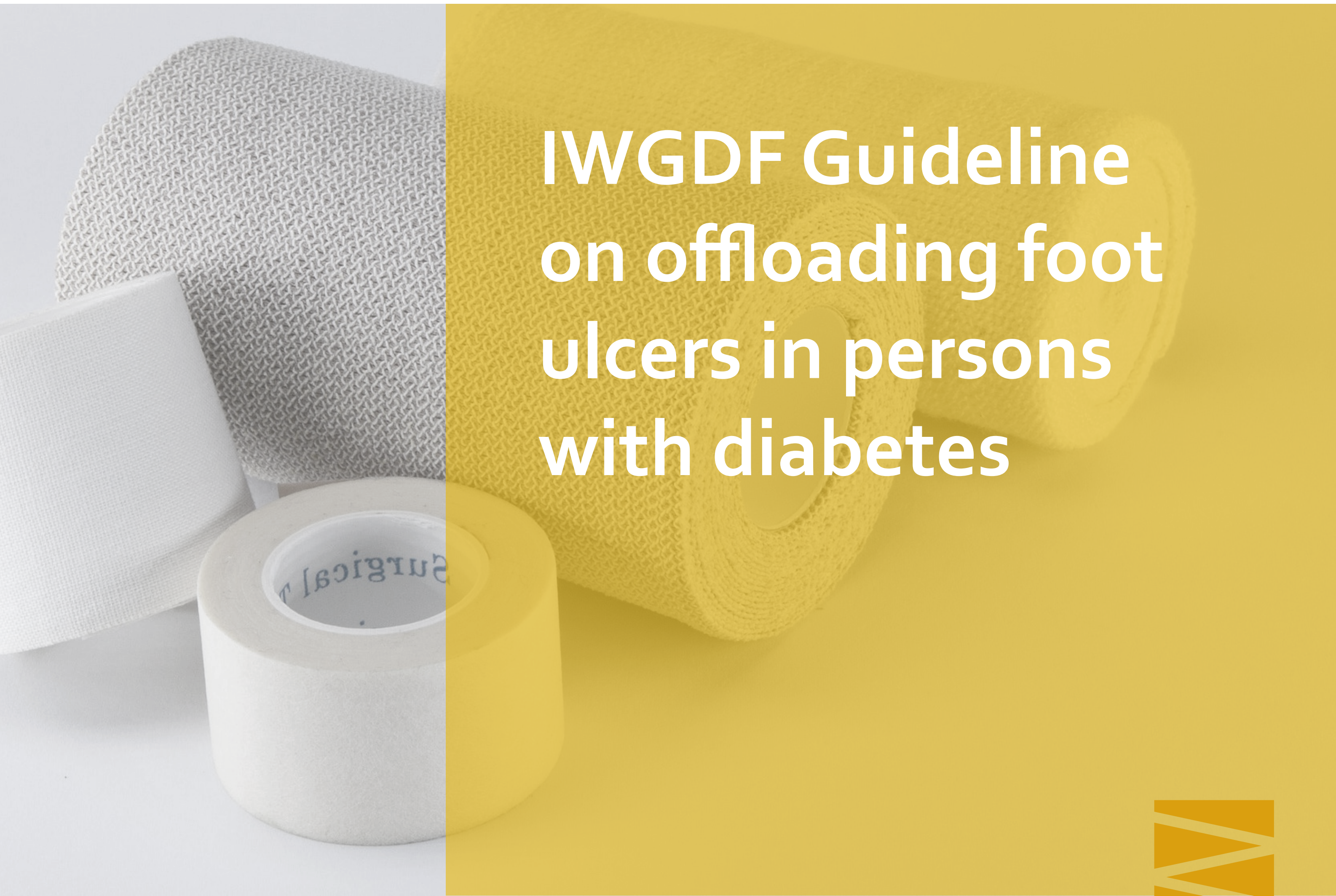
IWGDF Guideline on offloading foot ulcers in persons with diabetes



Part of the 2019 IWGDF Guidelines
on the Prevention and Management
of Diabetic Foot Disease

IWGDF Guidelines

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ABSTRACT

The International Working Group on the Diabetic Foot (IWGDF) has published evidence-based guidelines on the prevention and management of diabetic foot disease since 1999. This guideline is on the use of offloading interventions to promote healing foot ulcers in persons with diabetes and updates the previous IWGDF guideline.

We followed the GRADE methodology to devise clinical questions and critically important outcomes in the PICO format, to conduct a systematic review of the medical-scientific literature, and to write recommendations and their rationale. The recommendations are based on the quality of evidence found in the systematic review, expert opinion where evidence was not available, and a weighing of the benefits and harms, patient preferences, feasibility and applicability, and costs related to the intervention.

For healing a neuropathic plantar forefoot or midfoot ulcer in a person with diabetes, we recommend that a non-removable knee-high offloading device is the first-choice of offloading treatment. A removable knee-high and removable ankle-high offloading device are to be considered as the second- and third-choice offloading treatment, respectively, if contraindications or patient intolerance to non-removable offloading exist. Appropriately fitting footwear combined with felted foam can be considered as the fourth-choice offloading treatment. If non-surgical offloading fails, we recommend to consider surgical offloading interventions for healing metatarsal head and digital ulcers. We have added new recommendations for the use of offloading treatment for healing ulcers that are complicated with infection or ischemia, and for healing plantar heel ulcers.

Offloading is arguably the most important of multiple interventions needed to heal a neuropathic plantar foot ulcer in a person with diabetes. Following these recommendations will help health care professionals and teams provide better care for diabetic patients who have a foot ulcer and are at risk for infection, hospitalisation and amputation.

LIST OF RECOMMENDATIONS

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

   b) When using a non-removable knee-high offloading device to heal a neuropathic plantar forefoot or midfoot ulcer in a person with diabetes, use either a total contact cast or non-removable knee-high walker, with the choice dependent on the resources available, technician skills, patient preferences and extent of foot deformity present. (Strong; 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 a removable knee-high offloading device with an appropriate foot-device interface as the second-choice of offloading treatment to promote healing of the ulcer. Additionally, encourage the patient to consistently wear the device. (Weak; Low)
3. In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer for whom a knee-high offloading device is contraindicated or not tolerated, use a removable ankle-high offloading device as the third-choice of offloading treatment to promote healing of the ulcer. Additionally, encourage the patient to consistently wear the device. (Strong; Low)
4. a) In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer, do not use, and instruct the patient not to use, conventional or standard therapeutic footwear as offloading treatment to promote healing of the ulcer, unless none of the above-mentioned offloading devices is available. (Strong; Moderate)

   b) In that case, consider using felted foam in combination with appropriately fitting conventional or standard therapeutic footwear as the fourth choice of offloading treatment to promote healing of the ulcer. (Weak; Low)
5. In a person with diabetes and a neuropathic plantar metatarsal head ulcer, consider using Achilles tendon lengthening, metatarsal head resection(s), or joint arthroplasty to promote healing of the ulcer, if non-surgical offloading treatment fails. (Weak; Low)
6. In a person with diabetes and a neuropathic plantar digital ulcer, consider using digital flexor tenotomy to promote healing of the ulcer, if non-surgical offloading treatment fails. (Weak; Low)
7. a) In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer with either mild infection or mild ischemia, consider using a non-removable knee-high offloading device to promote healing of the ulcer. (Weak; Low)

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

   c) 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 ischemia, primarily address the infection and/or ischemia, and consider using a removable offloading intervention based on the patient's functioning, ambulatory status and activity level, to promote healing of the ulcer. (Weak; Low)

8. In a person with diabetes and a neuropathic plantar heel ulcer, consider using a knee-high offloading device or other offloading intervention that effectively reduces plantar pressure on the heel and is tolerated by the patient, to promote healing of the ulcer. (Weak; Low)
9. In a person with diabetes and a non-plantar foot ulcer, use a removable ankle-high offloading device, footwear modifications, toe spacers, or orthoses, depending on the type and location of the foot ulcer, to promote healing of the ulcer. (Strong; Low)

INTRODUCTION

Diabetes-related foot ulceration (DFU) results in a large global morbidity, mortality and cost burden (1-5). DFU annually affects around 26 million people worldwide (2, 4). Without appropriate care, these foot ulcers can lead to hospitalisation, amputation and death (1-5). Thus, healing of DFU is of paramount global importance (1-5).

Peripheral neuropathy affects around half of all people with diabetes and leads to loss of protective sensation in the feet (2-4). Elevated levels of mechanical stress in the presence of loss of protective sensation is one of the most common causes of DFU (2, 6-8). Mechanical 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 stress (7-9). Thus, the combination of loss of protective sensation and elevated mechanical stress leads to tissue damage and DFU (2, 6, 10). Once a DFU forms, healing is chronically delayed if the area is not effectively offloaded (2, 6, 10).

Multiple interventions are typically required to effectively heal a DFU, including local wound management, infection management, revascularisation and pressure offloading (11, 12). The first three of those interventions are covered in other parts of the International Working Group of the Diabetic Foot (IWGDF) Guidelines (12-15). In people with neuropathic DFUs, pressure offloading is arguably the most important of these interventions (10-12). There is a long standing clinical tradition of using different offloading devices, footwear, surgery, and other offloading interventions to heal DFUs (6, 10, 16-18). 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 (10, 12, 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 (10, 19). Over the last few years, several well-designed controlled studies have been performed in this field that add to the evidence base for offloading foot ulcers in patients with diabetes (20-23).

This guideline aims to update the previous IWGDF guideline on footwear and offloading. However, unlike the previous guideline, this guideline no longer includes footwear and offloading for the prevention of foot ulcers; it focusses only on offloading for the management of foot ulcers. Footwear and offloading for the prevention of foot ulcers is now covered by the IWGDF guideline on prevention (24). Other IWGDF guidelines in this series include those on peripheral artery disease, infection, wound healing and ulcer classification (25-28).

METHODS

In this guideline we have followed the GRADE methodology, which is structured around clinical questions in the PICO-format (Patient-Intervention-Comparison-Outcome), systematic searches and assessment of the available evidence, followed by developing recommendations and their rationale (29, 30).

First, a multidisciplinary working group of independent experts (the authors of this guideline) was installed by the IWGDF Editorial Board. The members of the working group devised the clinical questions, which were revised after consultation with external experts from various geographical regions and the IWGDF Editorial Board. The aim was to ensure the relevance of the questions for clinicians and other health care professionals in providing useful information on offloading interventions to heal foot ulcers in people with diabetes. We also formulated what we considered critically important outcomes relevant for daily care, using the set of outcomes defined by Jeffcoate et al. (11) as a reference guide.

Second, we systematically reviewed the literature to address the agreed upon clinical questions. For each assessable outcome we graded the quality of evidence based on the risk of bias of included studies, effect sizes, presence of inconsistency, and evidence of publication bias (the latter where appropriate). We then rated the quality of evidence as 'high', 'moderate' or 'low'. The systematic review supporting this guideline is published separately (31).

Third, we formulated recommendations to address each clinical question. We aimed to be clear, specific and unambiguous on what we recommend, for which persons, and under what circumstances. Using the GRADE system we provided the rationale for how we arrived at each recommendation, based on the evidence from our systematic review (31), expert opinion where evidence was not available, and a careful weighing of the benefits and harms, patient preferences, and financial costs (resource utilization) related to the intervention or diagnostic method (29, 30). Based on these factors, we graded the strength of each recommendation as 'strong' or 'weak', and for or against a particular intervention or diagnostic method. All our recommendations (with their rationales) were reviewed by the same international experts who reviewed the clinical questions, as well as by the members of the IWGDF Editorial Board.

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 (32).

RECOMMENDATIONS

A diagrammatic overview of the recommended offloading treatment approach to heal a foot ulcer in a person with diabetes can be found in Figure 1.

In this guideline, many different offloading interventions are mentioned. We refer to the glossary for a definition and description of each of these offloading interventions. Furthermore, many of the offloading devices and interventions recommended require specific training, skills, and experience to apply properly. As these specific skills and training are not described in the studies performed and may differ between 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 manage patients with a DFU.

What's new?
We have made several changes to the recommendations included in this updated 2019 IWGDF offloading guideline when compared to the previous IWGDF offloading guideline. The main changes are the following:

- Removed any recommendations on the prevention of foot ulcers (these are now covered in the updated 2019 IWGDF prevention guideline (24))
- Outlined clearly the first-, second-, third- and fourth-choice of offloading treatment to heal a neuropathic plantar forefoot or midfoot ulcer
- Added one new recommendation on considerations for choosing between either a total contact cast or non-removable knee-high walker
- Added three new recommendations on offloading treatments for people with neuropathic plantar forefoot ulcers that are complicated by infection or ischemia
- Added a new recommendation on offloading treatments for people with neuropathic plantar heel ulcers

OFFLOADING DEVICES

PICO 1: In people with a plantar DFU, are non-removable offloading devices compared to removable offloading devices effective to heal the DFU?

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

Rationale: Non-removable knee-high offloading devices consist of total contact casts (TCCs) and non-removable walkers (19). TCCs are custom-made, knee-high, non-removable casts and non-removable walkers are prefabricated, knee-high, removable walkers rendered irremovable by applying a layer of cast or tie wrap around the device. These walkers may involve a modular insole system or have an (custom) insole added. In any case, an appropriate foot-device interface is required, meaning that peak pressures are adequately distributed and reduced at the ulcer location. Non-removable offloading devices offer several benefits for healing a DFU over other offloading interventions, including better redistribution of pressure over the foot and lower leg and enforced adherence (6, 10, 19, 33). These factors play an important role in the healing of foot ulcers with non-removable offloading.

Our updated systematic review (31) identified five high-quality meta-analyses of controlled trials on this topic (33-37), with much overlap present between the meta-analyses on the trials included. All found that non-removable offloading devices result in significantly improved healing outcomes for neuropathic plantar forefoot ulcers when compared with removable devices (removable offloading devices or footwear) (33-37). For those meta-analyses reporting relative risks, they found non-removable offloading devices were 17-43% more likely than removable devices to heal a neuropathic plantar forefoot ulcer ($p<0.05$) (34, 36, 37). For those reporting time-to-healing, they found non-removable offloading devices healed ulcers 8-12 days quicker than removable devices ($p<0.05$) (33, 35). We conclude that non-removable knee-high offloading devices have clear healing benefits over removable devices. The quality of evidence is rated as high.

Possible adverse effects of non-removable offloading devices include muscle weakness, falls, new ulcers due to poor fitting, and knee or hip complaints due to the acquired limb-length discrepancy when wearing the device (38-40). One may consider a shoe raise for the contralateral limb to minimize this acquired limb-length discrepancy. In most randomized controlled trials (RCT), the wide variation in type of adverse events, relatively small sample sizes and low incidence of reported events prevented statistical testing between non-removable and removable devices (22, 23, 38, 41-43). However, two meta-analyses reported no differences in skin maceration or treatment discontinuation (combination of adverse events, voluntary withdrawal or losses to follow-up) (34, 36). Additionally, six RCTs described low overall incidences (0-20%) of adverse events, with no differences evident between non-removable and removable devices for these events, including falls, maceration, abrasions, new ulcers, infections and hospitalisations (22, 23, 38, 41-43). Nevertheless, clinicians and other health care providers should still be aware of these adverse events. We conclude non-removable and removable offloading devices have similar low incidences of harm.

Many patients are thought to not prefer non-removable knee-high offloading devices as they limit daily life activities, such as walking, sleeping, bathing, or driving a car (34). Two RCTs reported on patient preferences with one reporting lower patient satisfaction with non-removable compared with removable offloading devices (23) and the other reporting no differences in patient satisfaction or comfort (43). One large health technology assessment reported on qualitative interviews with 16 patients with DFU who were familiar with a variety of off-loading devices (34). They found that patients rated non-removable offloading devices as preferable after they understood the healing benefits of non-removable devices, even though they rated removable offloading devices as more comfortable, allowing greater freedom and mobility (34). Practitioners may not prefer some non-removable offloading, as surveys and epidemiological studies show low use of TCCs in clinical practice, but similar (and moderate) use of non-removable and removable walkers (16-18, 44). We conclude that non-removable and removable offloading devices may be equally preferred by both patients and clinicians.

Two RCTs reported on costs with one finding one-off device/material costs were higher for non-removable and removable walkers than for TCCs (38), and the other finding that TCCs and non-removable walkers were less expensive over the course of treatment than removable walkers (23). One large health technology assessment study systematically reviewed the literature and found no papers on economic evaluations of non-removable offloading devices (34). The authors then performed their own cost-effectiveness analysis, using existing literature and expert opinion, which showed that the cost per patient for three months of treatment (including all device/materials, dressings, consultations, labour, complication costs etc.) was lowest for non-removable walkers ($876) and TCCs ($1,137), compared with removable walkers ($1,629) and therapeutic footwear ($1,934) (34). They concluded that non-removable walkers and TCCs were superior to the other offloading interventions because they were both less expensive and more effective than removable walkers and therapeutic footwear. They also performed a cost utility analysis which also showed that the cost per patient for 6 months of treatment (including all treatment costs and heath gains from ulcers healed and quality of life) was again lowest for non-removable walkers ($2,431) and TCCs ($2,924), compared with removable walkers ($4,005) and therapeutic footwear ($4,940) (34). We conclude non-removable offloading devices to be more cost-effective than removable offloading devices.

Contraindications for the use of non-removable knee-high offloading devices, based predominantly on expert opinion, include presence of both mild infection and mild ischemia, moderate-to-severe infection, moderate-to-severe ischaemia, or heavily exudating ulcers (34-36, 39, 45). We refer to the IWGDF infection and PAD guidelines and the IWGDF definitions and criteria document for definitions on infection and ischemia (27, 28, 46). We identified no RCTs in this field that have included participants with these conditions, seemingly for safety reasons. However, we did identify controlled and non-controlled studies that indicate no additional adverse events in people with mild infection or mild ischaemia (39, 45, 47-51). One low-quality systematic review investigating mostly non-controlled studies of TCC use in people with ischaemia recommended an ankle brachial index threshold of >0.55 for safe use of a TCC (52). The use of non-removable knee-high offloading devices may also induce an increased risk of falls with several studies reporting abnormal gait changes and imbalance in people with DFU wearing knee-high offloading devices (53-55). However, in the aforementioned RCTs there was no increase in reported falls-related adverse events in those wearing non-removable knee-high offloading devices (22, 23, 38, 41-43). Further, studies investigating ankle foot orthoses, devices that share functional similarities to knee-high offloading devices, have shown ankle foot orthoses may help to improve balance and reduce falls in older people with neuropathy (56, 57). Future studies should specifically investigate the effect of knee-high offloading devices on risk of falls, and we suggest falls risk assessment should be done on a patient-by-patient basis.

In summary, the quality of the evidence from the meta-analyses performed was high, even though the quality of evidence from individual RCTs varied. All meta-analyses favoured the use of non-removable knee-high over removable offloading to heal neuropathic plantar forefoot ulcers without infection or ischemia present. These benefits outweigh the low incidence of harm, and with positive cost-effectiveness and mixed patient preference for the use of non-removable over removable offloading devices, we grade this recommendation as strong. We refer to recommendations 7a, 7b, and 7c for DFU that are infected or where ischemia is present.

PICO 2: In people with a plantar DFU, are total contact casts (TCC) compared to other non-removable knee-high offloading devices effective to heal the DFU?

Recommendation 1b: When using a non-removable knee-high offloading device to heal a neuropathic plantar forefoot or midfoot ulcer in a person with diabetes, use either a total contact cast or non-removable knee-high walker, with the choice dependent on the resources available, technician skills, patient preferences and extent of foot deformity present (Strong; Moderate).

Rationale: The TCC had been considered for decades the gold standard offloading intervention to heal a neuropathic plantar forefoot ulcer (19, 58). Our previous guideline broadened the recommendation to a non-removable offloading device (19), to include both a TCC and a prefabricated removable knee-high walker rendered non-removable with an appropriate foot-device interface. However, the previous guideline did not provide a recommendation on which one is preferable to use (19).

Our updated systematic review (31) identified one high-quality meta-analysis on this topic (34) that included three high-quality RCTs (23, 59, 60). The meta-analysis found no difference in ulcers healed using TCCs and non-removable walkers ($p=0.82$) (34). Another low-quality RCT also found no significant difference between a TCC and non-removable knee-high walker for ulcers healed ($p=0.99$) or time-to-healing ($p=0.77$) (61). However, none of these four RCTs was based on a sample size calculation for equivalence (59). Thus, the non-significant results of the individual RCTs may reflect low statistical power to detect differences, although the meta-analysis should have had sufficient power. We conclude that TCCs and non-removable knee-high walkers are equally effective to heal DFUs.

As healing outcomes were similar, we analysed effects on the surrogate outcomes of plantar pressures and weight-bearing activity (11). One RCT found a significantly greater plantar pressure reduction from barefoot pressure baselines in a knee-high walker compared with a TCC at the ulcer site (91% v 80%), the forefoot (92% v 84%) and midfoot (77% vs 63%) (all, $p<0.05$), but no difference in the rearfoot ($p=0.11$) (62). However, several non-controlled within-subject studies found no significant difference in plantar pressure reduction from standard footwear baselines in knee-high walkers compared with TCCs at the ulcer site, hallux and forefoot (63-66). We found no controlled studies investigating weight-bearing activity. We consider TCCs and non-removable knee-high walkers to have similar effects on reducing plantar pressures.

Three high-quality RCTs reported adverse events for TCCs and non-removable knee-high walkers and found no significant differences ($p>0.05$) (23, 59, 60). Additionally, one meta-analysis found no significant difference for treatment discontinuation between these two devices ($p=0.52$) (34). While the low numbers of adverse events and treatment discontinuations may have resulted in low power to detect differences, we consider these devices to have similarly low levels of harm. The same RCTs reported on patient preferences. One reported higher patient satisfaction with a non-removable knee-high walker than with a TCC ($p<0.05$) (60), whilst another reported no differences ($p>0.05$) (23). Two of these RCTs also found that it took a significantly longer time to apply and remove a TCC than a non-removable knee-high walker (by up to 14 minutes, $p<0.01$) (59, 60). We conclude that patient and practitioner preference for either device is mixed.

Four RCTs reported on the costs of using a TCC or non-removable knee-high walker. One low-quality RCT reported that the one-off device/material costs for a TCC were lower than for a non-removable offloading device ($20 v $35, $p<0.01$) (61). Three other, high-quality, RCTs reported that treatment costs were lower for non-removable knee-high walkers than for TCCs (23, 59, 60). One reported that device/material costs were lower ($158 v $211, p=not reported) (59), another that all offloading treatment costs (i.e. device/materials, cast changes, dressings, cast technician salary) were significantly lower ($162 v $727, $p<0.001$) (60), and the third that average costs per day of treatment were significantly lower with a non-removable walker than with a TCC (€83 v €243, $p<0.05$) (23). The cost-effectiveness analysis of a health technology assessment showed that the cost per patient for three months treatment was lower per patient for a non-removable walker than for a TCC ($876 v $1,137) (34). When the costs and healing probabilities were modelled over 1000 patients with a DFU, they reported the TCC would heal 15 more ulcers (741 v 726), but cost $260,420 more than the non-removable knee-high walker ($1.137 million v $0.876 million). Thus, from a population-based perspective they suggest that for each additional DFU healed using a TCC compared with using a non-removable walker would cost a service $17,923, and therefore would not be more cost-effective in most services (34). The same study found in a cost-utility analysis that the cost per patient for six months treatment were lower for a non-removable walker than for a TCC ($2,431 v $2,924) (34). We conclude that non-removable walkers are generally more cost-effective than TCCs.

In summary, based on one high-quality meta-analysis of three high-quality RCT's showing consistent results for healing between the TCC and non-removable knee-high walkers, and with a need for larger trials to test for equivalence, we rate the quality of evidence as moderate. Additionally, considering the equivalence in plantar pressure benefits and adverse events, and slight preference and lower costs for a non-removable knee-high walker, we grade this recommendation as strong. However, we recommend to base the choice for either a TCC or a non-removable knee-high walker on availability of the device/materials (i.e. resources), skills of available cast technicians, appropriateness of the device to fit the level of any foot deformity (i.e. a TCC with a severely deformed foot), and patient preferences.

PICO 3: In people with a plantar DFU, are removable knee-high offloading devices compared to other removable offloading devices effective to heal the DFU?

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 a removable knee-high offloading device with an appropriate foot-device interface as the second-choice of offloading treatment to promote healing of the ulcer. Additionally, encourage the patient to consistently wear the device (Weak; Low).

Rationale: There are circumstances when a non-removable knee-high offloading device is contraindicated (see rationale for recommendation 1) or cannot be tolerated by the patient. Intolerance by the patient can include refusal to wear the device or the patient's circumstances do not support its use, such as unable to use the device as part of the patient's job. A removable knee-high offloading device may be a solution to these conditions (19). A removable knee-high device redistributes peak pressures in a similar fashion as a non-removable knee-high device (6, 10, 19, 33), although one study showed higher peak pressures during walking after a TCC was bivalved and made removable (66). A removable knee-high device also does this more effectively than a removable ankle-high offloading device (such as ankle-high walker, forefoot offloading shoes, half-shoes, cast shoes, or post-operative sandal) (6, 10, 19, 33).

Our systematic review (31) identified one high-quality meta-analysis (34), that included two low-quality RCTs (38, 43), and found no difference in the proportion of plantar forefoot ulcers healed between removable knee-high and ankle-high offloading devices (healing sandal or half-shoe) (p=0.20) (34). A more recent high-quality RCT also found no difference in plantar forefoot ulcers healed between a removable knee-high device (bivalved TCC) and either a removable ankle-high cast shoe or forefoot offloading shoe, at either 12 weeks (p=0.703) or 20 weeks (p=0.305) (20). However, the authors noted the removable knee-high device group had significantly more deep ulcers (University of Texas grade 2) than both ankle-high device groups at baseline (p<0.05) (20). None of the RCTs conducted were sufficiently powered for equivalence. We conclude from the current evidence available that removable knee-high and removable ankle-high offloading devices have comparable effects on healing neuropathic plantar DFUs.

As healing outcomes were comparable between devices, we assessed surrogate measures (11). One high-quality RCT (20) found a removable knee-high device (bivalved TCC) had greater plantar pressure reductions from standard footwear baseline levels at the ulcer site than a removable ankle-high cast shoe or forefoot offloading shoe (67% v 47% v 26%, respectively, p=0.029) (20). Several within-subject studies also found that removable knee-high devices show greater forefoot plantar pressure reduction than removable ankle-high devices (53, 54, 64-67). Three RCTs investigated weight-bearing activity. One high-quality RCT found no differences in average daily step count between a removable knee-high device (bivalved TCC) and removable ankle-high cast shoe or forefoot offloading shoe device (4,150 v 3,514 v 4,447, respectively, p=0.71) (20), but it should be noted the study was not powered for this outcome. Another low-quality RCT found a large but non-significant reduction in daily steps in a removable knee-high device compared to a removable ankle-high half-shoe (768 v 1,462 steps, p=0.15) (38). A third, low-quality, RCT found significant reductions in average daily step count in those patients wearing a removable knee-high device compared to wearing a healing sandal (1,404 v 4,022, p<0.01) (43). We conclude that removable knee-high devices reduce plantar pressures at ulcer sites and weight-bearing activity more effectively than removable ankle-high devices, and therefore have more potential for healing plantar neuropathic forefoot ulcers when worn.

Adverse events for removable knee-high offloading devices are likely to be the same as for non-removable knee-high devices. However, ankle-high offloading devices may potentially have fewer adverse events compared with knee-high offloading devices as they either have lower or no device walls that reduce the risk for abrasions, lower-leg ulcers, imbalance, and gait challenges (33), and they may have lower treatment discontinuation (20). One high-quality meta-analysis including two low-quality RCTs (38, 43) found higher treatment discontinuation with removable knee-high devices compared with removable ankle-high devices ($p<0.01$) (34). One high-quality RCT found no differences in adverse events between a removable knee-high device and either a removable cast shoe or forefoot offloading shoe (45% v 30% v 25%, respectively, $p=0.377$) (20). Further, those events reported were mostly minor pressure points, blisters and abrasions; with smaller numbers of serious hospitalisation and fall events (15% v 5% v 5%, respectively, p=not reported) (20). A low-quality RCT also found no difference in adverse events for new ulcers or infections between removable knee-high and removable ankle-high devices (15% v 13%, $p>0.05$) (43). A third, low-quality, RCT reported no adverse events in either group (38). We conclude there is no clear difference in adverse events between removable knee-high and removable ankle-high offloading devices.

We identified one low-quality RCT reporting preference outcomes that found no difference in patient satisfaction, comfort or preference to wear again between wearing a removable knee-high and removable ankle-high offloading device ($p>0.05$) (43). The same study reported that the removable knee-high group was more non-adherent than the removable ankle-high group (11% vs 0% of participants were deemed non-adherent with their device and were removed from the study as drop outs, p=not reported) (43). A high-quality RCT also reported non-significantly higher non-adherence with removable knee-high offloading than with two removable ankle-high devices (17% vs 5% vs 5% of the time, $p=0.236$) (20). We conclude patients have similar preference for removable knee-high and ankle-high devices and non-adherence does not seem to be very different between devices, although one should note that these studies were not powered to detect a difference in non-adherence between devices.

One low-quality RCT reported on costs, finding that one-off device costs was more expensive for a removable knee-high offloading device (walker) than an ankle-high offloading device (half-shoe) ($150-200 v $25-75, p=not reported) (38). Based on only one, already rather old study, we provisionally conclude that the device costs of treatment are higher in removable knee-high devices than in removable ankle-high offloading devices.

Contraindications for the use of removable knee-high offloading devices, based predominantly on expert opinion, include presence of both moderate infection and moderate ischemia, or severe infection or severe ischaemia. We refer to the IWGDF infection and PAD guidelines and the IWGDF glossary for definitions on infection and ischemia (27, 28, 46) .

In summary, based on similar healing outcomes in a small number of mostly low-quality controlled studies, but consistently superior plantar pressure offloading and induced reduction of walking activity and thus superior healing potential in those studies and other non-controlled studies, we rate the quality of evidence favouring removable knee-high devices over removable ankle-high devices as low. Additionally, considering this healing benefit, no apparent differences in adverse events or preferences, and slightly higher non-adherence and treatment costs with removable knee-high offloading, we favour removable knee-high offloading over ankle-high offloading in our recommendation, but grade the recommendation as weak. Nevertheless, as such a device is removable and there is potential for non-adherence, we stress that the patient should (repeatedly) be educated on the benefit of adherence to wearing the device to improve the effectiveness of the device for healing (55).

Recommendation 3: In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer for whom a knee-high offloading device is contraindicated or not tolerated, use a removable ankle-high offloading device as the third-choice of offloading treatment to promote healing of the ulcer. Additionally, encourage the patient to consistently wear the device (Strong; Low).

Rationale: Overall, evidence indicates that removable and non-removable knee-high offloading devices give better clinical outcomes or potential for healing than ankle-high devices (see rationales for recommendations 1 and 2). However, there may be contraindications (see rationales for recommendations 1 and 2) or patient intolerance for wearing a knee-high device, such as expected or experienced device-induced gait instability, abrasions or other complications from the cast or device wall, or patient refusal to wear the device. Another reason may be lack of available knee-high offloading devices. In those cases, removable ankle-high offloading can be considered. This includes ankle-high walkers, cast shoes, half shoes, forefoot offloading shoes, post-operative healing shoes and custom-made temporary shoes.

Our systematic review identified (31) no controlled studies specifically comparing removable ankle-high devices to conventional or standard therapeutic footwear or other offloading interventions, for effectiveness of healing, surrogate healing outcomes, adverse events, patient preferences or costs.

Several non-controlled studies show that 70–96% of plantar foot ulcers can be healed in a reasonable time frame (mean 34–79 days) with ankle-high removable offloading devices, provided they are used regularly (68-72). Multiple within-subject studies also consistently found that a variety of removable ankle-high offloading devices were more effective in reducing plantar pressure at the forefoot than a variety of footwear interventions (custom-made, therapeutic, extra-depth, conventional or standard footwear) (53, 54, 64, 65, 73-77). No studies were found for weight-bearing activity or adherence. Thus, we conclude that removable ankle-high devices have higher potential for healing than conventional or therapeutic footwear or other non-knee-high offloading interventions when worn.

Adverse events comparing ankle-high offloading devices to footwear interventions have not been reported in the literature. Based on expert opinion, we consider ankle-high offloading devices to have a low adverse event rate, and comparable to conventional or therapeutic footwear. Adverse events may include minor abrasions, blisters, minor gait challenges or instability, and, with poor casting, new ulcers with cast shoes. However, it should be noted that the traditional form of half-shoes, that only support the midfoot and heel (71), contrary to a forefoot offloading shoe, are contraindicated owing to risk of midfoot fracture.

Two studies reported on patient preferences (74, 75). They showed that patient comfort was similar between ankle-high walkers and standard footwear (75), but was lower in different forefoot offloading shoe models compared with standard footwear (74). A recent study reported that the use of ankle-high walkers had similar patient comfort levels to athletic shoes when the contralateral leg had a shoe raise to compensate for leg-length discrepancy (53). Based on expert opinion, patients may prefer an ankle-high walker over a forefoot offloading shoe, because the latter has a significant negative rocker outsole that may cause problems during gait.

We found no studies comparing costs of ankle-high offloading devices with conventional or therapeutic footwear. The cost of treatment is likely to be low for some ankle-high offloading devices (e.g. cast shoes, forefoot offloading shoes), particularly when they require no replacement during treatment. However, costs for therapeutic footwear are expected to be higher than for these other ankle-high devices.

In summary, all evidence for this recommendation comes from cross-sectional studies and expert opinion, and therefore the quality of evidence for this recommendation is rated as low. When weighing the potentially higher healing benefits of removable ankle-high devices over conventional or therapeutic footwear, better outcomes on plantar pressure, with expected similar low incidence of harms, patient preferences, and costs we grade this recommendation as strong. In particular, for countries with low resources or lack of trained cast technicians, these removable ankle-high devices may be an appropriate offloading intervention for treating plantar neuropathic forefoot ulcers.

FOOTWEAR

PICO 4: In people with a plantar DFU, are conventional or standard therapeutic footwear compared to other (non-surgical) offloading interventions effective to heal the DFU?

Recommendation 4a: In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer, do not use, and instruct the patient not to use, conventional or standard therapeutic footwear as offloading treatment to promote healing of the ulcer, unless none of the above-mentioned offloading devices is available (Strong; Moderate).

Rationale: There are no studies that show the efficacy of conventional or standard-therapeutic footwear as the primary intervention to heal neuropathic plantar foot ulcers. In the few studies in which this footwear has been tested as a comparison intervention, the conventional or standard therapeutic footwear proved inferior to other offloading devices (custom-made or prefabricated, non-removable or removable, knee-high or ankle-high devices) to both reduce mechanical stress and effectively heal a neuropathic plantar forefoot ulcer. Two high-quality meta-analyses found non-removable knee-high offloading devices were 62-68% more likely to heal a neuropathic plantar forefoot ulcer than therapeutic footwear ($p<0.01$) (34, 37). Another high-quality meta-analysis (35), including two lower quality RCTs (49, 78), reported removable offloading devices were 76% more likely to heal these ulcers than therapeutic footwear, but the difference was non-significant ($p=0.184$) (35). A low quality RCT not included in the meta-analyses found no difference between TCCs, non-removable knee-high walkers or modified footwear for healing rates ($p=0.99$) and time-to-healing ($p=0.77$) (61).

Four low-quality RCTs reported adverse events using therapeutic footwear and all were compared to TCCs. Two found similar low proportions of abrasions or new ulcers for TCCs (0-4%) and footwear (0-4%, no p=not reported) (61, 79). Whilst another two found lower proportions of infections with TCC (0-3%) compared with footwear (19-26%) ($p<0.05$) (49, 78). One high-quality meta-analysis reported significantly more treatment discontinuations due to a combination of adverse events, voluntary withdrawal or losses to follow-up in those patients treated with TCCs compared to therapeutic footwear (p=0.003) (34).

One low-quality RCT reported on patient preference and found that those patients using TCCs and those using therapeutic footwear had no difference in an acceptance of treatment score (p="not significant") (79). One low-quality RCT reported the material costs for modified footwear were lower than for TCCs and non-removable walkers in treating patients with a foot ulcer ($7 v $20 v $35, respectively; $p<0.01$) (61). However, the aforementioned large health technology assessment showed therapeutic footwear was far less cost-effective than other non-removable (TCC and non-removable knee-high offloading device) and removable offloading devices (removable walkers) (34).

Taken together, based on data from multiple meta-analyses consistently favouring the use of offloading devices over conventional or standard therapeutic footwear to heal neuropathic plantar forefoot ulcers, we rate the quality of evidence as moderate. Based additionally on worse outcomes for adverse events and costs using therapeutic footwear, and similar outcomes for preferences, we grade this recommendation as strong.

OTHER OFFLOADING TECHNIQUES

PICO 5: In people with a plantar DFU, are any other offloading techniques that are not device or footwear-related, effective to heal a DFU?

Recommendation 4b: In that case, consider using felted foam in combination with appropriately fitting conventional or standard therapeutic footwear as the fourth choice of offloading treatment to promote healing of the ulcer (Weak; Low).

Rationale: Despite many practitioner surveys reporting high use of other offloading techniques (particularly for felted foam) (17, 18), there has been limited evidence to support any other offloading techniques to effectively heal a neuropathic plantar foot ulcer (10). Other offloading techniques 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 approach.

Our updated systematic review (31) identified just three low-quality controlled trials (70, 80, 81) on other offloading techniques to heal a neuropathic plantar foot ulcer. All three trials investigated felted foam padding (70, 80, 81). No controlled trials were identified for bed rest, crutches, wheelchairs, offloading dressings, callus debridement, foot-related strength and stretching exercises, or gait retraining to effectively heal DFUs.

One low-quality RCT showed significantly shorter time-to-healing with felted foam worn in a post-operative shoe when compared with a half-shoe used without the felted foam (81). Another low-quality RCT showed no difference in ulcer size reduction at 4 weeks between felt fitted to the foot worn in a post-operative shoe compared with felt fitted to a post-operative shoe (80). A low-quality retrospective cohort study found no differences in ulcers healed or time-to-healing between felted foam fitted to the foot in a post-operative shoe, felted foam fitted to a post-operative shoe, a walking splint or TCC (70). Additionally, two within-subject studies found that felted foam in addition to post-operative shoes moderately reduced plantar pressures over one week compared to post-operative shoes alone (82, 83). We conclude that felted foam used with an ankle-high offloading device may be more effective than wearing just the device alone, to reduce plantar pressure and heal a plantar neuropathic DFU. Furthermore, we consider the same effectiveness may be apparent if the felted foam was used with an appropriately fitting conventional or standard therapeutic footwear as opposed to just wearing the footwear alone.

The only two controlled studies reporting adverse events found similar levels of adverse events for the use of felted foam in combination with an ankle-high offloading device compared with an ankle-high device alone, including minor skin tear/maceration (10% v 20%) and new infection (25% v 23%) (80, 81). No controlled studies were identified that investigated patient preferences or costs; however, patients will likely value and prefer the use of felted foam as an easy-to-use modality. The costs of felted foam are relatively low, but it does require frequent replacement, by a clinician, the patient, a relative, or a home-care nurse. Based on the evidence from the studies performed, felted foam may be used in ankle-high offloading devices or when no offloading devices are available then may be used in addition to appropriately fitting conventional or standard therapeutic footwear. We define appropriately fitting footwear as providing sufficient room for the patients' foot shape and the added felted foam. This enables for some offloading treatment of the ulcer if other forms of offloading devices, as mentioned in recommendation 1 to 3, are not available. Whether the felted foam is fitted to the foot or to the shoe or insole does not make a difference in healing, although fitting it to the foot provides some offloading when the patient is non-adherent to wearing the shoes.

In summary, based on few low-quality controlled studies, and the difficulty in determining the added effect of felted foam in these studies, we rate the quality of evidence as low. Any benefit found with the use of felted foam will likely outweigh the harm. Together with a lack of information on costs and patient preference, we rated the strength of this recommendation as weak. Finally, based on the evidence from all offloading intervention studies performed and our expert opinion, felted foam may be used in addition to offloading devices, or if no offloading devices are available then felted foam may be used in combination with appropriately fitting conventional or standard therapeutic footwear as the fourth-choice of offloading treatment for healing the ulcer. However, felted foam should never be used as a single treatment modality.

SURGICAL OFFLOADING TECHNIQUES

PICO 6: In people with a DFU, are surgical offloading techniques compared to non-surgical offloading interventions effective to heal the DFU (O)?

Recommendation 5: In a person with diabetes and a neuropathic plantar metatarsal head ulcer, consider using Achilles tendon lengthening, metatarsal head resection(s), or joint arthroplasty to promote healing of the ulcer, if non-surgical offloading treatment fails (Weak; Low).

Rationale: Surgical offloading techniques have been traditionally used for plantar ulcers that are considered hard-to-heal with non-surgical offloading interventions (58). These techniques change the structure of the foot and therefore provide a more permanent offloading solution for areas of elevated mechanical stress, even when the patient is not adherent to wearing an offloading device. However, surgical offloading potentially comes with increased risk of complications (58). Surgical offloading is defined as a surgical procedure undertaken with the intention of relieving mechanical stress from a specific region of the foot, and typically include Achilles tendon lengthening, metatarsal head resection, osteotomy, arthroplasty, ostectomy, exostectomy, external fixation, flexor tendon transfer or tenotomy, and tissue fillers such as silicone or fat.

Our updated systematic review (31) identified one high-quality meta-analysis on this topic (84). This meta-analysis included two 2 RCTs, one high-quality (85) and one low-quality (86), and investigated Achilles tendon lengthening and gastrocnemius recession compared with TCC controls (84). It found no differences in proportion of ulcers healed or time-to-healing (84). The high-quality RCT did find small effects, but these were not statistically significant, on ulcers healed (100% v 88%, p=0.12) and time-to-healing (40.8 days v 57.5 days, p=0.14) favouring Achilles tendon lengthening with TCC compared with TCC alone in patients with reduced ankle dorsiflexion (85). Four retrospective non-controlled studies showed 80–95% healing in 3 months with Achilles tendon lengthening (87-90).

One high-quality RCT found that metatarsal head resection(s) in combination with therapeutic footwear compared with therapeutic footwear alone healed more ulcers (95% v 79%, p<0.05) with shorter time-to-healing (47 v 130 days, p<0.05) (91). Three low-quality retrospective controlled cohort studies also found metatarsal head resection(s) had shorter time-to-healing (by 21-350 days, p<0.05) than non-surgical offloading interventions (removable walker, healing sandals and therapeutic footwear) (92-94). Additionally, six non-controlled studies showed positive effects of single or pan metatarsal head resection in time-to-healing of plantar neuropathic metatarsal head ulcers, in patients in whom non-surgical treatment had failed (95-100).

Two small lower-quality retrospective controlled cohort studies investigated metatarsal-phalangeal joint arthroplasty in addition to TCC and found shorter time-to-healing (by 24-43 days, p<0.05) compared with non-removable offloading devices (TCC or non-removable walker) (101, 102). Four non-controlled studies showed between 91% and 100% healing of plantar, lateral, or dorsal toe ulcers using interphalangeal or metatarsal-phalangeal joint arthroplasty (103-106).

The potential harm of applying these surgical techniques includes post-operative complications, infection, gait problems, acute Charcot neuro-osteoarthropathy, ruptured Achilles tendons and transfer ulcers (87, 97, 99). The controlled trials reporting adverse events found mixed results (85, 91-93, 101, 102). These included a significant increase in heel ulcers after Achilles tendon lengthening compared with TCC alone (13% v 0%, $p<0.05$), but similar number of abrasions (13% v 18%), infection (3% v 0%), amputation (0% v 3%), falls (7% v 0%) and death (10% v 9%) (85). Most other trials compared surgical techniques to removable offloading devices or footwear and found mixed results on adverse events that were not significantly different between interventions, including infection (5-40% v 13-65%) and amputation (5-7% v 10-13%) ($p>0.05$) (91-93, 101). One recent low-quality controlled study of metatarsal head resection(s) found significant decreases in number of hospitalisations and infections compared with non-surgical offloading controls described as "non-weight bearing, and sometimes specialized footwear" ($p<0.05$) (94).

Only one controlled study reported on patient preferences, finding higher discomfort in a surgical offloading group during healing ($p<0.05$), but higher satisfaction after treatment when compared with therapeutic footwear ($p<0.01$) (91). We found no controlled trials investigating costs. Costs of treatment for surgical interventions are generally considered higher than for non-surgical treatment, although one study showed no difference in costs between metatarsal head resection and non-surgical treatment of a plantar foot ulcer (99).

In summary, there is some evidence to support surgical versus non-surgical offloading to improve time-to-healing of plantar foot ulcers that prove to be hard-to-heal after unsuccessful non-surgical treatment. However, based on the low number of controlled trials for each surgical intervention, the general low-quality of these trials and the mixed benefits, we consider the quality of evidence for this recommendation is low. When considering that the benefits predominantly relate only to time-to-healing and not to healing proportion, it is unclear if the benefits outweigh the potential harm. Patients may value and prefer surgical treatment after long and unsuccessful non-surgical treatment (such as with knee-high offloading devices). Thus, we rate the strength of this recommendation as weak. However, we recommend considering surgical offloading when non-surgical offloading treatment fails in healing the foot ulcer. Surgical offloading is contra-indicated when severe ischemia is present; the ischemia should be primarily addressed in that case.

Recommendation 6: In a person with diabetes and a neuropathic plantar digital ulcer, consider using digital flexor tenotomy to promote healing of the ulcer, if non-surgical offloading treatment fails (Weak; Low).

Rationale: Two recent systematic reviews were identified on the efficacy of digital flexor tenotomy on DFU outcomes (107, 108). Both reviews identified the same five non-controlled studies (109-113) and one of the reviews identified a sixth non-controlled study (114). The larger systematic review reported an overall healing rate of 97% in a mean 29.5 days (107). The majority of the studies that reported on adverse events, reported moderate incidences of infection (2-7%), transfer lesions (5-16%) amputations (2-9%) or ulcer recurrence (0-21%) (107). None reported patient preference or cost outcomes.

While controlled studies on this topic are lacking, we consider this procedure to be a promising intervention in patients with hammertoes and recalcitrant digital ulcers in particular that fail non-surgical treatment. However, the quality of the evidence for this recommendation is low. The possible benefits of digital flexor tenotomy may outweigh the potential harm. Patients who have digital ulcers that will not heal with non-surgical treatment may value and prefer treatment by flexor tenotomy, which may be performed in an outpatient setting, without need for subsequent immobilization. Costs and cost-effectiveness of this procedure have not been evaluated. Thus, we consider the strength of this recommendation to be weak.

OTHER ULCERS

PICO 7: In people with a plantar DFU complicated by infection or ischaemia, which offloading intervention is effective for healing the DFU?

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

Recommendation 7b: In a person with diabetes and a neuropathic plantar forefoot or midfoot ulcer with both mild infection and mild ischemia, or with either moderate infection or moderate ischaemia, consider using a removable knee-high offloading device to promote healing of the ulcer. (Weak; 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 ischemia, primarily address the infection and/or ischemia, and consider using a removable offloading intervention based on the patient's functioning, ambulatory status and activity level, to promote healing of the ulcer (Weak; Low).

Rationale: Many plantar ulcers seen in clinical practice are not purely neuropathic ulcers, but have some level of infection and/or ischemia present. Due to the neuropathic origin and mechanical stress that often caused and still affects these ulcers, they do require offloading. However, health care professionals should be more cautious about which kind of offloading to use and when to use them if ulcers are complicated by infection or ischaemia.

As identified in Recommendation 1, non-removable knee-high offloading devices can be considered for healing neuropathic plantar forefoot ulcers that have mild infection, mild-to-moderate amounts of exudate or mild ischaemia (34-36, 39, 45, 52). Non-removable offloading should not be used for moderate-to-severe infections or heavily exudating ulcers that require frequent local wound care or inspection, or moderate-to-severe ischaemia where there may be doubt on the potential for wound healing, or when both mild infection and mild ischaemia are present (34-36, 39, 45, 52). Removable knee-high offloading devices can be considered for healing ulcers with both mild infection and mild ischaemia present, or with heavy exudate, moderate infection or moderate ischaemia present, which all require frequent local wound care or inspection. However, if a neuropathic plantar forefoot ulcer is complicated by both moderate infection and moderate ischemia, or by severe infection or severe ischaemia, then the infection or ischemia should primarily be addressed and an offloading intervention should be applied based on the patient's function, ambulatory status, and activity level.

The overall quality of evidence for these recommendations are low as they are collectively based on only a few observational studies (39, 45, 47, 48), interpretations from small sub-groups of patients with these complications in some larger controlled trials (49-51), and expert opinion, but with the notion that these plantar ulcers still require offloading for healing (33, 34). Furthermore, based on the lack of evidence, data missing on harm and benefits, patient preferences and costs, the strength of these recommendations are weak.

PICO 8: In people with a plantar rearfoot DFU, which offloading intervention is effective to heal the DFU?

Recommendation 8: In a person with diabetes and a neuropathic plantar heel ulcer, consider using a knee-high offloading device or other offloading intervention that effectively reduces plantar pressure on the heel and is tolerated by the patient, to promote healing of the ulcer. (Weak; Low).

Rationale: Neuropathic plantar rearfoot ulcers are less prevalent than forefoot ulcers (115), but are considered more of a challenge to offload and heal (58). There is a paucity of evidence available on offloading interventions to treat plantar rearfoot ulcers (58).

Our updated systematic review (31) identified only one controlled study that specifically reported healing outcomes for plantar rearfoot ulcers (78). This low-quality RCT reported that those ulcers offloaded with a TCC had shorter time-to-healing than those using therapeutic footwear (69 days vs 107 days), but no statistical significance was reported (78). Another high-quality RCT compared a custom-made fiberglass heel cast with standard wound care in patients with heel ulcers, but of which most (72%) were non-plantar (21). The authors did not specifically report on plantar heel ulcers. This RCT is discussed under non-plantar ulcers.

As outcomes on healing were limited, we assessed surrogate measures for offloading as previously recommended (11) and identified three controlled trials investigating plantar pressure reductions. One high-quality RCT found slightly greater rearfoot plantar pressure reductions from baseline barefoot pressure in participants wearing a TCC compared with those wearing a knee-high walker, but this difference was not significant (54% v 40%, p=0.11) (62). Another high-quality RCT found a significant increase in rearfoot plantar pressures in those undergoing an Achilles tendon lengthening procedure in combination with a TCC compared with those treated with a TCC alone (70.6±28.1 vs 55.8±30.7 N/cm2, p=0.018) (116). The other low-quality non-randomized controlled trial reported rearfoot plantar pressures in a removable ankle-high walker intervention increased by 10% from baseline pressures in conventional footwear (117).

A number of cross-sectional within-subject designed studies also investigated the effect of different offloading interventions on rearfoot plantar pressures (65, 66, 118). Three investigated TCCs compared with knee-high walkers and found mixed results. One found TCCs had slightly greater rearfoot plantar pressure reduction (118), another found knee-high walkers reduced more rearfoot pressure (65), and a third found they were the same in pressure relief (66). Several others found removable knee-high devices (walkers and bivalved TCCs) had slightly greater rearfoot plantar pressure reductions than ankle-high devices (walkers, cast shoes, post-operative healing shoes) (65-67, 76), but not always to a statistically significant level (66, 67). Other studies found that removable ankle-high devices give greater rearfoot plantar pressure reduction than footwear (therapeutic and standard) (74-76). Heel-relief shoes are specifically designed to offload the heel, but have not been tested for efficacy on pressure relief to date.

No controlled studies specifically reported on adverse events when treating those with rearfoot ulcers. However, one RCT found an increase in new plantar heel ulcer development in those undergoing Achilles tendon lengthening in combination with a TCC to heal forefoot ulcers compared with a TCC alone, but did not report significance (13% v 0%) (85). Otherwise we suggest the adverse events from different offloading interventions would be similar to those to heal a forefoot DFU. Thus, we consider that non-removable and removable knee-high devices have similar low incidence of harm, but potentially slightly higher than removable ankle-high devices. No studies have reported on preferences or costs for treating plantar rearfoot ulcers.

In summary, there is some evidence that using knee-high offloading devices may be more effective in time-to-healing and reducing plantar pressures on the heel than other offloading interventions. However, based on one low-quality controlled trial comparing sub-groups and several non-controlled studies we rate the quality of evidence as low. When considering the benefits predominately related to small effects on time-to-healing and plantar pressure reductions compared to other offloading interventions, and given the paucity of data on harms, patient preferences and costs, we rate the strength of this recommendation as weak. Therefore, we recommend considering using a knee-high offloading device or any other offloading intervention that can demonstrate effective reduction of plantar pressure on the heel.

PICO 9: In people with a non-plantar DFU, which offloading intervention is effective to heal the DFU?

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

Rationale: Overall, there is very little evidence available on how to treat non-plantar foot ulcers. This is despite non-plantar DFU being prevalent and also needing relief from mechanical stress (115). Our updated systematic review (31) identified just one controlled trial that could partly address this topic (21). This large high-quality RCT compared a custom-made, fiberglass heel cast in additional to usual care with usual care alone ("usual care was not uniform") in patients that mostly (72%) had non-plantar heel DFUs (21). They found no differences in ulcer healing, adverse events or patient preferences, but did find the heel cast had higher overall costs (21). Although patients with non-plantar DFU made up the majority of included patients, the RCT did not report outcomes specifically for the non-plantar DFU (21).

Therefore, until new evidence becomes available and depending on the location of the non-plantar ulcer, we recommend that various modalities can be considered, including ankle-high offloading devices, modifications to conventional or therapeutic footwear, toe spacers, and orthoses. Footwear does not have to be therapeutic but can consist of properly fitting conventional footwear that prevents, or is modified to prevent, direct contact with the ulcer. The modality chosen should be based on the principal that it prevents any mechanical stress or contact with the ulcer and is an appropriate fit for the rest of the foot so as not to produce new lesions.

Based on the RCT and our expert opinion, we expect any potential harm such as lesions directly caused by these other modalities on the foot to be minimal. We also anticipate that patients will likely prefer the use of these modalities for treatment of their non-plantar foot ulcers, as they should increase the protection of their ulcer, compared with standard care. We also suggest the additional costs for applying these modalities are relatively low.

In summary, due to the paucity of data, we rate the quality of evidence for this recommendation as low. However, we assessed the strength of this recommendation as strong. This is based on our opinion that these modalities compared with standard wound care alone would produce benefits in terms of DFU healing, mechanical stress reduction and patient preference, that should outweigh any harms or small costs of treatment.

KEY CONTROVERSIES AND CONSIDERATIONS

1. Since the last guidelines, the TCC is no longer the only gold standard treatment option to effectively heal plantar forefoot ulcers. Prefabricated removable knee-high walkers that are rendered non-removable have been shown with more evidence over the last 4 years, to be as effective as the TCC. This has changed the traditional view on offloading, in which the main comparison was TCC versus any other offloading interventions, but is now non-removable knee-high offloading devices versus other offloading interventions. This has positive implications for those settings where casting materials or trained casting technicians are not available. In these settings, depending on patient preferences and fit, reliance on the correct use of prefabricated removable walkers made non-removable for offloading is appropriate.
2. In the large number of studies conducted on the efficacy of the TCC or non-removable knee-high walkers, many different versions, types and methods of devices and casts have been used. These different versions of devices may potentially lead to different outcomes and varied costs. Trials are needed in which these different versions of casting or walkers used are compared with each other, so that a more informed decision can be made on which type of cast or walker is best to use for non-removable knee-high offloading.

3. Likewise, there are many different offloading devices that are defined as an "ankle-high offloading device" such as ankle-high walker, forefoot offloading shoe, cast shoe, healing sandal, post-operative healing shoe, custom-made temporary shoe, etc. These devices can be just above-ankle or below-ankle, prefabricated or custom-made and may lead to different outcomes and varied costs. More consideration should be given to studying the efficacy of each of these ankle-high offloading devices in healing foot ulcers to determine which of these devices are most effective on healing and plantar pressure outcomes, so that more informed decisions can also be made in clinical practice on which type is best to use for removable ankle-high offloading.
4. Many RCTs on offloading do not directly measure the degree to which the mechanical stress on the ulcer has been changed by the offloading intervention. Such measurements improve not only our understanding of the role of offloading in healing but also other outcomes. A stronger focus is required on measuring the factors impacting on the mechanical stress levels that lead to different healing outcomes, such as plantar pressure, shear stress, weight-bearing activity that includes steps and standing duration, and adherence to using offloading devices.
5. Offloading studies have focused almost exclusively on the treatment of non-complicated neuropathic plantar forefoot ulcers. Little data are 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 are from clinical experience now much more common than years ago. We have now addressed these specific foot ulcers in separate PICOs and recommendations, which are largely based on expert opinion. High quality studies on offloading ulcers other than the non-complicated neuropathic plantar forefoot ulcer are still 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 intervention present with worse healing outcomes. A stronger focus is required, both in research and in clinical practice, on the measurement and improvement of offloading treatment adherence.
7. Surgical offloading has primarily been applied to heal foot ulcers in selected patients typically where other non-surgical offloading interventions have failed. More high-quality RCTs concerning surgical offloading procedures are required to determine the impact of surgical interventions on the healing of both non-complicated and complicated foot ulcers.
8. Information on harms and other adverse events are critical to determine whether to use an offloading intervention or not, and if so, which one. Most RCTs are underpowered to determine if there are any differences in adverse events between offloading interventions. It is unlikely a RCT will be established to test for adverse events as the primary outcome. However, if future trials collect the same adverse events with the same definitions there is the possibility of pooling adverse event data in more homogenous meta-analyses that may better answer questions on which interventions cause fewer or more adverse events. We recommend future trials ensure they collect adverse events based on standard definitions as recommended by Jeffcoate et al. (11).
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. While some cost studies have been performed since our previous guidelines in 2015, more attention is still warranted in view of the continuing pressure of healthcare cost containment.

10. The majority of interventions discussed are from studies from more economically developed countries with relatively temperate climates. While some of these interventions are broadly applicable, there is a need for more specific guidance on approaches to ulcer healing in these lower income regions where climate and/or resources may be a factor in which offloading device can be used, adherence to wearing the device and its efficacy.

CONCLUDING REMARKS

The global patient and economic burden of diabetic foot disease can be considerably reduced when evidence-based treatment is implemented by health-care professionals and multidisciplinary teams working on this medical problem. Arguably, offloading the foot ulcer, is one of the, if not the, most important intervention with the strongest evidence available for healing foot ulcers and reducing the global burden of diabetic foot disease. We think that following the recommendations for offloading treatment of diabetic foot ulcers in this guideline will help health care professionals and teams provide better care for persons with diabetes who have a foot ulcer and are at risk for infection, hospitalization and amputation.

We encourage our colleagues, especially those working in diabetic foot clinics, to consider developing some forms of surveillance (e.g., registries, pathways) to monitor and attempt to improve their outcomes in persons with diabetes and a foot ulcer. We also encourage our research colleagues to consider our key controversies and considerations and conduct well-designed studies (11) 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.

GLOSSARY

Adverse events 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 (abrasions, calls and blisters); new DFU formation; acute Charcot foot; infection; hospital admissions; amputation; 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: usually defined as the weight-bearing activity (average daily steps or strides of the foot on which the specific region of interest is located, e.g. DFU site).

Ankle-high offloading device: an offloading device that extends no higher up the leg than just above the ankle level. Includes ankle-high walker, forefoot offloading shoe, cast shoe, healing sandal, post-operative healing shoe, and 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. Examples are Mabal cast shoe, Ransart boot, or Scotch-cast boot.

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

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 pre-fabricated (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 (46).

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

Extra-depth footwear: Footwear constructed with additional depth and volume in order 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 on the foot. The footwear has a specific shape with a wedge design and the outsole portion missing in 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 heel and the midfoot as the only weight-bearing surfaces.
Healed DFU: see IWGDF definitions and criteria document (46).
Heel-relief shoe: shoe designed to offload the heel. The heel part is missing from the footwear, and its sole arrangement is constructed in such a way that the heel is not loaded when walking.
In-shoe orthoses: devices put inside the shoe to achieve some alteration in the function of the foot.
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).
Non-plantar: see IWGDF definitions and criteria document (46).
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 knee-high walker wrapped with a layer(s) of fiberglass cast material circumferentially rendering it non-removable to the patient (also known as "instant total contact cast").
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 treatment, 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 (46).
Plantar pressure: see IWGDF definitions and criteria document (46).
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 (pressure) from a specific region of the foot (e.g. Achilles tendon lengthening, metatarsal head resection, osteotomy, arthroplasty, ostectomy, exostectomy, external fixation, flexor tendon transfer or tenotomy, silicone injections, tissue augmentation, etc.).
Therapeutic footwear: Generic term for footwear designed to have some 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.
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 plantar DFU.

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CONFLICT OF INTEREST STATEMENTS

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All individual conflict of interest statement of authors of this guideline can be found at: *www.iwgdfguidelines.org/about-iwgdf-guidelines/biographies*

VERSION

Please note that this guideline has been fully refereed and reviewed, but has not yet been through the copyediting, typesetting, pagination and proofreading process. Thus, it should not be considered the Version of Record. This guideline might still contain errors or otherwise deviate from the later published final version. Once the final version of the manuscript is published online, this current version will be replaced.

REFERENCES

1. Boulton AJM, Vileikyte L, Ragnarson-Tennvall G, Apelqvist J. The global burden of diabetic foot disease. Lancet. 2005;366(9498):1719-24.
2. Armstrong DG, Boulton AJM, Bus SA. Diabetic Foot Ulcers and Their Recurrence. New England Journal of Medicine. 2017;376(24):2367-75.
3. Jeffcoate WJ, Vileikyte L, Boyko EJ, Armstrong DG, Boulton AJM. Current Challenges and Opportunities in the Prevention and Management of Diabetic Foot Ulcers. Diabetes Care. 2018;41(4):645-52.
4. Lazzarini PA, Pacella RE, Armstrong DG, Van Netten JJ. Diabetes-related lower-extremity complications are a leading cause of the global burden of disability. Diabetic Medicine. 2018;35:1297-9.
5. Lazzarini PA, Hurn SE, Kuys SS, Kamp MC, Ng V, Thomas C, et al. The silent overall burden of foot disease in a representative hospitalised population International Wound Journal. 2017;14(4):716-28.
6. Bus SA. The Role of Pressure Offloading on Diabetic Foot Ulcer Healing and Prevention of Recurrence. Plast Reconstr Surg. 2016;138(3 Suppl):179S-87S.
7. Lazzarini PA, Crews RT, Van Netten JJ, Bus SA, Fernando ME, Chadwick PJ, et al. Measuring Plantar Tissue Stress in People With Diabetic Peripheral Neuropathy: A Critical Concept in Diabetic Foot Management. Journal of Diabetes Science and Technology. 2019;0(0):1932296819849092.
8. Fernando ME, Crowther RG, Pappas E, Lazzarini PA, Cunningham M, Sangla KS, et al. Plantar pressure in diabetic peripheral neuropathy patients with active foot ulceration, previous ulceration and no history of ulceration: a meta-analysis of observational studies. Plos One. 2014;9(6):e99050.
9. Fernando M, Crowther R, Lazzarini P, Sangla K, Cunningham M, Buttner P, et al. Biomechanical characteristics of peripheral diabetic neuropathy: A systematic review and meta-analysis of findings from the gait cycle, muscle activity and dynamic barefoot plantar pressure. Clinical Biomechanics (Bristol, Avon). 2013;28(8):831-45.
10. Bus SA, van Deursen RW, Armstrong DG, Lewis JEA, Caravaggi CF, Cavanagh PR, et al. Footwear and offloading interventions to prevent and heal foot ulcers and reduce plantar pressure in patients with diabetes: a systematic review. Diabetes/Metabolism Research and Reviews. 2016;32:99-118.
11. Jeffcoate WJ, Bus SA, Game FL, Hinchliffe RJ, Price PE, Schaper NC. Reporting standards of studies and papers on the prevention and management of foot ulcers in diabetes: required details and markers of good quality. The Lancet Diabetes & Endocrinology. 2016;4(9):781-8.
12. Schaper NC, Van Netten JJ, Apelqvist J, Lipsky BA, Bakker K, on behalf of the International Working Group on the Diabetic F. Prevention and management of foot problems in diabetes: a Summary Guidance for Daily Practice 2015, based on the IWGDF Guidance Documents. Diabetes/Metabolism Research and Reviews. 2016;32:7-15.
13. Game FL, Apelqvist J, Attinger C, Hartemann A, Hinchliffe RJ, Löndahl M, et al. IWGDF guidance on use of interventions to enhance the healing of chronic ulcers of the foot in diabetes. Diabetes/Metabolism Research and Reviews. 2016;32:75-83.
14. Hinchliffe RJ, Brownrigg JRW, Apelqvist J, Boyko EJ, Fitridge R, Mills JL, et al. IWGDF guidance on the diagnosis, prognosis and management of peripheral artery disease in patients with foot ulcers in diabetes. Diabetes/Metabolism Research and Reviews. 2016;32:37-44.
15. Lipsky BA, Aragón-Sánchez J, Diggle M, Embil J, Kono S, Lavery L, et al. IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes. Diabetes/Metabolism Research and Reviews. 2016;32:45-74.
16. Wu SC, Jensen JL, Weber AK, Robinson DE, Armstrong DG. Use of pressure offloading devices in diabetic foot ulcers: do we practice what we preach? Diabetes Care. 2008;31(11):2118-9.
17. Raspovic A, Landorf K. A survey of offloading practices for diabetes-related plantar neuropathic foot ulcers. Journal of Foot and Ankle Research. 2014;7(1):35.
18. Quinton T, Lazzarini P, Boyle F, Russell A, Armstrong D. How do Australian podiatrists manage patients with diabetes? The Australian diabetic foot management survey. Journal of Foot and Ankle Research. 2015;8(1):16.

19. Bus SA, Armstrong DG, van Deursen RW, Lewis JEA, Caravaggi CF, Cavanagh PR, et al. IWGDF guidance on footwear and offloading interventions to prevent and heal foot ulcers in patients with diabetes. Diabetes/Metabolism Research and Reviews. 2016;32:25-36.

20. Bus SA, Netten JJv, Kottink AIR, Manning EA, Spraul M, Woittiez AJ, et al. The efficacy of removable devices to offload and heal neuropathic plantar forefoot ulcers in people with diabetes: a single-blinded multicentre randomised controlled trial. International Wound Journal. 2018;15(1):65-74.

21. Jeffcoate W, Game F, Turtle-Savage V, Musgrove A, Price P, Tan W, et al. Evaluation of the effectiveness and cost-effectiveness of lightweight fibreglass heel casts in the management of ulcers of the heel in diabetes: a randomised controlled trial. Health Technol Assess. 2017;21(34):1-92.

22. Najafi B, Grewal GS, Bharara M, Menzies R, Talal TK, Armstrong DG. Can't Stand the Pressure: The Association Between Unprotected Standing, Walking, and Wound Healing in People With Diabetes. J Diabetes Sci Technol. 2016;11(4):657-67.

23. Piaggesi A, Goretti C, Iacopi E, Clerici G, Romagnoli F, Toscanella F, et al. Comparison of Removable and Irremovable Walking Boot to Total Contact Casting in Offloading the Neuropathic Diabetic Foot Ulceration. Foot Ankle Int. 2016;37(8):855-61.

24. Bus SA, Lavery LA, Monteiro-Soares M, Rasmussen A, Raspovic A, Sacco ICN, et al. IWGDF Guideline on the prevention of foot ulcers in persons with diabetes. Diabetes/Metabolism Research & Reviews. 2019;in press.

25. Rayman G, Vas PR, Dhatariya KK, Driver VR, Hartemann A, Londahl M, et al. IWGDF Guideline on interventions to enhance healing of foot ulcers in persons with diabetes. Diabetes/Metabolism Research And Reviews. 2019;in press.

26. Monteiro-Soares M, Russell D, Boyko EJ, Jeffcoate WJ, Mills JL, Morbach S, et al. IWGDF Guideline on the classification of diabetic foot ulcers. Diabetes/Metabolism Research & Reviews. 2019;in press.

27. Lipsky BA, Senneville E, Abbas ZG, Aragon-Sanchez J, Diggle M, Embil JM, et al. IWGDF Guideline on the diagnosis and treatment of foot infection in persons with diabetes. Diabetes/Metabolism Research & Reviews. 2019;in press.

28. Hinchliffe RJ, Forsythe RO, Apelqvist J, Boyko E, Fitridge R, Hong JP, et al. IWGDF Guideline on the diagnosis, prognosis and management of peripheral artery disease in patients with a foot ulcer and diabetes. Diabetes/Metabolism Research & Reviews. 2019;in press.

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

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

31. Lazzarini PA, Jarl G, Gooday C, Viswanathan V, Caravaggi C, Armstrong DG, et al. Effectiveness of offloading interventions to heal foot ulcers and reduce mechanical stress in persons with diabetic foot ulcers: a systematic review. Diabetes/Metabolism Research and Reviews. 2019;in press.

32. Bus SA, Van Netten JJ, Apelqvist J, Hinchliffe RJ, Lipsky BA, Schaper NC. Development and methodology of the 2019 IWGDF Guidelines. Diabetes/Metabolism Research & Reviews. 2019;in press.

33. Martins de Oliveira AL, Moore Z. Treatment of the diabetic foot by offloading: a systematic review. J Wound Care. 2015;24(12):560, 2-70.

34. Health Quality Ontario. Fibreglass Total Contact Casting, Removable Cast Walkers, and Irremovable Cast Walkers to Treat Diabetic Neuropathic Foot Ulcers: A Health Technology Assessment. Ont Health Technol Assess Ser. 2017;17(12):1-124.

35. Elraiyah T, Prutsky G, Domecq JP, Tsapas A, Nabhan M, Frykberg RG, et al. A systematic review and meta-analysis of off-loading methods for diabetic foot ulcers. J Vasc Surg. 2016;63(2):59S-68S e1-2.

36. Lewis J, Lipp A. Pressure-relieving interventions for treating diabetic foot ulcers. Cochrane Database of Systematic Reviews. 2013(1).

37. Morona JK, Buckley ES, Jones S, Reddin EA, Merlin TL. Comparison of the clinical effectiveness of different off-loading devices for the treatment of neuropathic foot ulcers in patients with diabetes: a systematic review and meta-analysis. Diabetes/Metabolism Research and Reviews. 2013;29(3):183-93.

38. Armstrong DG, van Schie CHM, Nguyen HC, Boulton AJM, Lavery LA, Harkless LB. Off-loading the diabetic foot wound - A randomized clinical trial. Diabetes Care. 2001;24(6):1019-22.

39. Nabuurs-Franssen MH, Huijberts MS, Sleegers R, Schaper NC. Casting of recurrent diabetic foot ulcers: effective and safe? Diabetes Care. 2005;28(6):1493-4.

40. Wukich DK, Motko J. Safety of total contact casting in high-risk patients with neuropathic foot ulcers. Foot Ankle Int. 2004;25(8):556-60.

41. Armstrong DG, Lavery LA, Wu S, Boulton AJM. Evaluation of removable and irremovable cast walkers in the healing of diabetic foot wounds - A randomized controlled trial. Diabetes Care. 2005;28(3):551-4.

42. Caravaggi C, Sganzaroli A, Fabbi M, Cavaiani P, Pogliaghi I, Ferraresi R, et al. Nonwindowed nonremovable fiberglass offm-loading cast versus removable pneumatic cast (AircastXP diabetic walker) in the treatment of neuropathic noninfected plantar ulcers. Diabetes Care. 2007;30(10):2577-8.

43. Lavery LA, Higgins KR, La Fontaine J, Zamorano RG, Constantinides GP, Kim PJ. Randomised clinical trial to compare total contact casts, healing sandals and a shear-reducing removable boot to heal diabetic foot ulcers. International Wound Journal. 2015;12(6):710-5.

44. Prompers L, Huijberts M, Apelqvist J, Jude E, Piaggesi A, Bakker K, et al. Delivery of care to diabetic patients with foot ulcers in daily practice: results of the Eurodiale Study, a prospective cohort study. Diabetic Medicine: A Journal Of The British Diabetic Association. 2008;25(6):700-7.

45. Nabuurs-Franssen MH, Sleegers R, Huijberts MS, Wijnen W, Sanders AP, Walenkamp G, et al. Total contact casting of the diabetic foot in daily practice: a prospective follow-up study. Diabetes Care. 2005;28(2):243-7.

46. IWGDF Editorial Board. IWGDF Definitions and Criteria 2019 [Available from: *www.iwgdfguidelines.org/definitions-criteria*.

47. Ha Van G, Michaux C, Parquet H, Bourron O, Pradat-Diehl P, Hartemann A. Treatment of chronic plantar ulcer of the diabetic foot using an irremovable windowed fibreglass cast boot: prospective study of 177 patients. Diabetes Metab Res Rev. 2015;31(7):691-8.

48. Ha Van G, Siney H, Hartmann-Heurtier A, Jacqueminet S, Greau F, Grimaldi A. Nonremovable, windowed, fiberglass cast boot in the treatment of diabetic plantar ulcers: efficacy, safety, and compliance. Diabetes Care. 2003;26(10):2848-52.

49. Mueller MJ, Diamond JE, Sinacore DR, Delitto A, Blair VP, 3rd, Drury DA, et al. Total contact casting in treatment of diabetic plantar ulcers. Controlled clinical trial. Diabetes Care. 1989;12(6):384-8.

50. Udovichenko O, Galstyan G. Efficacy of removable casts in difficult to off-load diabetic foot ulcers: a comparative study. Diabetic Foot Journal. 2006;9(4):204-8.

51. Van De Weg FB, Van Der Windt DA, Vahl AC. Wound healing: total contact cast vs. custom-made temporary footwear for patients with diabetic foot ulceration. Prosthet Orthot Int. 2008;32(1):3-11.

52. Tickner A, Klinghard C, Arnold JF, Marmolejo V. Total Contact Cast Use in Patients With Peripheral Arterial Disease: A Case Series and Systematic Review. Wounds. 2018;30(2):49-56.

53. Crews RT, Candela J. Decreasing an Offloading Device's Size and Offsetting Its Imposed Limb-Length Discrepancy Lead to Improved Comfort and Gait. Diabetes Care. 2018;41(7):1400-5.

54. Crews RT, Sayeed F, Najafi B. Impact of strut height on offloading capacity of removable cast walkers. Clin Biomech (Bristol, Avon). 2012;27(7):725-30.

55. Crews RT, Shen BJ, Campbell L, Lamont PJ, Boulton AJ, Peyrot M, et al. Role and Determinants of Adherence to Off-loading in Diabetic Foot Ulcer Healing: A Prospective Investigation. Diabetes Care. 2016;39(8):1371-7.

56. Wang C, Goel R, Rahemi H, Zhang Q, Lepow B, Najafi B. Effectiveness of Daily Use of Bilateral Custom-Made Ankle-Foot Orthoses on Balance, Fear of Falling, and Physical Activity in Older Adults: A Randomized Controlled Trial. Gerontology. 2018.

57. Paton J, Hatton AL, Rome K, Kent B. Effects of foot and ankle devices on balance, gait and falls in adults with sensory perception loss: a systematic review. JBI database of systematic reviews and implementation reports. 2016;14(12):127-62.

58. Bus SA, Valk GD, van Deursen RW, Armstrong DG, Caravaggi C, Hlavácek P, et al. The effectiveness of footwear and offloading interventions to prevent and heal foot ulcers and reduce plantar pressure in diabetes: a systematic review. Diabetes/Metabolism Research & Reviews. 2008;24:S162-80.

59. Katz IA, Harlan A, Miranda-Palma B, Prieto-Sanchez L, Armstrong DG, Bowker JH, et al. A randomized trial of two irremovable off-loading devices in the management of plantar neuropathic diabetic foot ulcers. Diabetes Care. 2005;28(3):555-9.

60. Piaggesi A, Macchiarini S, Rizzo L, Palumbo F, Tedeschi A, Nobili LA, et al. An off-the-shelf instant contact casting device for the management of diabetic foot ulcers - A randomized prospective trial versus traditional fiberglass cast. Diabetes Care. 2007;30(3):586-90.

61. Miyan Z, Ahmed J, Zaidi SI, Ahmedani MY, Fawwad A, Basit A. Use of locally made off-loading techniques for diabetic plantar foot ulcer in Karachi, Pakistan. International wound journal. 2014;11(6):691-5.

62. Gutekunst DJ, Hastings MK, Bohnert KL, Strube MJ, Sinacore DR. Removable cast walker boots yield greater forefoot off-loading than total contact casts. Clin Biomech (Bristol, Avon). 2011;26(6):649-54.

63. Lavery LA, Vela SA, Lavery DC, Quebedeaux TL. Reducing dynamic foot pressures in high-risk diabetic subjects with foot ulcerations. A comparison of treatments. Diabetes Care. 1996;19(8):818-21.

64. Fleischli JG, Lavery LA, Vela SA, Ashry H, Lavery DC. 1997 William J. Stickel Bronze Award. Comparison of strategies for reducing pressure at the site of neuropathic ulcers. J Am Podiatr Med Assoc. 1997;87(10):466-72.

65. Götz J, Lange M, Dullien S, Grifka J, Hertel G, Baier C, et al. Off-loading strategies in diabetic foot syndrome–evaluation of different devices. International Orthopaedics. 2017;41(2):239-46.

66. Westra M, Netten JJv, Manning HA, Baal JGv, Bus SA. Effect of different casting design characteristics on offloading the diabetic foot. Gait Posture. 2018;64:90-4.

67. Begg L, McLaughlin P, Vicaretti M, Fletcher J, Burns J. Total contact cast wall load in patients with a plantar forefoot ulcer and diabetes. J Foot Ankle Res. 2016;9:2.

68. Dumont I, Tsirtsikolou D, Lepage M, Popielarz SM, Fayard A, Devemy F, et al. The Ransart boot – an offloading device for every type of diabetic foot ulcer? . EWMA Journal. 2010;10(2):46-50.

69. Dumont IJ, Lepeut MS, Tsirtsikolou DM, Popielarz SM, Cordonnier MM, Fayard AJ, et al. A proof-of-concept study of the effectiveness of a removable device for offloading in patients with neuropathic ulceration of the foot: the Ransart boot. Diabet Med. 2009;26(8):778-82.

70. Birke JA, Pavich MA, Patout CA, Jr., Horswell R. Comparison of forefoot ulcer healing using alternative off-loading methods in patients with diabetes mellitus. Adv Skin Wound Care. 2002;15(5):210-5.

71. Chantelau E, Breuer U, Leisch AC, Tanudjaja T, Reuter M. Outpatient treatment of unilateral diabetic foot ulcers with 'half shoes'. Diabet Med. 1993;10(3):267-70.

72. Hissink RJ, Manning HA, van Baal JG. The MABAL shoe, an alternative method in contact casting for the treatment of neuropathic diabetic foot ulcers. Foot Ankle Int. 2000;21(4):320-3.

73. Bus SA, Maas JC, Otterman NM. Lower-extremity dynamics of walking in neuropathic diabetic patients who wear a forefoot-offloading shoe. Clin Biomech (Bristol, Avon). 2017;50:21-6.

74. Bus SA, van Deursen RWM, Kanade RV, Wissink M, Manning EA, van Baal JG, et al. Plantar pressure relief in the diabetic foot using forefoot offloading shoes. Gait & Posture. 2009;29(4):618-22.

75. Bus SA, Waaijman R, Arts M, Manning H. The efficacy of a removable vacuum-cushioned cast replacement system in reducing plantar forefoot pressures in diabetic patients. Clin Biomech (Bristol, Avon). 2009;24(5):459-64.

76. Nagel A, Rosenbaum D. Vacuum cushioned removable cast walkers reduce foot loading in patients with diabetes mellitus. Gait Posture. 2009;30(1):11-5.

77. Raspovic A, Landorf KB, Gazarek J, Stark M. Reduction of peak plantar pressure in people with diabetes-related peripheral neuropathy: an evaluation of the DH Pressure Relief Shoe. J Foot Ankle Res. 2012;5(1):25.

78. Ganguly S, Chakraborty K, Mandal PK, Ballav A, Choudhury S, Bagchi S, et al. A comparative study between total contact casting and conventional dressings in the non-surgical management of diabetic plantar foot ulcers. J Indian Med Assoc. 2008;106(4):237-9, 44.

79. Caravaggi C, Faglia E, De Giglio R, Mantero M, Quarantiello A, Sommariva E, et al. Effectiveness and safety of a nonremovable fiberglass off-bearing cast versus a therapeutic shoe in the treatment of neuropathic foot ulcers: a randomized study. Diabetes Care. 2000;23(12):1746-51.
80. Nubé VL, Molyneaux L, Bolton T, Clingan T, Palmer E, Yue DK. The use of felt deflective padding in the management of plantar hallux and forefoot ulcers in patients with diabetes. The Foot. 2006;16(1):38-43.
81. Zimny S, Schatz H, Pfohl U. The effects of applied felted foam on wound healing and healing times in the therapy of neuropathic diabetic foot ulcers. Diabet Med. 2003;20(8):622-5.
82. Pabón-Carrasco M, Juárez-Jiménez JM, Reina-Bueno M, Coheña-Jiménez M. Behavior of provisional pressure-reducing materials in diabetic foot. Journal of Tissue Viability. 2016;25(2):143-9.
83. Raspovic A, Waller K, Wong WM. The effectiveness of felt padding for offloading diabetes-related foot ulcers, at baseline and after one week of wear. Diabetes Res Clin Pract. 2016;121:166-72.
84. Dallimore SM, Kaminski MR. Tendon lengthening and fascia release for healing and preventing diabetic foot ulcers: a systematic review and meta-analysis. J Foot Ankle Res. 2015;8:33.
85. Mueller MJ, Sinacore DR, Hastings MK, Strube MJ, Johnson JE. Effect of Achilles tendon lengthening on neuropathic plantar ulcers. A randomized clinical trial. J Bone Joint Surg Am. 2003;85-A(8):1436-45.
86. Allam AM. Impact of Achilles tendon lengthening (ATL) on the diabetic plantar forefoot ulceration. Egypt J Plast Reconstr Surg. 2006;30:43-8.
87. Holstein P, Lohmann M, Bitsch M, Jorgensen B. Achilles tendon lengthening, the panacea for plantar forefoot ulceration? Diabetes Metab Res Rev. 2004;20 Suppl 1:S37-40.
88. Laborde JM. Neuropathic plantar forefoot ulcers treated with tendon lengthenings. Foot Ankle Int. 2008;29(4):378-84.
89. Lee TH, Lin SS, Wapner KL. Tendo-achilles lengthening and total contact casting for plantar forefoot ulceration in diabetic patients with equinus deformity of the ankle. Operative Techniques in Orthopaedics. 1996;6(4):222-5.
90. Laborde JM. Midfoot ulcers treated with gastrocnemius-soleus recession. Foot Ankle Int. 2009;30(9):842-6.
91. Piaggesi A, Schipani E, Campi F, Romanelli M, Baccetti F, Arvia C, et al. Conservative surgical approach versus non-surgical management for diabetic neuropathic foot ulcers: a randomized trial. Diabet Med. 1998;15(5):412-7.
92. Armstrong DG, Fiorito JL, Leykum BJ, Mills JL. Clinical efficacy of the pan metatarsal head resection as a curative procedure in patients with diabetes mellitus and neuropathic forefoot wounds. Foot Ankle Spec. 2012;5(4):235-40.
93. Armstrong DG, Rosales MA, Gashi A. Efficacy of fifth metatarsal head resection for treatment of chronic diabetic foot ulceration. J Am Podiatr Med Assoc. 2005;95(4):353-6.
94. Motamedi AK, Ansari M. Comparison of Metatarsal Head Resection Versus Conservative Care in Treatment of Neuropathic Diabetic Foot Ulcers. J Foot Ankle Surg. 2017;56(3):428-33.
95. Giurini JM, Basile P, Chrzan JS, Habershaw GM, Rosenblum BI. Panmetatarsal head resection. A viable alternative to the transmetatarsal amputation. J Am Podiatr Med Assoc. 1993;83(2):101-7.
96. Griffiths GD, Wieman TJ. Metatarsal head resection for diabetic foot ulcers. Arch Surg. 1990;125(7):832-5.
97. Molines-Barroso RJ, Lazaro-Martinez JL, Aragon-Sanchez J, Garcia-Morales E, Beneit-Montesinos JV, Alvaro-Afonso FJ. Analysis of transfer lesions in patients who underwent surgery for diabetic foot ulcers located on the plantar aspect of the metatarsal heads. Diabet Med. 2013;30(8):973-6.
98. Patel VG, Wieman TJ. Effect of metatarsal head resection for diabetic foot ulcers on the dynamic plantar pressure distribution. Am J Surg. 1994;167(3):297-301.
99. Wieman TJ, Mercke YK, Cerrito PB, Taber SW. Resection of the metatarsal head for diabetic foot ulcers. Am J Surg. 1998;176(5):436-41.
100. Petrov O, Pfeifer M, Flood M, Chagares W, Daniele C. Recurrent plantar ulceration following pan metatarsal head resection. J Foot Ankle Surg. 1996;35(6):573-7; discussion 602.
101. Armstrong DG, Lavery LA, Vazquez JR, Short B, Kimbriel HR, Nixon BP, et al. Clinical efficacy of the first metatarsophalangeal joint arthroplasty as a curative procedure for hallux interphalangeal joint wounds in patients with diabetes. Diabetes Care. 2003;26(12):3284-7.

102. Lin SS, Bono CM, Lee TH. Total contact casting and Keller arthoplasty for diabetic great toe ulceration under the interphalangeal joint. Foot Ankle Int. 2000;21(7):588-93.

103. Kim JY, Kim TW, Park YE, Lee YJ. Modified resection arthroplasty for infected non-healing ulcers with toe deformity in diabetic patients. Foot Ankle Int. 2008;29(5):493-7.

104. Johnson JE, Anderson SA. One stage resection and pin stabilization of first metatarsophalangeal joint for chronic plantar ulcer with osteomyelitis. Foot Ankle Int. 2010;31(11):973-9.

105. Rosenblum BI, Giurini JM, Chrzan JS, Habershaw GM. Preventing loss of the great toe with the hallux interphalangeal joint arthroplasty. J Foot Ankle Surg. 1994;33(6):557-60.

106. Tamir E, Tamir J, Beer Y, Kosashvili Y, Finestone AS. Resection Arthroplasty for Resistant Ulcers Underlying the Hallux in Insensate Diabetics. Foot Ankle Int. 2015;36(8):969-75.

107. Bonanno DR, Gillies EJ. Flexor Tenotomy Improves Healing and Prevention of Diabetes-Related Toe Ulcers: A Systematic Review. J Foot Ankle Surg. 2017;56(3):600-4.

108. Scott JE, Hendry GJ, Locke J. Effectiveness of percutaneous flexor tenotomies for the management and prevention of recurrence of diabetic toe ulcers: a systematic review. J Foot Ankle Res. 2016;9:25.

109. Kearney TP, Hunt NA, Lavery LA. Safety and effectiveness of flexor tenotomies to heal toe ulcers in persons with diabetes. Diabetes Res Clin Pract. 2010;89(3):224-6.

110. Laborde JM. Neuropathic toe ulcers treated with toe flexor tenotomies. Foot Ankle Int. 2007;28(11):1160-4.

111. Rasmussen A, Bjerre-Christensen U, Almdal TP, Holstein P. Percutaneous flexor tenotomy for preventing and treating toe ulcers in people with diabetes mellitus. J Tissue Viability. 2013;22(3):68-73.

112. Tamir E, Vigler M, Avisar E, Finestone AS. Percutaneous tenotomy for the treatment of diabetic toe ulcers. Foot Ankle Int. 2014;35(1):38-43.

113. van Netten JJ, Bril A, van Baal JG. The effect of flexor tenotomy on healing and prevention of neuropathic diabetic foot ulcers on the distal end of the toe. J Foot Ankle Res. 2013;6(1):3.

114. Tamir E, McLaren AM, Gadgil A, Daniels TR. Outpatient percutaneous flexor tenotomies for management of diabetic claw toe deformities with ulcers: a preliminary report. Can J Surg. 2008;51(1):41-4.

115. Prompers L, Huijberts M, Apelqvist J, Jude E, Piaggesi A, Bakker K, et al. High prevalence of ischaemia, infection and serious comorbidity in patients with diabetic foot disease in Europe. Baseline results from the Eurodiale study. Diabetologia. 2007;50(1):18-25.

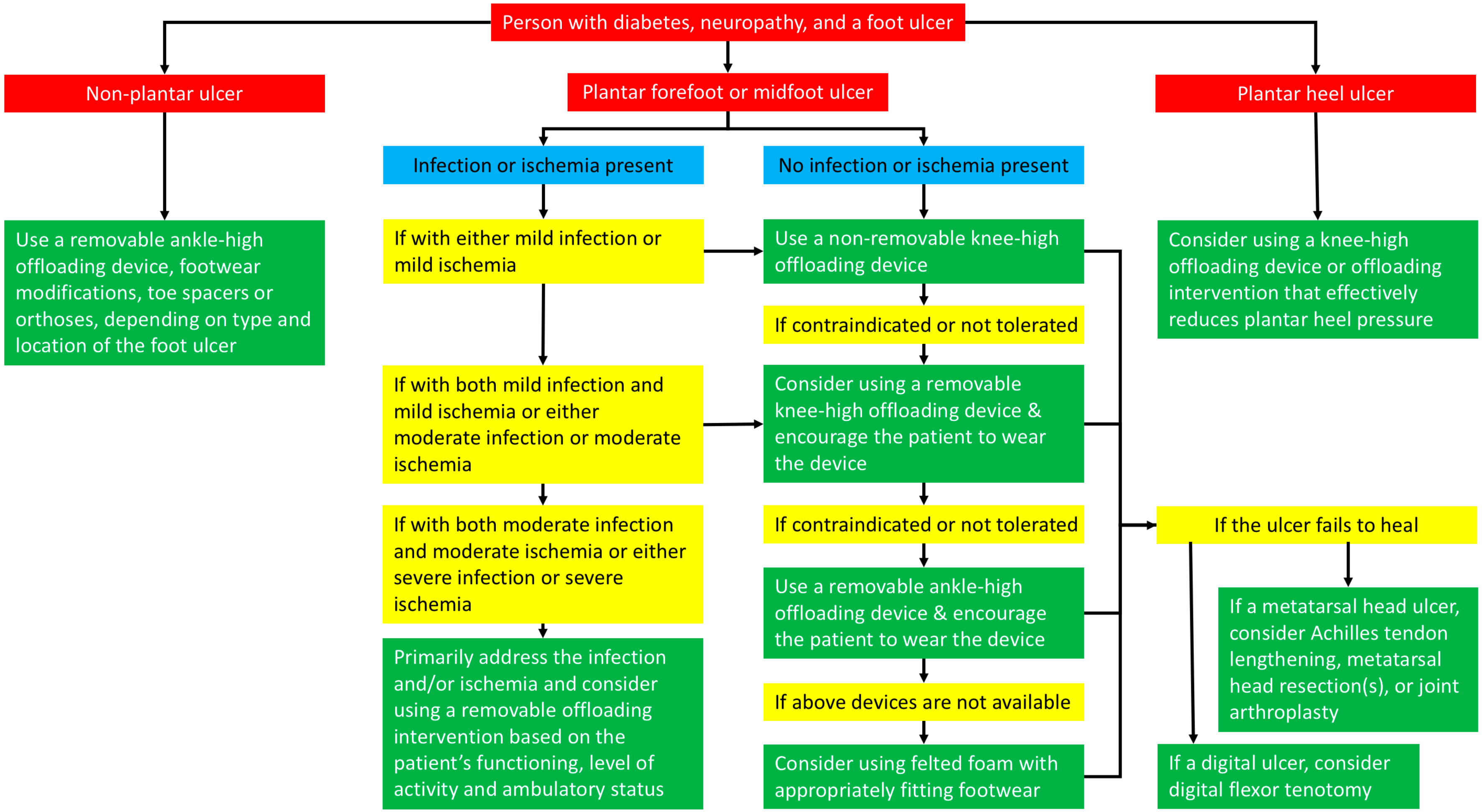
116. Maluf KS, Mueller MJ, Strube MJ, Engsberg JR, Johnson JE. Tendon Achilles lengthening for the treatment of neuropathic ulcers causes a temporary reduction in forefoot pressure associated with changes in plantar flexor power rather than ankle motion during gait. J Biomech. 2004;37(6):897-906.

117. Strakhova GY, Gorokhov SV, Ulyanova IN, Galstyan GR. Clinical efficacy and safety of a new method for pressure off-load for patients with diabetic foot syndrome: Ankle-foot pneumoorthosis with TM Orlett. Diabetes Mellitus. 2014;17(4):66-71.

118. Armstrong DG, Stacpoole-Shea S. Total contact casts and removable cast walkers. Mitigation of plantar heel pressure. J Am Podiatr Med Assoc. 1999;89(1):50-3.

FIGURES

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



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