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Review

Should weight-bearing activity be reduced during healing of plantar diabetic foot ulcers, even when using appropriate offloading devices?

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ABSTRACT

Physical activity is an essential part of general health and diabetes management. However, recommending weight-bearing physical activity for people with plantar diabetic foot ulcers is controversial, even when gold standard offloading devices are used, as it is commonly thought to delay healing. We aimed to narratively review relevant studies investigating the relationship between plantar diabetic foot ulcer healing and weight-bearing activity, plantar pressure and device adherence. We defined relevant studies as those from two systematic reviews, along with those identified since using a similar updated Pubmed search strategy. We identified six studies. One study found that more daily steps were associated

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with worse ulcer healing, three found no significant association between steps and ulcer healing, and in two others the association was unclear. Thus, there is weak evidence for an inverse relationship between weight-bearing physical activity and plantar ulcer healing while utilizing offloading devices. We propose a Diabetic foot Offloading and Activity framework to guide future research to find the optimal balance between the positive and negative effects of weight-bearing activity in the context of foot ulcers. We hope such future studies will shed more conclusive light on the impact of weight-bearing activity on healing of plantar diabetic foot ulcers.

Keywords:
Diabetic foot
Diabetic foot ulcer
Weight-bearing activity
Wound healing
Walking
Gait
Mobility limitations

Contents

1. Introduction

Weight-bearing physical activity in the presence of plantar diabetic foot ulcers (DFUs) is a controversial topic. On the one hand, high physical stresses on the plantar foot, for example occurring during physical activities such as standing and walking, are known contributors to delayed healing of plantar DFUs [1]. Therefore, the hallmark of treatment is protecting the ulcer from such high stresses using appropriate off-loading devices [1]. Yet, even when gold standard offloading devices are used, plantar stresses on the DFU are not completely eliminated and there are concerns that weight-bearing activity may result in unnecessary trauma to these ulcers and thus significantly delay healing [2]. On the other hand, physical activity is typically a crucial component of diabetes management aimed at keeping blood glucose levels within recommended levels, reducing risks of diabetes complications and promoting general physical and mental health [3–6]. Furthermore, there is some DFU and non-DFU wound research indicating exercise may aid wound healing [7–10]. Because of this dilemma, patients with plantar DFUs are commonly recommended to restrict their weight-bearing activity and increase non-weight-bearing activity, such as stationary cycling [1,4,11–13].

Recommendations to restrict weight-bearing activity, which for this population mainly concerns walking and standing, are similar to those that were long-held for patients with the most common risk factor for DFU, namely diabetic peripheral neuropathy (DPN). DPN was considered a contraindication for any undue weight-bearing activity as it was thought to significantly increase the risk of developing DFU in people with insensate feet [14]. However, research has indicated that weight-bearing activity may not in fact heighten the risk of developing DFUs as once thought [15], and international guidelines now recommend that people with DPN can carefully and progressively increase their weight-bearing activity [5,14,16,17]. With these new recommendations for people with DPN in mind, some clinicians and researchers are now questioning the benefit of restricting the weight-bearing activity of people with DFU that are utilizing recommended offloading devices [18]. Thus, there is uncertainty whether restricting weight-bearing activity should indeed be recommended for people with plantar DFUs. Yet, to the best of our knowledge, we are unaware of any review of physical activity and DFU healing in those using offloading devices. Thus, the aim of this paper was to review effects of weight-bearing activity in offloading devices on plantar DFU healing.

2. History of offloading DFUs

Offloading, "the relief of mechanical stress (pressure) from a specific region of the foot" [19], is a cornerstone in treatment of DFUs. Adequate offloading is especially important in reducing the elevated mechanical stress that typically caused the plantar DFU in the first place and if not addressed will prolong healing [20]. The historical intuitive reaction when clinicians were faced with a person with a plantar DFU was to recommend the person refrain from all weight-bearing activity [21]. Thus, offloading approaches that removed most mechanical stress were thought to be advantageous, such as bed rest, wheelchairs and crutches. Although widely used historically, these approaches have received very little research attention [21] and where they have been studied they have been typically found to be unsuccessful [22]. Reasons for the lack of success of these approaches were likely people's lack of adherence to these treatment regimens. This is probably not surprising considering this approach could mean months of complete non-weight bearing to heal a typical plantar DFU, and DPN often eliminates the trigger of pain that would typically 'encourage' people without DPN to reduce their weight-bearing activity on unprotected ulcers. Furthermore, prolonged non-weight bearing implies negative consequences for daily and social activities, as walking is the most commonly performed exercise among people with diabetes [23] and is an integral part of many occupations and daily activities [24]. Thus, an ideal solution would be using offloading interventions that effectively mitigate mechanical stresses on the ulcer, are used consistently during all weight-bearing activity and allow patients to maintain some ambulation during treatment.

Non-removable knee-high offloading devices were developed to try to meet these needs, such as the total contact cast (TCC) [25,26] and more contemporary "instant" TCC that consists of a knee-high walker rendered irremovable [27,28]. These non-removable knee-high offloading devices are now considered the gold standard treatment of uncomplicated forefoot and midfoot DFUs and are strongly recommended in international guidelines based on high quality evidence [1,21]. Non-removable knee-high offloading devices achieve the goals of effective offloading, high adherence, and healing [29], but only partly fulfill the goal of allowing patients to remain ambulatory during treatment. A recent systematic review concluded that patients with non-removable knee-high offloading do less weight-bearing activity compared to those wearing removable ankle-high devices [21], presumably because the former devices are difficult to walk with and cannot be removed, the so-called "ball-and-chain" effect [30]. However, before reviewing the potential effects of weight-bearing activity in offloading devices, a framework is needed to understand how offloading devices, weight-bearing activity and ulcer healing could be related.

3. The Diabetic foot Offloading and Activity (DOA) framework

The main mechanisms by which offloading devices reduce plantar pressure (vertical pressures and horizontal shear) and heal the ulcer, but also impact gait, balance, and daily activities, are summarized in the Diabetic foot Offloading and Activity (DOA) framework illustrated in Fig. 1. Each type of offloading device can thus be investigated with the help of this framework, to try to find the optimal balance between ulcer healing and side effects.

Knee-high non-removable devices can be used as an example to illustrate the use of the framework. These devices include at least three crucial common features that collectively facilitate a continuous transfer of mechanical stresses from an isolated local area of high stress to a more even distribution across the entire foot and lower leg. These features are: i) a cast wall that extends just below the distal aspect of the knee, ii) an immobilization of the ankle joint, iii) a rigid rocker sole, and iv) the inability to be removed and readily reapplied to the foot, which facilitates wearing the device at all times [31–35]. Adherence is an important consideration with offloading devices as it has been shown to positively impact healing [36], yet studies that objectively measured adherence with removable offloading devices have found average adherence levels to be fairly low [36,37]. The four reviewed features of knee-high non-removable devices lead to pressure reduction as described in the first box in Fig. 1. However, they result not only in less stress on the ulcer per step, but they also impair gait and balance [38] by presenting challenges to ambulation, such as a more pronounced hip hike, slower gait velocity, and smaller steps [35,39] contributing to patients taking fewer daily steps [40,41]. On one hand, these impairments reduce the magnitude and number of loading cycles on the ulcer and thereby potentially positively promote ulcer healing from that perspective (left column in Fig. 1). On the other hand, the forced reduction of weight-bearing activity may have negative side-effects in a number of other areas, such as independence in daily activities, working ability and muscle weakness, leading to social isolation

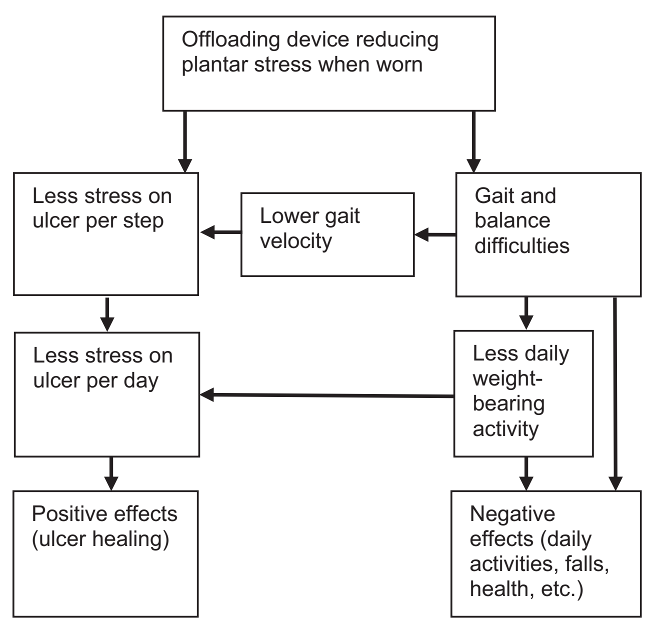

Fig. 1 – Diabetic foot Offloading and Activity (DOA) framework. The framework summarizes the mechanisms by which offloading devices promote ulcer healing but also may aggravate gait and balance difficulties which result in less weight-bearing activity and negative effects on daily activities, health, bone and muscle mass, joint flexibility, etc.

and reduced quality of life (right column in Fig. 1). Also, it is worth noting that many of the negative side-effects of non-removable knee-high devices, such as gait and balance impairments [42–45], low weight-bearing activity level [42], restrictions of daily activities, and low quality of life [46], are already common in this patient group [47–52]. Thus, the knee-high devices seem to increase pre-existing gait challenges and their consequences in a patient group that is already burdened.

While the positive association between the reduction of plantar pressure using certain offloading devices and healing has been extensively studied (left column in Fig. 1), it is not clear whether there is an association between the reduction of weight-bearing activity while using these devices and healing. To investigate this, we aimed to narratively review studies that simultaneously investigated weight-bearing activity, plantar pressure (or used knee-high devices known to optimally reduce plantar pressures), and device adherence (or used non-removable devices known to enforce adherence) in relation to plantar DFU healing.

4. Studies on weight-bearing activity and ulcer healing

Our search strategy involved initially identifying all relevant publications included in two systematic reviews published by the International Working Group on the Diabetic Foot on the effectiveness of offloading interventions to heal DFUs [21,53]. The search strategies for those publications are discussed in detail within the systematic review publications [21,53]. Seven relevant publications [36,40,41,54,55,56,57] were identified within the prior systematic reviews' references. In order to identify any new publications in the intervening period between the terminal date of the prior systematic reviews (August 13th 2018) and the drafting of the current publication, we searched for relevant publications in Pubmed using the search strings: (diabetic foot[MeSH Terms]) AND physical activity[MeSH Terms], (diabetic foot[MeSH Terms]) AND off-load*, (foot ulcer[MeSH Terms]) AND physical activity[MeSH Terms], and (diabetic foot[MeSH Terms]) AND off-load*. These searches were limited to publications occurring between August 1st, 2018 and January 21st, 2020. This search yielded no additional relevant publications. Lastly, we added two relevant conference abstracts [58,59] that we were aware of and which used datasets from some of the publications identified from the prior systematic reviews.

We were able to identify six studies (four randomized controlled trials [RCT] and two observational studies) that met our aims, with findings reported in nine publications [36,40,41,54–59]. The methodology and findings of these studies are summarized in Tables 1 and 2. With regards to measuring weight-bearing daily activity, all studies used activity monitors, ranging from simple pedometers to sophisticated accelerometers. In terms of plantar pressure measurements, one study measured plantar pressures at the ulcer site [55,56], while all studies included knee-high offloading devices. In terms of assessing adherence, one study used objective monitors [36,59], two used self-report [41,55,56], while the other three studies investigated non-removable offloading devices [40,54,57,58]. We will discuss the merits and impacts on healing of each study individually below.

Najafi et al. (2017) [54] compared a non-removable knee-high walker and removable knee-high walker in an RCT on people with DFU treated for up to 12 weeks. When comparing the non-removable and removable walker groups after four weeks, the non-removable walker group had significantly less daily standing time (6.8% vs. 11.9% of total activity, $p = 0.028$), less daily walking time (2.4% vs. 4.8%, $p = 0.049$), and non-significantly fewer daily steps (2994 vs. 5902, $p = 0.07$). Furthermore, among the non-removable walker group, significantly more ulcers healed at 12 weeks (70% vs. 40%, $p = 0.049$) and weekly ulcer area reduction was larger ($p < 0.001$). In the non-removable walker group, weekly ulcer area reduction correlated significantly and negatively with number of steps taken ($r = -0.33$) but not with daily standing time ($r = 0$, p-values not reported). In the removable walker group, ulcer area reduction correlated significantly and negatively with both standing duration ($r = -0.67$) and number of steps ($r = -0.36$, p-values not reported). However, as adherence to wearing the removable walker was not objectively assessed, the association found between weight-bearing activities and wound healing should be interpreted cautiously. When the authors compared participants with healed ($n = 22$) and non-healed ulcers ($n = 21$) at 12 weeks, the authors found more people wearing a non-removable walker in the group with healed ulcers compared to the group with non-healed ulcers (68% vs. 38%, $p = 0.049$), and those with a healed ulcer had shorter daily standing duration (5.7% vs. 11.4%, $p = 0.025$). In addition, those with healed ulcers had non-significantly shorter walking duration (1.9% vs 4.6% of 24 h daily activities, $p = 0.057$) and non-significantly fewer daily steps (2595 vs. 5586, $p = 0.104$). In a secondary analysis, reported in a conference abstract [58], Najafi et al. analyzed activity and ulcer healing during the two first weeks of the study period, when all participants were still in the study. There was a negative correlation between number of daily steps and weekly ulcer area reduction for both the non-removable walker group ($r = -0.50$, $p < 0.05$) and the removable walker group ($r = -0.46$, $p < 0.05$). Every 1000 daily steps reduced weekly healing rate (ulcer area reduction) by 5.0% with a non-removable walker and 5.4% with a removable walker. There was no significant correlation between daily standing time and weekly ulcer area reduction in the non-removable walker group ($r = 0.10$, $p > 0.05$). The correlation was significant in the removable walker group ($r = -0.64$, $p < 0.05$), where every 15 min of daily standing time reduced weekly healing rate (ulcer area reduction) by 3.5%. However, the results for the removable walkers should be interpreted with caution as adherence was not objectively assessed.

Saltzman et al. (2004) [57] investigated the effects of daily number of steps on time to ulcer healing in an observational study on a cohort of patients treated with a TCC for up to 13 weeks. Of the 40 participants, 32 (80%) healed with a median healing time of six weeks. On average, participants took 2083 steps per day (excluding the first 48 h after each cast application during which they were instructed to remain completely non-weight-bearing). Data from the step activity monitors and measurements of the ulcers were used to esti-

Table 1 – Summary of the methods of the studies.

Study	Design	n	Offloading devices	Measurements		
				Weight-bearing activity	Plantar pressures	Adherence
Najafi et al. (2017) [54], Najafi et al. (2019) [58]†	RCT	49	Non-removable knee-high walker (n = 23), removable knee-high walker (n = 26)	Different aspects of standing, sitting, lying and walking measured with PAMSys™ (BioSensics LLC, MA) incorporated in a shirt	Not measured	Not measured
Saltzman et al. (2004) [57]	Observational	40	TCC (n = 40)	Step count measured with StepWatch (Cyma, WA) embedded in the TCC	Not measured	Not measured
Bus et al. (2018) [55], van Netten et al. (2018) [56]‡	RCT	60§ / 31	Bivalved TCC (n = 20), removable ankle-high cast (n = 20), forefoot offloading shoe (n = 20)	Step count measured with StepWatch™ (Orthocare Innovations LLC, OK) worn around the ankle	Measured with PEDAR®-X system (Novel GmbH, Germany)	Self-report
Crews et al. (2016) [36], Vileikyte et al. (2017) [59]¶	Observational	79	Removable knee-high walker (n = 61), sandal (n = 13), "other" (n = 5)	Step count measured with Lifecorder Plus (Suzuken) at the hip	Not measured	Dual activity monitors
Armstrong et al. (2001) [40]	RCT	63	TCC (n = 19), removable knee-high walker (n = 20), half-shoe (n = 24)	Step count measured with Sportline (Campbell, CA)	Not measured	Not measured
Lavery et al. (2015) [41]	RCT	73	TCC (n = 23), removable knee-high walker (n = 27), healing sandals (n = 23)	Step count measured with unspecified pedometer worn at the waist	Not measured	Self-report

RCT, randomized controlled trial; TCC, total contact cast.†Secondary analysis of Najafi et al. (2017) [54]. ‡Secondary analysis of 31 participants from Bus et al. (2018) [55]. §Activity and plantar pressures were assessed in subset of 35 participants. ¶Secondary analysis of Crews et al. (2016) [36].

Table 2 – Summary of the results of the studies.

Study	Daily weight-bearing activity	Peak pressure at ulcer	Adherence	Ulcer healing
Najafi et al. (2017) [54], Najafi et al. (2019) [58]‡	Non-removable walker: 2994 steps, 6.8% standing time, 2.4% walking time. Removable walker: 5902 steps, 11.9% standing time, 4.8%; walking time.	Not measured	Not measured	Healed at 12 weeks, non-removable walker: 70%, removable walker: 40%. Weekly ulcer area reduction, non-removable walker: 24.2%, removable walker: 13.2%
Saltzman et al. (2004) [57]	TCC: 2083 steps	Not measured	Not measured	80% healed at 13 weeks
Bus et al. (2018) [55], van Netten et al. (2018) [56]§	Bivalved TCC: 8300 steps, ankle-high cast: 7028 steps, forefoot offloading shoe: 8894 steps	Bivalved TCC: 81 kPa, ankle-high cast: 176 kPa, forefoot offloading shoe: 107 kPa	Adherence (≥50% time worn), bivalved TCC: 82.7%, ankle-high cast: 94.8%, forefoot offloading shoe: 95.1%	Healed at 12 weeks, bivalved TCC: 58%, cast shoe: 60%, forefoot offloading shoe: 70%
Crews et al. (2016) [36], Vileikyte et al. (2017) [59]†	3335 steps. Mean walking duration: 6.7 h	Not measured	On average, devices were worn 59% of active time.	At six weeks, 24% healed and mean ulcer size reduction was 54%
Armstrong et al. (2001) [40]	TCC: 600 steps, walker: 768 steps, half-shoe: 1462 steps	Not measured	Not measured	Healed at 12 weeks, TCC: 89.5%, walker: 65.0%, half-shoe: 58.3%
Lavery et al. (2015) [41]	TCC: 1447 steps, walker: 1404 steps, healing sandals: 4022 steps	Not measured	Number of participants removed because of poor adherence, TCC: 0, walker: 3, healing sandals: 0. (Adherence levels were not reported)	Healed at 12 weeks, TCC: 69.6%, walker; 22.2%, healing sandals: 44.5%. Healing time, TCC: 5.4 weeks, walker: 6.7 weeks, healing sandal: 8.9 weeks

TCC, total contact cast. †Secondary analysis of Crews et al. [36] ‡Secondary analysis of Najafi et al. [54] §Secondary analysis of 31 participants from Bus et al. [55].

mate the impact of walking on ulcer healing. For median sized ulcers (radius 0.65 cm), it was estimated that a person who walked 0 daily steps would heal in 6.77 (95% confidence interval 5.22–9.62) weeks, whereas a person who walked 2083 daily steps (which was the median for the cohort) would heal in 7.70 (6.63–9.20) weeks, and those who walked 4166 (double of the median) daily steps would heal in 8.94 (6.79–13.08) weeks. Thus, like the study by Najafi et al. [54,58], the direction of the results would indicate that more daily steps are associated with worse healing. However, the large overlap of the confidence intervals indicates that the differences were not statistically significant [60].

Bus et al. (2018) [55] compared three removable offloading devices in an RCT: bivalved TCC, custom-made ankle-high cast shoe and forefoot offloading shoe. Adherence was self-reported. In a random subset of 35 participants, daily step count and plantar pressures were objectively measured. When comparing users of bivalved TCC, ankle-high cast and forefoot offloading shoe, there was no significant difference between the groups in daily step count after two weeks (8300 vs. 7028 vs. 8894, $p = 0.711$), ulcer healing at 12 weeks (58% vs. 60% vs. 70%, $p = 0.70$) and self-reported adherence $\geq$50% of daytime (82.7% vs. 94.8% vs. 95.1%, $p = 0.236$). Plantar pressures at the ulcer were significantly higher with ankle-high cast (176 kPa) than with bivalved TCC (81 kPa, $p = 0.004$) and forefoot offloading shoe (107 kPa, $p = 0.034$). Van Netten et al. [56] performed a secondary analysis on 31 of the participants using bivalved TCC ($n = 10$), ankle-high cast ($n = 7$) and forefoot offloading shoe ($n = 14$). The cumulative plantar tissue stress was calculated by multiplying the mean pressure–time integral at the ulcer by the mean number of daily steps. Comparing people whose ulcers had healed ($n = 21$) or had not healed ($n = 10$) at 12 weeks, there was non-significant lower daily step count (7222 vs. 9706; $p = 0.26$), similar peak pressure (108 vs. 107 kPa, $p = 0.97$) and peak pressure time integrals at the ulcer site (45 vs. 38 kPa*s, $p = 0.44$), and overall a non-significantly lower cumulative plantar tissue stress at the ulcer site (155 vs. 207 MPa*s/day, $p = 0.071$) in those who healed. Similar to the studies by Najafi et al. [54,58] and Saltzman et al. [57], the results indicate that more daily steps are associated with worse healing outcomes, but as with the study by Saltzman et al. [57], the difference was not statistically significant. Both this study and the one by Saltzman et al. [57] may have been underpowered as only some 30 participants were analyzed.

Crews et al.(2016) [36] investigated determinants of adherence to using removable knee-high walkers, sandals and "other" removable devices in a six-week observational study on people with plantar DFUs. Offloading adherence was a significant predictor of healing ($p < 0.05$). A secondary analysis, reported in a conference abstract [59], found a significant correlation (−0.29, $p < 0.05$) between daily step counts and smaller ulcer size at six weeks suggesting a potential benefit of increasing weight-bearing activity on ulcer healing. However, in a multiple regression analysis, this association was not significant (standardized coefficient = −0.13; $p = 0.091$), although offloading adherence (standardized coefficient = −0.17; $p < 0.05$) independently predicted ulcer healing in the model. Thus, it was concluded that offloading-adherent weight-bearing activity had no detrimental effect on healing within the study.

Armstrong et al. (2001) [40] compared a TCC, removable knee-high walker, and half-shoe in an RCT. When comparing number of daily steps with TCC (600), walker (768) and half-shoe (1462), significantly fewer steps were taken with a TCC than a half-shoe ($p = 0.04$). The differences between a TCC and a walker ($p = 0.67$) and between a walker and a half-shoe ($p = 0.15$) were not statistically significant. When comparing ulcer healing at 12 weeks with TCC (89.5%), walker (65.0%) and half-shoe (58.3%), results of walker and half-shoe were combined. The TCC resulted in a significantly higher proportion of healed ulcers ($p = 0.026$) compared to walker or half-shoe (89.5% vs. 61.4%). When comparing survival distributions (time to healing), healing time was shorter with TCC (33.5 days) than with walker (50.4 days, $p = 0.033$) and half-shoe (61.0 days, $p = 0.012$). However, plantar pressures and adherence were not measured for the removable devices. Thus, it is not possible to disentangle to what extent the superior healing found with the TCC was due to lower plantar pressures, lower weight-bearing activity, better adherence, or a combination of these factors.

Lavery et al. (2015) [41] compared a TCC, removable knee-high walker (with shear-reducing insole) and healing sandal in an RCT. Participants in the TCC and walker groups took a similar number of daily steps (1447 vs. 1404, $p > 0.05$). Participants randomized to a sandal took more daily steps (4022) than those randomized to TCC (1447, $p = 0.014$) or walker (1404, $p = 0.007$). With a TCC, a significantly higher proportion of ulcers healed (69.6%) at 12 weeks compared to a walker (22.2%, $p < 0.05$), but there was no significant difference between a TCC and a sandal (69.6% vs. 43.5%, $p > 0.05$). Time to healing was shorter for a TCC than a sandal (5.4 vs. 8.9 weeks, $p < 0.01$). Time to healing did not differ significantly between a TCC and a walker (5.4 vs. 6.7 weeks, $p = 0.22$). Adherence was assessed with self-report but the study only reported the number of participants excluded because of "poor compliance", without defining this. As plantar pressures were not measured, adherence levels were unclear and study attrition was high (especially in the walker group where only 55.6% of participants finished the study), it is difficult to judge whether weight-bearing activity affected ulcer healing.

5. Discussion

The aim of this paper was to review potential effects of weight-bearing activity in offloading devices on plantar DFU healing. We found a somewhat mixed picture. One study [54,58] found that more daily steps were associated with worse ulcer healing, three studies [36,55–57,59] found no significant association between step count and ulcer healing, and in two studies the association was unclear [40,41]. Collectively, the studies suggest there may potentially be an inverse relationship between weight-bearing activity, at least in the form of walking, in offloading devices on plantar DFU healing. However, the evidence is assessed to be weak because studies included in the review had several weaknesses. First, none of them had an experimental design with the primary aim of investigating the association between weight-bearing activity and ulcer healing, which limits the possibility to infer causality between weight-bearing activity and ulcer healing. Second, power seemed to be low in two studies where the direction of the results indicated a negative effect of weight-bearing activity on healing, but without reaching statistical significance [55–57]. Third, although we inferred plantar pressure reduction by only including studies using gold standard knee-high offloading devices that are known to most effectively reduce plantar pressures, plantar pressures were only measured in one study [55,56], and no study measured shear forces. Thus we cannot exclude the possibility that the negative effect of weight-bearing activity on ulcer healing in part was due to ineffective reduction of pressure and shear on the ulcer. Fourth, only one of the studies [54,58] assessed standing time in addition to walking. This is an important aspect as people with an active DFU can spend almost three times longer time standing than walking [54]. Fifth, only one of the studies objectively assessed adherence [36,59]. Although several studies included 'non-removable' devices, we recommend that adherence should always be assessed and reported as no device is strictly non-removable [61,62]. Rather, so-called non-removable devices imply different physical or psychological thresholds that patients can accept to prevent their future self from removing the device [63]. It is also worth noting that of the reviewed studies only three investigated activity-related side-effects (reporting no [40] or few [55,56] falls and moderate satisfaction with performance of daily activities [41]), although other studies have found that prolonged immobilization of the ankle joint with knee-high devices results in muscle atrophy [64], reduced range of motion [65] and loss of calcaneal bone mass [66]. Thus, future studies should include side-effects of restricted weight-bearing activity from a wider perspective, including both specific bodily side-effects (glycemic control, weight gain, loss of muscle mass, joint flexibility, and bone mass) and a wider health perspective, taking emotional and social aspects into account.

There has been an increasing awareness over time of the detrimental health effects of physical inactivity, making the historical recommendations of bed rest or wheelchair use for a number of health conditions obsolete [67]. However, it is still not uncommon for clinicians and researchers to recommend patients and study participants who use offloading devices for treatment of DFUs to reduce weight-bearing activity [28,68]. Furthermore, according to the Physical Stress Theory, the relationship between mechanical stress and tissue health is dynamic and non-linear in that body tissues respond to increases in (but not excessive) physical stress by increased tolerance to injury, and tissue adapts to decreased stress by decreased tolerance to injury [14,69]. This reduction in stress tolerance may explain why some studies have found high reulceration rates the first months after healing when patients start reloading plantar tissues after a period of offloading [51]. The Physical Stress Theory would suggest that activity and plantar tissue stress should be reduced to a yet to be determined 'safe' range of load stress during healing and then be gradually increased after healing to increase plantar tissue strength and reduce reulceration risk. It is intriguing that one study included in this review [54,58], suggested that up to 3000 daily steps would not negatively impact ulcer healing. More research is needed on how to best adapt physical activity and plantar tissue loading during ulcer healing and afterwards to promote healing and prevent reulceration, as current evidence is insufficient [16].

For future research and development, it would be interesting to investigate whether it would be possible to achieve ulcer healing with offloading devices designed to limit weight-bearing activity less than the traditional non-removable knee-high devices. Such a device should aim to find the optimal balance between both outcomes (healing and side-effects) depicted in Fig. 1. To achieve this, the device may need to let the ankle joint remain fully or partly mobile. However, accomplishing this while still reducing pressures at the ulcer as effectively as is possible with knee-high devices will be a challenge [33]. Also, the device needs to be associated with continuously high adherence, either by offering some physical or psychological threshold to remove it [63], or by including mechanisms to improve adherence, such as, an adherence monitoring system that provides feedback on adherence and reminders to use the device [2,70,71], or adaptations of the device to minimize its negative effects on gait and balance [36].

When future studies are undertaken, they need to investigate and compare different offloading devices in line with the framework illustrated in Fig. 1, that is, include objective measurements of plantar pressures, adherence, different aspects of weight-bearing activity (walking and standing) and side-effects, in addition to the traditional outcome focus on ulcer healing. By this, we may in future be able to judge whether any potential positive effect of reduced weight-bearing activity on ulcer healing is worth any potential negative side-effects, and design future offloading devices accordingly. Also, the proposed framework can be applicable to studies on ulcer prevention. While some evidence is now available that suggests weight-bearing activity can be increased for people at moderate or high-risk of ulceration, more research is needed in that field as well, and the proposed framework might be extended to include ulcer prevention following such future studies.

6. Conclusions

There is weak evidence for an inverse relationship between weight-bearing physical activity and plantar DFU healing while utilizing offloading devices. A Diabetic foot Offloading and Activity framework was proposed to guide future research on offloading devices to find the optimal balance between positive and negative effects of weight-bearing activity in the context of plantar DFU healing.

Authors contributions

GJ has drafted the manuscript. JJvN, PAL, RTC, BN, and MM have contributed to specific sections and edited the manuscript. All authors have contributed to discussions of the content and have read and approved the final manuscript.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: GJ is a consultant for Novo Nordisk and PAL has been a speaker consultant for Sanofi, Australia, but do not consider these relevant conflicts for this paper. JJvN, RTC, BN and MJM have no conflicts of interest to declare.

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