacy.

11. We encourage our colleagues, whether working in multidisciplinary diabetic foot clinics or in a solo practice, to consider developing some form of surveillance (e.g., registries, pathways) to monitor interventions and outcomes and attempt to improve their outcomes (e.g. through bench marking, best practice and research) for cohorts of persons with diabetes who have a foot ulcer (62-64).
12. We encourage our research colleagues to consider these key considerations and conduct well-designed studies according to published reporting standards (12) in areas of offloading in which we find gaps in the evidence base so to better inform the diabetic foot community in the future on effective offloading treatment for persons with diabetes and a foot ulcer.

CONCLUDING REMARKS

The large global disease and economic burdens caused by DFU can be considerably reduced when evidence-based treatment is implemented by health-care professionals and multidisciplinary teams. Offloading interventions are arguably one of the, if not the, most important interventions with the highest certainty of evidence available for healing neuropathic DFUs and reducing the global burden of these ulcers. Following the recommendations for evidence-based offloading treatments of people with diabetes and a foot ulcer in this guideline should help healthcare professionals and teams improve important outcomes for persons with a diabetes-related foot ulcer.

GLOSSARY

Achilles tendon lengthening: a surgical procedure used to lengthen a tight Achilles tendon and increase motion at the ankle joint (65).

Adverse events/effects in relation to offloading treatment: general or local complications related directly or indirectly to the intervention regardless of whether they are serious. These include but are not limited to: falls; new pre-ulcerative lesion formation (i.e. abrasions, callus and blisters); new DFU formation; acute Charcot foot; infection; hospital admissions; amputation; and death.

Adherence to offloading intervention: The extent to which a person's behaviour corresponds with agreed recommendations for treatment from a healthcare provider, expressed as quantitatively as possible; usually defined as the proportion of time using the prescribed offloading intervention of the total time in which the intervention is prescribed to be used (e.g. % of the total weight bearing time that the patient was wearing the prescribed offloading device).

Ambulatory activity: defined as the weight-bearing dynamic activity, often expressed as average daily steps or strides.

Ankle-high offloading device: an offloading device that extends no higher up the leg than just above the ankle and can be further sub-grouped into above ankle-high and below ankle-high offloading devices. Includes ankle-high walker, forefoot offloading shoe, cast shoe, healing sandal, post-operative healing shoe, and custom-made temporary shoe.

Above ankle-high offloading device: an offloading device that extends up the leg to just above the ankle, typically includes ankle-high walkers.

Below ankle-high offloading device: an offloading device that extends no higher up the leg then just below the ankle, and typically includes forefoot offloading shoe, cast shoe, healing sandal, postoperative healing shoe, custom-made temporary shoe.

Cast shoe: a removable plaster or fibreglass cast that extends to just below or at the ankle joint, moulded around the shape of the foot with total contact of the entire plantar surface.

Complicated DFU: a plantar DFU that is complicated by infection and/or ischaemia.

Conventional footwear: off-the-shelf footwear with no specific properties for fitting or intended therapeutic effect.

Custom-made insole: An insole that is custom-made to the individual's foot using a 2D or 3D impression of the foot, and that is often built-up in a multi-layer construction. This may also incorporate other features, such as a metatarsal pad or metatarsal bar. The insole is designed to conform to the shape of the foot, providing cushioning and redistribution of plantar pressure. The term "insole" is also known as "insert" or "liner"

Custom-made (medical grade) footwear: Footwear uniquely manufactured for one person, when this person cannot be safely accommodated in prefabricated (medical grade) footwear. It is made to accommodate deformity and relieve pressure over at-risk sites on the plantar and dorsal surfaces of the foot. In-depth assessment, multiple measurements, impressions or a mould, and a positive model of a person's foot and ankle are generally required for manufacture. This footwear includes a custom-made insole. Also known as "bespoke footwear" or "orthopaedic footwear".

Custom-made temporary shoe: a unique, usually handmade shoe that is manufactured in a short time frame and is used temporarily to treat a foot ulcer. The shoe is built on a positive model of the patient's foot to accommodate deformity and relieve pressure over the ulcer site on the plantar surface of the foot.

Diabetes-related foot ulcer (DFU): see IWGDF definitions and criteria document (36).

Digital flexor tenotomy: a surgical division of a tendon,(66) in this case a digital flexor tendon.

DFU healing: defined as number or percentage of healed DFUs by a fixed time (e.g., % of DFUs healed in 12 weeks of intervention), or time-to-healing a DFU.

Extra-depth footwear: Prefabricated footwear constructed with additional depth and volume to accommodate deformity such as claw/hammer toes and/or to allow for space for a thick insole. Usually a minimum of 5 millimetres (~3/16") depth is added compared to off-the-shelf footwear. Even greater depth is sometimes provided in footwear that is referred to as double depth or super extra-depth.

Footwear: defined broadly as any shoe-gear and including insoles.

Forefoot offloading shoe: prefabricated shoe especially designed for relieving forefoot locations. The footwear has a specific shape with a wedge design raising the forefoot above the rearfoot, a rocker outsole, and minimal support of the forefoot. These shoes are usually worn unilaterally.

Half-shoe: prefabricated shoe designed to offload the forefoot. The anterior part of the shoe is cut out, leaving the rearfoot and the midfoot as the only weight-bearing surfaces.

Healed DFU: see IWGDF definitions and criteria document (36).

Heel-relief shoe: shoe designed to offload the rearfoot. The rearfoot part is missing from the footwear, and its sole arrangement is constructed in such a way that the rearfoot is not loaded when walking.

In-shoe (semi-)rigid orthoses: device put inside the shoe to achieve pressure reduction or alteration in the function of the foot. Can be prefabricated or custom-made

Joint arthrodesis: a surgical procedure that involves the fusion of two bones in a joint to relieve pain and improve stability.(66)

Joint arthroplasty: a surgical procedure that involves the repair or reconstruction of a damaged joint to increase range of motion, relieve pain, and improve mobility.(66)

Knee-high offloading device: an offloading device that extends up the leg to a level just below the knee (e.g., knee-high total contact cast (TCC), knee-high removable walker).

Lesion: Any abnormality associated with damage to the skin, nails, or deep tissues of the foot, such as abrasions, blisters, callus, maceration, subcutaneous haemorrhage, transfer lesions, ulcers (36).

Metatarsal head resection: a surgical removal of part of a bone, organ or structure,(66) in this case a metatarsal head.

Metatarsal osteotomy: a surgical procedure in which a bone is divided or a piece of bone is excised (as to correct a deformity),(66) in this case a metatarsal.

Non-plantar: see IWGDF definitions and criteria document (36).

Non-removable offloading device: an offloading device that cannot be removed by the patient (e.g., TCC, removable knee-high walker rendered non-removable (non-removable walker), etc.).

Non-surgical offloading intervention: any intervention undertaken with the intention of relieving mechanical stress (pressure) from a specific region of the foot that does not involve a surgical procedure (includes offloading devices, footwear, and other offloading techniques).

Non-removable walker: prefabricated removable, mostly knee-high, walker rendered non-removable to the patient, by a healthcare professional circumferentially wrapping with a layer(s) of fiberglass cast material or other closure technique such as a tie wrap. Such a device is also known as "instant total contact cast". Manufacturers may also provide means to make the walker non-removable such as incorporating locking mechanisms into the walker

Offloading: the relief of mechanical stress (pressure) from a specific region of the foot.

Offloading device: any custom-made or prefabricated device designed with the intention of relieving mechanical stress (pressure) from a specific region of the foot (e.g., total contact cast (TCC), (non-)removable walker, knee-high walker, ankle-high walker, ankle foot orthoses, healing sandal, cast shoe, forefoot offloading shoe, etc.). Note that this excludes footwear.

Offloading intervention: any intervention undertaken with the intention of relieving mechanical stress (pressure) from a specific region of the foot (includes surgical offloading techniques, offloading devices, footwear, and other offloading techniques).

Other offloading techniques: any other technique undertaken with the intention of relieving mechanical stress (pressure) from a specific region of the foot that is not a surgical offloading technique, offloading device or footwear (e.g. bed rest, crutches, wheelchairs, offloading dressings, felted foam/padding, callus debridement, gait retraining, foot-related exercises, patient education, etc.).

PICO: the PICO process is a technique used to frame evidence-based clinical questions. PICO stands for: (P): Population; (I): Intervention; (C): Control; (O): Outcome.

Plantar: see IWGDF definitions and criteria document (36).

Plantar pressure: see IWGDF definitions and criteria document (36).

Post-operative healing shoe: prefabricated shoe with roomy and soft upper worn after an operation of the foot.

Removable offloading device: an offloading device that can be removed by the patient (e.g. removable walker, forefoot offloading shoe, cast shoe, healing sandal, etc.).

Rocker outsole: rigid outsole with a sharp transition that aims to rock the shoe forward. during late support to allow walking without extension of the metatarsal-phalangeal joints.

Shoe modification: modification to an existing shoe with an intended therapeutic effect, for example, pressure relief.

Standard therapeutic footwear: off-the-shelf shoe with intended therapeutic effect but without any customization to the patient's foot.

Surgical offloading intervention: a surgical procedure or technique undertaken with the intention of relieving mechanical stress from a specific region of the foot, and includes Achilles tendon lengthening, metatarsal head resection, osteotomy, arthroplasty, arthrodesis, ostectomy, exostectomy, external fixation, flexor tendon transfer or tenotomy, silicone injections, tissue augmentation.

Sustained healing: Days since a person has achieved a healed ulcer and gone without another foot ulcer at the same location (also known as ulcer-free days or remission at that same location) (36).

Therapeutic footwear: Generic term for footwear designed to have a therapeutic effect that cannot be provided by or in a conventional shoe. Custom-made shoes or sandals, custom-made insoles, extra-depth shoes, and custom-made or prefabricated medical grade footwear are examples of therapeutic footwear.

Toe orthosis: an in-shoe orthosis to achieve some alteration in the function of the toe.

Total contact cast (TCC): a custom-made, well-moulded, minimally padded, knee-high non-removable fiberglass or plaster cast that maintains total contact with the entire plantar surface and lower leg. The cast is often worn with an attachable sole that protects the cast and facilitates walking.

Ulcers healed: Intact skin, meaning complete epithelialization without any drainage of a previous foot ulcer site, and typically stated within a certain prespecified time frame (e.g. ulcers healed within 3 months).(36)

Ulcer area reduction: defined as the proportion of ulcer area reduction from baseline over a given period of time (e.g., % ulcer area reduction at 4 or 6 weeks from the start of the observation period) (1).

Uncomplicated DFU: non-infected, non-ischaemic neuropathic DFU.

CONFLICT OF INTEREST STATEMENTS

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

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AUTHOR CONTRIBUTIONS

SAB performed qualitative assessments, completed summary of judgements, and wrote recommendations for clinical questions 5, 8, 11, and 14, and wrote the manuscript. DGA and KKM performed qualitative assessments, completed summary of judgements, and wrote recommendations for clinical question 7, and critically reviewed and edited the manuscript. RTC and CG performed qualitative assessments, completed summary of judgements, and wrote recommendations for clinical questions 1-4, and 10, and critically reviewed and edited the manuscript. GJ performed qualitative assessments, completed summary of judgements, and wrote recommendations for clinical questions 5, 8, 11, and 14, and critically reviewed and edited the manuscript. VV and PAL performed qualitative assessments, completed summary of judgements, and wrote recommendations for clinical questions 6, 9, 12 and 13, and critically reviewed and edited the manuscript.

SAB acted as chair of the working group and PAL as secretary and they take full responsibility for the content of the manuscript.

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