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Publication date
2023

Document Version
Final published version

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Doctoral thesis, University of Amsterdam, the Netherlands.

The research in this thesis was embedded within Amsterdam Movement Sciences Research Institute, at the department of Rehabilitation Medicine, Amsterdam UMC, location AMC, University of Amsterdam, the Netherlands.

ISBN: 978-94-6361-892-2

Cover design, lay-out & printing by: Optima Grafische Communicatie (www.ogc.nl)

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Ter verkrijging van de graad van doctor
aan de Universiteit van Amsterdam
op gezag van de Rector Magnificus
prof. dr. ir. P.P.C.C. Verbeek
ten overstaan van een door het College voor Promoties ingestelde commissie,
in het openbaar te verdedigen in de Agnietenkapel
op dinsdag 17 oktober 2023, te 16:00 uur

door Renske Keukenkamp
geboren te Doetinchem

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‘Knowledge is a treasure, but practice is the key to it.’
- Lao Tzu -

Printing of this thesis was financially supported by:
Amsterdam UMC
Amsterdam Movement Sciences
Livit Ottobock Care
Buchrnhornen
Anna Fonds
OFOM

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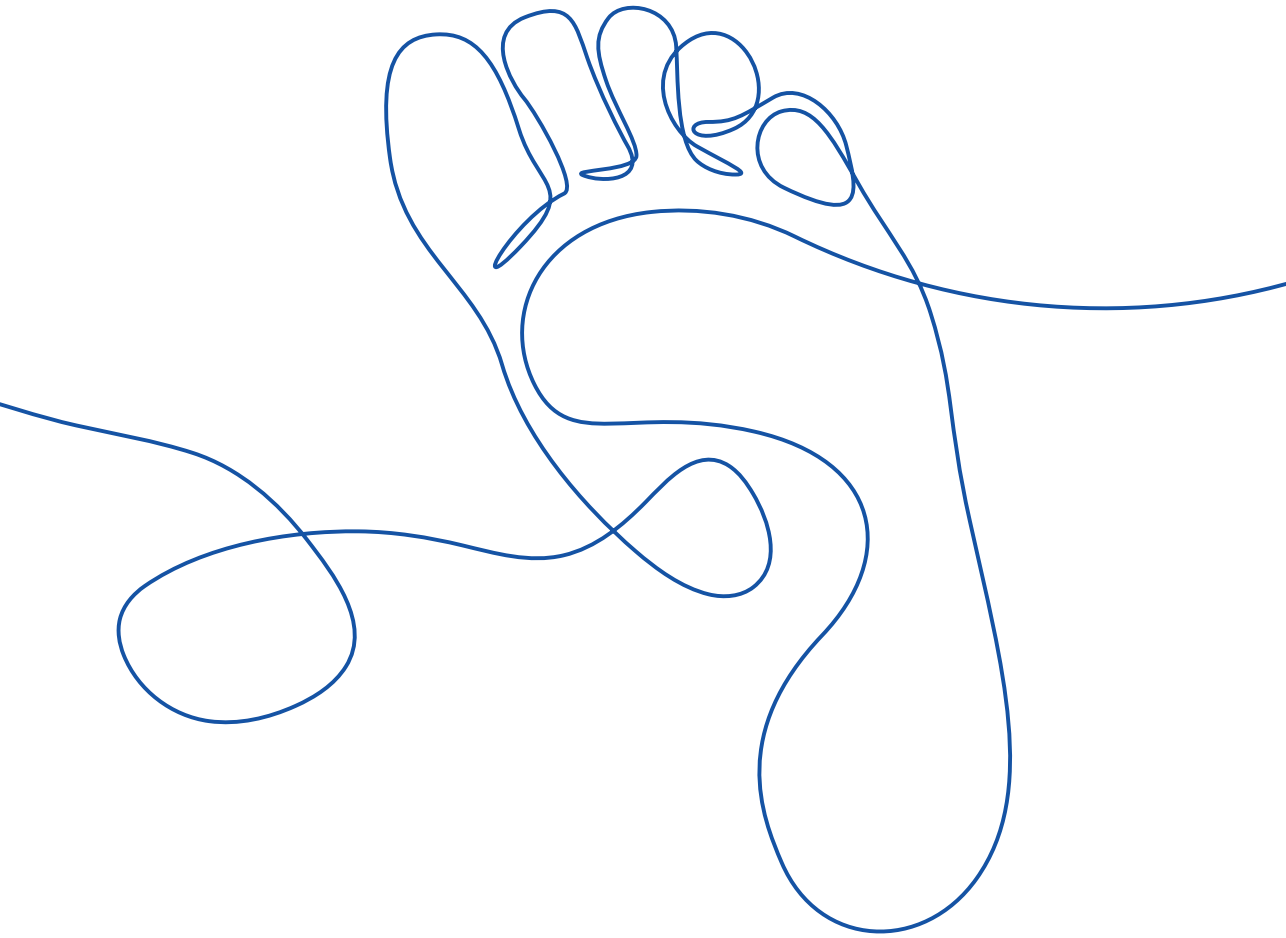

Chapter 1

General introduction

INTRODUCTION

Diabetes mellitus

Currently, 463 million people worldwide are diagnosed with diabetes mellitus, that is one in eleven adults.[1] This is predicted to rise to 578 million by 2030 and to 700 million by 2045.[1] This increase in diabetes prevalence will inevitably result in more chronic and acute diabetic complications, with profound effects on quality of life, demand on health services and economic costs.[2] The global burden is high, both in disability during life, with approximately 28.6 million years lived with disability,[3] and in deaths, with approximately 4.2 million deaths in 2019 as a result of diabetes and its complications.[1] For these reasons, continued efforts in clinical practice and research to reduce these complications of the disease are required.

Diabetic foot disease

A large part of the burden that is associated with diabetes is the result of cardiovascular, kidney, eye, and lower-extremity complications.[2, 4] In 2016, 131 million adults with diabetes were estimated to be affected by lower-extremity complications, most notably diabetic foot disease.[3] This includes several pathologies, such as ulceration, infection, Charcot neuro-osteoarthropathy, and destruction of foot tissue, often in combination with peripheral artery disease and/or peripheral neuropathy,[5] and ranks 10th in leading causes of global disease burden.[6] Up to 34% of people with diabetes experience a diabetic foot ulcer in their lifetime,[7] of which approximately half become infected[8-10] and approximately one fifth are followed by an amputation.[7, 10, 11] Once diabetic foot disease is present, quality of life is reduced,[12] and the risk of premature death is increased, in comparison with people with diabetes without foot disease.[13] With ulcer healing rates around 70% in 12 months,[14] ulcer treatment is lengthy and complex. Care should be organized in a multi-disciplinary setting, with offloading the ulcer and management of infection and peripheral artery disease as the primary focus.[5] But even if an ulcer has healed, ulcer recurrence risk remains high, with incidence of 40% within one year and 65% in 5 years.[7, 15] A previous foot ulcer is one of the strongest risk factors for developing a foot ulcer.[13] This means that people who heal from a foot ulcer are considered to be in remission and remain at high risk for re-ulcerating. Prevention of foot ulcers is especially important in this high-risk group, and is the focus of this thesis.

Pathogenesis of diabetic foot ulcers

Diabetic foot ulcers have a variety of causes, and a number of factors associated with their development. Of these, two key risk factors are peripheral neuropathy and peripheral artery disease, present in up to 25% of all people with diabetes.[7, 14, 16] Three types of peripheral neuropathy can be distinguished, which mostly co-occur[7]:

1. Motor neuropathy, where the nerves of the intrinsic foot muscles are damaged, leading to an imbalance between the flexor and extensor muscles and ultimately foot deformity and biomechanical abnormalities.
2. Sensory neuropathy, resulting in loss of protective sensation (LOPS), with subsequently the inability to detect trauma occurring in the foot.
3. Autonomic neuropathy, with decreased sweating and ultimately dry skin susceptible to tears/skin breakdown and infection.

All three types of neuropathy lead to abnormal biomechanical loading of the foot, which results in high mechanical stress at specific locations. Callus development is a typical response to this high mechanical stress, with a further increase in the mechanical load on the foot, and often subcutaneous hemorrhage developing underneath the callus and ultimately breakdown of the skin.[7]

Other risk factors for foot ulceration are foot deformity, a history of foot ulceration, any level of lower-extremity amputation, increased mechanical stress, as well as trauma, blisters and end-stage renal disease.[7, 16-18] Using these risk factors, people with diabetes can be stratified according to their ulcer risk. Two such stratification models are recommended in (inter)national guidelines (Table 1).[5, 19] Using these risk stratification systems, people with diabetes at risk for ulceration can be identified. This is an important first step towards setting up a proper treatment plan for ulcer prevention.

Both guidelines stratify people with diabetes with LOPS or peripheral artery disease and a history of foot ulceration in the group at highest risk for developing a new foot ulcer (Table 1). The Dutch guideline also added an inactive Charcot neuro-osteoarthropathy as a high-risk factor for ulcer development (Table 1). This complex and severe complication of diabetes[20, 21] is associated with significant morbidity and premature mortality.[20, 22] Charcot neuro-osteoarthropathy might require a specific ulcer prevention approach, however, due to its low incidence (0.1 to 0.3% among people with diabetes)[20, 23] it is often used as an exclusion criterion in intervention studies and therefore understudied in ulcer prevention trials.

Ulcer prevention

With lifetime ulcer incidence rates of up to 34%, and ulcer recurrence rates of up to 100% in the only study with a 10-year follow-up,[7] ulcer prevention is of fundamental importance. International and national guidelines on ulcer prevention outline five cornerstones of foot ulcer prevention treatment[16, 19]:

1. Identifying the at-risk foot. Foot disease may exist in people with diabetes, without having symptoms. According to these guidelines, all persons with diabetes should be examined once a year for signs or symptoms of LOPS or PAD.

2. Regularly inspecting and examining the at-risk foot, when LOPS or PAD is present.
3. Educating the patient, family and health care professionals, aimed at improving a patient's foot self-care knowledge and self-protective behavior and to enhance their motivations and skills to facilitate adherence to this behavior.
4. Treating risk factors for ulceration, such as removing abundant callus, treating ingrown or thickened nails, and treating fungal infections.
5. Ensuring routine wearing of appropriate footwear, that accommodates the shape of the foot, and redistributes peak plantar pressures.

Table 1. Risk classification systems used in international and Dutch guidelines.

Ulcer risk	Grade	Characteristics IWGDF	Characteristics Dutch guidelines
Very low	0	No LOPS and no PAD	No LOPS and no PAD
Low	1	LOPS or PAD	LOPS or PAD, without signs of local increased pressure[#]
Moderate	2	LOPS + PAD, or LOPS + foot deformity, or PAD + foot deformity	LOPS or PAD, or LOPS + signs of local increased pressure, or PAD + signs of local increased pressure
High	3	LOPS or PAD, *and* one or more of the following: -history of a foot ulcer -a lower extremity amputation -end-stage renal disease	History of foot ulceration or amputation Inactive Charcot neuro-osteoarthropathy End-stage renal disease or dialysis

Note: IWGDF, International Working Group on the Diabetic Foot; LOPS, loss of protective sensation; PAD, peripheral artery disease; [#]Signs of local increased pressure are defined as: abundant callus, and/or signs of inflammation (swelling, redness or warmth), and/or subcutaneous hemorrhages, and/or blisters.

Appropriate footwear

The fifth cornerstone, ensuring routine wearing of appropriate footwear, is the focus of this thesis. It is well known that walking barefoot or in inappropriate footwear is an important cause of ulceration, as this increases the local mechanical repetitive stress on the foot.[5, 17, 24, 25] It is for this reason that wearing of appropriate footwear at all times is recommended for people with diabetes at risk of foot ulceration.[26] Appropriate footwear is footwear that accommodates the shape of the foot, especially in the presence of deformities, and redistributes peak plantar pressure from at-risk regions to regions at lower risk with lower pressures.[26] Depending on foot structure and the degree of deformity present, foot biomechanics may be altered in such a way that off-the-shelf footwear can no longer adequately accommodate the foot shape, and semi-custom-made footwear (custom-made insoles worn in off-the-shelf (extra depth) shoes) or fully custom-made footwear (custom-made insoles worn in custom-made shoes) is required. Fully custom-made footwear is uniquely manufactured for an individual, and made from a positive last from the person's foot and ankle. Custom-made insoles usually consist of a multi-layer construction, in which features such as a metatarsal bar or metatarsal pad can be incorporated.[26] Two recent meta-analyses found offloading custom-made

footwear to be effective in reducing the incidence of diabetic foot ulcers.[25, 27] However, these meta-analyses also showed some important knowledge gaps: first, there is limited research into the pressure-reducing characteristics of different types of offloading footwear included in the studies in these meta-analyses; second, there is an evidence gap regarding appropriate footwear for people with an inactive Charcot neuro-osteoarthropathy, the single greatest predictor of high barefoot plantar pressure;[28] and third, for offloading with custom-made footwear to be effective, the footwear needs to be worn consistently.[29] Yet, this adherence to wearing appropriate footwear was not taken into account in both meta-analyses, while it is known that adequate adherence is not always the case, from both research studies and clinical experience.[30]

Adherence

The World Health Organization (WHO) defines adherence as "the extent to which a person's behavior corresponds with agreed recommendations from a health care provider".[31] According to the WHO, adherence should be seen as a multidimensional phenomenon determined by the interplay of five dimensions: 1) social and economic factors, 2) health-system-related factors, 3) condition-related factors, 4) therapy-related factors and 5) patient-related factors (Figure 1).[31]

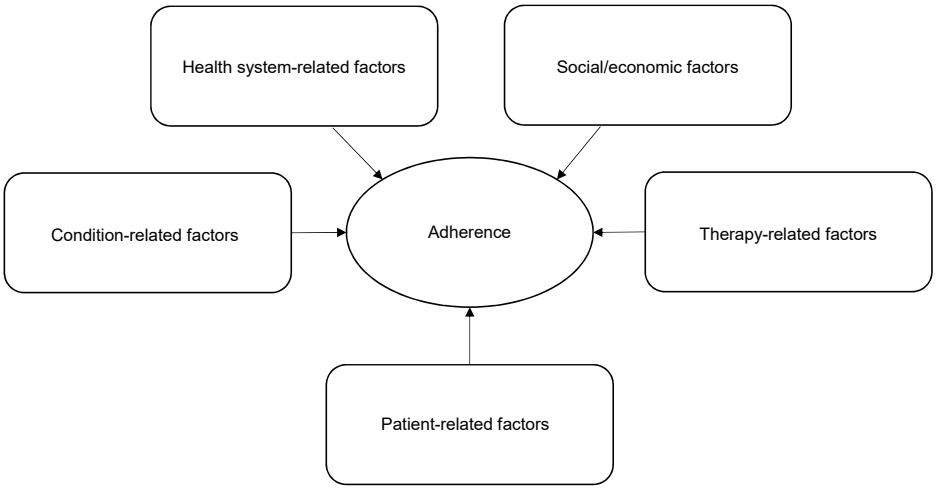

Figure 1. WHO model of adherence, where adherence is seen as a multidimensional phenomenon determined by the interplay between five dimensions.[31]

A systematic review found that adherence to medical treatment was low in persons with diabetes, where treatment regimen is complex, and expected or actual efficacy is not always high, compared to diseases with less complex treatments and better efficacy, such as human immunodeficiency virus, cancer and gastrointestinal disease.[32] Persons

with diabetes who were non-adherent to taking their medication showed worse health outcomes (such as a higher mortality and hospitalization rates, and worse blood pressure, cholesterol- and glycosylated hemoglobin levels),[32] confirming the importance of adherence to treatment.

In diabetic foot disease, adherence to self-care also plays an important role in clinical outcomes, especially in the prevention of foot ulceration. Persons with diabetes at risk of developing diabetic foot ulcers are recommended to: inspect on a daily basis their feet and the inside of the footwear; to daily wash their feet and use emollients to moisturize dry skin; cut toe nails straight across; avoid using chemical agents or plasters or any other technique to remove callus or corns; and, protect their feet by wearing appropriate footwear that redistributes and thereby reduces plantar pressure to prevent ulceration.[16] Especially this last recommendation has been an important topic in clinical care and research in people with diabetic foot disease.

Adherence to wearing custom-made footwear

Several studies have investigated adherence to wearing custom-made footwear. Three studies showed that only 22-36% of people with diabetes and neuropathy, vascular disease, or foot deformity wore their prescribed footwear more than 80% of the day.[33-35] Breuer et al. and Chantelau et al. found that 60% and 72%, respectively, wore their prescribed footwear more than 60% of the day,[36, 37] while Churchman et al. reported 35% of participants to wear their prescribed footwear more than 9 hours per day.[38] Although it is clear from these studies that prescribed footwear is only worn part of the day, the studies are outdated. The prescribed footwear used in these studies is not representative of the prescribed footwear currently used in the Netherlands, and results can therefore not be generalized to the current Dutch situation. Even though there are signals that adherence to wearing custom-made footwear is still low, specifically indoors, recent evidence is lacking.

In addition to not being representative of the current Dutch situation, these studies are also limited by using self-report to assess adherence, with different methods used and different adherence definitions. Subjective measurement of adherence may lead to reduced accuracy and reliability due to the risk of reporting bias such as social desirability in answering. These disadvantages can mostly be overcome with objective measurements, as this rules out incorrect participant recall or overstating footwear use. Objective methods have been used in studies on offloading diabetic foot ulcers with a removable cast walker, by means of accelerometry-based activity monitors worn on both the cast and the hip.[39, 40] However, because of their properties, these activity monitors are not suitable for measurements inside the shoe.

In 2012, at the start of the research project that resulted in this thesis, objective data on adherence to wearing custom-made footwear were not available in the Netherlands. However, a sensor to objectively monitor wearing of footwear (the @monitor) had just been developed.[41] The @monitor consists of two temperature sensors, measuring on both sides of the monitor, and uses the resultant temperature difference to determine if a shoe is worn or not. The @monitor can be fitted inside the footwear. When used in combination with activity monitoring, adherence to wearing footwear while walking can be objectively and quantitatively assessed.[41] This monitor was therefore used in the research for this thesis, aiming to gain insight in adherence to wearing custom-made footwear and the determinants of this adherence in persons with diabetes who are at high risk for ulceration.

Interventions to improve footwear adherence

Insight in (determinants of) adherence to wearing custom-made footwear is a first step in understanding people's behavior. If adherence is insufficient, interventions to improve the adherence are needed. At the start of the research for this thesis, there was no data available on interventions that aim to improve footwear adherence. A key aspect for interventions to help improve adherence is that they should target modifiable contributing factors. According to a model on footwear use (Figure 2), adapted from a model on usage of assistive technologies in general, there are potential avenues to improve adherence.[42] According to the model, use of custom-made footwear is influenced by the patients' acceptance of the footwear. The acceptance is influenced by 1) the perceived relative advantage and 2) the contextual factors. The perceived relative advantage is based on usability factors, such as appearance, comfort and ease of use. The contextual factors are factors concerning communication, service with healthcare providers, and the opinion of others (Figure 2). In line with these avenues, within this thesis we aimed to influence 1) the contextual factors, specifically communication, by using motivational interviewing as a behavior change technique, and 2) the perceived relative advantage of custom-made footwear, specifically the usability factors, by developing custom-made footwear specifically for indoor use.

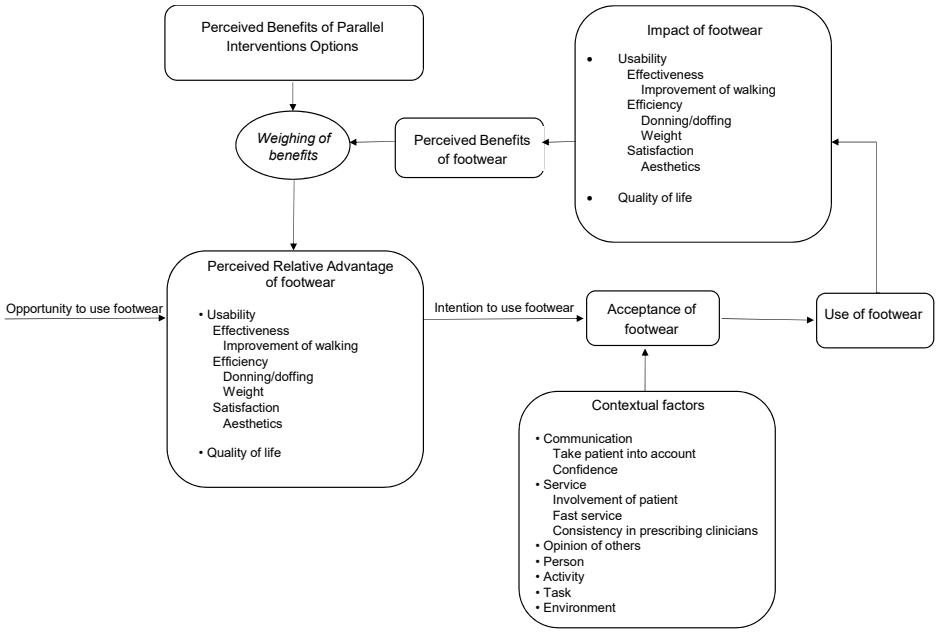

Figure 2. Conceptual model for predicting footwear use.[42] The use of footwear is dependent on the acceptance of footwear. The acceptance is influenced by usability factors (perceived relative advantage) and contextual factors. When footwear is used, the impact of the footwear on the usability factors determine the individuals' perceived benefits. These are weighed against the benefits of parallel interventions options, such as using other (not custom-made) footwear or walking barefoot, to determine again the perceived relative advantage.

Motivational interviewing

Motivational interviewing is an evidence-based technique that enhances motivation for change by exploring and resolving ambivalence to change.[43, 44] It uses several change and counselling techniques, aiming to elicit 'change talk'.[45, 46] Change talk is when a person presents arguments for change (i.e., revealing consideration of, motivation for, or commitment to change), and is the result of a directive strategy of the caregiver. This focus on behavior change makes motivational interviewing an attractive tool for addressing patient engagement to self-care.[44, 47] Although motivational interviewing has proven to be effective in behaviour change in people with addictions, obesity, musculoskeletal care, and diabetes,[48-51] no studies exist on behavior change specifically in people with diabetes-related complications. By applying the technique in people who are non-adherent to wearing their custom-made footwear, we hope to remove barriers and enhance motivation for behavior change, making it more likely to accept and therefore use the footwear.

Custom-made indoor footwear

Non-adherence to wearing prescription custom-made footwear is particularly high when people are at home, due to the perception of the footwear being heavy, difficult to don and doff, warm and dirty, or out of habit. Apparently, people weigh the same shoe characteristics differently for indoor use vs. outdoor use. With non-adherence being higher at home, we developed a custom-made shoe specifically for indoor use. When developing the shoe, we considered the needs of the users in their home situation, as well as the necessary set of requirements for custom-made footwear. Therewith, we aimed to increase the perceived relative advantage, increasing the acceptance and thereby the use of protective pressure-relieving footwear.

Aims of this thesis

In this thesis, the first aim was to gain insight in the adherence to wearing custom-made footwear and the determinants of adherence in a group of people with diabetes with a high risk for plantar foot ulceration, and in a subgroup of people with diabetes, recently healed plantar foot ulcer and a Charcot midfoot deformity. Secondly, the aim was to gain insight in how adherence to wearing custom-made footwear in people with diabetes and a healed plantar ulcer can be improved by assessing the effects of motivational interviewing and the provision of custom-made footwear that is specifically designed for indoor use.

Outline

In **chapter 2** the results of the study on adherence to wearing prescribed custom-made footwear in persons with diabetes at high risk for plantar foot ulceration and determinants of adherence are reported. In **chapter 3** a specific subgroup of people with diabetes, Charcot midfoot deformity and a plantar foot ulcer history, is investigated with regard to plantar pressure, footwear adherence and plantar foot ulcer recurrence. In **chapter 4** the efficacy and feasibility of motivational interviewing to improve footwear adherence is assessed. In **chapter 5** a new design for custom-made footwear for indoor use is developed, and users' needs and expectations for this footwear is evaluated, and in **chapter 6** the effect of this custom-made indoor footwear on footwear adherence in short-term and long-term is investigated. Finally, in **chapter 7** the main findings of this thesis, methodological considerations, clinical implications and recommendations for future research are discussed.

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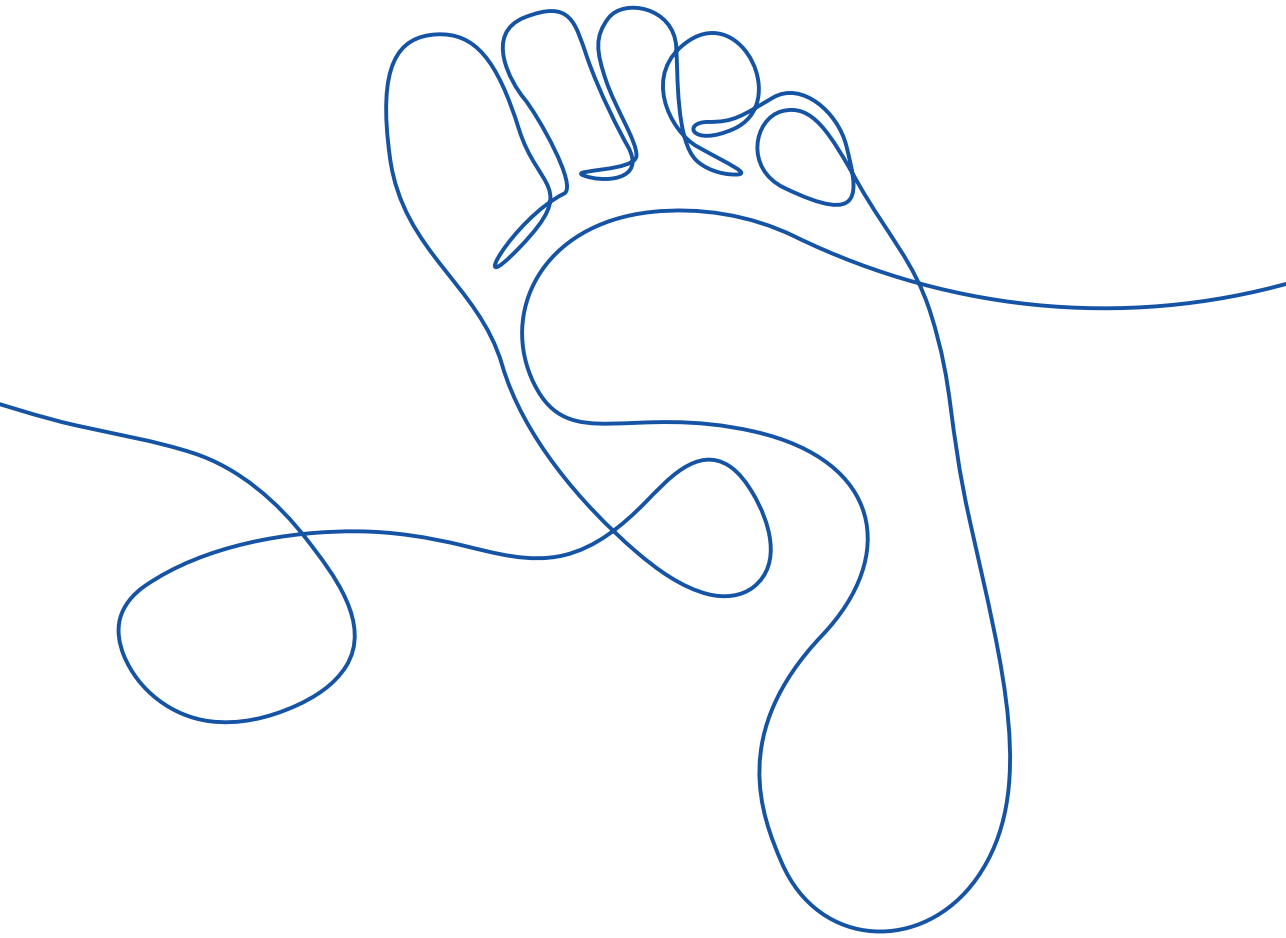

Chapter 2

Adherence to wearing prescription custom-made footwear in patients with diabetes at high risk for plantar foot ulceration

Roelof Waaijman, Renske Keukenkamp, Mirjam de Haart, Wojtek P. Polomski, Frans Nollet, Sicco A. Bus

Diabetes Care. 2013;36:1613-8

ABSTRACT

Objective: Prescription custom-made footwear can only be effective in preventing diabetic foot ulcers if worn by the patient. Particularly, the high prevalence of recurrent foot ulcers focuses the attention on adherence, for which objective data is nonexisting. We objectively assessed adherence in patients with high risk for ulcer recurrence and evaluated what determines adherence.

Research Design and Methods: In 107 patients with diabetes, neuropathy, a recently healed plantar foot ulcer, and custom-made footwear, footwear use was measured during 7 consecutive days using a shoe-worn, temperature-based monitor. Daily step count was measured simultaneously using an ankle-worn activity monitor. Patients logged time away from home. Adherence was calculated as the percentage of steps that prescription footwear was worn. Determinants of adherence were evaluated in multivariate linear regression analysis.

Results: Mean±SD adherence was 71±25%. Adherence at home was 61±32%, over 3959±2594 steps, and away from home 87±26%, over 2604±2507 steps. In 35 patients with low adherence (<60%), adherence at home was 28±24%. Lower BMI, more severe foot deformity, and more appealing footwear were significantly associated with higher adherence.

Conclusions: The results show that adherence to wearing custom-made footwear is insufficient, in particular at home where patients exhibit their largest walking activity. This low adherence is a major threat for reulceration. These objective findings provide directions for improvement in adherence, which could include prescribing specific offloading footwear for indoors, and they set a reference for future comparative research on footwear adherence in diabetes.

INTRODUCTION

Custom-made footwear is recommended and often prescribed to patients with diabetes, peripheral neuropathy, and foot deformity, to prevent foot ulceration and further complications such as infection and amputation.[1] Elevated plantar pressures and ill-fitting footwear are important risk factors of ulceration.[2, 3] Custom-made footwear aims to reduce ulcer risk by reducing foot pressures and providing proper fit.[4-6] It is clear that to be effective in ulcer prevention, prescription footwear should be worn by the patient, in particular when being ambulant.[7] Because annual ulcer recurrence rates are high, up to 40% found in one study,[8-10] poor adherence may be a factor in this outcome. Patient self-report studies show that only 22-36% of diabetic patients with peripheral neuropathy, vascular disease, or foot deformity wear their prescription footwear regularly (>80% of the day).[11, 12] This is unfortunate, since it has been shown that ulcer recurrence rate can be substantially reduced when patients adhere to wearing pressure-relieving footwear.[13] Nonadherence is therefore a major issue in high-risk diabetic patients that determines clinical outcome.

To date, adherence to footwear use has been assessed using subjective methods, including questionnaires, face-to-face interviews, or diaries.[11-14] Subjective methods are known to have issues with accuracy and reliability, and may lead to a response bias or to missing data.[15-17] Furthermore, these methods do not accurately distinguish between active and nonactive periods. In removable below-the-knee walkers used for offloading diabetic foot ulcers, adherence was measured objectively,[18] but the accelerometer-based sensors used were not developed to fit inside a shoe. Therefore, we use a new adherence-to-treatment monitoring system (the @monitor, developed at the Academic Medical Center in Amsterdam), which is small enough to fit inside the patients' shoe and has been proven to be valid and reliable in determining moments of donning/doffing and feasible in use in diabetic foot patients.[19]

Objective data on footwear adherence in patients who have diabetes and are at high risk for ulceration are not available. Adherence is most appropriately obtained during ambulation, when pressures on the foot are highest. Furthermore, adherence may vary according to where the patient is (at home or away from home)[14] or according to what day of the week or time of day it is. Knowledge about adherence and about what determines adherence is valuable in addressing issues of footwear effectiveness and can direct or even reform footwear prescription practice. Therefore, the aim of this study was to objectively assess adherence to wearing prescribed custom-made footwear during ambulation in patients with diabetes at high risk for ulceration, and to assess the determinants of adherence in this patient group.

RESEARCH DESIGN AND METHODS

Patients were selected from the database of a randomized controlled trial on custom footwear effectiveness (DIAbetic Foot Orthopedic Shoe [DIAFOS], clinical trial reg. no. NTR1091), in which patients were consecutively recruited from the outpatient multidisciplinary foot clinics of 10 Dutch hospitals. The first 120 patients in this trial who were assessed for adherence were included in the current study. Inclusion criteria were diagnosed diabetes, loss of protective sensation as confirmed by 10-g Semmes Weinstein monofilament and vibration perception threshold testing,[20] a prior plantar forefoot or midfoot ulcer that healed in the 18 months before inclusion in the trial, and prescription custom-made footwear. Exclusion criteria were bilateral amputation proximal to the tarso-metatarsal joint, nonambulatory status, unlikelihood to survive 18 months' follow-up, and inability to follow the study instructions. Written informed consent was obtained from each patient prior to inclusion in the trial, which was approved by all involved local research ethics committees.

Footwear

Patients wore fully custom-made footwear (i.e., custom insoles in custom shoes) or semi custom-made footwear (i.e., custom insoles in off-the-shelf extra-depth shoes). The footwear was prescribed by a rehabilitation medicine specialist and manufactured by a shoe technician, both of whom were experienced in treating diabetic foot patients. Shoes were mostly ankle high or boot style and were in some cases tibia high. The footwear generally had a stiffened rubber outsole with roller configuration and multidensity insoles.

Instrumentation

Data on footwear use was collected using a temperature-based adherence-to-treatment monitor, the @monitor, which has previously been described in detail.[19] In short, the @monitor measures 35x15x5 mm (length X width X height) and integrates two digital-to-digital temperature sensors (one on each flat side of the monitor), a battery, and a data logger. The @monitor samples temperatures at a maximum 1-min interval giving a 14-day collection period. The @monitor is placed in a plastazote foam pad and taped to the inner lateral shoe border just below ankle level. Only thin adhesive tape (covering the @monitor) and the patient's sock separate the @monitor from the leg. Because the temperature difference across the @monitor when wearing the footwear is unequal to the temperature difference when not wearing the footwear, footwear use can be determined. Response of the @monitor to donning and doffing footwear is immediate, with temperature change present at the next measurement sample. The @monitor has been shown accurate in determining moments of donning and doffing of footwear

(mean 0.4- min difference with an accurately kept log [95% CI: 0.2-0.6]) and feasible for use by high-risk diabetic patients.[19] Using a docking station and custom software, start date and time, number of days of data collection, and sample frequency are defined. Temperature readouts are exported to a text file after data collection.

Ambulatory activity was recorded using a step activity monitor (Stepwatch, Orthocare Innovations), which was strapped to the lateral side of the leg above the ankle. The step activity monitor stores the number of steps per minute over a maximum period of 14 days. Measurement accuracy is optimized by personalizing body height and type of gait of the patient (normal, fast, and slow) in the settings of the monitor, and verified by a light on the monitor that blinks at each of the first 40 steps taken by the patient after initialization. The error between counted steps and measured steps with the StepWatch is 0.3%.[21]

Procedures

At baseline, demographic, socioeconomic, disease-related, and foot complication history data were collected and a foot examination was performed. Each patient received brochures and standard verbal information from the researcher on diabetic foot care and the need to wear prescribed footwear as much as possible, preferably with each step taken. Because of the break-in period of footwear, data on adherence were collected a minimum of 3 months after footwear delivery. Three months after footwear delivery, perceived footwear aesthetics and comfort were scored on a visual analogue scale using the Questionnaire of Usability Evaluation.[22]

To avoid change in behavior of the patient during the measurement, patients were informed that foot temperature (not adherence) would be measured. The sample frequency of the @monitor was set at the maximum one sample per minute. Both the @ monitor and the step activity monitor were synchronized to local time on the same personal computer before each measurement. Shoes were equipped with the @monitor, and the step activity monitor was strapped to the ankle. If a patient had more than one pair of prescription custom-made shoes, a second pair was also equipped with the @ monitor. If a patient had more than two pair of prescription shoes, the patient was asked to wear only those two pair equipped with the @monitor. Each patient was asked to wear the step activity monitor for seven consecutive full days, at all times, except when taking a shower or bath or when discomfort was felt. Patients were also instructed not to remove the @monitor from the shoes. Additionally, they were asked to write down in a daily log the time periods (from [hh:mm] to [hh:mm], where h is hour and m is minute) that they were away from home, were cycling, or did not wear the step activity monitor. Patients returned the monitors and log after the measurement through postal mail.

Data analysis

Recordings with <4 days of step activity or without a weekend day included were considered incomplete and were excluded from analysis. The @monitor and step activity monitor data were analyzed using Matlab R2011a software (MathWorks, Natick, MA).[19] For patients with two pair of custom-made shoes in the study, data were accumulated. For each measurement day, step count and total wearing time were calculated. Adherence was calculated from the cumulative number of steps over the full measurement period as follows:

$$Adherence = \frac{\sum steps\ wearing\ prescribed\ footwear}{\sum steps}$$

When step activity was recorded during periods that the @monitor did not record footwear use, it was assumed that the patient walked either barefoot or in non-prescription footwear. The reported time periods in the daily log that patients were cycling were used to filter the step count data to keep walking-only data. Reported time in the daily log for being away from home was used to separate step count, wearing time, and adherence data for periods at home and for periods away from home. Subgroup analyses were done for the patients with adherence ≥80% ($adherence_{high}$) and adherence <60% ($adherence_{low}$). To compare outcomes with previous studies that used subjective methods, we also calculated adherence as percentage of daytime that the prescription footwear was worn. We assumed out-of-bed daytime to be 16 h.

Determinants of adherence

As potential determinants of adherence, the following factors were taken into account: age, sex, education level (low, medium, and high), living status, employment, diabetes type, diabetes duration, cumulative months of past ulceration, history of amputation, presence of peripheral arterial disease, BMI, HbA_{1c}, severity of foot deformity, daily step count, variation in daily step count over the measurement period, type of footwear, and perceived footwear aesthetics and footwear comfort.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics 19 (SPSS, Chicago, IL). Mann-Whitney *U* tests assessed baseline differences between included and excluded patients. Descriptive analyses were done on baseline patient characteristics and on outcomes for wearing time, adherence, and step activity. Paired *t* tests assessed differences in adherence between being at home and away from home, and between weekdays and weekend days. One-way ANOVA tested for differences in adherence between participating centers and between patient subgroups ($adherence_{high}$ vs. $adherence_{low}$).

Pearson correlation coefficients were calculated between adherence and wearing time and between adherence and daily step count. For all above tests, a significance level of $p<0.05$ was used. Univariate regression analysis ($p<0.10$) was used to assess the association between variation in step count and time away from home and to assess factors significantly associated with adherence. Significant univariate factors were entered in a multivariate regression analysis of adherence (with backward selection, $p<0.10$).

RESULTS

Thirteen of the 120 included patients were excluded from analysis because of incomplete (<4 days) step activity data (N=10), technical failure (N=2), or refusal to wear the step activity monitor (N=1). Baseline characteristics did not differ significantly between excluded and analyzed patients, except for sex (relatively more women were excluded, $p=0.018$).

Of the remaining 107 patients, 93 (87%) were men, 103 (96%) were Caucasian, 76 (71%) had diabetes type 2, and 89 (83%) wore fully custom-made footwear. Mean±SD age was 63.8±9.6 years and diabetes duration 17.3±11.9 years, Thirty-five patients had one pair of prescription custom-made shoes, and 72 had two pair. Footwear age at assessment of adherence was 1.4±0.9 years. We had 6.5±0.9 days of analyzed data per patient. Seventy-nine patients (74% of total group) had complete reports of time spent away from home. The step activity monitor was not worn during 3.5±9.6% of the day, and nonuse occurred mostly at night. Patients donned and doffed their footwear 1.3±0.9 times per day.

Outcome data for step count and adherence are shown in Table 1. Footwear adherence was 71±25% (range 10-100%). When patients were at home, adherence was significantly lower than when away from home ($p<0.001$), while daily step count was significantly higher at home ($p<0.001$). Adherence was <60% between 8pm and 10am, and <40% between midnight and 8am (Figure 1). Both adherence and step count were significantly lower during weekend days than weekdays ($p<0.001$). Adherence and daily step count were not significantly correlated ($r=0.14$, $p=0.16$). Correcting for cycling had a negligible effect on adherence.

Patients wore their prescribed footwear 9.4±4.4 h/day, at home 6.4±4.6 h, and away from home 3.5±2.7 h. Wearing time was 59±27% of daytime. Twenty-nine percent of patients wore their prescription footwear >80% of daytime. Wearing time was significantly correlated with adherence ($r=0.87$, $p<0.001$). Adherence was not significantly different between participating centers ($p=0.16$), and neither was daily step count ($p=0.35$), or wearing time ($p=0.59$). Day-to-day variation in step count increased significantly when patients were more away from home (β=181 steps/h [95% CI 80-282], $p<0.001$).

Table 1. Data on daily step count and adherence.

	Daily step count			Adherence (%)		
	Total group	$Adherence_{low}$ group	$Adherence_{high}$ group	Total group	$Adherence_{low}$ group	$Adherence_{high}$ group
Full measurement period (*n*=107)	6397±3494	5849±3720	6885±3543	71±25	40±15	92±6*
Walking only (*n*=107)	5967±3129	5505±3301	6300±3199	71±25	40±15	91±7*
Cycling only (*n*=28)	1642±1647	1507±1388	1790±1813	78±37	44±39	94±24*
At home (*n*=79)	3959±2594††	3988±2131††	3917±2947	61±32††	28±24††	83±17*†
Away from home (*n*=79)	2604±2507	1867±2661	3051±2441	87±26	69±31	95±22*
Weekday (*n*=107)	6686±3573	5959±3543	7252±3761	72±25	42±17	92±6*
Weekend day (*n*=107)	5734±3628$^{\#}$	5542±4160	6056±3545$^{\#}$	66±30$^{\#}$	34±24	89±11$^{\#*}$

Data are means±SD. $Adherence_{high}$ group, adherence ≥80%; $Adherence_{low}$ group, adherence <60%. $^{*}p$<0.001, significantly different from the $adherence_{low}$ group. $^{\dagger}p$<0.05. $^{\dagger\dagger}p$<0.01, significantly different from away from home. $^{\#}p$<0.05, significantly different from weekday.

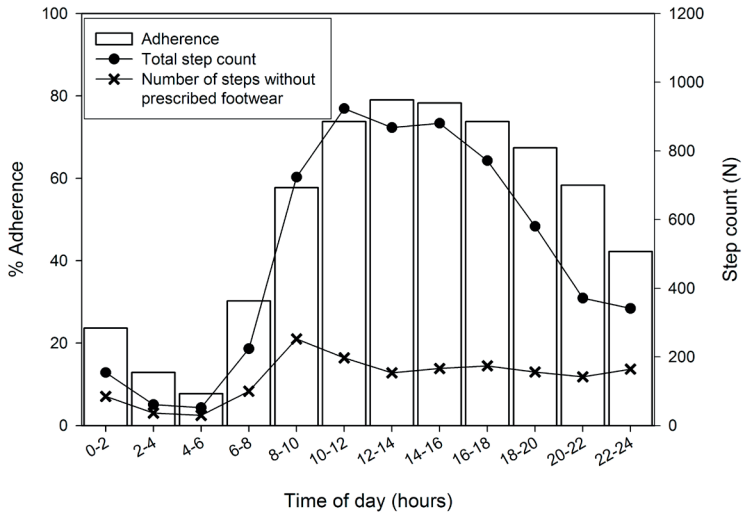

Figure 1. Mean adherence, total step count, and the number of steps taken without wearing prescribed footwear during 2-h time slots over the day.

Thirty-three percent of the patients had adherence <60% (Figure 2). In this $adherence_{low}$ group, adherence was 40±15% and was 2.5 times higher for away from home than for at home (Table 1). In the $adherence_{high}$ group, adherence was 85±12% and was 1.1 times higher for away from home than for at home. Daily step count was not significantly different between the adherence subgroups (p=0.19) (Table 1).

In the univariate regression analysis, a lower BMI, a history of amputation, more severe foot deformity, more variation in daily step count, and a better perception of footwear aesthetics were significantly associated with higher adherence (Table 2). In the mul-

tivariate analysis, all these factors except history of amputation remained significant (R^2=0.18, p<0.10) (Table 2).

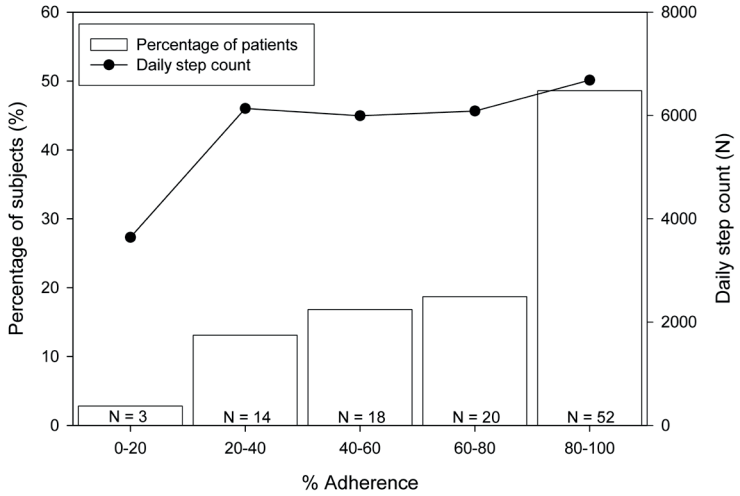

Figure 2. Distribution of patients across five subgroups of adherence. Also shown is the mean daily step count for each subgroup.

CONCLUSIONS

Adherence to wearing prescription custom-made footwear is important to prevent ulceration in high-risk patients with diabetes. With use of objective methods to measure adherence, the study results showed that 71% of the steps taken were in prescription custom-made footwear, while, among individuals, differences in adherence were large (10-100%). Adherence was much lower at home than away from home, which substantiates earlier studies that use subjective data.[14] In particular, in the patient group with low adherence (<60%), adherence at home was poor (28% compared with 69% away from home). Patients were significantly more active at home than away from home, which corresponds with previous data.[24] This further amplifies the problem of footwear use at home, increasing the cumulative stress on an inadequately protected foot. Therefore, interventions aimed to increase adherence should primarily target the home situation, e.g., through the prescription of special off-loading footwear for indoors.

When calculating adherence in similar units to what most previous studies did, our results show that 29% of the patients wore their prescribed footwear >80% of the daytime. This is comparable to these earlier studies that used mailed questionnaires (with a less-than-optimal response rate) and face-to-face interviews and that showed that 22-36% of

Table 2. Outcomes for the univariate and multivariate regression analysis on determinants of adherence.

Variable		Univariate regression		Multivariate regression	
	N or mean ± SD	ß (95% CI)	*p*	ß (95% CI)	*p*
Age (years)	63.8±9.6	0.120 (-0.380 to 0.620)	0.639		
Sex (male/female)	93/14	4.263 (-9.833 to 18.359)	0.555		
Diabetes type (1/2)	31/76	-5.408 (-15.855 to 5.039)	0.313		
Diabetes duration (years)	17.3±11.9	0.080 (-0.324 to 0.484)	0.701		
BMI (kg/m^2)	31.1±6.0	-0.939 (-1.717 to -0.161)	0.020*	-0.747 (-1.544 to 0.051)	0.066*
PAD grade (I/II)[a]	60/45	7.324 (-2.288 to 16.936)	0.138		
HbA_{1c} (%)	7.4±1.4	0.297 (-3.284 to 3.878)	0.871		
Cumulative past ulcer months [log(months)]	2.00±1.18	0.491 (-3.639 to 4.621)	0.816		
History of amputations (no/yes)	69/38	11.017 (1.291 to 20.743)	0.029*		
Severity of deformity (no/mild/moderate/severe)[b]	4/37/50/16	8.615 (2.464 to 14.766)	0.006*	6.831 (0.545 to 13.118)	0.034*
Education level (low/medium/high)	63/21/23	-1.796 (-7.629 to 4.037)	0.548		
Living with others (no/yes)	29/78	4.16 (-6.524 to 14.844)	0.447		
Employed (no/yes)	82/25	-3.44 (-14.807 to 7.923)	0.549		
Daily step count (per 1000 steps)	6397±3494	0.985 (-0.901 to 2.870)	0.158		
Variation in daily step count (per 1000 steps)	2.101±1.411	3.956 (0.651 to 7.261)	0.021*	3.655 (0.307 to 7.003)	0.033*
Type of footwear (fully custom-made/semi custom-made)	89/18	-1.747 (-14.621 to 11.127)	0.788		
Perceived footwear aesthetics (VAS score)	6.8±2.6	1.861 (-0.025 to 3.747)	0.056*	1.975 (0.176 to 3.775)	0.032*
Perceived footwear comfort (VAS score)	8.1±1.8	-0.226 (-2.988 to 2.536)	0.873		

Data are *N* or means±SD for descriptive data and unstandardized linear regression coefficients (95% CIs) for regression analysis. PAD, peripheral arterial disease; VAS, visual analogue scale. *Significant association ($p<0.10$). [a]Presence of peripheral arterial disease was classified according to a diabetic foot ulcer classification system for research purpose.[23] [b]Severity of deformity was classified as “no”, “mild” (i.e., presence of pes planus, pes cavus, hallux valgus, hammer toes, or lesser toe amputation), “moderate” (i.e., hallux or ray amputation, prominent metatarsal heads, or claw toes) or “severe” (i.e., Charcot deformity or [fore]foot amputation). The most severe deformity present determined classification.

diabetic patients at risk for ulceration wear their prescription footwear all day,[11, 12] or at least >80% of daytime.[14] These consistent outcomes across studies reinforce the problem of nonadherence in this patient group. Furthermore, they show that interpretations may vary based on which method is chosen to report adherence (percentage of daytime versus percentage of steps). A major disadvantage of subjective methods is that they lack the sensitivity, accuracy, and reliability to measure adherence during ambulant and non-ambulant periods added with the risk of reporting bias. Therefore, these methods lack the ability to accurately assess adherence when it is most important, namely when the foot is loaded most. This strongly supports the use of objective methods to assess true adherence in a patient. Using these methods, our study still showed that on average 29% of steps were taken without wearing custom-made footwear. Nonadherence was largest during the late-evening, night, and early-morning hours when patients may walk more on a hard bathroom or kitchen floor. This further increases the risk for ulcer recurrence.

The multivariate regression analysis showed that patients with more severe deformity had higher adherence to prescribed footwear, maybe because these patients have no other choice than to wear custom-made footwear or because they are more aware of its benefits. Patients with higher BMI were less adherent, which may reflect overall difficulty with adhering to a healthy life style in overweight or obese patients. More day-to-day variation in activity was positively associated with adherence, probably because patients who spent more time away from home (higher adherence) were the ones more variable in activity. Finally, patients who perceived their footwear as more attractive were more adherent, which seems intuitive, although previous studies are inconclusive on this association.[14, 25] Despite these significant associations, overall explained variance in adherence was only 18%, which implies that optimizing any of these predicting factors may have a limited effect on adherence. More research is needed to further elucidate why patients are adherent or not.

The objective data collected on adherence provide an excellent basis for further exploration of predictors of adherence and have great value in guiding footwear prescription practice and diabetic foot treatment. In many chronic diseases, adherence to treatment is a major problem and influenced by social and economical factors, the health care team, disease characteristics, therapy, and patient-related factors.[26] Therefore, objective footwear adherence data could be used to assess patient groups with different social-economic or cultural backgrounds, ethnicity, or past experiences with foot complications. Assessment of adherence in different regions or at different centers may provide information on more or less successful prescription and health care practices. Effects of patient education and other interventions can be accurately determined.

Finally, objective adherence data could be used to explore reasons for nonadherence and to individualize type and frequency of footwear prescription.[19] Effectively, these analyses could shape and potentially reform the prescription and use of specialist diabetic footwear.

Some limitations apply. First, we did not measure adherence while standing, even though patients spend twice as much time standing than walking[27] and forces equal to body weight are applied to the foot. Custom-made footwear was worn 9.4 h/day and was strongly associated with adherence. We therefore suggest that adherence may be as high in standing as in walking. Second, we measured adherence objectively, but we were still dependent on daily kept logs for periods of cycling, being away from home, and nonuse of the step activity monitor. This increases the chance for missing data or unreliable data. More objective ways to evaluate these events should be further explored, as well as methods to assure that patients do not take off the step activity monitor during measurement. Nonuse of the step activity monitor may under- or overestimate adherence. We verified from the daily kept logs that nonuse occurred only during 3.5% of the day, suggesting a negligible impact on the adherence values. Third, we attempted to avoid a conscious change in behavior by blinding the patient for the goal of the measurement, but we have no confirmation whether we succeeded. Finally, we did not measure adherence to wearing nonprescription footwear (e.g., off-the-shelf shoes, sandals, slippers), and therefore we lack information on the amount of barefoot walking, which is the most hazardous walking condition.

In conclusion, the results show that adherence to wearing prescribed custom-made footwear is insufficient in neuropathic diabetic patients with prior foot ulceration, in particular at home where they exhibit their largest walking activity. This low adherence is a major threat for re-ulceration in this high-risk patient group. Improvement of adherence could therefore include the prescription of specific protective footwear for indoors, while the importance of wearing prescription footwear should be further promoted. The objective data collected on adherence have great value in guiding clinical practice and provide an excellent basis to further explore predictive factors of adherence, to perform comparative research, and to investigate interventions that aim to improve adherence.

ACKNOWLEDGEMENTS

The DIAFOS trial was supported by project grants from the Dutch Diabetes Research Foundation (project 2007.00.067), the Dutch Branch Organization for Orthopedic Shoe Technicians (NVOS-Orthobanda) and Foundation for the Development of Orthopedic

Footwear (OFOM), and the Dutch Organization for Health Research and Development (ZonMw, project 14350054).

The Academic Medical Center in Amsterdam collaborates with nine other multidisciplinary diabetic foot centers and nine orthopedic footwear companies in the Netherlands in the DIAFOS trial on the effectiveness of custom-made footwear to prevent foot ulcer recurrence. The authors gratefully acknowledge the contribution of Mark Arts (Academic Medical Center, Amsterdam, the Netherlands) in collecting data for the study and also acknowledge the following persons for their contribution in patient recruitment and footwear prescription: T.E. Busch-Westbroek, MD; P.J.A. Mooren (Academic Medical Center, Amsterdam); J.W.E. Verlouw, MD; I. Ruijs and H. van Wessel (Maxima Medical Center, Veldhoven, the Netherlands); J.P.J. Bakker, MD, PhD; C. van den Eijnde (Medical Center Alkmaar, the Netherlands); D. Wever, MD; H. Wessendorf (Medisch Spectrum Twente, Enschede, the Netherlands), R. Dahmen, MD; B. Koomen (Slotervaart Hospital, Amsterdam, the Netherlands), J.G. van Baal, MD, PhD; R. Haspels (Ziekenhuisgroep Twente, Almelo, the Netherlands); J. Harlaar, PhD; V. de Groot, MD, PhD; J. Pulles (VU Medical Center, Amsterdam, the Netherlands); R. Lever; G. du Mont (Spaarne Hospital, Hoofddorp, the Netherlands); H.G.A. Hacking, MD; J. de Bruin (St. Antonius Hospital, Nieuwegein, the Netherlands); H. Berendsen, MD and W. Custers (Reinier de Graaf Gasthuis, Delft, the Netherlands).

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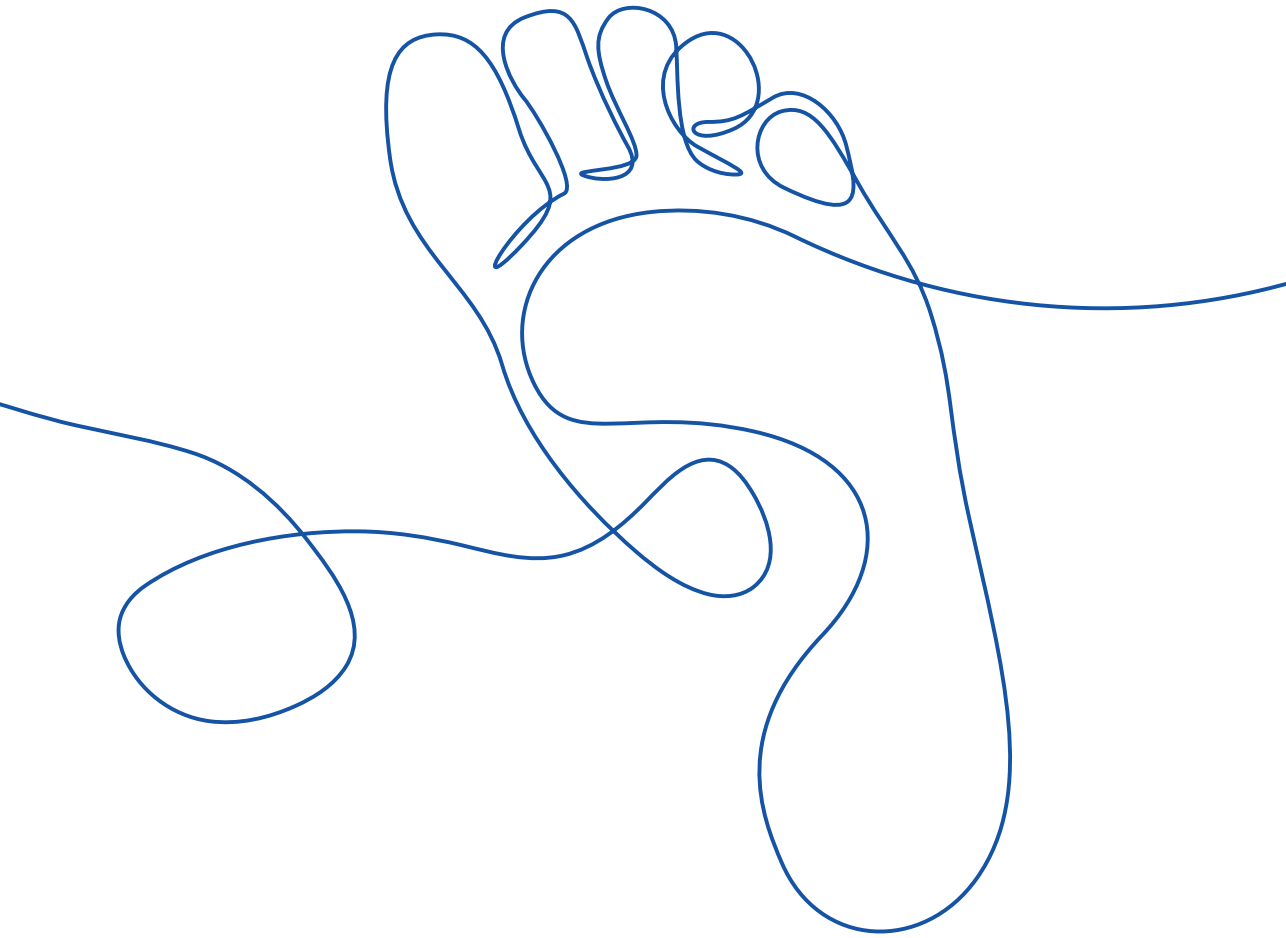

Chapter 3

Foot ulcer recurrence, plantar pressure and footwear adherence in persons with diabetes and Charcot midfoot deformity: a cohort analysis

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Diabetic Medicine. 2020;00:e14438

ABSTRACT

Aims: To investigate people with Charcot midfoot deformity with regard to plantar pressure, footwear adherence and plantar foot ulcer recurrence.

Methods: Twenty people with diabetes, Charcot midfoot deformity, plantar foot ulcer history and custom-made footwear were assessed with regard to barefoot and in-shoe plantar pressures during walking, footwear adherence (% of daily steps over 7-day period) and plantar foot ulcer recurrence over 18 months. In a cohort design, they were compared to 118 people without Charcot foot (non-Charcot foot group) with custom-made footwear and similar ulcer risk factors.

Results: Median (interquartile range) barefoot midfoot peak pressures were significantly higher in the Charcot foot group than in the non-Charcot foot group [756 (260-1267) vs. 146 (100-208) kPa, $p<0.001$]. In-shoe midfoot peak pressures were not significantly higher in the Charcot foot group [median (interquartile range) 152 (104-201) vs. 119 (94-160) kPa] and significantly lower for all other foot regions. Participants in the Charcot foot group were significantly more adherent, especially at home, than participants in the non-Charcot foot group [median (interquartile range) 94.4% (85.4, 95.0) vs. 64.3% (25.4, 85.7), $p=0.001$]. Ulcers recurred in 40% of the Charcot foot group and in 47% of the non-Charcot foot group ($p=0.63$); midfoot ulcers recurred significantly more in the Charcot foot group (4/8) than in the non-Charcot foot group (1/55; $p=0.001$).

Conclusions: Effective offloading and very high footwear adherence were found in people with diabetes and Charcot midfoot deformity. While this may help protect against plantar foot ulcer recurrence, a large proportion of such people still experience ulcer recurrence. Further improvements in adherence and custom-made footwear design may be required to improve clinical outcome.

INTRODUCTION

Charcot neuro-osteoarthropathy is a complex and severe condition that can have devastating consequences for affected feet.[1, 2] Diabetes is the most common cause of Charcot neuro-osteoarthropathy[3] which occurs exclusively in those people affected by peripheral neuropathy. Without appropriate treatment, the condition may result in gross alteration of foot structure and function.[1, 2] Moreover, Charcot neuro-osteoarthropathy has a profound negative effect on quality of life[4] and is associated with significant morbidity and premature mortality.[1, 5] It is considered a rare complication, with an incidence ranging from 0.1% to 0.3% among people with diabetes,[1, 6] although it may be more prevalent due to difficulties with diagnosis.[1, 7]

Evidence-based treatment for the acute Charcot neuro-osteoarthropathy does not exist. Treatment primarily aims at achieving a stable and plantigrade foot that remains ulcer- free, through immobilization and offloading with a total contact cast or removable walker.[2, 8-11] Delay in diagnosis and continued weight-bearing without total contact cast support may lead to severe deformity.[2, 12] Deformity occurs mostly in the midfoot and frequently as rocker-bottom, which is a significant risk factor for ulceration.[13] Typical management following the acute stage includes gradual weight-bearing and continued off-loading with custom-made footwear in order to prevent (recurrent) ulceration.[7, 14, 15] However, only few non-comparative studies exist on the efficacy of offloading management of the Charcot foot beyond the acute phase.[14, 16] Ulceration rates of 49% and 65% over a 4- to 9-year follow-up were reported in people with Charcot foot wearing accommodative or custom-made footwear.[15, 17] Furthermore, 1-year ulcer incidence was found to drop from 73% to 10% in people with Charcot after provision of custom-made footwear.[18] However, none of these studies measured the offloading characteristics of the footwear prescribed.

The presence of Charcot deformity is often an exclusion criterion in ulcer prevention trials, and thus hardly studied. Charcot deformity was recently identified as the single greatest predictor of high barefoot plantar pressures in the midfoot region in people with diabetes and a history of ulceration.[19] Furthermore, objective measures show that adherence to wearing custom-made footwear is insufficient in people with diabetes at high risk for foot ulceration, which has implications for ulcer recurrence.[20, 21] A literature review shows that the risk of developing a recurrent foot ulcer is 40% within 1 year after healing;[22] therefore, this group in remission is an important one to target for ulcer prevention. Footwear offloading and adherence have, however, not been investigated in the Charcot foot population. Neither has ulcer recurrence after recent healing for which custom-made footwear is prescribed. The aim of the present study, therefore, was to as-

sess barefoot and in-shoe plantar pressures, footwear adherence and plantar foot ulcer recurrence in people with diabetes, Charcot midfoot deformity and plantar foot ulcer history, and to compare these outcomes to those in people with the same risk factors but without a Charcot foot.

PARTICIPANTS AND METHODS

Study design

We conducted a cohort analysis of data obtained from a multicenter randomized controlled trial on the effectiveness of custom-made footwear to prevent plantar foot ulcer recurrence in people with diabetic foot disease (the Diabetic Foot Orthopedic Shoe (DIAFOS) trial).[20] Reporting is carried out according to the recommendations set out in the STROBE checklist for cohort studies (https://www.strobe-statement.org/).

Participants

Participants from 10 outpatient clinics in the Netherlands were enrolled if they met the following inclusion criteria: type 1 or type 2 diabetes; age ≥18 years; loss of protective foot sensation as a result of peripheral neuropathy; and a recently healed plantar foot ulcer (<18 months prior to study entry). All participants received newly prescribed fully or semi custom-made footwear at study entry. Fully custom-made footwear comprises custom-made insoles worn in custom-made shoes, whereas semi custom-made footwear comprises custom-made insoles worn in off-the shelf diabetes-specific shoes. People with bilateral amputation proximal to the metatarsals, inability to walk unaided and comorbidity that would make 18 months' survival (i.e., the length of follow-up) unlikely, were excluded. Participants were randomized to either pressure-improved and preserved custom-made footwear, as guided by 3-monthly in-shoe plantar pressure measurements, or to usual care (i.e., non-improved custom-made footwear).

Procedures

On entry into the trial, demographic and disease-related data were collected, a foot assessment was undertaken and barefoot and in-shoe plantar foot pressures were measured. In the participants with pressure-improved footwear, recorded in-shoe pressures were used to identify a maximum of three regions of interest per foot that were targeted for pressure improvement. These regions were the previous ulcer location and the two highest peak pressure locations in the forefoot or midfoot. If peak pressure exceeded 200 kPa, the footwear was subject to a maximum three rounds of modifications, with the goal of reducing peak pressure by at least 25% or to an absolute level below 200 kPa.[20] A detailed description of the modification protocol can be found elsewhere.[23]

For the present study, the in-shoe pressure data *after* footwear modification at entry were used for analysis for the participants with pressure-improved footwear. For the usual care participants, the single measured in-shoe pressure data at entry were used. Each participant was followed for 18 months or until plantar foot ulcer recurrence. A foot ulcer was defined as a cutaneous erosion through the dermis without reference to time present.[24] Ulcer recurrence for the study was defined as an ulcer appearing on any plantar site on either foot in a person whose plantar foot ulcer had previously healed.

Foot assessment

History of plantar foot ulceration and Charcot neuro-osteoarthropathy were confirmed via medical records that included foot and ankle radiographs. Midfoot Charcot deformity was diagnosed from clinical assessment by the participant's physician and from consensus between four investigators who assessed photographs of the foot. With the participant's foot weight-bearing, these photographs were taken from a medial, lateral, anterior and posterior view, and non-weight bearing from a medial, anterio-lateral and anterio-medial view. Other commonly encountered foot deformities were recorded in a similar fashion. The presence of peripheral neuropathy was diagnosed using methods and definitions described elsewhere.[20]

Custom-made footwear

Participants wore and were tested for plantar pressure in their newly prescribed custom-made footwear and in the custom-made footwear they already possessed. Footwear was prescribed by a rehabilitation specialist and manufactured by a shoe technician in each of the participating centers; both specialist and technician were experienced in the management of people with diabetic foot disease. See elsewhere for technical details on the custom-made footwear.[20]

Plantar pressure measurement and analysis

Barefoot dynamic plantar pressures were measured with an Emed-X pressure platform (Novel, Munich, Germany) at a 100-Hz sampling rate. The two-step method at a self-selected speed over five walking trials for each foot was used.[25] In-shoe dynamic plantar pressures were recorded at a 50-Hz sampling frequency using a Pedar-X in-shoe pressure measurement system (Novel, Munich, Germany). A minimum of 12 midgait steps per foot were collected at a self-selected walking speed, independent from the speed chosen for barefoot pressure measurement.[26] Pressure analysis was undertaken using Novel multimask software (version 13.3.65). The mean peak pressures at the previous ulcer location, and, in case of ulcer recurrence, the new ulcer location, were used for analysis, as well as mean peak pressures for four anatomical foot regions: the heel, midfoot, forefoot (i.e., metatarsal 1-5) and toes (hallux, digits 2-5).

Adherence

Footwear use and daily step activity were assessed objectively at least 3 months after baseline for 7 continuous days. Footwear use was measured with the @monitor (Department of Medical Technology and Innovation, Amsterdam UMC, Amsterdam, The Netherlands). This is a small temperature-based sensor that was placed inside the two pairs of custom-made shoes that the participant used most. The @monitor provides valid and reliable data.[27] Daily step activity was recorded simultaneously using an activity monitor strapped above the ankle (StepWatch; Orthocare Innovations LLC, Oklahoma City, OK, USA). Participants were instructed to wear the StepWatch at all times, except when having a shower or bath. Footwear adherence was calculated from these measurements and expressed as the percentage of cumulative steps taken in the 7-day period that custom-made footwear was worn. Participants recorded time spent away from home so that adherence could be calculated for both at-home and away-from home periods.[21]

Selection of participants and feet

Of the 171 trial participants, those wearing semi custom-made footwear (n=28) were excluded for the present study, to match study groups on participants only wearing fully custom-made shoes. Participants with missing barefoot plantar pressure data (n=5) were also excluded. The remaining 138 participants were divided into two groups: those with Charcot midfoot deformity (Charcot foot group) and those without (non-Charcot foot group). All participants with Charcot diagnosis had midfoot deformity. One foot per participant was selected for barefoot and in-shoe pressure analysis. The foot with the highest degree of deformity was selected for the non-Charcot foot group. Foot deformity was classified as 'absent', 'mild' (i.e., pes planus, pes cavus, hallux valgus or limitus, hammer toes, lesser toe amputation), 'moderate' (i.e., hallux rigidus, hallux or ray amputation, prominent metatarsal heads, claw toes) or 'severe' (i.e., forefoot amputation, and pes equines).[20] In case of equal degree of deformity, the foot with the highest barefoot peak pressure, irrespective of location, was chosen. Where both feet saturated the pressure platform at 1275 kPa, the left foot was selected. For the Charcot foot group, the affected foot was selected. One participant had bilateral Charcot; in this case, the foot with the highest barefoot peak pressure was included.

Statistical analysis

Participant characteristics, barefoot and in-shoe peak pressure, footwear adherence and daily step activity were summarized using descriptive statistics. For normally distributed data, expressed as mean±SD, independent sample *t*-tests were used to compare differences between study groups; for non-normally distributed data, expressed as median [interquartile range (IQR)], Mann-Whitney *U* tests were used. Proportions of participants with a foot ulcer were compared using Fisher's exact test. *P* values <0.05

were considered significant, with Bonferroni correction applied in case of multiple testing of dependent variables. Statistical analyses were performed using SPSS 24.0 (SPSS Inc., Chicago, IL, USA).

Ethics

All participants provided written informed consent prior to entering the trial. Ethical approval was obtained from the medical ethics committee of Amsterdam UMC, University of Amsterdam (project MEC07/133).

RESULTS

Group characteristics

Twenty participants in the Charcot foot group and 118 in the non-Charcot foot group were analysed and compared. Eight Charcot foot participants (40%) and 63 non-Charcot foot participants (53%) had pressure-improved custom-made footwear. Demographic and disease characteristics are shown in Table 1; no significant differences (after Bonferroni adjustment) were found between study groups, except for location of previous ulcers. Most previous ulcers in the non-Charcot foot group were found at the hallux and metatarsal head regions, and none in the midfoot. In the Charcot foot group, most previous ulcers were found at the metatarsal head 1 region and at the midfoot.

Plantar pressure

Barefoot and in-shoe plantar pressure data are summarized in Table 2. Median (interquartile range) barefoot peak pressures in the midfoot were significantly higher in the Charcot foot group than the non-Charcot foot group [756 (260-1267) kPa vs 146 (100-208) kPa; $p<0.001$]. No other region showed a significant group difference in barefoot peak pressure. In-shoe peak pressure at the midfoot was non-significantly higher in the Charcot foot group than the non-Charcot foot group: 152 (104-20) kPa vs 119 (94-160) kPa. In-shoe peak pressure in the heel, forefoot, toes, and at the new ulcer location were significantly lower in the Charcot foot group ($p<0.01$).

Adherence

Median (IQR) overall adherence to wearing the prescribed custom-made footwear was significantly higher in the Charcot foot group than non-Charcot foot group: 95.3 (80.3-98.5)% vs 75.9 (54.9-90.2)%; $p<0.001$ (Table 3). In particular, adherence at home was different between groups: 94.4 (85.4-95.0)% for the Charcot foot group vs 64.3 (26.4-85.7)% for the non-Charcot foot group ($p=0.001$). Groups exhibited a comparable daily step count of approximately 6600 steps ($p=0.82$).

Table 1. Baseline participant characteristics.

Characteristic	Charcot foot group	Non-Charcot foot group	*p*
Participants, *N*	20	118	-
Age, years	61.6±8.8	63.2±10.5	0.46
Male gender, *n* (%)	15 (75)	100 (85)	0.33
Median (IQR) BMI, kg/m^2	29 (26-33)	31 (27-34)	0.34
Type 2 diabetes, *n (%)*	13 (65)	84 (71)	0.60
Median (IQR) diabetes duration, years	18 (9-25)	12 (7-26)	0.48
HbA_{1c} (*N*=129)			
mmol/mol	68±15	59±15	0.02
%	(8.4±1.3)	(7.5±1.4)	0.02
Loss of protective sensation[b], *n (%)*			
Based on abnormal SW monofilament	20 (100)	116 (98)	1.00
Based on vibration perception threshold >25 volts (*N*=132)	17 (89)	98 (87)	1.00
Vibration perception threshold, volts (*N*=131)[c]	50 (48-50)	50.0 (43-50)	0.98
Peripheral arterial disease (*N*=131)[d], *n (%)*	5 (28)	40 (35)	0.79
Location previous ulcer, *n* (%)			
Hallux	3 (15)	32 (27)	0.40
Digits 2-5	3 (15)	23 (19)	0.77
Metatarsal 1	7 (35)	27 (23)	0.27
Metatarsal 2-5	0	31 (26)	<0.01[a]
Heel	0	1 (0.8)	1.00
Medial midfoot	5 (25)	0	<0.001[a]
Lateral midfoot	2 (10)	0	0.02
Base metatarsal 1-2	0	4 (3.4)	1.00

Abbreviations: IQR, interquartile range; SW, Semmes-Weinstein. Data are expressed as mean±SD, unless otherwise indicated. [a]Significantly different between study groups (p<0.01, after Bonferroni correction). [b]Loss of protective sensation was confirmed present in both feet by the inability to sense the pressure of a 10-g SW monofilament at any of the three plantar foot sites (hallux, first and third metatarsal head) or a vibration of 25 volts at the hallux from a biothesiometer (maximum measurable value 50 volts). [c]In nine participants, the vibration perception threshold could only be measured in one foot because of hallux amputation. [d]Peripheral arterial disease was confirmed as present when pedal pulses were non-palpable and the ankle-brachial index was <0.9 in the foot that was selected for analysis. In seven participants, peripheral arterial disease data were missing.

Ulcer recurrence

Table 4 summarizes the data on plantar foot ulcer recurrence. Eight of the 20 participants (40%) in the Charcot foot group had a recurrent plantar ulcer in 18 months, vs 55 of the 118 (47%) in the non-Charcot foot group (p=0.63). In the Charcot foot group, seven of eight (88%) ulcers recurred in the same foot as where the previous ulcer was present, of which four (57%) recurred at the previous ulcer site. Four of the eight ulcers (50%) were in participants with pressure-improved footwear. In the non-Charcot foot group, 45 of 55 (82%) ulcers developed in the foot as where the previous ulcer was present, of which 35 (78%) recurred at the previous ulcer site. Twenty-nine of 55 ulcers (53%) were in participants with pressure-improved footwear. In the Charcot foot group, significantly

Table 2. Barefoot and in-shoe plantar peak pressure data.

	Charcot foot group	*n*	Non-Charcot foot group	*n*	*p*
Barefoot peak plantar pressure					
New ulcer location	752 (491-1079)	8	849 (503-1186)	55	0.82
Heel	299 (258-407)	20	327 (245-409)	118	0.66
Midfoot	756 (260-1267)	20	146 (100-208)	118	<0.001[a]
Forefoot	1066 (716-1253)	19	1091 (822-1238)	118	0.64
Toes	186 (83-447)	20	223 (95-331)	113	0.98
In-shoe peak plantar pressure					
New ulcer location	141 (92-190)	7	219 (167-306)	55	<0.01[a]
Heel	153 (125-197)	20	190 (163-223)	118	<0.01[a]
Midfoot	152 (104-201)	20	119 (94-160)	118	0.03
Forefoot	195 (125-216)	20	219 (178-287)	118	<0.01[a]
Toes	100 (65-165)	20	153 (114-202)	118	<0.01[a]

Data are expressed as median (interquartile range). [a]significantly different between study groups (p<0.01, after Bonferroni correction).

Table 3. Adherence and daily step count data.

	Charcot foot group	*n*	Non-Charcot foot group	*n*	*p*
Adherence[b], %	95 (80-99)	17	76 (55-90)	103	<0.001[a]
Adherence at home[c], %	94 (85-95)	12	64 (26-86)	68	0.001[a]
Adherence away from home[c], %	100 (100-100)	12	99 (93-100)	68	0.03
Mean±SD daily step count	6592±3145	16	6600±3447	111	0.82

Data are expressed as median (interquartile range), unless otherwise indicated. [a]Significantly different between study groups (p<0.02, after Bonferroni correction). [b]Adherence was not measured in 18 participants due to drop out (n=4), development of an ulcer during the trial (n=9), refusal to participate (n=1) or for other reasons (n=4). [c]In an additional 40 participants, data on being at home or away from home, which was completed through daily logs, were missing.

more plantar ulcers recurred at the midfoot than in the non-Charcot foot group (four of eight vs. one of 55, respectively; p=0.001). Two of four midfoot ulcers (50%) in the Charcot foot group and the midfoot ulcer in the non-Charcot foot group developed in participants with pressure-improved footwear.

DISCUSSION

This study was a comprehensive analysis of biomechanical factors, treatment adherence behavior, and plantar foot ulcer recurrence in people with Charcot midfoot deformity compared with those without. Participants with Charcot midfoot deformity

showed a significant 5.2-fold greater median barefoot peak pressure at the midfoot and a non-significant 1.3-fold greater median in-shoe peak pressure at the midfoot than non-Charcot foot participants. In-shoe midfoot peak pressures in the Charcot foot group were 80% lower than their barefoot peak pressures and nearly all were <200 kPa. At all other foot regions, in-shoe peak pressures in the Charcot foot group were significantly lower than in the non-Charcot foot group. The Charcot foot participants were significantly more adherent in wearing their custom-made shoes than the non-Charcot foot participants. This was especially the case when at home, with median values close to 100% in the Charcot foot group. The combination of low in-shoe peak pressure and very high footwear adherence in the Charcot foot participants may have helped reduce the incidence of ulcer recurrence. Still, a large proportion of Charcot foot participants had plantar foot ulcer recurrence, similar to the non-Charcot foot group; significantly more midfoot ulcers developed in the Charcot foot group.

The significantly higher barefoot and non-significantly higher in-shoe peak pressures found in the midfoot in the Charcot foot group can be expected from the major change in foot architecture. By losing the plantar arch as a result of bone, joint and soft-tissue damage, deformity occurs at the midfoot. This extends to the typical rocker bottom foot,[1] which was found in some of the Charcot foot participants in the study. Such midfoot (rocker bottom) deformity changes the structural weight-bearing surface and leads to increased load on the skin. This is attributable to, among other factors, an absence of a cushioning subcutaneous fat-pad. This can ultimately result in ulceration. The midfoot deformity is the characteristic difference between the Charcot foot and non-Charcot foot groups, and possibly the sole biomechanical difference, as barefoot peak pressures in other foot regions were similar between groups. The highest barefoot and in-shoe peak pressures in both groups were found under the metatarsal heads, as observed previously.[28] This suggests that, while the midfoot is targeted for offloading in people with Charcot midfoot deformity, pressure redistribution over the entire plantar surface is important. Our data show this can be effectively achieved with custom-made footwear.

Footwear adherence in the Charcot foot group was significantly higher than in the non-Charcot foot group, especially when participants were at home. Overall median adherence was close to 100% in the Charcot foot group, with some non-adherence only found when participants were at home. A possible explanation for the very high adherence may be that, with midfoot deformity, the base of support is reduced when barefoot. This may further increase the balance disturbance already caused by the neuropathy. Therefore, by necessity, these people may increase their base of support by wearing their custom-made footwear. Alternatively, the prolonged periods of casting in the acute phase of Charcot neuro-osteoarthropathy (up to 9 months) may have made this group

more aware of the risk of complications, the loss of mobility and decline of quality of life, and thus more motivated to wear their prescribed footwear.

Incidence of plantar foot ulcer recurrence was not significantly different between groups and similar to rates found in other studies of high-risk people with diabetes.[22] Comparisons with other studies in people with Charcot foot are hampered by a wide variation in follow-up periods, patient inclusion criteria and footwear provided.[15, 17, 18] More ulcers in the Charcot foot group recurred at the midfoot than in the non-Charcot foot group: 50% vs 2%. The higher midfoot peak pressures, combined with previous ulcer history at the midfoot in 35% of Charcot foot participants best explains this. The other 50% of foot ulcers in the Charcot foot group recurred at the metatarsal heads, where barefoot peak pressures were also high. The trial from which the current data was obtained showed that high footwear adherence, in combination with improved and low in-shoe peak pressures, substantially reduces risk for plantar foot ulcer recurrence in high-risk people with diabetes.[20, 29] Thus, the close to optimal footwear adherence and seemingly low in-shoe peak pressures may have protected against ulcer recurrence compared to when these conditions would not have been met. Nevertheless, the incidence of ulcer recurrence in the Charcot foot group was still high and not different from that in the non-Charcot foot group. A number of factors may play a role here. First, while the in-shoe midfoot peak pressures were reduced by 80% from barefoot, they still may have been too high to help prevent ulceration effectively. A target pressure that is advocated for footwear provision is 200 kPa,[20, 29, 30] but this pressure threshold was defined based on pressures measured in the forefoot. A different threshold may apply to the midfoot, being more vulnerable after a major change in foot architecture and lack of protective subcutaneous fat tissue present. Second, despite the close to optimal adherence outcomes, the few percent non-adherence remaining at home may have left the Charcot foot participants unprotected and with increased risk for ulcer recurrence. Further improvements in midfoot offloading and footwear adherence may be needed and should be further investigated. Also other factors related to bone, joint and soft-tissue involvement (i.e., strength, movement, extensibility), shear and vascular components, and the effect of surgical reconstruction of the foot should be further studied. Clinicians should therefore regard offloading and adherence as only two of a number of issues that need to be addressed to help prevent plantar foot ulcer recurrence in people with Charcot midfoot deformity.

A strength of the present study is that objective biomechanical and behavioral measures are used in a comprehensive analysis of plantar foot ulcer recurrence in a homogeneous group of people with Charcot midfoot deformity. Few studies exist on the management of the Charcot foot beyond the acute phase, despite its importance given the associated morbidity and mortality. The limitations of the study mainly originate from using

existing data from a randomized controlled trial on footwear efficacy.[20] This determined the imbalance between groups with 20 Charcot foot participants and 118 non-Charcot foot participants. This is, however, in line with the low incidence of Charcot neuro-osteoarthropathy in the diabetes population. Furthermore, being a clinical trial, we did not randomly include people with Charcot from the general patient population; neither did we include people with Charcot foot who had no plantar foot ulcer history. These factors may affect footwear adherence and ulcer outcome. Also, we relied heavily on peak pressure as an outcome of Charcot midfoot deformity. While many bony and soft-tissue changes will show as a change in peak pressure, factors such as shear and small vessel blood flow are probably also important in skin breakdown. Finally, approximately half of the participants had pressure-improved footwear, which potentially biases the in-shoe pressure results within study groups, in particular, in the already-small Charcot foot group. This is not expected, however, to influence the comparison between study groups as the proportion of participants with pressure-improved footwear was comparable between groups and because peak pressures in improved and non-improved footwear showed substantial overlap.

In conclusion, our findings show effective offloading of pressures inside custom-made footwear and very high adherence to wearing this footwear in people with diabetes at high risk for foot ulceration who have Charcot midfoot deformity. While this may have reduced plantar foot ulcer recurrence incidence compared to less effective or less worn footwear, incidence of recurrence was comparable to high-risk people without Charcot foot who showed higher in-shoe peak pressures and lower adherence. Further improvements in adherence and custom-made footwear design that include the use of region-specific target pressures may be required, among other options, to improve clinical outcome in people with diabetes and Charcot midfoot deformity.

ACKNOWLEDGEMENTS

The data in this study were obtained from the DIAFOS trial, a multicentre randomized controlled trial on the effectiveness of custom-made therapeutic footwear to prevent ulcer recurrence in people with diabetes. The authors acknowledge the contribution of M. L. Arts and R. Waaijman for collecting data for the DIAFOS trial and the following for recruiting participants for the study: J. W. E. Verlouw, I. Ruijs, J. P. J. Bakker, D. Wever, R. Dahmen, J. G. van Baal, R. Haspels, V. de Groot, W. P. Polomski, H. G. A. Hacking and H. Berendsen.

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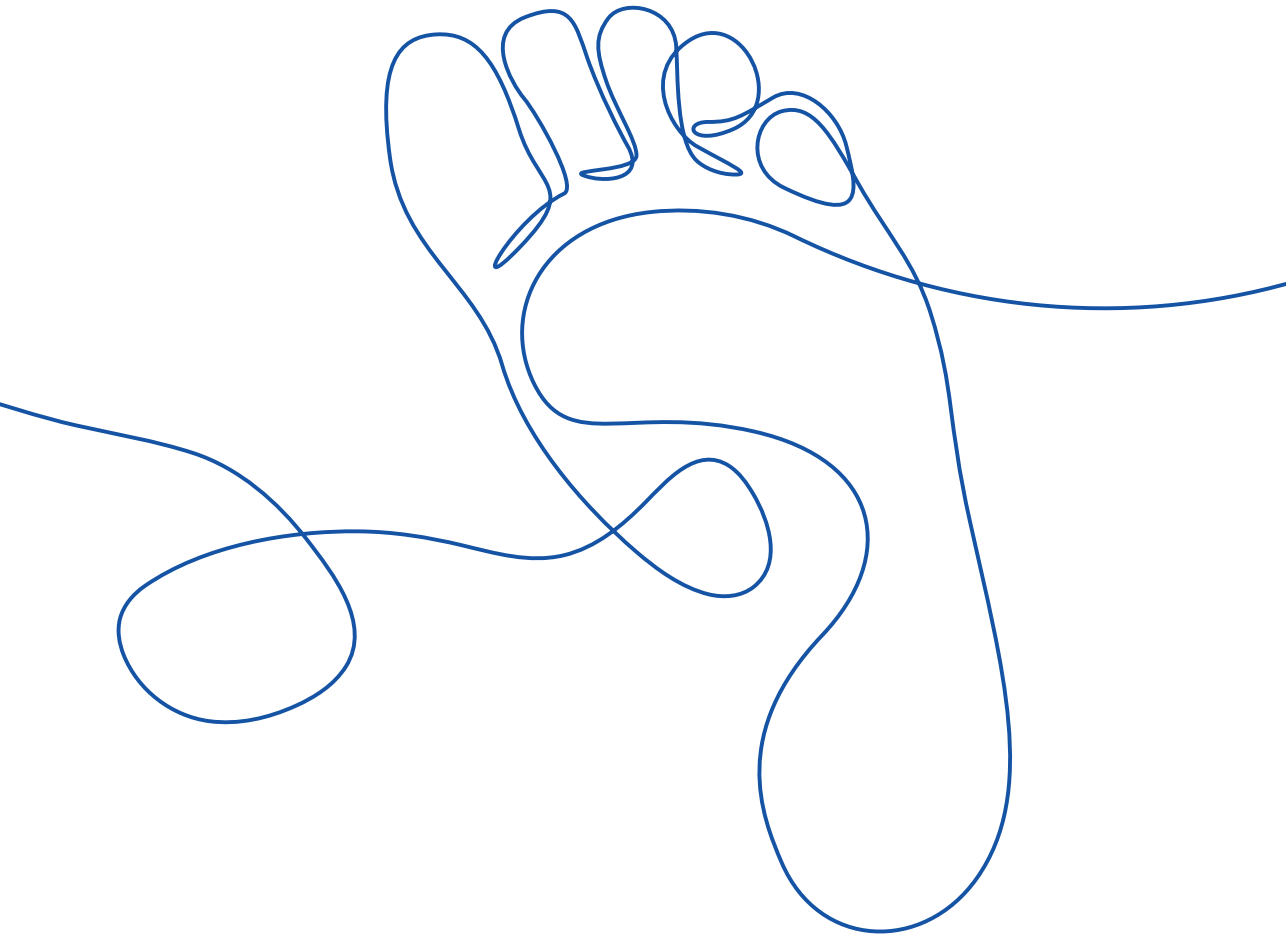

Chapter 4

An explorative study on the efficacy and feasibility of the use of motivational interviewing to improve footwear adherence in persons with diabetes at high risk for foot ulceration

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Journal of the American Podiatric Medical Association 2018;108(2):90-99

ABSTRACT

Background: In this explorative study we assessed the effect and feasibility of using motivational interviewing to improve footwear adherence in persons with diabetes who are at high risk for foot ulceration and show low adherence to wearing prescribed custom-made footwear.

Methods: Thirteen individuals with diabetes, ulcer history, and low footwear adherence (i.e., <80% of steps taken in prescription footwear) were randomly assigned to standard education (i.e., verbal and written instructions) or to standard education plus two 45-min sessions of motivational interviewing. Adherence was objectively measured over 7 days using ankle- and shoe-worn sensors and was calculated as the percentage of total steps that prescribed footwear was worn. Adherence was assessed at home and away from home at baseline, at 1 week and 3 months after the intervention. Feasibility was assessed for interviewer proficiency to apply motivational interviewing and for protocol executability.

Results: Median (range) baseline, 1-week and 3-month adherence at home was 49% (6%-63%), 84% (5%-98%), and 40% (4%-80%), respectively, in the motivational interviewing group, and 35% (13%-64%), 33% (15%-55%), and 31% (3%-66%), respectively, in the standard education group. Baseline, 1-week, and 3-month adherence away from home was 91% (79%-100%), 97% (62%-99%) and 92% (86%-98%), respectively, in the motivational interviewing group, and 78% (32%-97%), 91% (28%-98), and 93% (57%-100%), respectively, in the standard education group. None of the differences were statistically significant. Interviewers proficiency was good and the protocol could be successfully executed in the given time frame.

Conclusions: Footwear adherence at home increases 1 week after motivational interviewing to clinically relevant but not statistically significant levels (i.e., 80%), but then returns over time to baseline levels. Away from home, adherence is already sufficient at baseline and remains so over time. The use of motivational interviewing seems feasible for the given purpose and patient group. These findings provide input to larger trials and provisionally suggest that additional or adjunctive therapy may be needed to better preserve adherence.

INTRODUCTION

Foot ulceration is one of the major health problems for people with diabetes mellitus. It is estimated to affect 19% to 34% of people with diabetes at some time in their lives.[1] Foot ulceration is an important precursor to foot infection and amputation. Furthermore, it negatively affects quality of life[2] and leads to a substantial economic burden.[3] Therefore, prevention of ulceration is of paramount importance.

Preventative treatment often involves the use of prescription custom-made footwear, aiming to reduce ulcer risk by redistributing and reducing foot pressures and providing proper fit.[4, 5] Our research group found that pressure-improved custom-made footwear is effective in preventing foot ulcer recurrence, if it is worn as recommended.[6] However, in this study, half of the patients were shown to have low adherence, i.e., less than 80% of the steps taken per day were in prescribed footwear. Moreover, footwear adherence at home was much lower than away from home, although patients walked significantly more at home.[7] These results confirm previously reported findings on footwear adherence in this patient population,[8, 9] and demonstrate that nonadherence is a problem in high-risk persons with diabetes and should, therefore be improved.

Apart from good footwear, patient education is a cornerstone of preventative treatment[10] and is generally aimed at increasing knowledge, improving self-care behavior and adherence to treatment. However, the evidence base to support patient education to prevent foot ulceration in persons with diabetes is small.[10] The common method used and studied in patient education is the provision of information. However, to change one's behavior may require additional intervention. Brief interventions using motivational interviewing are shown to be evidence-based methods in several domains, mainly in substance use disorders, but also in health behaviors related to diet, exercise programs, and treatment adherence.[11, 12] Although not all studies report positive outcomes, several reviews suggest that motivational interviewing is effective in diabetes care.[13-15] Motivational interviewing is a person-centered, directive method for enhancing motivation for change by exploring and resolving ambivalence to change.[16] Such ambivalence to change in behavior may also exist in persons with diabetes who are nonadherent to wearing prescribed protective footwear.

The effect of motivational interviewing on footwear adherence has not yet been investigated in persons with diabetes who are at high foot ulcer risk. Given the suggested conceptual behavioral similarity with nonadherence in general diabetes care, we hypothesize that motivational interviewing has a positive effect on footwear adherence. Because of the complete lack of existing knowledge on efficacy and feasibility, we aimed

to explore the effect of motivational interviewing on footwear adherence and to assess the feasibility of applying motivational interviewing in persons with diabetes who are at high risk for foot ulceration and who have low adherence to wearing prescribed custom-made footwear.

PATIENTS AND METHODS

Patients

Patients were recruited from the outpatient diabetic foot clinic of the Academic Medical Center in Amsterdam, the Netherlands. Inclusion criteria were age 18 or older, diabetes mellitus type 1 or 2, history of foot ulceration, and the possession of prescription footwear dispensed at least 3 months before inclusion. The exclusion criteria were current foot ulcer, inability to walk, participation in another study that may influence the study outcomes, and inability to read and understand the study instructions. From each patient, written informed consent was obtained prior to inclusion. The Medical Ethical Committee of the Academic Medical Center approved the study.

Randomization and blinding

This study was designed as an explorative trial in which participants were randomly allocated to one of two study arms in a balanced manner. First, a 7-day baseline measurement of footwear adherence was conducted in each patient. Those who wore their prescribed footwear for less than 80% of the steps taken either inside or outside their homes were classified as having low adherence. These patients were randomly assigned to either standard education (control group) or to standard education plus two sessions of motivational interviewing (intervention group). To ensure a balanced treatment allocation, block randomization with variable block sizes was used. A sealed envelope randomization sequence was created and managed by an independent investigator. Participants were not blinded to treatment allocation, but we blinded them at baseline to the goal of monitoring treatment adherence. The participants' rehabilitation medicine specialist was blinded to treatment allocation. Participants were asked not to disclose their study allocation to their rehabilitation medicine specialist.

Interventions

Each patient in the study received standard education, which consisted of written and verbal information given by the rehabilitation medicine specialist at footwear delivery on the proper use of footwear and the importance of wearing this footwear to prevent complications. Written information included a brochure providing shoe-wearing advice.

Motivational interviewing was given in addition to standard education in the intervention group, and consisted of two 45-min sessions, 1 week apart. It focused mainly on enhancing the patient's knowledge and motivation for change. The sessions followed a protocol developed by the investigators. During the first session of motivational interviewing, first the patients' footwear adherence over 1 week measured at baseline was presented and discussed. This data was presented in a histogram containing the day-by-day total footwear adherence, the adherence for being at home and away from home, and the average daily step count. An example histogram can be found elsewhere.[17] Second, the reasons for low adherence were discussed with the patient, as well as the reasons why the patient would wear the footwear. Subsequently, the patient was presented with outcomes of studies showing evidence-based data on the importance of wearing prescription footwear, specifically, the results of two randomized controlled trials on the topic.[6, 18] The second session focused on the change in behavior and goal setting. First, the patient was asked about the advantages and disadvantages of wearing and not wearing the prescribed shoes, and answers were recorded in a table format and then discussed. Second, the readiness to change footwear-wearing behavior was examined by asking the patient how relevant a change in behavior would be, and subsequently, how confident the patient was that he or she could achieve and maintain a change in behavior. Relevance and confidence wear assessed using a 10-point scale. This part was concluded with asking the following question: "Do you want to change your footwear-wearing behavior?" If the answer was "yes", an intention-to-change plan was made. This plan contained the following items: goal setting in changing footwear use, with options ranging from 'not willing to change', to 'change instantly'; determining a percentage of footwear use that the patient wants to achieve; and discussing the measures of self-control to achieve this goal, which could include avoiding activities, persons or places that may evoke nonadherence; initiating behavioral alternatives; and defining rewards and alternative rewards when short-term goals are achieved.

In both sessions, principles and techniques of motivational interviewing were applied, in order to evoke change talk: 1) basic skills such as the ability to ask open-ended questions, provide affirmations and summaries, and engage in reflective listening; 2) strategies to elicit change talk, such as asking evocative questions, query extremes, looking back and forward, and using change rulers; and 3) principles of motivational interviewing, such as expressing empathy, developing discrepancy, rolling with resistance, and supporting self-efficacy and autonomy.[16]

The two investigators (R.K. and S.A.B.) conducting the motivational interviewing with the participants underwent a training programme consisting of 1) a 16-hour group training in motivational interviewing; 2) three 2-hour private training sessions aimed at managing

the specific motivational interviewing study protocol; 3) two simulation sessions with persons with diabetes with direct verbal feedback from the trainer; and 4) written and verbal feedback from the trainer after the first two motivational interviewing sessions in the study. This feedback was based on recorded and systematically coded interviews using the Coding System for Integrity of Treatment-Motivational Interviewing (CoSIT-MI). The CoSIT-MI is a Dutch validated instrument that measures therapists' proficiency in conducting motivational interviewing; it includes all of the items on the Motivational Interviewing Treatment Integrity code.[19] A health psychologist (M.J.M.) educated in training motivational interviewing by the Motivational Interviewing Network Trainers was responsible for the training.

Assessments

Footwear adherence was assessed at baseline, and at 1 week and 3 months after the intervention. In addition, at baseline, demographics and disease characteristics of each patient were collected.

Footwear adherence was determined through a continuous 7-day objective assessment of footwear use and daily step activity. Footwear use was assessed using the @ monitor (Department of Medical Technology and Innovation, Academic Medical Center, Amsterdam, the Netherlands), a small, temperature-based sensor placed inside the prescribed shoes.[7, 17] Footwear use was assessed at 1-min intervals according to previously described methods.[17] A maximum of 2 pairs of prescribed shoes were fitted with the @ monitor. If patients had more pairs of prescription footwear, they were instructed not to wear these other pairs during the 7-day measurement.

Daily step activity was measured simultaneously and synchronously with footwear use using a step activity monitor strapped around the ankle (StepWatch; Orthocare Innovations LLC, Edmonds, Washington, USA). The StepWatch records number of steps at 1-min intervals. Patients were instructed to wear the StepWatch at all times, which included sleeping, showering and bathing. In previous studies, the @monitor and StepWatch activity monitor proved to be valid and reliable.[17, 20]

Patients were asked to complete a daily log during the 7-day assessment for the periods that they were cycling, away from home, or not wearing the step activity monitor. Monitors and log were returned through postal mail after the 7-day assessment.

The feasibility of applying motivational interviewing was assessed by evaluating 1) the proficiency of the investigators who conducted the interviews using the CoSIT-MI (assessed by the trainer) and 2) the recorded motivational interviewing sessions for aspects

such as duration of the sessions, success in executing and completing the protocol, and ability of the patient to comprehend the protocol components (as judged by the investigator).

Data analysis

Footwear adherence and daily step count were calculated from raw data from the monitors using custom-built software in Matlab R2014 (The MathWorks, Inc., Natick, Massachusetts, USA). A minimum of four complete days of recording, including one weekend day, was required for inclusion in the analysis. Periods of cycling were subtracted from the step activity data. When both the @monitor and the step activity monitor showed activity during recording, it was assumed that the patient walked with the prescribed shoes. If only step activity was recorded, we assumed barefoot walking or walking in nonprescribed shoes.

Adherence was defined as the percentage of total steps during the full recording period that the prescribed footwear was worn and was calculated as:

$$Adherence = \frac{\sum steps\ wearing\ prescribed\ footwear}{\sum steps}$$

To differentiate between adherence at home or away from home, the reported time moments in the daily log that the patient was away from home were used.

Statistical analysis

Descriptive statistics were used for patient characteristics, adherence, and step count. Differences in patient characteristics were assessed with the Mann-Whitney *U* test and the Fisher exact test. The Friedman test was used to assess differences in adherence and step count within groups, and the Mann-Whitney *U* test for between-group differences. For all of the tests, a significance level of $p<.05$ was used. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp, Armonk, New York, USA). Individual results of patients randomized to the motivational interviewing group are described as case reports.

RESULTS

A flow diagram for patient inclusion and analysis is shown in Figure 1. Thirteen patients were randomized to either the intervention (n=6) or control (n=7) group. One patient in the motivational interviewing group dropped out because of withdrawing participation.

Two patients in the standard education group dropped out because of a fractured foot (n=1) and death (n=1). These events were not related to the study intervention. Baseline characteristics of the ten analyzed subjects are presented in Table 1.

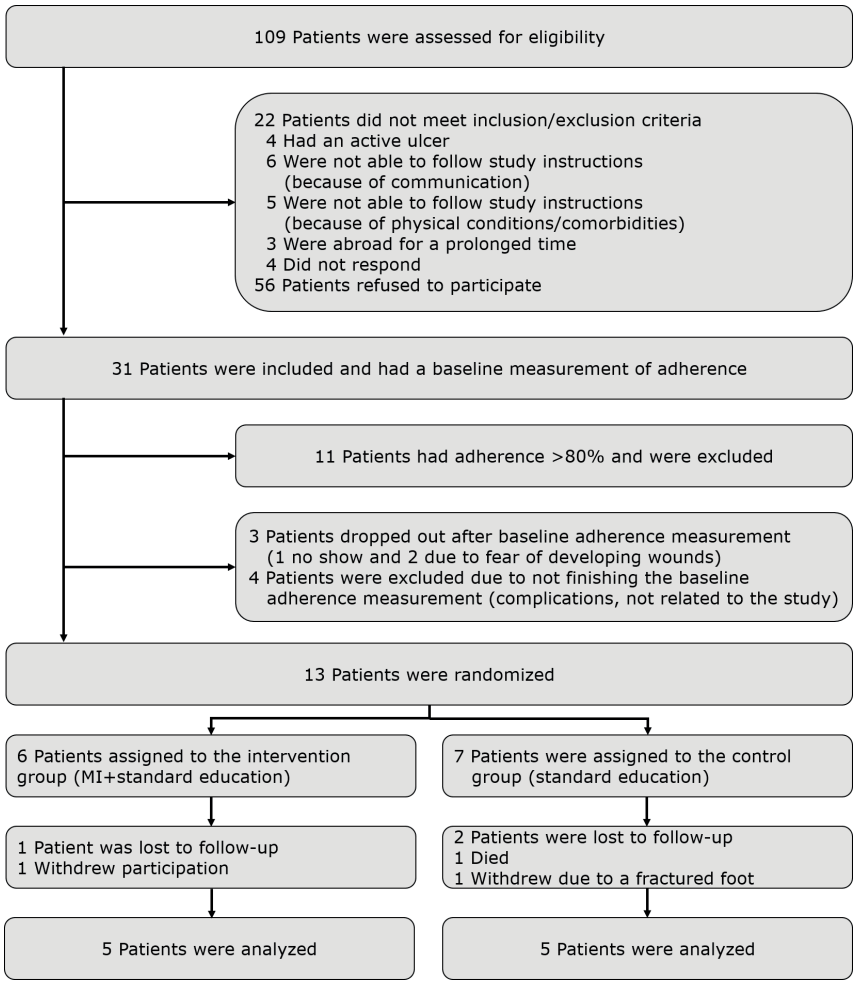

Figure 1. Study flow diagram. MI, motivational interviewing.

Table 1. Baseline characteristics.

Characteristic	Motivational interviewing group (n=5)	Standard education group (n=5)
Age (median [range] [years])	57 [51-73]	62 [45-65]
Sex, M/F (No.)	5/0	4/1
BMI (median [range])	24.2 [22.6-32.6]	27.8 [21.2-37.8]
Diabetes, type 1/2 (No.)	1/4	1/4
Diabetes duration (median [range] [years])	29 [15-47]	17 [14-49]
HbA_{1c} (median [range] [mmol/mol])	55 [38-82]	62 [52-98]
Loss of protective sensation (No.)	5	5

Note: No significant differences between groups were found. Of the 13 patients randomized, three were excluded from analysis: one in the motivational interviewing group because of withdrawing participation and two in the standard education group because of a fractured foot and death (not related to the study intervention).
Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HbA_{1c}, hemoglobin A_{1c}.

Adherence

Results for footwear adherence are shown in Table 2. Median footwear adherence in the motivational interviewing group was 67% at baseline, 90% at 1 week, and 56% at 3 months after the intervention. In the standard education group, median adherence was 45% at baseline, 47% at one week, and 59% at 3 months. Median adherence at home was 49% at baseline, 84% at 1 week, and 40% at 3 months in the motivational interviewing group, and 35%, 33% and 31%, respectively, in the standard education group. Adherence away from home was 91% at baseline, 97% at 1 week, and 92% at 3 months in the motivational interviewing group, and 78%, 91%, and 93%, respectively, in the standard education group. None of the changes within and between the groups were statistically significant.

Daily step count

Results for daily step count are shown in Table 3. In the motivational interviewing group, the median daily step count at home was 8200 at baseline, 6973 at 1 week, and 5367 at 3 months after the intervention. Away from home, this was 2587, 2536, and 3122, respectively. In the standard education group, the median daily step count at home was 3897 at baseline, 3919 at 1 week, and 4229 at 3 months. Away from home, this was 2931, 4244, and 3228, respectively. None of the changes within and between the groups were statistically significant.

Case reports

The individual results on overall adherence for participants in the motivational interviewing group are shown in Figure 2.

Table 2. Footwear adherence, overall, at home and away from home at baseline and 1 week and 3 months after the intervention.

Footwear adherence	Motivational interviewing group	Standard education group	*p*
Overall (%)			
Baseline	67 (30-72)	45 (22-77)	.55
1 week	90 (30-98)	47 (32-74)	.56
3 months	56 (28-90)	59 (22-78)	>.99
At home (%)			
Baseline	49 (6-63)	35 (13-64)	.84
1 week	84 (5-98)	33 (15-55)	.41
3 months	40 (4-80)	31 (3-66)	>.99
Away from home (%)			
Baseline	91 (79-100)	78 (32-97)	.22
1 week	97 (62-99)	91 (28-98)	.49
3 months	92 (86-98)	93 (57-100)	.73

Note: Data are given as median (range). No significant differences at $p<.05$ within and between groups were found.

Table 3. Daily step count overall, at home and away from home, at baseline and 1 week and 3 months after the intervention.

Daily step count	Motivational interviewing group	Standard education group	*p*
Overall			
Baseline	10788 (4047-15348)	6113 (4400-13918)	>.99
1 week	9367 (5757-12175)	9199 (6430-13444)	.90
3 months	10218 [5656-12663)	7458 (2772-15809)	>.99
At home			
Baseline	8200 (1843-10279)	3897 (2617-9888)	.55
1 week	6973 (5418-8081)	3919 (2607-7303)	.19
3 months	5367 (3298-8878)	4229 (1621-7523)	>.99
Away from home			
Baseline	2587 (566-5887)	2931 (1303-6779)	>.99
1 week	2536 (1637-5201)	4244 (2251-9784)	.34
3 months	3122 (2340-7262)	3228 (1151-8286)	>.99

Note: Data are given as median (range). No significant differences at $p<.05$ within and between groups were found.

Case 1 was a man from Surinam origin, aged 51 years and employed, who had type 2 diabetes for more than 25 years. This patient recalled having his last ulcer years ago; exact data were missing. His overall adherence at baseline was 67%. Adherence at home was 63%, away from home 100%. After the intervention, adherence at home increased to 95% at 1 week, and decreased to 57% at 3 months. Adherence away from home decreased slightly to 96% at 1 week, and 89% at 3 months. During the motivational interviewing session, he was able to explain why it was important to wear the prescribed

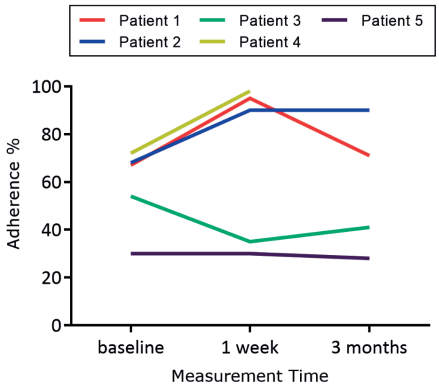

Figure 2. Individual overall footwear adherence for the motivational interviewing group across the three time points.

footwear. Reasons for not wearing the shoes inside the house were that donning and doffing of his shoes was more difficult than with his slippers, he spent a lot of time on the couch, and he thought he hardly took steps inside his home (although his data showed 4886 steps per day in the house, which was 89% of his total number of daily steps). He mentioned that he never saw the benefit of wearing his prescription shoes indoors, but after discussing the importance of wearing shoes based on scientific results, he clearly understood and even reiterated the benefits and importance and was prepared to wear his prescription shoes more at home. In his intention-to-change plan he stated that he would wear his shoes at home, every day, all of the time, starting right away.

Case 2 was a white man aged 64 years, retired, with type 1 diabetes for more than 40 years. Previous foot ulcers occurred in 1983 and 2011. His overall footwear adherence at baseline was 68%; at home this was 62%, away from home 87%. One week after the intervention, adherence increased to 90%, which was retained after 3 months at 90%. Adherence at home increased to 84% at 1 week, and was 80% at 3 months. During the motivational interviewing sessions, it seemed that the patient was not aware of the high amount of steps he took daily inside his home (8200 steps, 76% of his total number of daily steps). He did not have a clear reason for not wearing his prescribed shoes at home, other than that it was out of habit. The patient expressed his satisfaction with the prescribed shoes several times. He did not have any problem with shoe comfort or appearance. After providing the information on scientific results, he realized the importance of the protective properties of his prescribed shoes and was able to name several (future) benefits of wearing the shoes (i.e., staying active and independent). In his intention-to-change plan, he planned to increase adherence at home from 62% to 75%, on a gradual basis. His confidence in wearing his shoes more often was rated as a 9 on a 10-point scale.

Case 3 was a 57-year-old white man who was employed during inclusion in the study, but was forced to stop working for health reasons after the baseline measurement. He was diagnosed as having type 2 diabetes more than 15 years ago. He was familiar with having foot ulcers on a regular basis since 2007. His overall adherence was 54% at baseline, 35% at 1 week and 41% at 3 months after the intervention. Adherence at home was very low and did not increase after the intervention: 26%, 28% and 22%, respectively. When the results of his baseline measurements were discussed, he was surprised that he took so many steps inside his home (8223 steps per day, 60% of his total number of daily steps). The most notable comment he made was about the utility and perception of his shoes. Although he saw some advantages of wearing the shoes (support and protection), he firmly believed that the shoes were the cause of his ulcers. His treating rehabilitation medicine specialist did not agree with him. Moreover, because he perceived his prescription shoes to be heavy, difficult to put on and move around with, and because he reported sitting on the couch much of his time, he considered it easier not to wear them inside. He rated the importance of wearing his shoes more often as a 6.5 on a 10-point scale. His confidence in wearing his shoes more often was not rated. With several reservations, he stated in his intention-to-change plan that he would start wearing his prescribed shoes more often to achieve a level of 75% adherence at home.

Case 4 was a 73-year-old white man with type 2 diabetes who dropped out after the first follow-up measurement due to health reasons. Between the baseline measurement and the motivational interviewing sessions, he received prescribed custom-made shoes that were specially designed as indoor shoes. He experienced less pain while walking and was therefore very motivated to wear these indoor shoes.

Case 5 was a white man aged 56 years, unemployed, with type 2 diabetes for more than 15 years. No changes were seen in adherence at home 1 week and 3 months after the intervention. He was not willing to change his shoe-wearing behavior because he felt this would give noise disturbance for his neighbors.

Feasibility

Assessment and coding by the trainer using the CoSIT-MI of a 20-min part of the first two motivational interviewing sessions showed that basic skills were applied 54 and 49 times by investigator 1 and 2, respectively; and in 13 and 11 instances, respectively, a strategy to elicit change talk was applied. Use of the principles of motivational interviewing was scored on a 7-point scale as a mean of 6 for one investigator and a mean of 5.5 for the other. The study protocol dictated two 45-min sessions of motivational interviewing, however in four of the five patients the protocol was completed in one session, with a mean duration of 53 min.

Most of the protocol items, such as showing the adherence outcomes, providing information on the topic, discussing the reasons for low adherence, and examining readiness to change, were well understood by the participants. Discussing the advantages and disadvantages of both wearing and not wearing their prescribed footwear proved to be difficult at times due to the repetitive nature of the questions asked. We also found some unease in the use of a 10-point scale or percentage improvement score and in making the distinction between the relevance of and the confidence in changing behavior, being new concepts to them. In each patient we were able to complete the protocol by formulating an intention-to-change-plan and setting a new goal in footwear use.

DISCUSSION

The aim of this study was to explore the effects of motivational interviewing compared with standard education on adherence to wearing prescribed footwear and the feasibility of applying motivation interviewing in high-risk patients who have low footwear adherence. When patients are away from home, the study results show that footwear adherence was already high at baseline in both study groups, increased somewhat at 1 week, and remained high over time. Adherence to wearing prescribed footwear does, therefore, not seem an issue when patients are away from home. When at home, footwear adherence changed from a median baseline percentage of 49% to 84% at 1 week in the motivational interviewing group. This difference did not reach statistical significance due to the small number of patients tested, but it does represent a relatively large change, which we consider clinically relevant because it passes the threshold of 80% that we use to classify someone as adherent.[6,7] Three months after the intervention, adherence had returned to baseline values (i.e., 40%). Only small (a few percent) changes in footwear adherence when at home were seen in the standard education group. Such a clinically relevant, although nonsignificant, short-term improvement in adherence in the intervention group suggests that there may be potential for motivational interviewing in the short-term, also considering that patients were most active inside the house, which confirms earlier data.[7] This needs further study and confirmation in larger trials. The lack of effect found at 3 months should be a focus of further investigation into methods to preserve adherence over time.

The relative increase in adherence in the short-term followed by a decline over time is in line with outcomes of other studies that used motivational interviewing as method for lifestyle change, as were reviewed by Hettema et al.[11] The 72 studies included in this meta-analysis tested the efficacy of motivational interviewing on outcomes such as alcohol use, smoking, treatment compliance and diet and exercise. Overall, a rapid

positive impact of motivational interviewing was seen, with a gradual decrease in effect over time. Specifically for diabetes, a chronic and complex condition, behavioral change is not easy, as the disease often requires multiple behavioral changes (e.g., medication, food intake, exercise).[21] Adherence has been shown to become compromised when several lifestyle behaviors are targeted at the same time.[21, 22] Nevertheless, the studies reviewed by Hettema et al also showed that when motivational interviewing was used in addition to standard treatment, the effect seemed to endure over time. This seems in contrast to what we found and may be explained by the fact that most of the standard treatment in the reviewed studies was counseling-style treatment, which uses more one-on-one time with the client than the standard education used in the present study. According to Hettema et al,[11] the persisting effect over time with the addition of motivational interviewing to other counseling-style treatment suggests a synergistic effect. Such a possible synergistic effect needs to be explored in relation to footwear adherence, and this may include boosting sessions of motivational interviewing over time or the additional use of other therapies such as cognitive behavioral therapy, or contingency management interventions.

Cases 1 to 3 represented what may be considered a typical, a successful and a unsuccessful outcome, respectively. The subject in case 1 showed a short-term increase and a long-term decrease in adherence. Owing to the focus on wearing behavior at home and the information provided, the patient immediately understood the need to wear his shoes more often, without the effect being persistent, maybe because of lack of enduring behavioral mechanisms. The patient in case 2 showed a successful improvement in footwear adherence from an already quite high adherence level at baseline. Being surprised to find so many steps taken at home, he understood the need to improve and clearly saw the benefits of wearing his prescribed shoes at home. Furthermore, he was very confident that he could change his behavior, which is important for success. The patient in case 3 frequently reulcerated and was clearly unhappy with the weight and comfort of his prescribed shoes. He held the shoes responsible for his foot ulcers. His rating of importance to change was low. Under these circumstances, changing behavior is challenging, effectively creating a paradox: the shoe that is prescribed to protect the foot is perceived as the cause of the problem. The adherence data of the patient in case 4 suggest that custom-made shoes that are prescribed specifically for indoor use, being lighter in weight, clean and easy to don and doff, may be a good option to resolve a low footwear adherence. This option awaits further research. The patient in case 5 seems to show that when no ambivalence is experienced about shoe-wearing behavior, it will be hard to find motivation for change. Thus, as each of the 5 cases show, clues seem to be present as to why patients are able or unable to change their shoe-wearing habits.

Perception of the benefits of the prescribed footwear seems to play an important role, which corresponds to earlier findings on this topic.[23]

The application of motivational interviewing in the present study seemed to be feasible for the patient group and purpose studied. The investigators were sufficiently trained for enhancing motivation for change in these high-risk diabetic patients using a short, feedback-driven training program. The literature suggests that motivational interviewing can profitably be delivered by a range of professionals with a minimum investment of time in medical care settings.[24] Thus, this can be of interest for podiatric physicians and orthopedic shoe technicians because of their close involvement with prevention and treatment of the diabetic foot. Patients were generally able to understand the protocol and its components, and the investigators were able to complete the protocol in the scheduled time. In most cases, one session seems sufficient to complete the protocol. The discussion of the advantages and disadvantages of wearing and not wearing the prescribed footwear may be simplified by discussing only the advantages and disadvantages of either wearing or not wearing the footwear. And patients may have to be better introduced to specific characteristics of the protocol, such as the use of a 10-point scale and a percentage change scoring system and in understanding the difference between the relevance of and the confidence in change in behavior. Such adaptations to the protocol may result in a better understanding and, therefore, an easier transition to change in behavior.

The patient sample in this study was small because we aimed to assess preliminary effects and the feasibility of using motivational interviewing for the purpose of improving footwear adherence in high-risk diabetic patients, something that has not been done before.[25] The small sample does prevent drawing definite conclusions on efficacy. Despite the small study sample, the data seem to show some clinically meaningful outcomes that correspond to what the literature shows about the effects of motivational interviewing. The results provide relevant input for larger-sized studies. Another limitation was that patient blinding to the goal of the adherence measurement was lost in follow-up measurements because the results at baseline were discussed with the patient during the motivational interviewing sessions. We are not sure whether this affected patient behavior and study outcome. The lack of change in adherence over time in the standard education group, which did not receive feedback on adherence after baseline, combined with the return of adherence to baseline levels in the motivational interviewing group suggests that such an influence was not the case. The systematic difference in daily step count between groups can partly be explained by the way the data are described, using median and not mean outcomes. Seasonal effects were not present.

CONCLUSIONS

Nonsignificant but clinically meaningful short-term positive effects of motivational interviewing on adherence to wearing prescribed custom-made footwear at home, where walking activity is higher than away from home, were found in persons with diabetes who are at high risk for foot ulceration. Such effects were not seen in patients who receive standard education. However, the effects of motivational interviewing do not seem to persevere over time. Additional or adjunctive therapy may be needed to preserve effects on footwear adherence over time. The application of motivational interviewing seems feasible for the purpose and the population of patients studied. These data provide input to larger trials that should be sufficiently powered and include blinding of the patient to the initial adherence assessment, and that should confirm or refute our findings and hypotheses. Because of their close involvement in the long-term preventative care of this high-risk diabetic patient group, podiatric physicians and orthopedic shoe technicians may be valuable providers of motivational interviewing.

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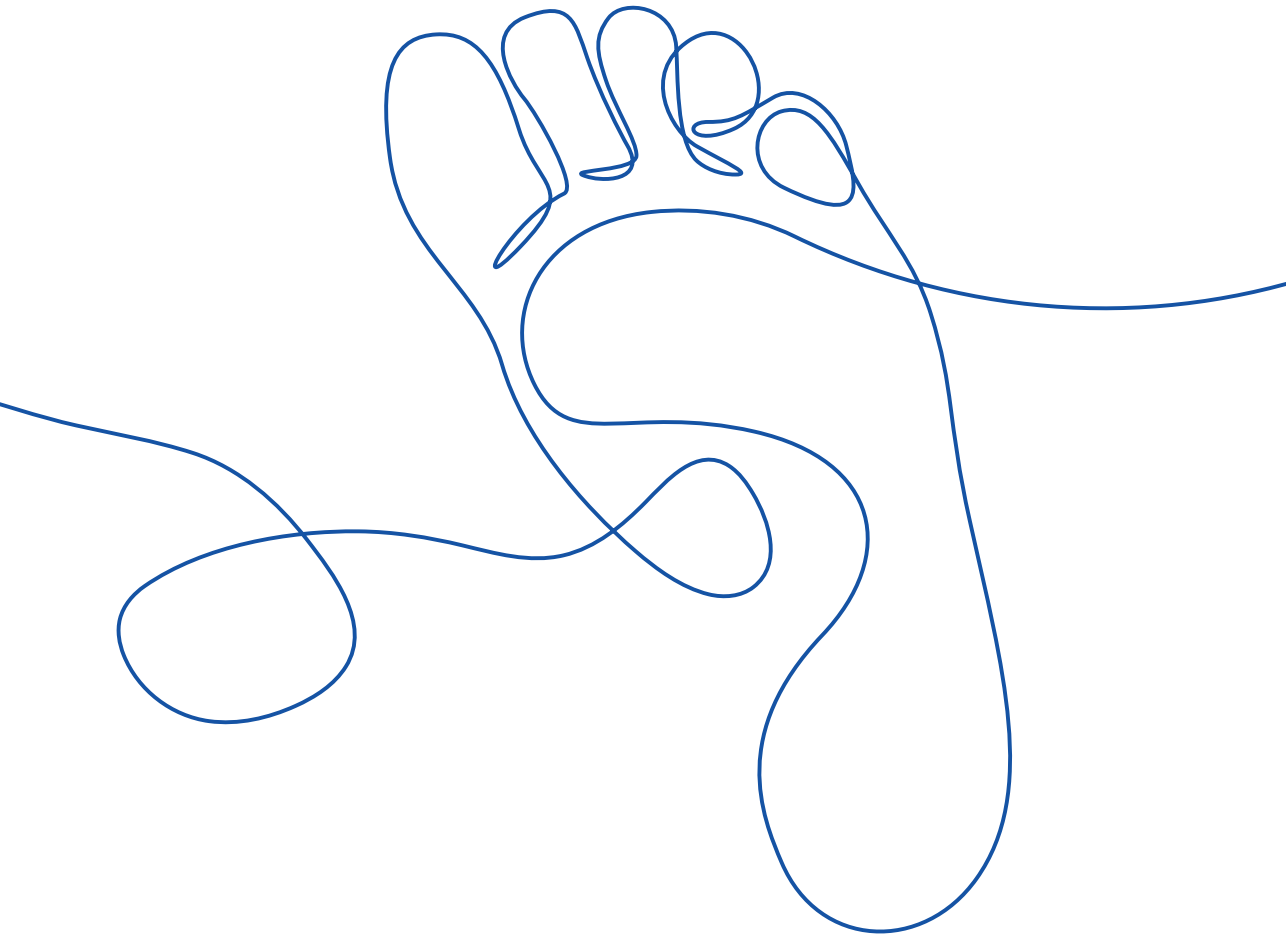

Chapter 5

Users' needs and expectations and the design of a new custom-made indoor footwear solution for people with diabetes at risk of foot ulceration

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Disability and Rehabilitation 2022;44(26):8493-8500

ABSTRACT

Purpose: To assess users' needs and expectations regarding custom-made indoor footwear, and to design such footwear with similar biomechanical efficacy and better usability compared to regular custom-made footwear in people with diabetes at risk for foot ulceration.

Materials and methods: Multidisciplinary systematic design approach. Needs and expectations regarding indoor footwear were evaluated via a questionnaire in 50 high foot ulcer risk people with diabetes using custom-made footwear. We systematically designed indoor footwear, and manufactured this for nine participants. Primary requirement was similar plantar pressure compared to participants' regular custom-made footwear.

Results: Eighty-two percent of participants expressed a need for custom-made indoor footwear and 66% expected such footwear to increase their adherence. The custom-made indoor footwear had the same bottom construction as participants' regular custom-made footwear, but with softer and more light-weight upper materials. Peak pressures were similar or lower, while qualitative evaluation showed better usability and lower costs for indoor footwear.

Conclusions: People with diabetes at risk of foot ulceration expressed a clear need for custom-made indoor footwear, and expected such footwear to increase their adherence. Our indoor footwear design provides adequate pressure relief, with better usability, and can be produced at lower costs compared to regular custom-made footwear.

INTRODUCTION

Foot ulceration is a frequent complication of diabetes mellitus and an important precursor to foot infection and amputation.[1] It affects 19 to 34% of people with diabetes and places a high burden on patients and carers, as well as healthcare systems.[2, 3] In the first year after healing of a diabetic foot ulcer, roughly 40% of patients experience a recurrent foot ulcer, while after 3 years this is almost 60%.[2] It is therefore important to focus on the prevention of foot ulceration.

International guidelines recommend custom-made footwear as key preventative intervention.[4, 5] The aim of such footwear is reducing ulcer risk by redistributing and lowering peak plantar pressures and providing a proper fit.[4] Adequate protective footwear helps prevent ulcer recurrence, if the footwear is worn consistently.[6, 7] However, footwear adherence is often low in people with diabetes who are at risk of ulceration.[6, 8-10]

To improve adherence, it is important to understand factors associated with non-adherence. However, evidence on associations between footwear adherence and personal, disease or behavioural factors such as gender, diabetes duration, ulcer history and activity levels, is absent, unclear, or conflicting.[10] Predictors for non-adherence are more likely to be found in an individual's assessment of the footwear itself or individual strategies towards their use.[11-14] For example, perceived benefit of custom-made footwear was the only predictor for its use in multivariate analyses in one study in people with diabetes at high ulcer risk,[11] and one of the strongest predictors in a cross-sectional study in people with diabetes with low, moderate and high ulcer risk.[14] However, this perception can be determined by a variety of factors, such as usability factors weight, ease of use, and aesthetics, but also by costs, clinical expectations, health literacy and acceptance.[10, 11, 15, 16] As weighing of these factors depends on individual preferences,[15] no general intervention to improve adherence has yet been successful.[17]

Rather than focusing on an intervention to improve the perceived benefit of protective footwear, a contextual approach could prove more beneficial. Adherence to wearing footwear differs between contexts, such as its location (e.g., indoor vs. outdoor) or its purpose (e.g., work vs. leisure).[18, 19] In people with diabetes at high ulcer risk, footwear adherence is especially low indoors, while patients are most active inside their home.[12, 20, 21] Targeting this context may offer opportunities to improve adherence. The only study that specifically investigated reasons for this low adherence indoors found that participants considered footwear weight and donning/doffing mostly a problem when inside.[21] In addition, footwear that is also worn outside can often be dirty, and people can have a habit to take off their footwear when arriving at home.[21] Following

these reasons, it can be expected that custom-made footwear purposely designed for indoor use may improve adherence.

Indoor footwear should not only overcome the barriers in indoor usability, it should still have adequate biomechanical offloading capacity as it replaces the regular custom-made footwear of the user.[4] Several orthopedic footwear companies have tried to create such custom-made indoor footwear. However, no systematic design approach and evaluation, integrating users' and professionals' perspectives, has been followed. The aim of this study was to follow such an approach to (1) assess users' needs and expectations regarding custom-made indoor footwear, and (2) design custom-made indoor footwear with similar biomechanical efficacy and better usability compared to regular custom-made footwear.

MATERIAL AND METHODS

We used a multidisciplinary systematic design approach and evaluation by means of two studies, integrating perspectives of users (people with diabetes at risk of ulceration in possession of regular custom-made orthopedic footwear), clinicians, orthopedic shoe technicians, medical insurers, and researchers. Both studies were coordinated by the clinical research team (authors of this paper) and took place in three orthopedic footwear companies that work within a multidisciplinary diabetic foot outpatient clinic in a hospital setting. User inclusion criteria were the same for both studies: type 1 or 2 diabetes mellitus, at moderate to high risk for foot ulceration (International Working Group on the Diabetic Foot (IWGDF) risk 2 or 3),[4] and in possession of regular custom-made footwear (defined as custom-made insoles worn in custom-made shoes).[4] Exclusion criteria for both studies were inability to read Dutch and inability to adhere to study requirements, for evaluating the design the following additional exclusion criteria were applied: a foot ulcer at the time of recruitment, Charcot deformation, amputation at or beyond the tarsometatarsal level, or another condition requiring high-cut footwear (i.e., mid-tibia level or higher) at all times. The requirement for ethical review was waived under the Medical Research Involving Human Subjects Act by the local ethics committee (reference number W17_405 #17.474).

Assessment of users' needs and expectations regarding custom-made indoor footwear

Study design

Questionnaire.

Questionnaire

A questionnaire was designed to assess users' needs and expectations regarding custom-made indoor footwear and assessed the following domains: (1) need for custom-made indoor footwear, (2) use and usability of current custom-made footwear, (3) expectations of indoor footwear and willingness of financial contribution, and (4) current living conditions. The questionnaire was based on the Monitor Orthopedic Shoes (MOS), a validated questionnaire that measures the most relevant aspects of footwear usability from a user's perspective[22] and further customized for this study, with help of a patient representative from the Dutch Diabetes Patient Society, which represents the interests of all persons with diabetes. It consisted of five-point Likert scale questions, multiple choice and open-ended questions. Questions on financial contributions were added because custom-made footwear in the Netherlands costs on average 1500 Euros to produce. These costs are reimbursed by healthcare insurers, with the exception of patients' "own contribution" of 129 Euros per pair.

Recruitment

Three certified orthopedic shoe technicians (one per company) were instructed to invite a minimum of 15 eligible persons who fulfilled the inclusion criteria. Persons who agreed to participate in the survey were approached by a member from the research team. Depending on their preference, the questionnaire could be completed on paper and returned in a pre-stamped envelope or completed online with Typeform™ (Barcelona, Spain). If necessary, a postal reminder was sent after one month.

Statistical analysis

We used descriptive statistics to summarize participant characteristics and questionnaire responses.

Design and evaluation of custom-made indoor footwear

Study design

Multidisciplinary three-phase footwear design and cross-sectional within-subject evaluation.

Phase 1: Defining and prioritizing requirements. A multidisciplinary team of specialists was formed, and consisted of a rehabilitation specialist, four orthopedic shoe technicians (all with >5 years of experience in the field of diabetic foot disease), three management representatives from three different footwear companies, a healthcare insurer, four human movement scientists, and the patient representative, who advocated the interests of the intended users. Based on discussions within the multidisciplinary team and aligned with the results from the needs assessment, a consensus set of 12 require-

ments for custom-made indoor footwear was created (Table 1). The key requirement was to have similar peak plantar pressures (±10%) compared to the participants' regular custom-made footwear.

Phase 2: Designing the indoor footwear. In the next phase, the multidisciplinary team held four meetings to evaluate the design, manufacturing, and testing of the indoor footwear. During the first meeting an orthopedic shoe technician from each company presented a preliminary model. Its quality was discussed using the set of requirements (Table 1). One model best fitted the key requirements of pressure distribution and other characteristics, and was unanimously chosen as the leading type. This model was subsequently adapted by each orthopedic shoe technician and discussed at the second meeting.

Table 1. Requirements for custom-made indoor footwear.

Key requirement
Peak plantar pressure is comparable to regular custom-made footwear
Other requirements
Easy donning and doffing
Lighter in weight than regular custom-made footwear
Regulating heat and breathable
Appearance satisfactory for indoor use
More comfortable than regular custom-made footwear
Safe to use
Good durability
No, or minimal, increase of shear forces compared to regular custom-made footwear
To be worn alternately with regular custom-made footwear
Improves adherence to indoor footwear use
Cheaper to produce than regular custom-made footwear

Phase 3: Selection of participants; manufacturing and evaluating the indoor footwear. When all agreed on its properties, the indoor footwear was custom-made for nine participants (three per company, selected by the orthopedic shoe technician). Nine participants were considered a sufficiently large convenience sample to obtain adequate first impressions when manufacturing the footwear and to provide participants with an opportunity to wear it in real-life. The indoor footwear was made on the shoe last of the participants' regular custom-made footwear. In-shoe plantar pressure measurements were taken in both indoor and regular custom-made footwear (see next section). If peak pressure in the indoor *or* regular footwear exceeded 200 kPa or peak pressure in the indoor footwear was >10% higher than in the regular footwear, the orthopedic shoe technician modified the footwear until pressure requirements were satisfactory.[23, 24]

Participants were asked for qualitative feedback on usability aspects of the indoor footwear. During the third and fourth meeting of the multidisciplinary team, peak pressure outcomes were presented and discussed, along with the other requirements. Consensus on the final design, including all materials to be used, was reached.

In-shoe plantar pressure measurements

Dynamic in-shoe peak plantar pressures were measured with the Pedar-X in-shoe pressure measurement system (Novel GmbH, Munich, Germany) at a 50-Hz sampling frequency. Participants walked undisturbed over a flat surface in the regular clinical evaluation rooms at the three participating companies. The length of the walkway varied from 4 to 8 meters. Participants were asked to walk at a comfortable speed. At one of the companies, walking speed was quantitatively measured and controlled, where speed had to be within 5% of the first attempt; at the other two companies, similarity of walking speed between trials and conditions was judged qualitatively. The first and last step of each walk were discarded. The walk was repeated until a minimum of 12 midgait steps per foot were collected.[25] Novel multimask software (version 13.3.65) was used for pressure analysis. The mean peak pressures at eight anatomical foot regions were calculated for the left and right foot separately: the toes (hallux, dig 2-3 and dig 4-5), forefoot (metatarsal head 1, metatarsal head 2-3 and metatarsal head 4-5), midfoot and heel.

Statistical analysis

Participant characteristics and in-shoe peak pressures were summarized with descriptive statistics. Wilcoxon's signed rank tests were used to compare differences in in-shoe peak pressure between indoor and regular custom-made footwear for the eight anatomical regions of both the left and right foot, with alpha at 0.05 and (with a total 16 comparisons) the Holm-Bonferroni method to correct for multiple testing (i.e., sorting the *p* values from lowest to highest; comparing the *p* values to nominal alpha levels with alpha=alpha/16=0.05/16=0.003125 for the smallest *p* value, etc.). Statistical analyses were performed using SPSS 26.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Assessment of end-users' needs and expectations regarding custom-made indoor footwear

Participants

A total 58 participants were provided with the questionnaire to assess their needs and expectations regarding custom-made indoor footwear. The response rate was 90%

(n=52). Two responders were excluded because they did not have diabetes mellitus and were erroneously invited to participate, 50 responders were analyzed. Mean (SD) age of the responders was 69 (13) years and 48% were male (n=24); this was 67 (6) years and 83% male (n=5) for the non-responders.

Custom-made footwear use and usability

Of the responders, 92% reported to wear their custom-made footwear for 6-7 days per week. A total of 50% wore their custom-made footwear inside their house >8 h per day, 22% 4-8 h per day, 14% 0-4 h per day, and another 14% never wore their custom-made footwear inside the house - they walked barefoot or in prefabricated footwear. The most frequently reported reason for not or hardly wearing their custom-made footwear inside the house was that the footwear was too heavy (43%). Almost all responders (92%) left their beds at least once during the night, with 24% doing so three times or more. Only 4% wore their custom-made footwear when getting out of bed during the night, most (58%) reported to walk barefoot or on socks during the night as donning/doffing custom-made footwear would require too much effort. Concerning usability, most responders (76%) indicated they were satisfied with their custom-made footwear. Most frequently reported negative usability characteristics concerned the footwear being too heavy or difficulty with donning and doffing (Table 2).

Needs, expectations and priorities for custom-made indoor footwear

Of the responders, 64% were unfamiliar with the concept of custom-made indoor footwear. After explanation, 82% indicated they felt a need for such footwear. The majority of responders (66%) expected to wear indoor footwear more frequently inside their home than their regular custom-made footwear, if it would be provided to them. Most responders expected for indoor footwear that negative usability characteristics (e.g., ulceration, difficulties donning and doffing) would not or hardly be present (Table 2). Positive usability characteristics like easy maintenance and good durability were more frequently expected than an appealing appearance (Table 2). Prevention of ulceration was seen as most important feature of such footwear, while prevention of skin irritation, easy donning and doffing and good fit were also considered important (Table 3). Participants varied in what they were willing to contribute financially, with 20% indicating they would contribute 0 Euros, 26% 1-50 Euros, 32% 51-100 Euros and 22% 101-200 Euros.

Design and evaluation of custom-made indoor footwear

Indoor footwear design

The final design of the indoor footwear included two types, to provide patients with a choice concerning the vamp material (Figure 1). The vamp of type A was made from Alcantara®, and therefore also included a strengthened toecap and collar. The vamp of

Table 2. Usability characteristics of participants' regular custom-made footwear and expected presence or absence thereof in custom-made indoor footwear.

Regular custom-made footwear			
Negative usability characteristics	Not or hardly present	No opinion	Present or very much present
Skin irritation	66 (33)	16 (8)	18 (9)
Ulceration	82 (41)	12 (6)	6 (3)
Sweating	82 (41)	16 (8)	2 (1)
Cold feet	72 (36)	10 (5)	18 (9)
Too much weight	46 (23)	32 (16)	22 (11)
Difficulty donning & doffing	48 (24)	30 (15)	22 (11)
Fit (too tight)	70 (35)	26 (13)	4 (2)
Custom-made indoor footwear			
Negative usability characteristics	Not or hardly present	No opinion	Present or very much present
Ulceration	88 (44)	10 (5)	2 (1)
Inadequate fit	84 (42)	14 (7)	2 (1)
Skin irritation	74 (37)	24 (12)	2 (1)
Difficulty donning & doffing	74 (37)	18 (9)	8 (4)
Too much weight	70 (35)	28 (14)	2 (1)
Sweating	66 (33)	34 (17)	-
Cold feet	60 (30)	34 (17)	6 (3)
Positive usability characteristics	Not or hardly present	No opinion	Present or very much present
Good durability	-	22 (11)	78 (39)
Easy maintenance	-	34 (17)	66 (33)
Appealing appearance	6 (3)	64 (32)	30 (15)

Data expressed as % (*n*) of responders.

Table 3. Importance of usability characteristics of custom-made indoor footwear.

	Important or very important	No opinion	Not or hardly important	Item ranked as #1 priority
Prevention of ulceration	100 (50)	0	0	54 (27)
Prevention of skin irritation	96 (48)	4 (2)	0	25 (12)
Good fit	96 (48)	4 (2)	0	6 (3)
Easy donning and doffing	92 (46)	4 (2)	4 (2)	4 (2)
Flexibility of the material	86 (43)	14 (7)	0	4 (2)
Prevention of cold feet	70 (35)	26 (13)	4 (2)	4 (2)
Weight	74 (37)	20 (10)	6 (3)	2 (1)
Durability	78 (39)	16 (8)	6 (3)	-
Maintenance	70 (35)	28 (14)	2 (1)	-
Appearance	42 (21)	40 (20)	18 (9)	-
Prevention of sweating	40 (20)	50 (25)	10 (5)	-

Data expressed as % (*n*) of responders. One responder did not answer the priority question.

type B was made from felt. All materials of both types of the final design are presented in Figure 1 and Table 4. The bottom of the shoe was designed such that it had the same biomechanical properties as the regular custom-made footwear, i.e., the same heel, outsole and rocker profile, and the same custom-made insole.

Participants

Nine participants (mean age (SD) 63 (14) years; 78% male (n=7)) were provided with indoor footwear as part of their regular foot care.

Peak plantar pressures

The indoor footwear showed similar peak plantar pressures in all regions compared with the regular custom-made footwear (Table 5). After one or two rounds of modifications, some participants still presented with peak pressures >200 kPa, but further modifications were not required in the judgement of the orthopedic shoe technician; peak pressures >200 kPa were less frequently present in indoor footwear (Table 5).

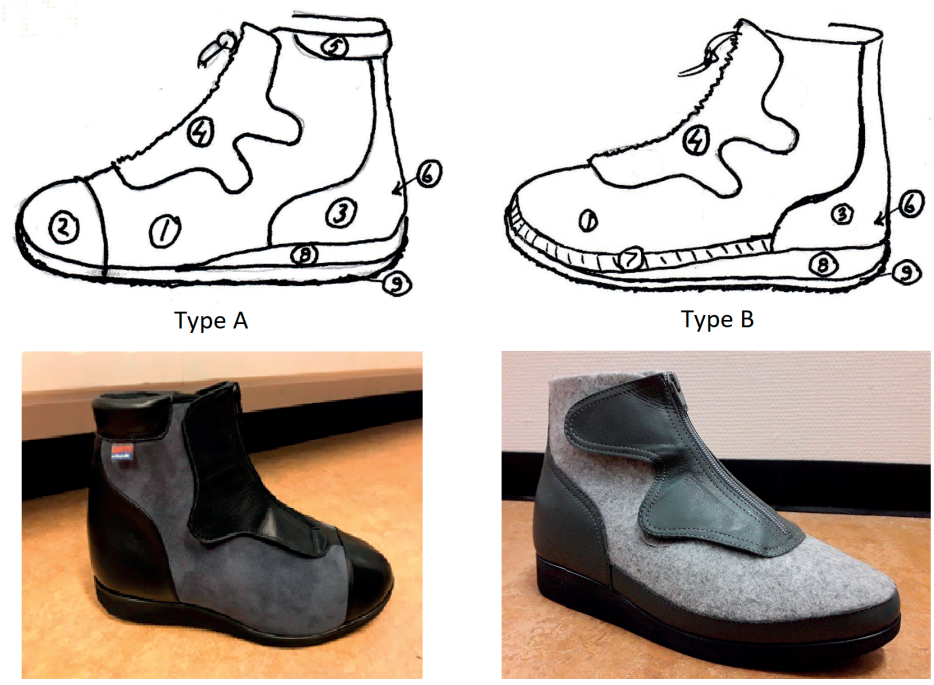

Figure 1. Schematic drawing with features and two images of the two types of custom-made indoor footwear design (see Table 4 for explanation of the numbers and material details).

Table 4. Features of the indoor footwear design.

Feature	Specification
(1) Vamp	Type A: Alcantara® (4mm microfibre); Type B: Felt (tweed extra 953)
(2) Toe part	Type A: leather; Type B: no toe part
(3) Heel cap	Leather
(4) Upperpart	A combination of leather, Velcro fastener and a zipper. The Velcro fastener was used for optimal fitting and allows individual adjustment, with two fixations on both the lateral and medial side. The zipper had a metal ring to support opening and closure.
(5) Collar	Type A: leather with 8mm sponge inside; Type B: no collar.
(6) Contrefort	Thermoplastic reinforcement material (Rhenoflex® 1.2 mm or Teefe® 15).
(7) Protective welt	A: none. B: leather
(8) Heel	Wedged ethylene vinyl acetate, shore 60. Heel height was similar to the regular custom-made footwear. Heel rounding was similar to regular custom-made footwear.
(9) Outsole	Ethylene vinyl acetate, 4-6 mm, shore 40, to enhance foot progression and create more stiffness.
Rocker profile	The pivot point and angle of the pivot point were identical to the regular custom-made footwear. Adjustment was permitted, dependent on the insole type that is used (a more flexible insole might need more rocker profile).
Insole	The insole was identical to the insole of the regular custom-made footwear and made on the same shoe last. A 2.2mm-thick full-length rigid insole was added under the normal insole for additional stiffness (Redoma® Texon T97®).
Height	Ankle-high (i.e., approximately 2-5 centimetres above the ankle).
Stitching	40/3 (Gunze count)

Qualitative evaluation of requirements

All participants reported the indoor footwear to be easy to don and doff, lighter in weight, acceptable in cosmetic appearance, and comfortable to wear. Orthopedic shoe technicians in the multidisciplinary project group estimated that the indoor footwear could be fabricated for around 350 Euros per pair, excluding any overhead costs, and provided the indoor footwear could be manufactured with the existing last of the regular footwear. Detailed breakdown of all costs associated with producing the indoor footwear was outside the scope of the project. Other requirements (heat regulation, safety, shear, durability and adherence) could not be assessed in this study.

Table 5. Peak plantar pressures of the indoor and regular footwear per anatomical region.

Foot region	Indoor footwear[a]	Regular custom-made footwear[a]	Median difference[a,b]	*p*[c]	PP>200 kPa Indoor footwear[d]	PP>200 kPa Regular custom-made footwear[d]
Right foot						
Hallux	162 (26-254)	156 (63-213)	-2 (-70-115)	0.594	2	2
Digits 2-3	109 (43-153)	114 (69-194)	-6 (-41-20)	0.110	0	0
Digits 4-5	99 (41-134)	78 (54-161)	-5 (-27-46)	0.953	0	0
Metatarsal 1	140 (38-257)	163 (63-257)	-22 (-33-5)	0.049	2	3
Metatarsal 2-3	193 (56-260)	189 (74-280)	-17 (-63-30)	0.025[c]	2	4
Metatarsal 4-5	114 (44-187)	108 (66-198)	0 (-27-46)	0.314	0	0
Midfoot	89 (62-135)	102 (71-133)	0 (-31-6)	0.889	0	0
Heel	197 (93-239)	214 (110-313)	-10 (-105-16)	0.249	4	5
Left foot						
Hallux	106 (60-398)	104 (63-514)	1 (-122-30)	0.678	1	3
Digits 2-3	112 (63-209)	99 (53-223)	21 (-61-87)	0.260	1	1
Digits 4-5	87 (76-260)	98 (54-209)	0 (-21-51)	0.575	1	1
Metatarsal 1	126 (71-232)	157 (63-226)	-3 (-49-30)	0.678	2	2
Metatarsal 2-3	147 (100-245)	155 (74-283)	1 (-66-27)	0.678	2	2
Metatarsal 4-5	130 (95-260)	135 (71-215)	2 (-29-45)	0.859	1	1
Midfoot	132 (99-165)	132 (75-174)	4 (-68-39)	0.343	0	0
Heel	176 (124-274)	193 (110-271)	3 (-69-38)	0.859	3	4

PP: Peak pressure. [a]Data expressed as median (range) peak pressure, in kPa. [b]Difference is peak pressure in indoor footwear minus custom-made footwear; a negative score means lower pressures in the indoor footwear. [c]Cut-off for *p* values to be considered statistically significant was corrected for multiple testing with Holm-Bonferroni method; with the smallest *p* value (p=0.025) being larger than its corrected cut-off (alpha/16=0.05/16=0.003125), all differences are considered statistically not significant. [d]Data expressed as *n*.

DISCUSSION

To improve adherence to wearing custom-made footwear, and ultimately prevent foot ulcers in people with diabetes, we developed custom-made indoor footwear via a multidisciplinary systematic design and evaluation approach. We integrated perspectives of users (people with diabetes at moderate-to-high risk for ulceration in possession of custom-made orthopedic footwear), clinicians, orthopedic shoe technicians, researchers and insurers, and incorporated their needs and expectations in a set of 12 criteria the indoor footwear needed to fulfill. The primary criterion (i.e., similar offloading capacity as regular custom-made footwear)[4] was assessed quantitatively in a group of nine users, and we found this criterion to be met. This indoor footwear is thereby a new offloading device in the armamentarium for diabetic foot ulcer prevention.

We found the need for indoor footwear to be high, and participants expected such footwear to increase their use of prescribed footwear. Participants indicated ulcer prevention to be the most and appearance the least important requirement for indoor footwear. Other factors discriminating indoor from regular custom-made footwear, according to user needs, were the importance given to easy donning and doffing, flexibility of the materials, and prevention of cold feet. Finding appearance to be the least important characteristic was unexpected, as this is often considered important by people with diabetes assessing their prescribed protective footwear.[11, 13, 26] Apparently, people impose different requirements on footwear that is made specifically for indoor use. This can be explained by indoor footwear not being visible for other people, and thereby not being seen as a visible representation of their disease in social situations.[27] Imposing different requirements on indoor footwear was also seen in the importance given to easy donning and doffing, a frequent complaint in relation to low indoor use of regular custom-made footwear, and flexibility of materials. The finding that the majority of participants indicated prevention of ulceration or skin irritation to be the most important factor is supported by the results in a recent multi-ethnic population in Singapore,[28] but different from a study in a similar Dutch population, where only 5% of participants assessed this as a priority.[11] However, that study was done more than 10 years ago, and has led to increased education and attention for communication and explaining the need for orthopedic footwear in this population.[11, 16] Despite the importance given to the ulcer protective characteristics of the footwear, we found that most participants leave their bed at night with their feet unprotected, and some never use their regular footwear at home, which is in line with earlier research.[12, 20, 21] As every step without protection imposes a risk of ulcer development, unprotected walking during the night is undesirable.

We used a set of 12 predefined requirements to design custom-made indoor footwear, based on these results and additional multidisciplinary input. The key requirement was for the indoor footwear to have similar offloading capacity as a person's regular footwear, as plantar pressure reduction is the most important criterion for ulcer prevention footwear, and the indoor footwear is to replace the regular custom-made footwear inside the home.[4] We would have accepted up to 10% higher peak plantar pressures in comparison to regular footwear because of lower walking speed inside one's house than either outside or in the gait lab, with subsequent lower pressures,[29, 30] but found peak plantar pressures to be similar in the indoor footwear. While it remains important to confirm this in a larger group of participants, we conclude that biomechanically and from a user's perspective our design is fit for use in everyday practice.

The remaining requirements concerned a variety of usability, durability and outcome characteristics, and costs. While some of these requirements need to be assessed in

studies with a longer follow-up and more participants (e.g., temperature regulation, safety, shear forces, durability, and – most importantly – adherence), all other requirements were satisfactorily met. Participants were positive about the indoor footwear's usability, which may contribute to increased adherence.[10, 13, 26] However, investigating the effects of providing indoor footwear on adherence is beyond the scope of this study and will be assessed in another study. Also, adherence is a multidimensional phenomenon,[31] and the importance attached to the various requirements of indoor footwear varied between individuals in our needs assessment. It remains important to consider individual preferences when discussing the provision of indoor footwear and whether such a footwear solution matches their needs.

The companies involved estimated that the indoor footwear can be produced for 25-35% of the cost of regular custom-made footwear, provided it is made on an existing shoe last, and in addition to regular custom-made footwear. Another reason for these lower costs comes from using less durable materials compared to regular custom-made footwear. This is justified as indoor footwear will experience less "wear and tear". However, while most participants were willing to contribute financially to its provision, coverage of most production costs through healthcare insurance or systems alike, remains a requirement for implementation.

A limitation of this study was its potential for selection bias, with orthopedic shoe technicians inviting their patients for participation. However, participants were picked arbitrarily, without using a specific procedure, characteristics of participants and their usability assessments were similar to other studies,[11, 13] there was adequate variation in answers provided, and in the plantar pressure evaluation participants were their own controls. Second, while "not increasing shear forces" was included as one of the requirements, with no reliable measurement system available we were limited by not being able to assess this requirement.[32] Third, we were not able to quantitatively control walking speed during plantar pressure measurements at two locations. However, visual observations showed no difference in walking speed between regular and indoor custom-made footwear, and this was confirmed quantitatively at the one location where speed could be measured.

In daily clinical practice in the Netherlands, custom-made indoor footwear is occasionally already prescribed by specialists in rehabilitation medicine and manufactured by orthopedic footwear companies. However, large variation is present in design and production, and likely efficacy, as these are all made based on clinical experience and without following a systematic design approach. With the current study, we were the first to follow such an approach, integrating perspectives of users and professionals,

and providing evidence for important biomechanical and usability requirements. The resultant indoor footwear is described within this paper with sufficient detail for others to also start implementing the prescription and production of indoor footwear that meets all requirements.

In future research, it is needed to investigate various clinical, behavioral and product outcomes. Most importantly, this concerns investigating if indoor footwear indeed improves adherence to wearing prescription preventative footwear, as well as its effect on foot ulcer prevention. Factors such as climate, culture and religious beliefs might also play a role in wearing of and satisfaction with indoor footwear,[18, 19] and it remains to be investigated if these and other individual preferences can be satisfactorily dealt with in the current design.

CONCLUSIONS

People with diabetes at moderate-to-high risk for foot ulceration and in possession of regular custom-made footwear express a clear need for special custom-made footwear for indoor use, and expect such footwear to increase their adherence. Following a multidisciplinary systematic design approach, we designed custom-made indoor footwear with adequate offloading properties, better usability and at lower costs than participant's regular custom-made footwear. This indoor footwear can be made in daily clinical practice, while its effect on footwear adherence and ulcer prevention needs to be evaluated in further studies.

ACKNOWLEDGEMENTS

We would like to thank the orthopedic footwear companies, their orthopedic shoe technicians and their management representatives for their time and energy dedicated to the project: Livit Orthopedie (Jan Pulles, Carlijn Renee, Esther Mik), Buchrnhornen BV (Frans Buchrnhornen, Bart van Heerebeek), OIM Orthopedie (Sjakko Lieben, Yvette Kerkum, Cock Vergeer). We would also like to thank Diabetes Vereniging Nederland [Diabetes Association Netherlands] (Dayline Coffie, Olof King) and CZ Zorgverzekering [CZ Health Insurance] (Marjan Peelen, Tanja Bastiaansen, Dion van Bommel) for their participation in the project group, and MyOrthopedics (Vincent Bergmans) for providing all details on the materials of the indoor footwear.

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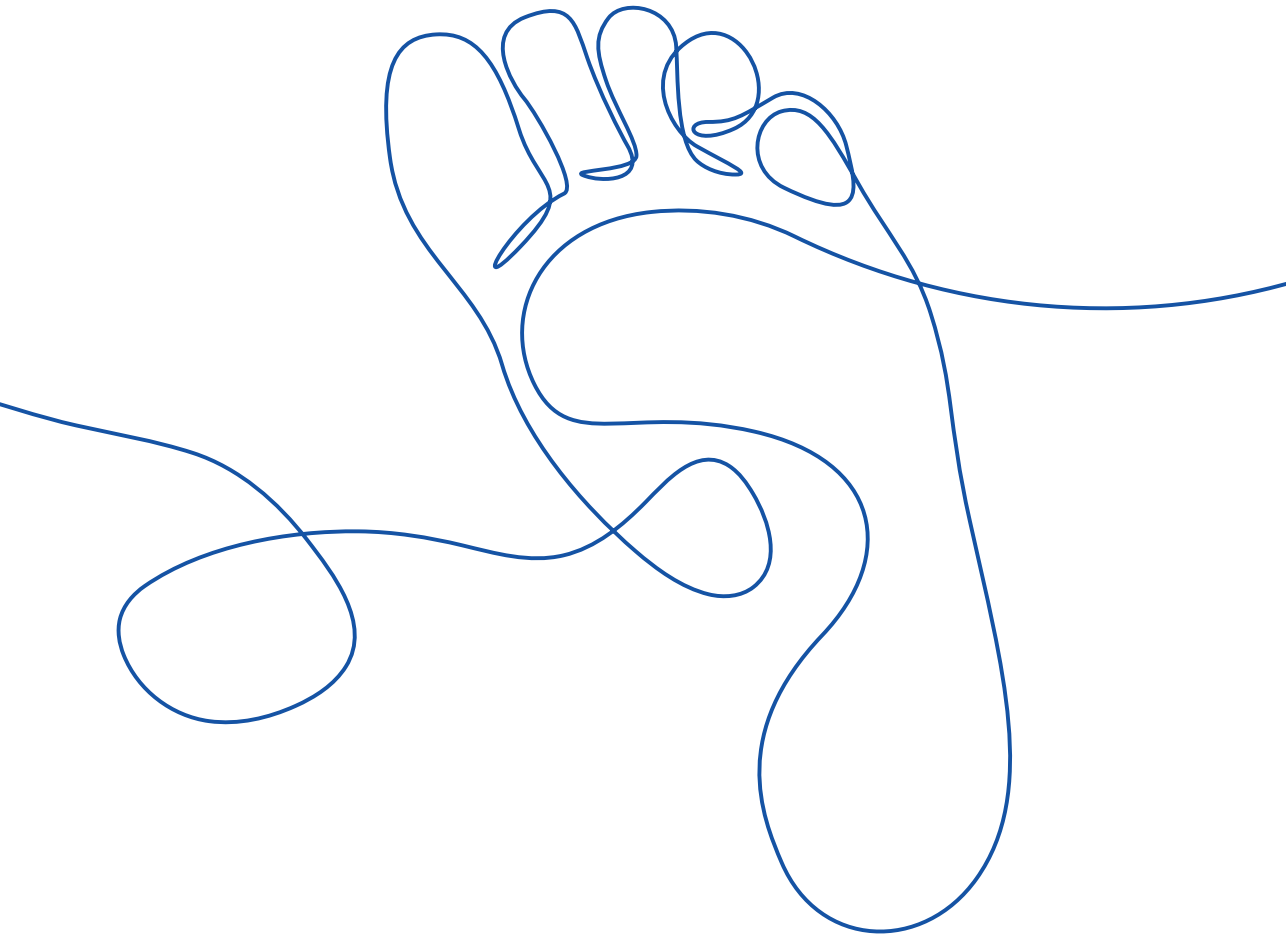

Chapter 6

Custom-made footwear designed for indoor use increases short-term and long-term adherence in people with diabetes at high ulcer risk

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BMJ Open Diabetes Research and Care 2022;10:e002593

ABSTRACT

Introduction: To explore changes in footwear adherence following provision of custom-made indoor footwear in people with diabetes at high risk for plantar foot ulceration and in possession of regular custom-made footwear.

Research Design and Methods: Adherence indoors and outdoors was assessed objectively as percentage of steps custom-made footwear was worn, at baseline (in regular custom-made footwear), 1 and 12 months after providing custom-made indoor footwear (in both indoor and regular footwear). Primary group: participants with low (<80%) baseline indoor adherence; secondary group: participants with high (≥80%) baseline indoor adherence. Peak plantar pressures of the indoor footwear were compared with the regular custom-made footwear. Footwear usability was evaluated at 3 months via a questionnaire. At 12 months, ulcer recurrence was assessed through participant/prescriber reporting.

Results: Of 31 participants, 23 had low baseline indoor adherence (<80%). Overall adherence in this group increased statistically significant from median 65% (IQR:56%-72%) at baseline to 77% (60%-89%) at 1 month (p=0.002); and 87% (60-93%) at 12 months (p<0.001). This was due to a significant increase in adherence indoors: baseline: 48% (21%-63%); 1 month: 71% (50%-83%) (p=0.001); 12 months: 77% (40%-91%) (p<0.001). Mean peak plantar pressures were comparable between the indoor and regular custom-made footwear. Participants were positive about usability. One-year ulcer recurrence rate was 26%.

Conclusions: Footwear adherence increased in the short-term and long-term after provision of custom-made indoor footwear in people at high risk of diabetic foot ulceration with low baseline adherence, because they actively wore their newly provided indoor footwear inside their house. Footwear adherence may be helped by using both regular and indoor custom-made footwear in clinical practice; the effect on ulcer recurrence should be investigated in future trials.

INTRODUCTION

Foot ulceration affects up to 30% of all people with diabetes in their lifetime, and places a high burden on patients and carers, as well as the healthcare system.[1] Once a foot ulcer has healed, recurrence within 1 year is around 40%, and 60% within 3 years.[1] Due to this high risk for foot ulceration and its recurrence, its prevention is of fundamental importance.

Custom-made footwear is an effective intervention to help prevent foot ulceration,[2, 3] and is recommended in international guidelines.[4] The aim of such footwear is to reduce ulcer risk by redistributing and lowering mechanical stress at high-risk regions and providing a proper fit.[4] For footwear to achieve this, it needs to be worn.[5, 6] However, adherence to wearing custom-made footwear is a challenge in people with diabetes at high ulcer risk, and they frequently wear footwear that is not protective or go barefoot (or in socks only) when weight-bearing.[4, 5, 7, 8] Adherence is particularly low indoors, while approximately 60% of their daily steps are taken indoors.[9-11] Interventions to specifically increase footwear adherence indoors are needed for this high-risk population.[5]

Research on adherence-increasing interventions, however, is limited; a recent systematic review found only one study that attempted to increase footwear adherence, by using motivational interviewing.[12] This resulted in some improvement in footwear adherence 1 week after motivational interviewing, but a return of adherence to baseline levels after 3 months, with especially low adherence indoors.[9] Participants provided various reasons for their low indoor adherence, such as the weight of the footwear, difficulties with donning and doffing, and difficulties moving around inside the house with their custom-made footwear.[9] Custom-made footwear specifically designed for indoor use might overcome these drawbacks and improve adherence.

We developed custom-made indoor footwear based on an evaluation of needs and preferences of people with diabetes and on a set of design rules such footwear should fulfil.[13] The most important was similar offloading efficacy compared with a person's regular custom-made footwear,[13] because indoor footwear may improve adherence by increasing wearing time indoors and can replace time that regular custom-made footwear would otherwise be worn. We aimed to explore the short-term and long-term changes in footwear adherence following the provision of such custom-made indoor footwear in people with diabetes at high risk for foot ulceration and regular custom-made footwear.

RESEARCH DESIGNS AND METHODS

Study design and setting

A prospective non-controlled intervention study (pre-post design) in three multidisciplinary diabetic foot outpatient clinics.

Participants

Inclusion criteria were: type 1 or 2 diabetes mellitus; moderate to high risk for foot ulceration (International Working Group on the Diabetic Foot risk 2 or 3);[4] and in possession of custom-made footwear (i.e., custom-made insoles worn in custom-made footwear). Exclusion criteria were: presence of a foot ulcer; Charcot foot deformation or active Charcot's neuroarthropathy; amputation at or beyond the tarsometatarsal level; necessity to wear high-cut footwear (midtibia level or higher) at all times; and inability to walk unaided. Participants who took part in a preceding survey to assess needs and expectations regarding custom-made indoor footwear and expressed a need for such footwear were invited.[13] Written informed consent was obtained from all participants prior to inclusion. The Medical Ethics Review Committee of the Amsterdam University Medical Center waived the requirement for ethical review of the study under the Medical Research Involving Human Subjects (WMO) (W17_405#17.474).

Custom-made footwear

Prior to the study, all participants possessed custom-made footwear that was prescribed by a rehabilitation medicine specialist and manufactured by a certified orthopedic shoe technician from each of the three participating multidisciplinary clinics. The footwear consisted of custom-made insoles worn in custom-made shoes, both handmade from a positive last of the foot. The shoe had rocker profile outsoles, and multidensity insoles with pressure relieving elements.[14] This custom-made footwear is from here onwards referred to as 'regular footwear'.

Custom-made indoor footwear

During the study, participants were provided with custom-made footwear specifically intended for indoor use (referred to as 'indoor footwear' from here onwards), in addition to their regular custom-made footwear. To ensure the same biomechanical offloading capacity as the regular footwear, the indoor footwear (Supplementary data) was built on the same shoe last, was ankle-high (i.e., above ankle but below midtibia level), and was fitted with a custom-made insole similar to the insole used in the regular footwear.[13] This similarity in offloading capacity was the key characteristic as determined in our pilot study,[13] because people may replace wearing of their regular footwear inside their house with wearing the indoor footwear. To maintain an optimal biomechanical environment,

similarity in offloading between regular and indoor footwear is important, and this was objectively assessed (see sections '*Procedures'* and '*In-shoe plantar pressure measurements'* for more information). To facilitate usability, the shoe outsole was a light-weight material, the vamp was made of either microfiber (Supplementary data Type A), or felt (Supplementary data Type B), and held together with a combination of leather, Velcro fastener and a zipper. Prior to the start of the study, participants were informed that the indoor footwear would be provided free of charge.

Procedures

On study entry, demographic and disease-related data were collected. Loss of protective sensation was assessed with a 10g Semmes-Weinstein monofilament,[15] foot amputations were documented by clinical assessment, and photographs of the feet were taken. Baseline adherence was determined by measuring step count with an activity monitor at the ankle and footwear use with a temperature sensor (see '*Adherence*' section for details).

After this baseline visit, the indoor footwear was manufactured, and on its delivery, in-shoe plantar pressures were measured in both the participants' regular and indoor footwear (see *'In-shoe plantar pressure measurements'* section for details). If necessary, the footwear was modified until peak pressures were similar between the two footwear types.[4, 6, 16] One month after provision, adherence was again determined, now in the combination of regular and indoor footwear. At 3 months, a questionnaire was sent to the participants to evaluate (1) usability, (2) satisfaction and (3) appearance of the indoor footwear, and (4) the willingness to pay for the indoor footwear if prescribed in clinical practice. The questionnaire was based on the Monitor Orthopedic Shoes,[17] and consisted of questions scored on a 5-point Likert-scale. The response options were combined to three categories: 'not or hardly present', 'neutral' and '(very much) present'. At 12 months, adherence was again determined in the combination of regular and indoor footwear. Any ulcer (recurrence) that had occurred in the previous 12 months was identified based on participant or orthopedic shoe technician reports.

Adherence

Footwear adherence was determined by combining seven consecutive days of footwear use and daily step count measurements. Footwear use was measured with a small temperature-based sensor (@monitor, Department of Medical Technology and Innovation, Academic Medical Center, Amsterdam, The Netherlands), placed inside the custom-made footwear and recording temperature at 1-min intervals. The one or two pairs of footwear that were most frequently used, or three after provision of the indoor footwear, were provided with the @monitor. Simultaneously, daily step count

was recorded with an activity monitor strapped above the ankle (StepWatch, Orthocare Innovations LLC, Oklahoma, USA). Participants were instructed to wear the StepWatch at all times, except when showering or bathing. Time spent outdoors, cycling and not wearing the StepWatch were logged by the participants in a report form.

Footwear use and daily step count were obtained for each measurement day, and analyzed with custom-built software in Matlab R2018a (MathWorks, Natick, Massachusetts, USA).[10] Only valid recordings (i.e., a minimum of 4 days of combined step count and footwear use measured, including one weekend day) were included in analyses.[18, 19] Barefoot walking or walking in non-prescribed footwear was assumed when the StepWatch showed activity and the @monitor did not show footwear usage. The daily activity log was used to differentiate between indoor and outdoor adherence. Adherence was defined as the percentage of steps while wearing prescribed footwear and calculated as the ratio between the cumulative number of steps with prescribed footwear worn and the total number of steps taken. 'Low indoor adherence' was defined as <80% of the total steps indoors taken in prescribed footwear.[6]

In-shoe plantar pressure measurements

In-shoe peak plantar pressures were measured dynamically with the Pedar-X in-shoe pressure measurement system (Novel GmbH, Munich, Germany) at a 50 Hz sampling frequency. To increase generalizability, participants were asked to walk at a comfortable speed, over a flat surfaced walkway. The first and last step of each walk were discarded. Plantar pressure data were collected over a minimum of 12 midgait steps per foot per condition, as determined to be valid and reliable.[20] Pressures were analyzed with Novel multimask software (V.13.3.65). The mean peak pressures at eight anatomical foot regions were calculated for the left and right foot separately: the toes (hallux, dig 2-3 and dig 4-5), forefoot (metatarsal head 1, metatarsal head 2-3 and metatarsal head 4-5), midfoot and heel.

Statistical analysis

Patient characteristics, adherence, daily step count, total wearing time and in-shoe peak plantar pressures were summarized using descriptive statistics. Separate analyses were undertaken for participants with low indoor adherence (<80%, primary group) and high indoor adherence (≥80%) at baseline. Independent samples t-tests and Fisher's exact tests were used to compare patient characteristics between low-adherence and high-adherence groups. Wilcoxon signed rank test was used to compare adherence, step count and wearing time between both follow-up moments and baseline. Paired sample t-test was used to compare in-shoe peak plantar pressures between indoor and regular custom-made footwear for the eight anatomical regions of both the left and right foot. A

Bonferroni-corrected significance level of $p<0.025$ (0.05/2) was used for adherence and wearing time, as two primary analyses were done, and $p<0.004$ (0.05/12) for peak plantar pressures. Wilcoxon effect sizes (r) were calculated for adherence and wearing time as follows: $r=Z/\sqrt{(N)}$. Statistical analyses were performed using SPSS V.26.0 (SPSS Inc). In case of missing adherence data at baseline, adherence was imputed using missing value analysis regression in SPSS, with wearing time as predictor. First observation carried backward was used to impute missing adherence data at 1 month, and last observation carried forward for missing adherence data at 12 months follow-up. Data were not imputed in case of death.

RESULTS

Participants

Thirty-four participants completed baseline measurements; three dropped-out during follow-up (Figure 1). Twenty-three participants had low indoor adherence at baseline, and eight had high adherence (Table 1). Of the 31 analyzed participants, 13 were female (42%), mean (SD) age was 69.3 (9.9) years, and 24 had type 2 diabetes (77%), with no difference between low-adherence and high-adherence groups (Table 1).

Missing data

Adherence data were missing for three participants at baseline (equipment failure), three at 1 month (equipment failure, hospitalization and missed visit) and eight at 12 months follow-up (two equipment failure, one untraceable, five missed visit). Analyses on the imputed dataset and on available cases provided similar results; we used the imputed dataset for reporting.

Footwear adherence, wearing time, and step count

In participants with low baseline adherence, overall adherence increased significantly from baseline (65%) to 1 month (77%; $p=0.002$; $r=0.66$), and from baseline to 12 months (87%; $p<0.001$; $r=0.74$; Table 2). Adherence indoors increased significantly from 48% to 71% ($p=0.001$; $r=0.74$), and 77% ($p<0.001$; $r=0.78$), respectively. Adherence outdoors was high at baseline (94%) and improved non-significantly to 98% and 99%, respectively (Table 2). Ten of 23 participants (44%) with low baseline adherence improved to high adherence (>80% of steps) at 1 month and 12 participants (55%) at 12 months. Similar to adherence, time that custom-made footwear (indoor and regular) was worn increased significantly from 8.6 hours/day to 9.3 hours/day ($p=0.0014$; $r=0.68$) and 12.0 hours/day ($p=0.002$; $r=0.75$; Table 2), respectively. Wearing time at 1 and 12 months was evenly distributed between indoor and regular footwear (Table 2).

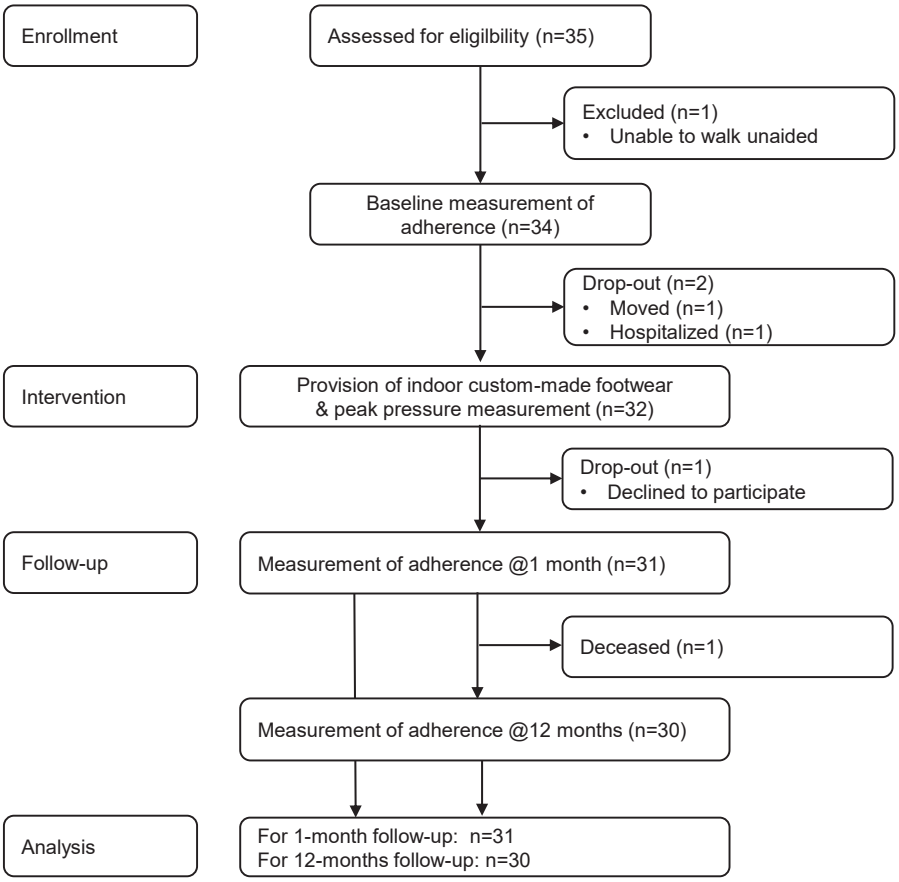

Figure 1. Flow diagram summarizing participants included and excluded from analysis.

Table 1. Participant characteristics.

	Baseline indoor adherence low (n=23)	Baseline indoor adherence high (n=8)	*p*	All participants (n=31)
Age (years)	68.3±11.2	72.1±4.2	0.357	69.3±9.9
Female gender	39(9)	50(4)	0.689	42(13)
BMI (kg/m^2)	30±7	32±8	0.614	31±7
Type 2 diabetes	78(18)	75(6)	1.0	77(24)
Diabetes duration (years)*	19.5±15.7	19.5±10.2	0.997	19.5±14.5
LOPS, based on abnormal monofilament perception	100(23)	100(8)	-	100(31)
Amputation†	22(5)	25(2)	1.0	23(7)
Digiti	(3)	(2)		(5)
Ray/Forefoot	(2)	0		(2)

Data are expressed as mean±SD, or % (n). No significant differences were found between the groups baseline indoor adherence 'low' and 'high'. *Diabetes duration was available from n=27. †Amputation up to tarsometatarsal level. BMI, body mass index; LOPS, loss of protective sensation.

Table 2. Adherence in % of steps taken in prescribed footwear, wearing time indoor and regular footwear in hours a day, and indoor footwear relative to total wearing time.

	Baseline indoor adherence low (n=23)			Baseline indoor adherence high (n=8)			All participants (n=31)		
	Baseline	1 month	12 months	Baseline	1 month	12 months	Baseline	1 month	12 months
	Adherence								
Overall	65 (56-72]	77 (60-89) *p*=0.002* *r*=0.66ǂ	87 (60-93) p<0.001* r=0.74	96 (93-97)	94 (91-96) *p*=0.306 *r*=0.36	95 (79-97) *p*=0.203 *r*=0.45	71 (60-90)	83 (67-94) *p*=0.006* *r*=0.49	90 (69-95) *p*=0.003* *r*=0.54
Indoor	48 (21-63]	71 (50-83) *p*=0.001* *r*=0.74	77 (40-91) *p*<0.001* *r*=0.78	94 (91-95)	93 (89-94) *p*=0.268 *r*=0.41	93 (93-96) *p*=0.496 *r*=0.26	57 (34-87)	77 (52-93) *p*=0.002* *r*=0.62	84 (55-93) *p*=0.001* *r*=0.65
Outdoor	94 (85-98]	98 (92-100) *p*=0.135 *r*=0.34	99 (94-100) *p*=0.028 *r*=0.52	99 (99-100)	100 (100-100) *p*=0.034* *r*=0.80	100 (100-100) *p*=0.034* *r*=0.80	96 (86-99)	100 (100-100) *p*=0.059 *r*=0.37	100 (100-100) *p*=0.010* *r*=0.51
	Wearing time indoor and regular footwear								
Overall	8.6 (4.9-9.8]	9.3 (7.4-12.6) *p*=0.001* *r*=0.68	12.0 (8.1-14.2) *p*=002* *r*=0.75	14.7 (14.2-15.4)	14.6 (13.1-15.1) *p*=0.309 *r*=0.39	17.9 (10.5-15.4) *p*=*0*.735 *r*=0.13	9.4 (6.5-12.2)	11.5 (8.2-4.4) *p*=0.004* *r*=0.54	12.9 (8.7-15.1) *p*=0.005* *r*=0.57
	Wearing time indoor footwear relative to total wearing time								
Indoor footwear	NA†	4.7 (2.9-7.1)	5.7 (2.0-7.1) *p*=0.796 *r*=0.07	NA	10.3 (6.5-11.9)	3.9 (3.5-10.4) *p*=0.173 *r*=0.56	NA	5.7 (2.9-7.8)	5.6 (2.6-7.3) *p*=0.548 *r*=0.13
Regular footwear	8.6 (4.9-9.8]	4.5 (3.3-6.6)	5.4 (3.1-9.0) *p*=0.796 *r*=0.07	14.7 (14.2-15.4)	4.7 (2.7-8.2)	5.7 (3.2-11.9) *p*=0.173 *r*=0.56	9.4 (6.5-12.2)	4.6 (3.2-7.4)	5.6 (3.3-10.7) *p*=0.249 *r*=0.25

Data are expressed as median (IQR). *Significantly different between baseline and follow-up (Bonferroni-corrected level of significance: $p<0.025$ [0.05/2]).†NA=not applicable; because the indoor footwear was provided only after baseline measurement. Please note that values are median; hours of indoor and regular footwear cannot be added up. ǂ*r*=Wilcoxon effect size.

Table 3. Daily step count at various time points.

	Baseline indoor adherence low (n=23)			Baseline indoor adherence high (n=8)			All participants (n=31)		
	Baseline	1 month	12 months	Baseline	1 month	12 months	Baseline	1 month	12 months
Overall	5580 (3562-7187)	3722 (2726-5797) *p*=0.355	3921 (2179-6864) *p*=0.179	5976 (3769-6857)	3321 (2135-5025) *p*=0.176	3591 (2145-6504) *p*=0.249	5580 (3145-7016)	3522 (2509-5567) *p*=0.124	3790 (2206-6410) *p*=0.101
Indoor	3202 (2405-4887)	2694 (2156-4326) *p*=0.744	2307 (1721-2966) *p*=0.88	4147 (2685-4759)	2904 (1605-4476) *p*=0.398	2050 (1518-6463) *p*=0.893	3345 (2418-4809)	2799 (2056-4342) *p*=0.677	2050 (1751-3303) *p*=0.204
Outdoor	1744 (1084-3332)	835 (517-2467) *p*=0.286	1375 (339-2536) *p*=0.650	1591 (929-2440)	859 (418-1122) *p*=0.091	716 (305-1761) *p*=0.080	1593 (831-2527)	847 (492-1447) *p*=0.074	1326 (353-2262) *p*=0.167
Relative use of indoor footwear indoors	NA[†]	59 (29-74)	45 (15-71)	NA	81 (43-86)	45 (20-65)	NA	62 (37-76)	45 (20-66)
Relative use of indoor footwear outdoors	NA	2 (0-10)	0 (0-1)	NA	1 (0-6)	0 (0-39)	NA	1 (0-9)	0 (0-1)

Data are expressed as median (IQR) or %. [†]NA=not applicable; because the indoor footwear was provided only after baseline measurement. No significant differences were found between baseline and follow-up ($p<0.05$).

In participants with high indoor adherence at baseline, both adherence (Table 2) and wearing time (Table 2) remained high. They wore the indoor footwear 10.3 hours/day at 1 month and 3.9 hours/day at 12 months.

All participants took more steps indoors compared with outdoors, and had a non-significantly lower daily step count during follow-up compared to baseline (Table 3). In participants with low baseline adherence, 59% of indoor steps were in the indoor footwear at 1 month and 45% at 12 months. In participants with high adherence at baseline, this was 81% and 45%, respectively. The indoor footwear was hardly used outdoors (range: 0-2%).

Peak plantar pressures

Peak plantar pressures in all regions of the indoor footwear were comparable with the regular footwear (Table 4). Peak pressures >200 kPa were less frequently present in indoor footwear (Table 4).

Table 4. Peak plantar pressures for indoor and regular custom-made footwear.

		Indoor footwear*	Regular footwear*	Mean difference (95%CI)†‡	% difference	*p*
Hallux	Left	121±46	122±53	-1 (-12 to 11)	-1%	0.908
	Right	124±47	128±66	-4 (-18 to 9)	-3%	0.525
MTH1	Left	141±40	145±60	-4 (-21 to 14)	-3%	0.653
	Right	146±40	153±72	-8 (-28 to 13)	-5%	0.467
MTH2-3	Left	145±36	151±56	-6 (-22 to 10)	-4%	0.460
	Right	157±43	157±52	-1(-13 to 12)	-1%	0.916
MTH4-5	Left	121±39	124±45	-3 (-15 to 9)	-2%	0.599
	Right	124±48	123±52	0 (-9 to 10)	0%	0.972
Midfoot	Left	117±38	115±35	2 (-8 to 12)	2%	0.634
	Right	112±29	115±36	-4 (-12 to 4)	-3%	0.343
Heel	Left	187±52	201±76	-14 (-33 to 3)	-7%	0.112
	Right	185±58	209±69	-24 (-47 to -1)	-10%	0.046

*Data are provided as mean±standard deviation kPa. †Mean difference is peak pressure in indoor footwear minus custom-made footwear; a negative score means lower pressures in the indoor footwear. ‡No significant differences were found between indoor and regular footwear (Bonferroni-corrected level of significance: $p<0.004$ [0.05/12]). MTH: metatarsal head.

Usability of indoor footwear

Response rate for the usability questionnaire was 90% (n=28). Most responders (79%) were satisfied or very satisfied with the indoor footwear (Table 5), and 68% felt that it met their expectations. The indoor footwear was considered appealing by 43% of the respondents. All but one of the respondents reported negative usability aspects ‘difficult to don and doff’, ‘too heavy’, ‘too tight fit’, and ‘skin irritation’ as neutral or not or hardly

Table 5. Satisfaction and usability characteristics of participants' indoor footwear.

Overall satisfaction	(Very) unsatisfied	Neutral	(Very) satisfied
	7 (2)	14 (4)	79 (22)
Positive usability characteristics	Not or hardly present	Neutral	(Very much) present
Good durability	-	50 (14)	50 (14)
Easy maintenance	10 (3)	29 (8)	61 (17)
Appealing footwear	-	57 (16)	43 (12)
Negative usability characteristics	Not or hardly present	Neutral	(Very much) present
Too much sweating*	85 (22)	15 (4)	-
Too heavy*	88 (23)	8 (2)	4 (1)
Cold feet†	89 (24)	11 (3)	-
Difficult to donn and doff	89 (25)	7 (2)	4 (1)
Too tight fit†	93 (25)	4 (1)	4 (1)
Ulceration†	93 (25)	4 (1)	4 (1)
Skin irritation†	93 (25)	4 (1)	4 (1)

Data expressed as % (n) of responders. *Missing data n=2. †Missing data n=1.

present (Table 5). The largest group of responders (36%) were willing to pay between €0 and €50 for the indoor footwear; 32% between €50 and €100.

Ulcer recurrence

Eight of the 31 participants (26%) developed a recurrent ulcer during follow-up, of which four had low indoor adherence at baseline. Seven out of eight ulcers were plantar, of which five in the forefoot and two locations unknown; one ulcer was dorsal, caused by skin getting caught in the zipper of the indoor footwear.

DISCUSSION

We assessed changes in footwear adherence after provision of custom-made indoor footwear in people with diabetes at high risk for foot ulceration and already in possession of regular custom-made footwear. People with low baseline indoor adherence significantly increased their adherence in the short-term and long-term after provision of indoor footwear, predominantly as a result of increasing their indoor adherence, as well as wearing time. Adherence remained high in people with high baseline indoor adherence; they wore their indoor footwear for substantial amounts of time in the short-term and long-term. Ulcer recurrence in 12 months was 26%, with mostly plantar ulcers. The indoor footwear had similar offloading capacity as regular custom-made footwear, and almost all participants were satisfied with the indoor footwear and were neutral or

positive about usability aspects. Custom-made indoor footwear in addition to regular custom-made footwear therefore seems a useful intervention to improve adherence to wearing prescribed footwear in people with diabetes at high risk for foot ulceration.

Adherence strongly improved both in the short-term and long-term from additionally providing a pair of custom-made indoor shoes. As expected, indoor adherence improved the most, because the intervention specifically targets indoor adherence, and because indoor adherence was lowest at baseline and therefore had most potential to increase. People with low adherence at baseline (i.e., <80% of steps indoors in protective footwear) showed absolute 23% and 29% improvements in adherence in the short-term and long-term, respectively. At 12 months, 55% of this group was highly adherent. Outdoor adherence was already high at baseline in this group, and remained high over time, showing that footwear adherence is not so much an issue outdoors. However, participants were clearly more active inside their homes compared with outside, even more than found in previous studies.[9-11] This again stresses the importance of an intervention specifically targeting indoor adherence. In line with increased adherence, wearing time also increased. This suggests that the higher percentage of steps taken in protective footwear was the result of an increase in hours the footwear was worn.

Adherence and wearing time in participants with high baseline adherence remained high over time. Given the high baseline adherence of 96%, little opportunity for increased adherence was possible for this group. Important, however, was that most steps indoors were taken in the indoor footwear at 1 month, and still almost half at 12 months. This indicates that people with high adherence also benefit from the provision of indoor footwear and suggests that its provision should not be limited to those with low indoor adherence.

Almost all participants were satisfied with their indoor footwear, and most scored positive on usability aspects. Earlier research showed that difficulties with donning and doffing, as well as the weight of the footwear, are reasons for low indoor adherence.[9] These usability aspects were considered in the indoor footwear design. The positive usability scores, in combination with the increased adherence, suggest a successful design of the indoor footwear for most people.

The ulcer recurrence rate was 26% in 12 months, lower than found in a review,[1] but still considerable given the increase in adherence. Although high footwear adherence combined with pressure-reducing footwear reduces the risk for plantar foot ulcer recurrence,[6] it does not eliminate risk completely. The recurrence rate found in our study may be explained by the improved, but still not optimal adherence in some cases. For people

at high risk, every step without protection may be one too much. Second, the target peak pressure of 200 kPa[6, 21, 22] used in the design of the indoor footwear may still be too high for some people, for instance in case of ample weight-bearing activity, resulting in excessive plantar cumulative tissue stress.[23, 24] Although our results suggest that indoor footwear potentially may help in ulcer prevention, its effectiveness should be assessed in a randomized controlled trial (RCT) with ulcer recurrence as a primary outcome. However, as indoor footwear in itself may not be enough to remove all barriers in ulcer prevention, this intervention should preferably be combined with additional preventative interventions as part of an RCT using a personalized treatment approach for ulcer prevention.[25]

A strength of the present study was the objective measurement of footwear adherence, as recommended for diabetic foot disease research.[26] While this might affect adherence due to participants' awareness of being monitored,[27] such an effect would be similar for baseline and follow-up measurements, and there is therefore no reason to assume that the improvement in adherence was caused by something other than the intervention. Another strength was that adherence was assessed in both the short-term and the long-term, providing a more valid and robust outcome. The lack of a control group not receiving indoor footwear or a control group with off-the-shelf footwear could be seen as a study limitation. However, we aimed to explore the effect of the intervention on adherence, for which a pre-post design is suitable. Nevertheless, we recommend to include a control group in future trials with this intervention. A limitation was how foot ulcer recurrence was assessed. Being a secondary outcome, full details and independent outcome assessment of ulcers were not obtained. While this limits interpretation regarding ulcer severity, the current finding of 26% ulcer recurrence is a useful indication of the potential effect of this single intervention on ulcer recurrence and can be used for power calculations to inform future RCTs. Finally, we had to deal with missing data, with equipment failure one of the main causes. However, we estimate a limited effect of missing data, as we could use wearing time for imputation, which is strongly related to adherence,[10] and because the imputed data analysis showed similar results to analysis of the non-imputed data.

This is the first study that explored the effect of providing custom-made indoor footwear in addition to regular footwear on footwear adherence. Even though adherence was still low in some participants and many of them did not take every step indoors with the prescribed footwear, the results do suggest that the provision of indoor footwear in addition to regular footwear can be a useful intervention in daily practice for people with diabetes at high risk for ulceration. With costs being higher than participants are willing to pay, reimbursement is required.

CONCLUSIONS

Adherence to wearing custom-made footwear increased in the short-term and long-term after provision of custom-made indoor footwear with adequate offloading properties for people at high risk of diabetic foot ulceration. This was because they wore their custom-made indoor footwear inside their house and positively assessed its usability. Due to the substantially improved adherence, the combination of wearing custom-made indoor and regular footwear produces a more continuous low-pressure environment for the foot at risk. Implementation of this intervention may have a positive effect on ulcer recurrence, but this should be investigated in future trials.

ACKNOWLEDGEMENTS

The authors acknowledge the contribution of the orthopedic footwear companies for manufacturing the custom-made indoor footwear: Livit Orthopedie (Jan Pulles, Carlijn Renee, Esther Mik), Buchrnhornen BV (Frans Buchrnhornen, Bart van Heerebeek), OIM Orthopedie (Sjakko Lieben, Yvette Kerkum, Cock Vergeer) and MyOrthopedics (Vincent Burgmans), and Diabetes Vereniging Nederland [Diabetes Association Netherlands] (Dayline Coffie, Olof King) and CZ Zorgverzekering [CZ Health Insurance] (Marjan Peelen, Tanja Bastiaansen, Dion van Bommel) for their participation in the project group.

SUPPLEMENTARY DATA

The two types of custom-made indoor footwear used in this study

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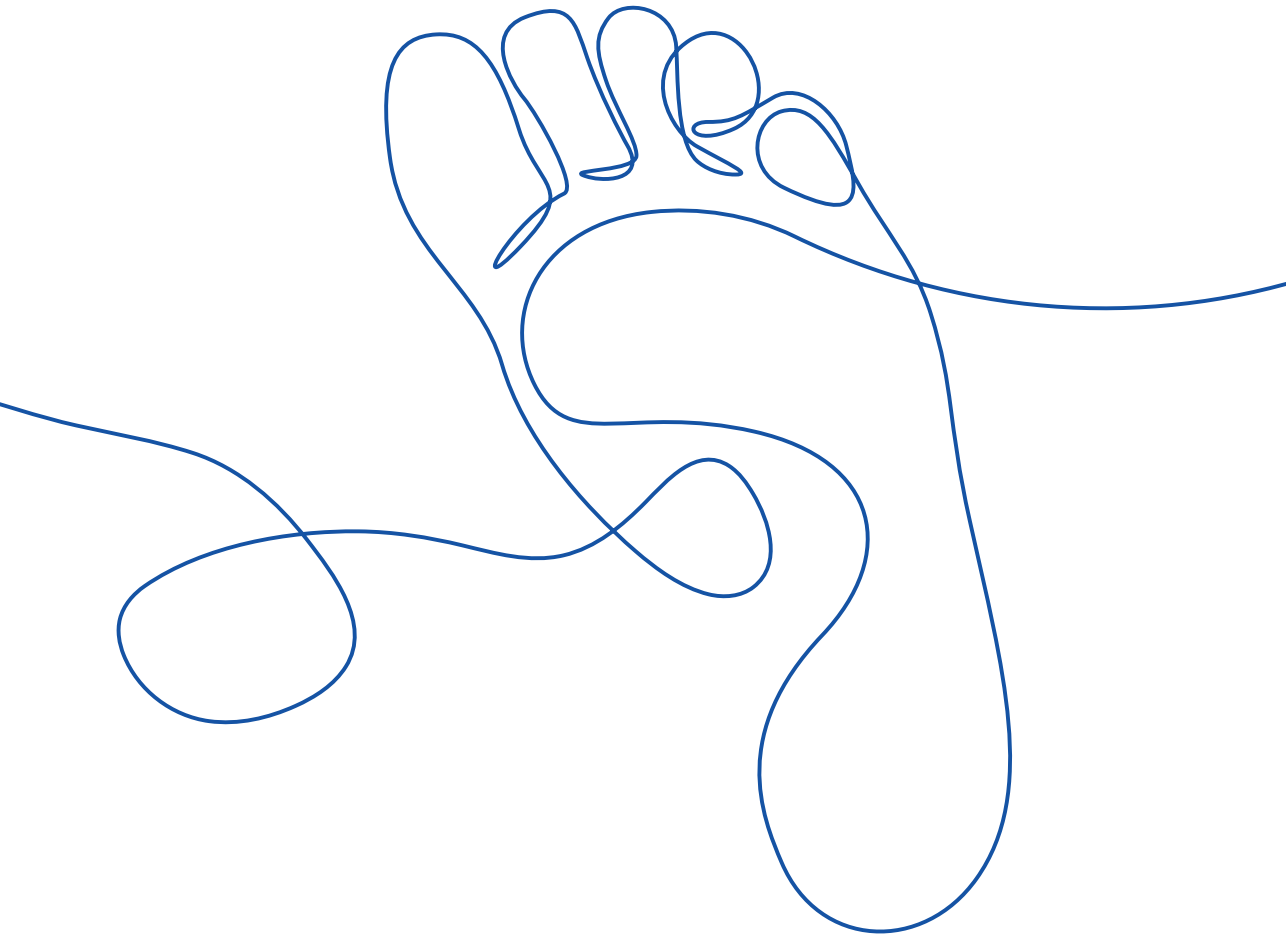

Chapter 7

General discussion

GENERAL DISCUSSION

The overall aim of this thesis was twofold: 1) to gain insight in the adherence to wearing custom-made footwear and in the determinants of adherence in a group of people with diabetes who are at high risk for plantar foot ulceration, and in a subgroup of people with diabetes, a recently healed plantar foot ulcer and a Charcot midfoot deformity, and 2) to gain insight in how adherence to wearing custom-made footwear in people with diabetes and a healed plantar ulcer can be improved by assessing the effects of motivational interviewing and the provision of custom-made footwear that is specifically designed for indoor use. In this final chapter, the main findings and methodological considerations are discussed against the background of the current literature, and clinical implications and recommendations for future research are addressed.

MAIN FINDINGS

In **chapter 1**, two models were introduced as a framework for the studies in this thesis. First, the WHO model of adherence that is focused on factors influencing adherence in general and that uses a 'static' perspective (Figure 1). And second, a conceptual model for explaining footwear use and its consequences that uses a 'dynamic' perspective (Figure 2).[1,2] Both models assume adherence is influenced by several variables, resulting in enhancing or inhibiting effects on adherence, and thereby showing the complexity of adherence to health behavior.[1] In practice, the decision to use custom-made footwear is made at least daily, often multiple times per day. While the WHO model gives a clear overview of factors that influence adherence, the conceptual model better shows how interventions may impact daily decision-making, and how this may change over time. Moreover, the conceptual model takes the consequences of use or non-use of the footwear into account, and incorporates a focus on use and usability of the footwear itself, which the WHO model does not. To place findings of the current thesis in a broader theoretical perspective, a model is needed. Because a validated adherence model currently does not exist, both models are used in the last chapter of this thesis.

Adherence to wearing custom-made footwear, and its determinants

Custom-made footwear can only be of benefit when it is worn. Although several studies have investigated adherence to wearing custom-made footwear in people with diabetes, it was assessed with a variety of subjective methods, which have clear drawbacks,[3-8] and which has recently been shown to be not valid for use in research.[9] It was therefore important to measure adherence objectively and reliably, and gain insight in factors contributing to (objectively measured) footwear adherence. In **chapter 2**, the adherence

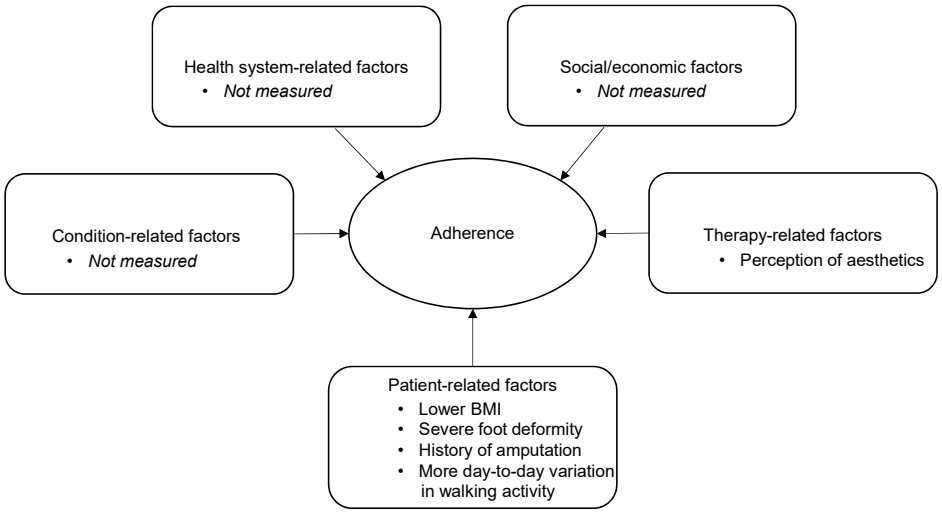

Figure 1. The WHO model of adherence,[1] with factors found to be associated with adherence to wearing custom-made footwear as found in this thesis, added to the model.

to wearing custom-made footwear was objectively assessed during seven consecutive days, by combining footwear use (measured with a shoe worn temperature-based monitor) and walking activity (measured with an ankle-worn activity monitor). In a group of 107 participants, 71% of the steps were taken while wearing prescribed custom-made footwear. Adherence was significantly lower at home (61%) than away from home (87%), with more steps taken at home (3995 vs. 2604 steps per day). A subgroup analysis in participants with low adherence (<60%) showed even lower adherence at home (28%) compared with adherence away from home (69%). The low adherence and high walking activity at home is in correspondence with earlier studies by MacFarlane et al. and Armstrong et al.[3, 10] Thus, compared to when being away from home, the foot is less protected when a person at high risk of diabetes-related foot ulceration is inside the home, with increased cumulative stress as a result and increasing the risk for ulcer recurrence. This is a clear indication that interventions aiming to improve footwear use should mainly target the use at home.

A multivariate regression analysis in the group of 107 participants showed that, from the perspective of usability or therapy-related factors, the only factor associated with a higher adherence was a better perception of footwear aesthetics. Although this may seem self-evident, with the idea widespread in clinical practice, previous studies were inconclusive about this association.[3, 11] Other factors that were associated with higher adherence were all patient-related, and also accounted for in the WHO model: lower BMI, severe foot deformity, a history of amputation, and more day-to-day variation

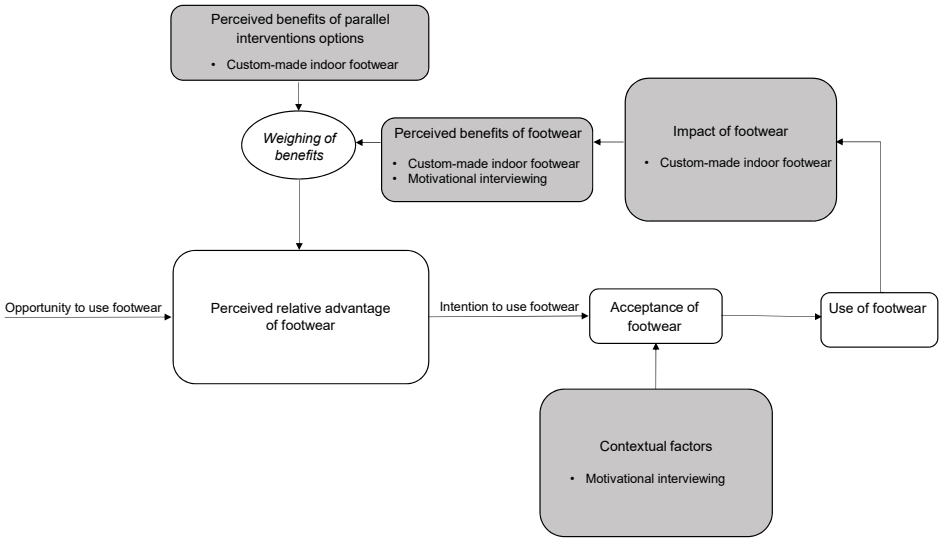

Figure 2. The conceptual model for predicting footwear use,[2] with the interventions investigated in this thesis indicated (in grey) in the areas that they impacted.

in walking activity (Figure 1). However, overall explained variance in the multivariate analysis was only 18%, and a recent systematic review found no conclusive evidence for any single factor to accurately predict adherence.[12]

It thus appears difficult to predict footwear adherence based on usability, therapy- or patient-related factors.[13-15] This has several implications: 1) the effect of optimizing any of these determinants on improving adherence may be limited; 2) rather than the determinants themselves, the importance given to each of these determinants by an individual should be taken into account. This importance influences the weighing of the benefits and thereby the perceived relative advantage, and as such affects footwear adherence (Figure 2). And 3) that other factors, such as related to the health system, social/economic status, physical condition, and behavior should also be considered in future research.

Footwear adherence and ulcer recurrence in Charcot midfoot deformity

Charcot midfoot deformity is a rare, but complex and severe condition among people with diabetes. People with a Charcot midfoot deformity are often excluded from studies on diabetic foot ulcer prevention, hence limited knowledge on offloading management and clinical effect thereof beyond the acute phase exist. In **chapter 3**, a comprehensive analysis of adherence to wearing custom-made footwear, biomechanical factors and plantar foot ulcer recurrence was performed in people with Charcot midfoot deformity (n=20). Outcomes were compared with 118 participants without a Charcot midfoot

deformity, but with similar ulcer risk factors. Participants were drawn from the same population as participants in **chapter 2**. In people with a Charcot midfoot deformity, adherence to wearing custom-made footwear was close to optimal (95%), and significantly higher than in the group without a Charcot midfoot deformity (76%). In particular, adherence at home was substantially higher (94% vs 64%), which is also in contrast with the outcomes of **chapter 2**. One of the factors that may explain the high adherence in the Charcot group is their decreased base of support resulting from the midfoot deformity. A disturbed static and dynamic balance, already caused by peripheral neuropathy, may necessitate an increased base of support from the shoes worn, only achievable in this group by means of wearing their custom-made footwear. Consequently, the immediate impact of wearing custom-made footwear is higher in people with a Charcot midfoot deformity, and therefore, according to the conceptual model, the perceived relative advantage of the footwear will be higher in this group. This then increases the chance of accepting and adhering to using the footwear. Another explanatory factor may be a higher intrinsic motivation to wear custom-made footwear because of a more severe disease history, with for example, prolonged periods of casting with loss of mobility and reduction in quality of life in the acute Charcot phase. This is a patient-related factor according to the WHO model of adherence, and according to the conceptual model, the perceived relative advantage of wearing their shoes will be higher for the Charcot group in this case, as the advantage of lowering the risk to undergo prolonged casting again outweighs any perceived disadvantage of wearing custom-made footwear.

With regard to biomechanical factors, barefoot midfoot peak pressures were significantly higher in the group with Charcot midfoot deformity than in those without, confirming the changed architecture of the foot.[16] The in-shoe midfoot peak pressures were comparable between groups, while all other foot regions showed significantly lower in-shoe peak pressures in the Charcot group, suggesting that offloading by the footwear was effective. One might expect that the effective offloading in combination with the close to optimal adherence in the Charcot group would thus result in lower ulcer recurrence rates.[17] However, plantar ulcer recurrence over 18 months follow-up in the group with a Charcot midfoot deformity was comparable to that of the group without (40% vs 47%, respectively) and similar to rates found in other studies in people with diabetes at high risk for ulceration.[18] Based on research evidence, the in-shoe pressure threshold that is used as target for evaluating custom-made footwear that is provided in clinical practice is 200 kPa.[17, 19, 20] Possibly, the changed foot architecture and the absence of protective subcutaneous fat in the midfoot makes the Charcot foot more vulnerable for ulceration, and a lower threshold than 200 kPa may be required to help prevent ulcers in the midfoot in this population. Furthermore, footwear adherence was close to but not exactly 100%, and the number of steps taken without using protective footwear might have

been sufficient to increase ulcer recurrence risk in this vulnerable group, where every unprotected step can be one too much. This suggests that further improvements in custom-made footwear design and in adherence in general may be required to improve clinical outcome in people with a Charcot midfoot deformity.

Improving footwear adherence

In the second part of the thesis, the aim was to study two separate interventions that may improve adherence to wearing custom-made footwear. In **chapter 4**, motivational interviewing was investigated as intervention to increase the acceptance of footwear by 1) changing the contextual factors, such as communication and service and by 2) influencing the perceived benefits of footwear, by aiming to have participants emphasize the advantages of using custom-made footwear. The effect on footwear adherence was explored by randomly assigning thirteen participants with diabetes, high ulcer risk and low footwear adherence to standard education, or to standard education plus two 45-min sessions of motivational interviewing. The results showed an increase in adherence one week after the motivational interviewing from a median 67% (range 30%-72%) to 90% (range 30%-98). Although the increase was statistically non-significant due to the small number of participants, the effect was considered clinically relevant because most participants increased their adherence levels above the threshold of 80% that has been used in previous research to distinguish adherent from non-adherent people.[17] Away from home, baseline adherence was already high in both study groups and remained high over time. At home, baseline footwear adherence was low and improved from a median 49% (range 6%-63%) at baseline to 84% (range 5%-98%) one week after motivational interviewing, while no increase was seen in the standard education only group. However, three months after the intervention, adherence had returned to baseline levels in the intervention group. The temporary increase in footwear adherence in the intervention group suggests that motivational interviewing has the potential to influence acceptance of footwear by changing contextual factors, and can contribute to the behavior change needed in this group with low footwear adherence (Figure 2). However, the intervention did not have an effect on the long term. This was also found in a meta-analysis of 72 studies that used motivational interviewing as a stand-alone intervention for any form of behavioral change.[21] Combined effect sizes of all studies showed an effect size of 0.77 up to 1 month after the intervention, that decreased to 0.39 at 1-3 months, and 0.11 at >12 months. This indicates that, for a lasting effect on behavior change, repeat or booster sessions of motivational interviewing, or additional interventions may be needed.[21] Interestingly, when motivational interviewing was used in addition to other counseling-style treatments, the effect endured over time, with an effect size maintained around 0.60.[21] This synergistic effect may also be a requirement to preserve footwear adherence in the population studied in this thesis and can for

example be achieved by combining motivational interviewing with cognitive behavior therapy.[22]

Motivational interviewing was feasible for the given purpose and patient group. Basic proficiency was good for the interviewers, following approximately 26 hours of training, and the protocol was straightforward to execute. These outcomes are similar to results found in a recent systematic review investigating the effects of motivational interviewing training.[23] A systematic review of studies comparing trained and untrained groups found that practitioners working in diabetes care were successful in acquiring and applying motivational interviewing skills after a median training duration of 16 hours.[24] This suggests that motivational interviewing can be delivered by a range of professionals, and with a relatively small time investment for training.[24, 25]

The motivational interviewing sessions also provided insight into the reasons for not wearing prescribed footwear at home, and the (in)ability to change behavior. Perception of the benefits of the prescribed footwear seemed to play an important role, corresponding to earlier findings,[13] and covered by the factors "usability" and "quality of life" in the conceptual model (Figure 2). For example, it was repeatedly mentioned that the custom-made footwear was too heavy, and difficult to don and doff. Another reason for not wearing prescribed footwear at home was that participants were convinced that hardly any steps were taken at home (which was not in line with their measured data), and therefore did not need protective footwear at home. In addition, in one case no clear reason could be given, other than that taking of his shoes when going inside the house was a habit, while in another case it was the participants (erroneous) perception that the ulcers were caused by the custom-made footwear. To our knowledge, this was the first study that specifically explored factors for not wearing prescribed footwear at home.

In a published qualitative meta-synthesis, where perceptions and experiences of people with diabetes and foot ulceration were explored, the discomfort of wearing the footwear was also mentioned.[26] The studies in this meta-synthesis did not differentiate between being at home or away from home. It seems likely that the dissatisfaction with factors such as weight and difficulty with donning and doffing are magnified when being at home, especially when the perception is that not many steps are taken at home.

The low adherence indoors in combination with most steps taken indoors found in **chapter 2**, and the reasons for not wearing custom-made footwear at home reported in **chapter 4**, seemed to offer an opportunity for improvement when targeting this specific setting (i.e., footwear use at home). The solution investigated in **chapters 5 and 6** was indoor footwear, targeting therapy-related factors and the perceived relative advantage

of custom-made footwear. In **chapter 5**, the needs and expectations for custom-made indoor footwear were first evaluated via a questionnaire in 50 participants with diabetes and high foot ulcer risk, and already using 'regular' custom-made footwear. Participants indicated a clear wish for using indoor footwear, and they expected such footwear to increase their prescribed-footwear use. From the perspective of usability, appearance was scored as the least important requirement for indoor footwear, and ulcer prevention as the most important requirement. Easy donning and doffing, flexible materials and prevention of cold feet were also scored as important. Appearance as least important characteristic was in contrast with the results of previous studies where it was often found to be important.[11, 13, 27] It seems that different requirements are imposed on indoor custom-made footwear compared to regular custom-made footwear. This can partly result from indoor footwear being less visible beyond the comfort (and safety) of a person's own home, and therefore not perceived by the wearer to draw unwanted attention to their disease,[26, 28] and partly because there is a greater need for comfort in an indoor situation. Based on the outcomes in **chapter 5**, custom-made footwear for specific use indoors was designed according to a systematic approach. A set of 12 requirements was defined and prioritized, with the main requirement being similar offloading capacity as the regular custom-made footwear, being the footwear that would be replaced for indoor use. The indoor footwear was tested in a small group of nine users that already possessed regular custom-made footwear. Peak plantar pressure measurements showed similar or lower pressures than in the regular custom-made footwear, and a qualitative evaluation showed better usability and lower costs for the indoor footwear compared to the regular custom-made footwear.

In **chapter 6**, the effect of having custom-made indoor footwear on footwear use was evaluated in 23 participants with low (<80%) baseline indoor adherence, and 8 participants with high (>=80%) baseline indoor adherence. After provision of the indoor footwear, adherence to wearing custom-made footwear increased significantly in both the short-term (1 month) and long-term (12 months) in the low-adherent participants. Adherence remained high in high-adherent participants, with an increase in use indoors. Eight of the 31 participants (26%) developed a recurrent ulcer during one-year follow-up, of which half had low indoor adherence at baseline. Participants were generally satisfied with their custom-made indoor footwear, and scored most usability aspects positively. According to the WHO model, the indoor footwear changes the therapy-related factor by adding a new pair of footwear. With therapy-related factors influencing adherence, this explains the improved adherence. However, it fails to explain *why* adherence improved. For this, the conceptual model offers a lead. The custom-made indoor footwear improves custom-made footwear adherence by increasing the perceived benefits, or removing the perceived disadvantages of custom-made footwear in the home situation

(such as too much weight or difficulty in donning and doffing). The increased perceived benefits allow for new weighing of benefits in relation to parallel intervention options (e.g. regular footwear or no footwear), This leads to an increase of the perceived relative advantage of the indoor footwear, and subsequently an increase in acceptance and use of the custom-made footwear (Figure 2).

METHODOLOGICAL CONSIDERATIONS

Study design and risk of bias

The small sample sizes in some of the studies in this thesis can be seen as a limitation. The sample assessed in the Charcot study in **chapter 3** originated from a randomized controlled trial.[17] Recruiting 20 participants, also reflects the low incidence of Charcot neuro-osteoarthropathy in the diabetes population. However, given the 0.1-0.3% incidence of Charcot neuro-osteoarthropathy,[29, 30] the sample ratio (20 participants with a Charcot midfoot deformity vs. 118 participants without a Charcot midfoot deformity) can actually be seen as a strength. Further, the sample size is similar to other studies on the Charcot foot.[31-34] The other studies were explorative in nature, for which the sample sizes were considered sufficient to obtain relevant results. This explorative character, however, is associated with higher risk of bias. For example, there may have been selection bias during recruitment for the prototype design study **(chapter 5)** and the adherence study **(chapter 6)**, for which participants were invited by their orthopedic shoe technicians. However, the baseline characteristics of the participants and usability assessments were comparable to what is generally found in other studies.[13, 27] Further, information bias could have been present during the studies where adherence measurements took place. Participants were attempted to be blinded for the goal of the measurement to avoid a change in behavior, by informing them that foot temperature would be measured instead of footwear use. Although this was not formally evaluated afterwards, informal assessment indicated that participants were unaware of the real aim of the measurement. This unawareness of the real aim of measuring footwear use was also seen in the subsequent studies in this thesis, and in ongoing studies (NTR8839). Results of the baseline adherence measurements in the motivational interviewing study **(chapter 4)** were discussed with the participant during the motivational interviewing sessions. Hence, the blinding for the follow-up measurements was lost on purpose. Two further findings, suggest that information bias was limited. First, there was no change in adherence over time in the standard education group, who did not receive feedback on adherence after baseline but were informed about the purpose of measuring foot temperature. Second, adherence returned to baseline levels in the motivational interviewing group, despite that participants now knew what was being measured. This suggests that

no effect was present of knowing the real purpose of the measurement. Lutjeboer et al. found that being aware of the monitoring of footwear use increases adherence with approximately one hour per day only.[35] The information provided to the participants on the purpose of the measurements in their study was more detailed and comprehensive compared with the studies in this thesis. This suggests that the effect in the studies in this thesis was likely negligible.

Adherence measurement

The studies in this thesis measured adherence objectively, which is a strength. Objective measurements result in more valid and reliable data than data collected through self-reporting.[9] However, the diary that was completed by participants to distinguish if a person was at home or away from home was a subjective method. Second, the pedometer worn around the ankle to measure step count could be removed by the participant. This increased the chance of incomplete measurement of the number of steps taken, resulting in lower validity. Although removing the pedometer would result in an underestimation of activity data, the exact effect on adherence is unknown. Depending on whether the pedometer is removed while wearing or not wearing the custom-made footwear, an under- or overestimation of adherence may occur, and on average the effect may be limited. Moreover, by instructing participants to note the periods that the pedometer was not worn in their daily diary, it was possible to filter out these periods. The effect of pedometer non-wearing on adherence was thereby minimized. Third, adherence was measured for seven consecutive days. Although measuring physical activity for seven days is valid and reliable,[36, 37] no such data exists to determine if this period can be seen as representative for the use of footwear. A longer period of measurement may increase validity. Fourth, for feasibility reasons, a maximum of two pairs of custom-made footwear per participant were equipped with the adherence sensor. Some participants possessed more than two pairs, and were then asked to limit their use to these two pairs during the seven days of measurement. Non-prescribed footwear was not measured, although this would have provided valuable information on use of any type of footwear. As a result, it is not clear if the steps that were not taken in custom-made footwear were taken barefoot or in non-prescribed footwear. It is known, however, that of these two conditions, barefoot walking creates the largest risk of foot ulceration.[38] Nevertheless, this is not seen as a limitation in relation to our primary outcome measure, as the focus of this thesis was on adherence to wearing custom-made footwear. A fifth limitation is that information on the time that participants are standing is lacking from the data obtained. The time spent standing can be twice as much as the time while walking in this population.[39] With standing, the foot is continuously loaded. Although peak pressures are lower in standing than in walking, there are indications that prolonged moderate foot loading can delay wound healing.[39] It is therefore possible that

the time standing also plays a role in ulcer recurrence. Insight in wearing custom-made footwear while standing would provide valuable information in this context. Sixth, the temperature sensor was placed in a foam pad that was taped to the inner surface of the lateral shoe border, just below the lateral malleolus. This visible location created the risk of participants being aware of the measurement. Moreover, the relatively large pad was sometimes difficult to place inside the footwear without becoming uncomfortable. This resulted in some missing data, when placing became impossible. Nowadays, smaller sensors are available that can be incorporated in the insole, making it imperceptible for the participant.[35] Currently, studies with these smaller sensors, where longer periods of measurements and standing time are also taken into account are performed by our and other research groups (NTR8839).[40, 41]

CLINICAL IMPLICATIONS

The insights from this thesis on footwear adherence, its determinants, and possible interventions to improve adherence, have implications for daily clinical practice.

First, the results of the studies indicate that footwear adherence measurements should be implemented in daily foot care. One of the recommendations in the current national and international guidelines is to prescribe therapeutic footwear for people at risk for foot ulceration and to motivate the user to wear the footwear at all times.[42, 43] Good footwear alone will not have the desired effect, unless the footwear is worn as recommended. Measuring adherence provides insight in wearing behavior, making it possible to give objective feedback and discuss areas of concern. This will likely help improve footwear adherence.

Second, the measurements and interventions can identify personal factors in shoe-wearing behavior. For example, in the study reported in **chapter 4** it was discovered through motivational interviewing that one of the participants was not willing to wear the prescribed footwear. He was convinced that his custom-made footwear was the cause of his ulcers. This phenomenon has also been described in a recent review.[26] Without first attempting to resolve such barriers, it will be challenging to improve footwear adherence. It is therefore recommended for clinical practice to first identify reasons of non-use of the prescribed footwear when footwear adherence is found to be low. This could take place during normal consultations hours with healthcare professionals. This is preferably done embedded in a motivational interviewing session, but should as a minimum follow the basic principles of motivational interviewing during a normal consultation. The (inter)national guidelines on ulcer prevention recommend educating the

patient, family and health care professionals. The aim is to improve self-care knowledge and self-protective behavior and to enhance their motivations and skills to facilitate adherence.[43, 44] Extending this by exploring reasons for non-use will likely eventually lead to better outcomes on ulcer prevention.

Third, people with low adherence while being indoors can benefit from having custom-made indoor footwear. This implies that prescribers and shoe technicians should become familiar with this prescription option and apply it in patient care. Such indoor footwear should follow the design rules as used in these studies **(chapters 5 and 6)**. The design developed in this study provides evidence for adequate pressure relieve and good usability. Moreover, it can be produced at relatively low cost compared to the already existent custom-made footwear **(chapter 5)**. When provision of custom-made footwear is discussed with the intended user, a careful consideration has to be made on providing custom-made indoor footwear. Its value can be found in improving footwear adherence, but also in improving usability and satisfaction. Key aspects include the ratio between indoor and outdoor activity, and satisfaction with the usability of the current custom-made footwear. Reimbursement options may play a role in whether such footwear can be successfully implemented in everyday foot care.

RECOMMENDATIONS FOR FUTURE RESEARCH

With current prediction models on factors contributing to footwear adherence still insufficiently accurate, adherence depends on multiple, partly unknown factors. It is therefore recommended to continue research into these factors, as they are essential in guiding practitioners to potential successful interventions. Besides usability, therapy- and patient-related factors, also health-system related, social/economic related and condition-related factors should be considered in future research. Furthermore, the personal weighing of each of these determinants by the individual needs to be measured. Prediction models might be more successful if focused less on predicting adherence in people with diabetes at a group level, and more on interventions to improve adherence on an individual level, taking the individual wishes and characteristics into account. This idea is supported by the shift that is already seen in clinical care from a one approach for all to a more personalised approach, which will likely lead to better care towards ulcer prevention.[45] Such studies may also test and improve theoretical models on adherence, such as the two used in this thesis (Figure 1 and Figure 2).

Several studies indicated that a single-factor approach will have a limited effect on adherence to health behaviors.[1, 45] The studies in this thesis were also based on a single-factor

approach. The initial improvement in footwear adherence in the short-term, but decline in the long-term in the study where motivational interviewing was applied **(chapter 4)**, allows for two recommendations for future research. First, to sustain a long-term effect of motivational interviewing, this single-factor approach can be extended by repeat or booster sessions of motivational interviewing. Second, investigating if a multi-factor approach can better preserve footwear adherence. It is likely that combining interventions increases the chance of higher acceptance of the footwear and therefore better footwear adherence. Motivational interviewing could for example be used in addition to other counseling-style treatment, such as cognitive behavior therapy. Inspired by the results of the explorative study on motivational interviewing, an RCT that assesses the effect of motivational interviewing combined with digital shoe-fitting on footwear adherence is ongoing.[40] Furthermore, providing custom-made indoor footwear improved footwear adherence in both the short-term and the long-term **(chapter 5 and 6)**. It is therefore recommended to confirm these results in an RCT design, and study the effect of providing indoor footwear on ulcer prevention in this group at high ulceration risk. An ongoing RCT of which its design is based on several studies in this thesis aims at reducing ulcer recurrence with the help of a state-of-the-art personalised approach. This includes the provision of indoor footwear and multiple sessions of motivational interviewing (NCT05236660).

In research, as well as in clinical practice, a 200 kPa peak pressure threshold level is used as a target pressure for the provision of footwear. This is based on pressure measurements in the forefoot or midfoot.[17, 19, 20] One can argue whether this one threshold for all foot regions and activities is desirable in the complex area of diabetic foot disease. In **chapter 3**, the comparable ulcer recurrence rate between the Charcot and non-Charcot groups, suggests that for Charcot midfoot deformities another pressure threshold than 200 kPa might be required. Recently, a data-driven footwear design algorithm has been developed, including an algorithm aiming to effectively reduce peak plantar pressure.[46] Although this algorithm takes the different foot types and deformities into account, the cut-off threshold for all foot types, deformities and regions is kept at 200 kPa. It is therefore recommended to strengthen such an algorithm by defining subgroups or specific foot regions with their own target pressure thresholds.

GENERAL CONCLUSION

This thesis provides insight into the adherence to wearing custom-made footwear and its determinants in people with diabetes who are at a high risk for plantar foot ulceration, and in a subgroup of people with Charcot midfoot deformity. People with diabetes and

custom-made footwear wear their prescribed footwear less at home, compared to being away from home. However, they take more steps while at home, aggravating the problem of lower adherence. This poses a greater risk for ulcer recurrence compared to when being away from home, and interventions aiming to improve footwear adherence in this group of persons at high ulcer risk should therefore specifically target the situation at home. Furthermore, patient-related and therapy-related factors do not sufficiently explain if people with diabetes use their prescribed footwear. This suggests that other factors possibly also play a role, and possibly should be assessed on an individual level.

This thesis also provides insight into the effects of behavioral and shoe-specific interventions on adherence to wearing custom-made footwear in people with diabetes and a healed plantar ulcer. Two sessions of motivational interviewing improve footwear use only in the short-term. Custom-made footwear that was specifically designed for indoor use improves footwear use in the short-term and the long-term. Indoor footwear is therefore a helpful intervention for clinical practice to reduce non-adherence to wearing custom-made footwear. Altogether, the findings reported in this thesis provide several relevant options for improving clinical practice and give clear indications for further research, aiming to help prevent foot ulcer recurrence in people with diabetes.

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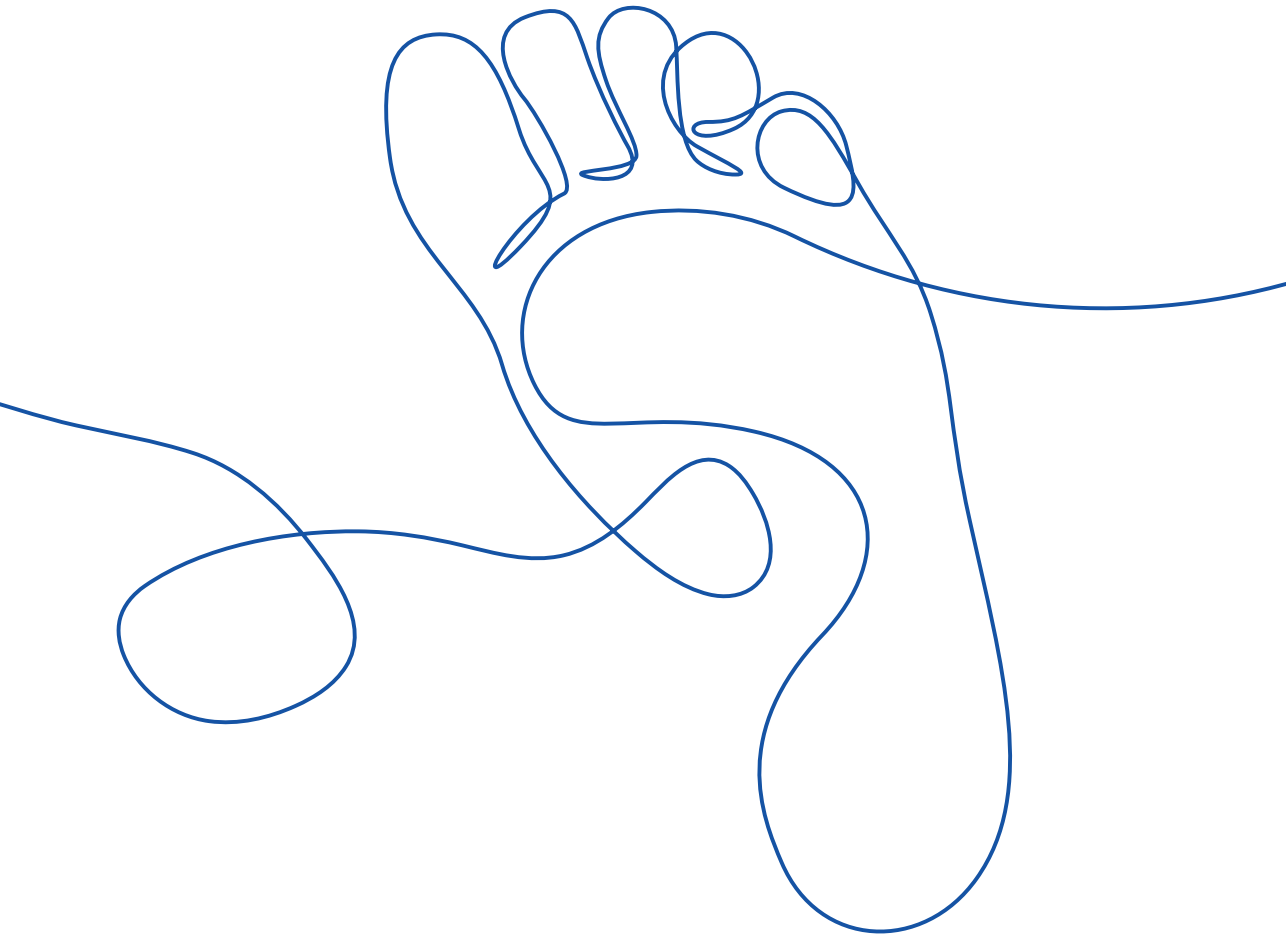


Summary

SUMMARY

The number of people with diabetes is still increasing worldwide, and with that its acute and chronic complications. One of the most frequently occurring complications is diabetic foot disease, which includes several pathologies. The development of a foot ulcer is one of these, and occurs in up to 34% of people with diabetes. A key risk factor for foot ulceration is polyneuropathy, which leads to abnormal biomechanical loading of the foot. This results in high mechanical stress at specific locations that can ultimately lead to skin breakdown. Once an ulcer is present, quality of life is reduced, and risk of infections, amputations, and premature death is increased. Foot ulcer treatment is complex, and even after successful healing 40% of patients develop a recurrent ulcer within one year. The major impact of ulcers on quality of life, and the demand on health services and economic costs thereof, makes ulcer prevention of fundamental importance.

Custom-made footwear that is being worn can help prevent foot ulceration, by providing proper fit and redistributing peak plantar pressures. Ensuring routine wearing of custom-made footwear is therefore recommended in (inter)national guidelines on ulcer prevention. Even though there are signals that adherence to wearing custom-made footwear is low in daily practice, recent evidence is lacking. The aim of this thesis was therefore twofold. First, to gain insight in the adherence to wearing custom-made footwear and the determinants of adherence in a group of people with diabetes who are at high risk for plantar foot ulceration and in a subgroup of people with Charcot midfoot deformity. Second, to gain insight in how adherence to wearing custom-made footwear in people with diabetes and a healed plantar foot ulcer could be improved by assessing the effects of motivational interviewing and the provision of custom-made footwear that was specifically designed for indoor use.

The outline and aims of this thesis were introduced in **chapter 1**. It provided insight in the problem of diabetic foot disease, specifically diabetic foot ulceration. The pathogenesis of diabetic foot ulcers was explained, as well as the risk of ulcer recurrence. The current guidelines on foot ulcer prevention were summarized, with a focus on the key cornerstone of this thesis: ensuring the routine wearing of appropriate footwear.

The study in **chapter 2** objectively assessed adherence to wearing custom-made footwear during seven consecutive days in 107 people with diabetes at high risk for ulcer recurrence. Moreover, determinants of adherence were evaluated. Seventy-one percent of steps were taken with custom-made footwear and adherence was significantly lower at home than away from home, while more steps were taken at home. Therefore, interventions aiming to improve adherence should mainly focus on the situation at home.

Determinants associated with higher adherence were better perception of footwear aesthetics, lower BMI, severe foot deformity, history of amputation, and more day-to-day variation in activity. However, overall explained variance was only 18%, which indicated that predicting footwear adherence is difficult. It was therefore recommended to continue to research not only these usability, therapy- and patient-related and factors, but also other factors, such as health-system related, social/economic related and condition-related factors.

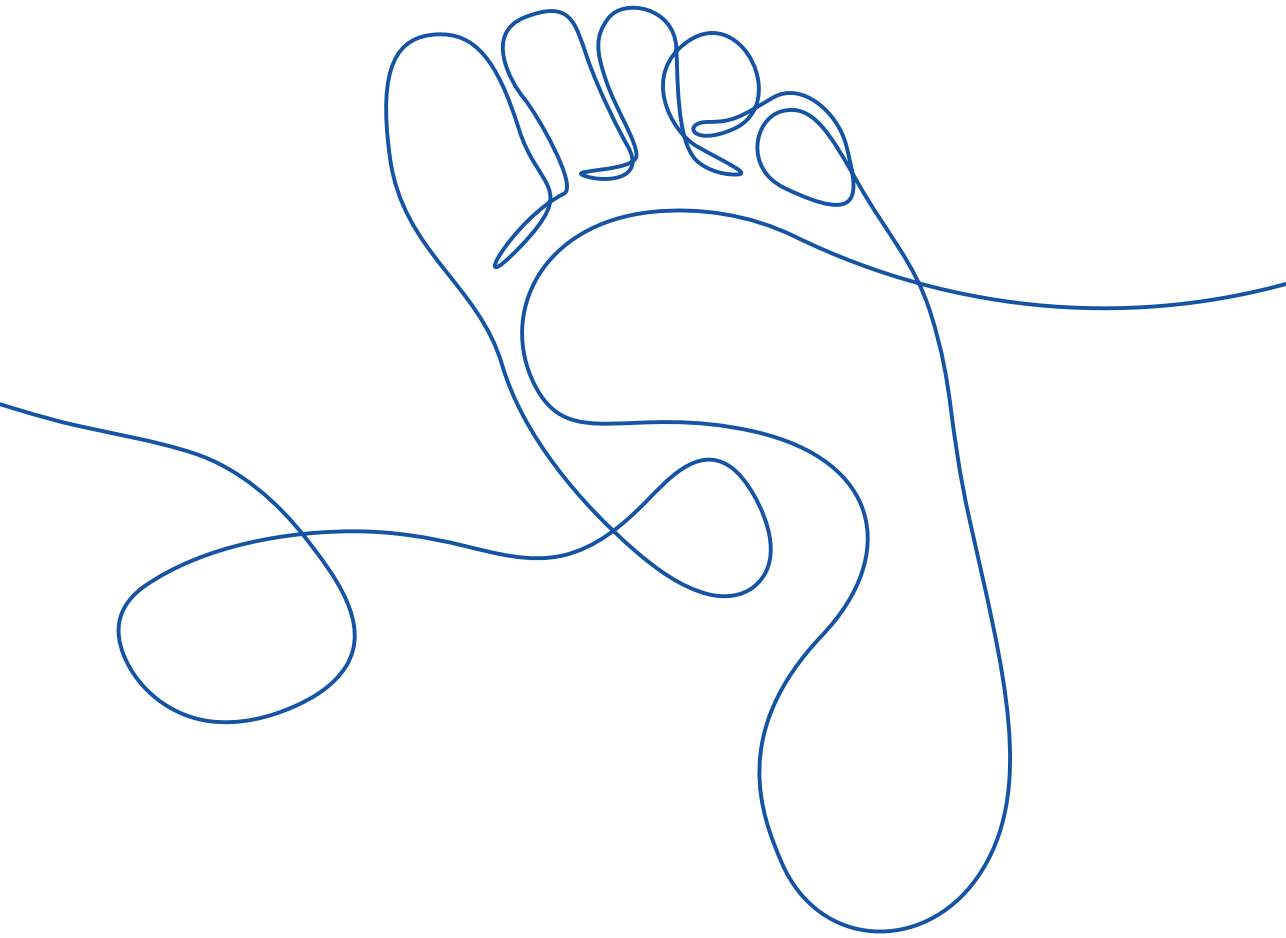
The research described in **chapter 3** focused on people with diabetes at high risk for foot ulceration with custom-made footwear and a Charcot midfoot deformity. In twenty participants, footwear adherence, biomechanical factors and plantar foot ulcer recurrence over 18 months were analyzed. This group was compared with 118 participants without a Charcot midfoot deformity, but with custom-made footwear and high risk for ulceration. People with a Charcot midfoot deformity were significantly more adherent than people without a Charcot midfoot deformity. Adherence at home was particularly higher in this group. Barefoot midfoot peak pressures were significantly higher in the group with Charcot midfoot deformity, while in-shoe midfoot peak pressures were comparable with the group without Charcot midfoot deformity, and significantly lower for all other foot regions. Plantar ulcer recurrence in 18 months in the group with a Charcot midfoot deformity was comparable to that of the group without Charcot midfoot deformity. These results suggest that further improvements in both adherence and custom-made footwear design are required to reduce ulcer recurrence risk in people with a Charcot midfoot deformity.

In **chapter 4**, the effect of using motivational interviewing on footwear adherence was assessed in people with diabetes who are at high risk for foot ulcer recurrence and show low adherence to custom-made footwear. In this explorative trial, thirteen participants were randomly assigned to standard education, or standard education plus two 45-min sessions of motivational interviewing. Overall, adherence improved one week after motivational interviewing. This was mainly the result of an increase in adherence at home. Although the increase was statistically non-significant due to the small number of participants, the effect was considered clinically relevant. Three months after the motivational interviewing sessions, adherence had returned to baseline levels. The increase in the short-term and decrease in the long-term was also seen in other studies on behavioral change that used motivational interviewing as intervention. This might indicate that repeat or booster sessions, or additional interventions might be needed to preserve the improved footwear adherence.

The research described in **chapter 5** focused on evaluating the needs and expectations of custom-made footwear especially designed for indoor use. Fifty participants, with diabetes at high foot ulcer risk, and already in the possession of 'regular' custom-made footwear completed a questionnaire. A clear need for custom-made indoor footwear was indicated and they expected that such footwear would improve their footwear adherence. Ulcer prevention was scored as the most important requirement for indoor footwear, and cosmetic appearance as the least important requirement. Other important requirements were easy donning and doffing, flexible materials and prevention of cold feet. As a result of these outcomes, a set of requirements for custom-made indoor footwear was systematically established by a multi-disciplinary team, and the resulting shoe design tested in nine users. The most important requirement, i.e., similar offloading as the regular custom-made footwear, was achieved. Users scored the indoor footwear as superior in usability and, moreover, it could be produced at lower cost than regular custom-made footwear.

In **chapter 6**, the effect of custom-made indoor footwear on footwear adherence was evaluated in people with diabetes at high risk for plantar for ulceration and already in the possession of regular custom-made footwear. Twenty-three participants with low (<80%) baseline indoor adherence, and 8 participants with high (>=80%) baseline indoor adherence were provided with custom-made indoor footwear. Adherence to wearing custom-made footwear increased significantly in both the short-term and the long-term in participants with low indoor adherence at baseline. This was due to a significant increase in adherence at home. High-adherent participants sustained their high adherence, with increased indoor use. Eight of the 31 participants developed a recurrent ulcer, four of them had low indoor adherence at baseline. The indoor and regular custom-made footwear had comparable mean peak plantar pressures. Participants were generally satisfied with their custom-made indoor footwear and scored most usability aspects positively. It was therefore recommended to confirm these results in a randomized controlled trial, and to study the effect of custom-made indoor footwear on preventing foot ulceration in this group at high ulceration risk.

The main findings of the studies in this thesis were discussed in **chapter 7** by using the two adherence models that were introduced in **chapter 1**. Methodological considerations were described, and recommendations for clinical practice and future research were given.



Samenvatting

SAMENVATTING

Het aantal mensen met diabetes neemt wereldwijd nog steeds toe, en daarmee ook het aantal acute en chronische complicaties. Een van de meest voorkomende complicaties is diabetische voetziekte, wat verschillende ziektebeelden omvat. De ontwikkeling van een voetulcus (voetwond) is daar één van. Tot wel 34% van de mensen met diabetes krijgt hier in hun leven mee te maken. Een belangrijke risicofactor voor het krijgen van een voetulcus is polyneuropathie, wat leidt tot een abnormale biomechanische belasting van de voet. Dit resulteert in hoge mechanische stress op specifieke locaties, wat uiteindelijk kan leiden tot huidbeschadiging. Als een voetulcus eenmaal is ontstaan, neemt de kwaliteit van leven af en neemt het risico op infecties, amputaties en vroegtijdig overlijden toe. De behandeling van voetulcera is complex en zelfs na succesvolle genezing ontwikkelt 40% van de patiënten binnen een jaar een recidief voetulcus. Vanwege de grote impact op de kwaliteit van leven, de gezondheidszorg en bijbehorende economische kosten is het voorkomen van voetulcera van fundamenteel belang.

Orthopedisch maatschoeisel dat wordt gedragen kan een voetulcus voorkomen door een goede pasvorm te bieden en piekdrukken te herverdelen. Het routinematig dragen van orthopedisch maatschoeisel wordt daarom aanbevolen in (inter)nationale richtlijnen voor de preventie van voetulcera. Hoewel er signalen zijn dat het dragen van orthopedisch maatschoeisel in de dagelijkse praktijk weinig wordt nageleefd, ontbreekt recent wetenschappelijk bewijs. Het doel van dit proefschrift was daarom tweeledig. Ten eerste, inzicht krijgen in de therapietrouw van het dragen van orthopedisch maatschoeisel en de determinanten van therapietrouw bij een groep mensen met diabetes met een hoog risico op plantaire voetulcera en bij een subgroep van mensen met een Charcot middenvoetsdeformatie. Ten tweede, inzicht krijgen in hoe de therapietrouw van het dragen van orthopedisch maatschoeisel bij mensen met diabetes en een genezen plantair voetulcus verbeterd kan worden, door de effecten te onderzoeken van motiverende gespreksvoering en het verstrekken van orthopedisch maatschoeisel dat speciaal ontworpen is voor gebruik binnenshuis.

In **hoofdstuk 1** zijn de opzet en doelstellingen van dit proefschrift geïntroduceerd. Het probleem van diabetische voetziekte, in het bijzonder het diabetische voetulcus, is inzichtelijk gemaakt. De pathogenese van een diabetisch voetulcus is uitgelegd, evenals het risico op een recidief voetulcus. De huidige richtlijnen voor preventie van voetulcera zijn samengevat, met de nadruk op het belangrijkste onderdeel daarvan voor dit proefschrift: het waarborgen van het routinematig dragen van adequaat schoeisel.

In de studie in **hoofdstuk 2** is de therapietrouw van het dragen van orthopedisch maatschoeisel gedurende zeven opeenvolgende dagen objectief gemeten bij 107 mensen met diabetes en een hoog risico op het krijgen van een recidief voetulcus. Tevens zijn determinanten van therapietrouw geëvalueerd. Van alle stappen werd 71% gezet met orthopedisch maatschoeisel. De therapietrouw was thuis significant lager dan buitenshuis, terwijl er thuis meer stappen werden gezet. Interventies gericht op het verbeteren van therapietrouw zouden daarom vooral gericht moeten zijn op de thuissituatie. Factoren geassocieerd met hogere therapietrouw waren een betere perceptie van de schoenesthetiek, lagere BMI, ernstige voetafwijkingen, een voorgeschiedenis van amputaties en meer variatie in dagelijkse activiteit. Echter, de totale verklaarde variantie was slechts 18%, wat aangaf dat het verklaren van therapietrouw op basis van de gemeten variabelen moeilijk was. Het werd daarom aangeraden om niet alleen deze bruikbaarheid-, therapie- en patiëntgerelateerde factoren te onderzoeken, maar in toekomstig onderzoek ook andere factoren mee te nemen, zoals factoren gerelateerd aan de gezondheidszorg, sociaal-economische omstandigheden en diabetes.

Het onderzoek in **hoofdstuk 3** richtte zich op mensen met diabetes en een hoog risico op een voetulcus die orthopedisch maatschoeisel hebben en een Charcot middenvoetsdeformatie. Bij twintig deelnemers zijn therapietrouw, biomechanische factoren en het optreden van een recidief voetulcus gedurende een periode van 18 maanden geanalyseerd. Deze groep is vergeleken met 118 deelnemers met een hoog risico op een voetulcus, in het bezit van orthopedisch maatschoeisel, maar zonder een Charcot middenvoetsdeformatie. Mensen met een Charcot middenvoetsdeformatie waren significant therapietrouwer dan mensen zonder een Charcot middenvoetsdeformatie. Met name de therapietrouw thuis was hoger in deze groep. De blootsvoetse piekdruk onder de middenvoet was significant hoger in de groep met Charcot middenvoetsdeformatie, terwijl de piekdruk in de schoenen onder de middenvoet vergelijkbaar was ten opzichte van de groep zonder Charcot middenvoetsdeformatie en significant lager voor alle andere regio's onder de voet. Het aantal recidive voetulcera in 18 maanden in de groep met Charcot middenvoetsdeformatie was vergelijkbaar met dat van de groep zonder Charcot middenvoetsdeformatie. Dit suggereerde dat zowel de therapietrouw als het design van orthopedisch maatschoeisel verder verbeterd moet worden om bij te dragen aan het verminderen van recidive voetulcera bij mensen met een Charcot middenvoetsdeformatie.

In **hoofdstuk 4** is het effect van motiverende gespreksvoering onderzocht op de therapietrouw van het dragen van schoeisel bij mensen met diabetes die niet therapietrouw zijn en die een hoog risico op re-ulceratie hebben. In deze exploratieve studie werden dertien deelnemers willekeurig toegewezen aan standaard voorlichting of standaard

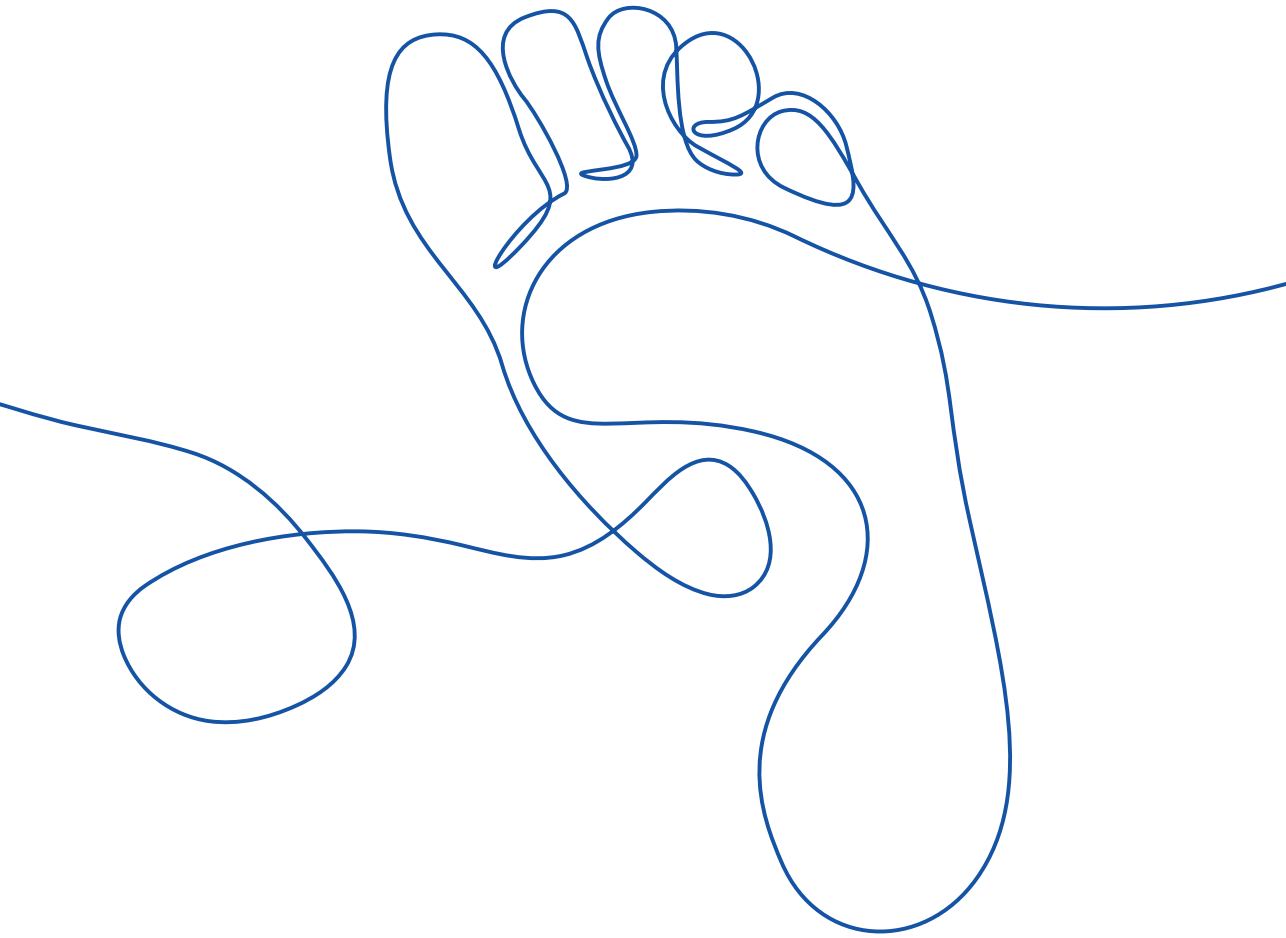
voorlichting plus twee sessies van 45 minuten motiverende gespreksvoering. De totale therapietrouw verbeterde een week na de motiverende gespreksvoering. Dit was voornamelijk het gevolg van een toename van de therapietrouw thuis. Hoewel de toename statistisch niet significant was vanwege het kleine aantal deelnemers, werd het effect beschouwd als klinisch relevant. Drie maanden na de motiverende gespreksvoering was de therapietrouw terug op het uitgangsniveau. De toename op korte termijn en afname op lange termijn werd ook gezien in andere studies naar gedragsverandering die motiverende gespreksvoering gebruikten als interventie. Mogelijk zijn herhaal- of boostersessies, of aanvullende interventies nodig om een toegenomen therapietrouw te behouden.

Het onderzoek in **hoofdstuk 5** richtte zich op de evaluatie van de behoefte aan en verwachtingen van orthopedisch maatschoeisel speciaal ontworpen voor gebruik binnenshuis (orthopedische huisschoen). Vijftig deelnemers met diabetes en een hoog risico op voetulcera, die al in het bezit waren van 'regulier' orthopedisch maatschoeisel, kregen een vragenlijst voorgelegd. Er was een duidelijke behoefte aan een orthopedische huisschoen en de verwachting was dat dergelijk schoeisel de schoentevredenheid verbetert. Preventie van ulcera werd als belangrijkste eis gezien voor een orthopedische huisschoen en het uiterlijk van de schoen als minst belangrijke eis. Andere belangrijke eisen waren gemakkelijk aan- en uittrekken, flexibele materialen en het voorkomen van koude voeten. Naar aanleiding van deze uitkomsten werd door een multidisciplinair team systematisch een pakket van eisen opgesteld waaraan de orthopedische huisschoen moest voldoen. Het resulterende schoenontwerp werd getest bij negen gebruikers. Aan de belangrijkste eis, een vergelijkbare drukverdeling ten opzichte van het reguliere orthopedische maatschoeisel, werd voldaan. De gebruikers scoorden de orthopedische huisschoen als superieur in gebruiksvriendelijkheid en bovendien kon de schoen tegen lagere kosten worden geproduceerd dan regulier orthopedisch maatschoeisel.

In **hoofdstuk 6** is het effect van orthopedische huisschoenen op de therapietrouw van het dragen van schoeisel geëvalueerd bij mensen met diabetes en een hoog risico op voetulcera en die al in bezit waren van regulier orthopedisch maatschoeisel. Drieëntwintig deelnemers met een lage (<80%) therapietrouw binnenshuis en acht deelnemers met een hoge (>=80%) therapietrouw binnenshuis kregen orthopedische huisschoenen. De totale therapietrouw van het dragen van orthopedisch maatschoeisel nam zowel op korte termijn als op lange termijn significant toe bij deelnemers die een lage therapietrouw hadden op baseline. Dit was het gevolg van een significante toename van de therapietrouw binnenshuis. Deelnemers met een hoge therapietrouw op baseline behielden dit, waarbij de therapietrouw binnenshuis toenam. Acht van de 31 deelnemers ontwikkelden een recidief ulcus; vier van hen hadden een lage therapietrouw binnenshuis op

baseline. De orthopedische huisschoen en het reguliere orthopedische maatschoeisel hadden vergelijkbare gemiddelde plantaire piekdrukken. De deelnemers waren over het algemeen tevreden met hun orthopedische huisschoen en scoorden deze positief op de meeste gebruiksaspecten. Daarom werd aanbevolen om deze resultaten te bevestigen in een gerandomiseerde studie, om het effect van orthopedische huisschoenen op het voorkomen van ulcera in deze groep met een hoog risico op voetulcera te evalueren.

De belangrijkste bevindingen van de studies in dit proefschrift werden besproken in **hoofdstuk 7** en geplaatst in de in **hoofdstuk 1** geïntroduceerde therapietrouwmodellen. Daarnaast werden methodologische overwegingen bediscussieerd, en aanbevelingen gedaan voor de klinische praktijk en toekomstig onderzoek.



Dankwoord

DANKWOORD

En dan is het proefschrift af! Dat komt zeker niet alleen door mijn eigen inzet. Veel dank aan iedereen die hier aan bijgedragen heeft, in het bijzonder:

Alle deelnemers die belangeloos hun tijd en energie in de studies hebben gestoken. Dank dat jullie meerdere malen langskwamen voor de metingen, en mij zo gastvrij ontvingen tijdens de huisbezoeken.

Mijn begeleidend team, prof. dr. Sicco Bus, prof. dr. Frans Nollet en dr. Jaap van Netten. Beste Sicco, dankjewel dat je mij de mogelijkheid gaf om onderzoek te doen naast mijn werk in het bewegingslab. Dat dat zou resulteren in een proefschrift had ik van te voren niet bedacht. Ik bewonder je onderzoekskwaliteiten, focus en oog voor detail. Beste Frans, in de klinische zorg werken we al jaren prettig samen, en in dit PhD-traject was je als promotor naast Sicco wat meer op de achtergrond. Toch was je altijd bereikbaar op momenten dat dat nodig was en voorzag je me van heldere en kritische feedback, dank daarvoor. Beste Jaap, ik wens elke PhD-student een dagelijkse begeleider zoals jou toe. Je heldere en snelle communicatie, kritisch maar motiverend, en je vermogen om in te schatten wat ik nodig had hebben me veel werkplezier gegeven. Ik vind het heel leuk dat ik nu nog steeds met je samenwerk in de klinische zorg.

De leden van mijn promotiecommissie, prof. dr. Max Nieuwdorp, prof. dr. Frank Snoek, prof. dr. Nathalie van der Velde, dr. Fieke Koopman, prof, dr. Noël Keijsers en dr. Louise Sabelis. Dank voor jullie kritische beoordeling van mijn proefschrift.

I would like to thank my co-authors dr. Ruth Barn and prof. Jim Woodburn for their collaboration and helpful insights during the writing of the article on Charcot midfoot deformities.

Dank ook aan co-auteurs dr. Mirjam de Haart en dr. Maarten Merkx voor hun bijdrage. Beste Mirjam, jij gaf mij de kans om als auteur mee te schrijven aan het eerste artikel in dit proefschrift, dat ben ik nooit vergeten. Beste Maarten, dank voor je trainingen in motiverende gespreksvoering, ik heb er nog steeds profijt van.

Het multidisciplinaire team van het huisschoenen-project, in het bijzonder de orthopedische schoenmakers Jan Pulles, Bart van Heerenbeek en Sjakko Lieben. Wat mooi om te zien dat jullie het concept nog steeds toepassen in de dagelijkse praktijk.

Mijn collega's van het Amsterdam UMC Center for Diabetic foot Complications. Het is een voorrecht om met zo'n bevlogen team van artsen, podotherapeuten, physician assistants, doktersassistenten, wondverpleegkundigen, orthopedische schoenmakers, bewegingslaboranten en onderzoekers de zorg rondom de diabetische voet vorm te geven. Drs. T.E. Busch-Westbroek, beste Tessa, jouw ervaring, sterke klinische blik en verantwoordelijkheid naar je patiënten toe, maken dat ik elke patiënt met diabetische voetziekte jou als arts gun. Dank ook voor je wetenschappelijke bijdrage aan mijn artikelen. Prof. dr. Max Nieuwdorp, beste Max, je omschreef ons team eens als de bastaards. Het voorkomen en oplossen van complicaties aan de voet lijkt soms wat ondergewaardeerd in de gezondheidszorg, maar we doen het met zijn allen graag. Met het VUmc team nu ook aan onze zijde kan de zorg alleen maar beter worden. Ik vind het dan ook heel leuk dat ik met jou en dr. Louise Sabelis over de inhoud van mijn proefschrift mag discussiëren tijdens mijn verdediging. Jan en Ghizella, we werken nauw en fijn samen om de patiënt de juiste schoen mee naar huis te geven. Jan, na zoveel jaar samenwerken weet ik nog steeds niet wanneer je een grap maakt of serieus bent, het maakt ook niet uit. Dank voor jullie kundigheid en gezelligheid.

Collega's en oud-collega's bewegingslaboranten, Hilde, Nicoline, Roelof, Tim, Jennefer, Jessie, Jana, Jaap, Niels, Chantal, Marjolein P, Koen, Elza, en leidinggevenden Marleen en Marjolein vd K. Dank voor de fijne samenwerking in het lab. En dank aan de huidige laboranten dat jullie mij in de eindfase hier en daar de tijd gaven om aan een artikeltje te schaven, een response in te dienen en dit proefschrift af te ronden. Hilde, dat jij straks aan mijn zijde staat als paranimf voelt zo vanzelfsprekend. Wat hebben we de afgelopen jaren veel gedeeld over werk-, thuis- en andere zaken. Dankjewel voor je hulp bij de laatste loodjes van het promoveren, en dat je zo'n fijne collega bent.

(oud-)Collega's buiten het lab. Dank voor de fijne samenwerking, gezelligheid en lunchwandelingen. In het bijzonder bedankt aan mijn oud-collega's Erik Slim, Mark, Roelof, Dominique, Fieke en Eva. Beste Erik, ik zette als onderzoeksassistent tijdens jouw PhD-traject mijn eerste stappen in het doen van onderzoek. De stap van voetproblemen als gevolg van lepra naar de diabetische voet was daardoor een logische. Mark en Roelof, ik mocht jullie assisteren tijdens jullie PhD-traject en dit was mijn eerste ervaring met het meedraaien in een heuse RCT. Wie had toen kunnen denken dat jouw artikel Roelof, het eerste artikel van mijn proefschrift zou worden. Ik niet! Fijn dat we nog regelmatig bijkletsen tijdens een etentje, borrel of congres. Het is altijd weer gezellig als vanouds! Dominique, Fieke en Eva, we leerden elkaar kennen op de afdeling Revalidatiegeneeskunde, en hoewel twee van jullie zijn uitgefladderd zien we elkaar nog met enige regelmaat tijdens onze etentjes in de lekkerste restaurants van Amsterdam. Heel fijn! En wat bijzonder dat jij mijn opponent bent Fieke.

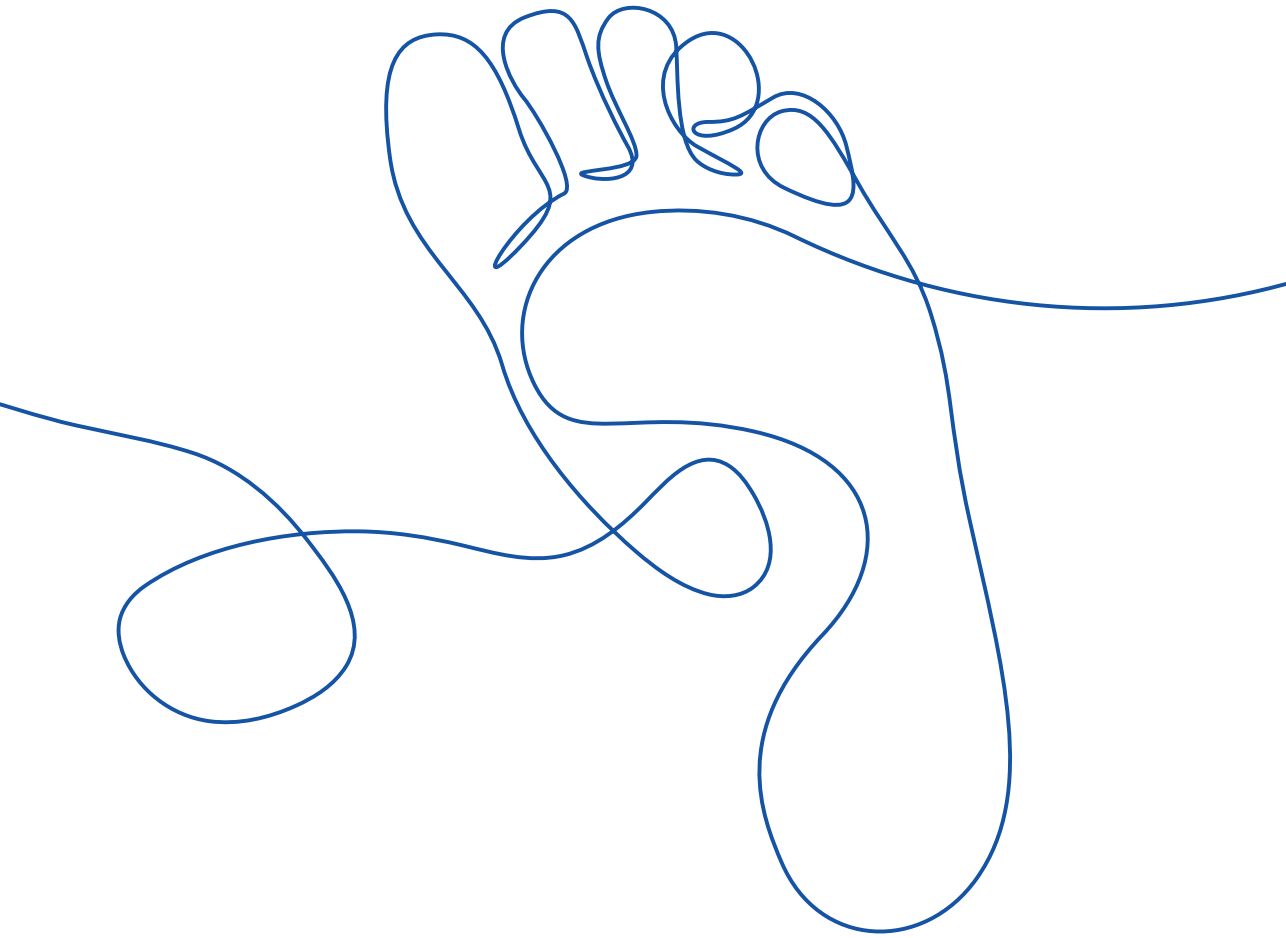
Mijn lieve vrienden, die soms geen idee hadden waar ik nou precies mee bezig was maar toch geïnteresseerd bleven en support gaven als dat nodig was. Lars, Sabrina en Simone, we leerden elkaar kennen op de peuter- en kleuterschool, en onze vriendschap is nooit meer overgegaan. Als we elkaar (na meestal lange tijd) weer zien, zijn onze gesprekken hetzelfde, lachen we nog net zo hard om elkaar en voelt het altijd als vanouds. Yvette, wat begon als een goede buur, is uitgegroeid tot een goede vriendin. Ondanks de drukte weten we meestal wel ergens een gaatje te vinden om bij te kletsen in een koffietentje, tijdens een wandeling of een etentje. Ik kan altijd op je terugvallen als dat nodig is, dankjewel daarvoor.

Nelie, ik ontmoette je in Australië, waar we beiden stage liepen. Na een aantal geslaagde uitstapjes aldaar, werd al snel duidelijk dat we samen meer wilden zien van de wereld. En dat lukte! Wat een bonus dat ik jouw grote vriendin Anne leerde kennen, en we inmiddels al jaren onze uitjes, vakanties en etentjes met zijn drieën voortzetten. Lieve meisjes, dank voor jullie vriendschap, gezelligheid en voor het feit dat ik altijd mezelf kan zijn. Ik ben zo blij dat jullie mijn paranimfen zijn!

En niet te vergeten, mijn familie en schoonfamilie. Bedankt voor jullie steun, betrokkenheid en interesse. Lieve papa en mama, het was soms lastig uit te leggen waar ik nu al die tijd mee bezig was, hoewel het op het eind steeds concreter werd. Dank jullie wel voor die keren dat Lou en Teun bij jullie konden spelen en logeren, terwijl ik in jullie werkkamer met vers geperste jus d'orange en uitzicht op de mooie bloementuin verder kon werken aan dit proefschrift. Lieve Martine, je bent er altijd voor mij, wat fijn dat jij mijn zus bent.

Lieve Lou en Teun, door jullie enthousiasme, verwondering om de kleinste dingen en onophoudelijke knuffels leren jullie mij elke dag weer te relativeren en te leven in het hier en nu. Dankjulliewel daarvoor.

Lieve Tim, het was soms een bumpy ride, maar wel een die ik met niemand anders had willen doen. Ik hou van je optimisme, je blik op de wereld en je vertrouwen in mij. Ik ben je ongelooflijk dankbaar voor je liefde en steun, en de ruimte die je me gaf om te kunnen werken aan dit proefschrift. Op naar mooie nieuwe avonturen met zijn viertjes!



Curriculum Vitae & Portfolio

CURRICULUM VITAE

Renske Keukenkamp was born on February 11th 1978, in Doetinchem, The Netherlands. She graduated from high school at the Ulenhof College in Doetinchem in 1996. Between 1997 and 2001 she studied Physiotherapy at the Hogeschool Arnhem en Nijmegen, in Nijmegen. After obtaining her Bachelor's degree, she started working as a physiotherapist. During her work as a physiotherapist, she decided to deepen her knowledge by enrolling in a Biomedical Sciences program with a specialization in Human Movement Sciences, at the Radboud University in Nijmegen in 2002. After completing a research internship at the University of Queensland in Gold Coast, Australia, she obtained her Master's degree in 2005.

In 2007, Renske started working at the Laboratory for Clinical Movement Analysis, at the department of Rehabilitation Medicine of Amsterdam UMC, location AMC. She conducts a range of clinical human movement measurements, such as 3D-gait analysis, electromyography, walking energy cost, muscle force and foot pressure assessments. Her work primarily focuses on neuromuscular disorders, orthotics, diabetic foot disease and custom-made footwear, while also incorporating teaching and research.

The first research project she participated in, was a project on functioning with leprosy impairments in the Netherlands in 2007. This was followed by her involvement in the Actigait study in 2009, which assessed the effect of an implanted functional electrical stimulation device on walking skills in stroke patients with drop foot. In 2010, she took her first steps into the area of diabetic foot disease by assisting in the DIAbetic Foot Orthopedic Shoe (DIAFOS) trial. This study resulted in the first publication of this thesis. Subsequently, Renske conducted a study in 2013 to assess the efficacy of motivational interviewing on footwear adherence in people with diabetic foot disease. This study resulted in the second publication of her thesis.

In 2018, Renske was offered to pursue a PhD program that would allow her to build on her previous publications about diabetic foot disease. Specifically, she would conduct further research on the topic of adherence to wearing custom-made footwear in persons with diabetes who are at high risk for developing plantar foot ulcers. This resulted in the remaining publications for this thesis.

Currently, she continues to work at the Laboratory for Clinical Movement Analysis with the aim of developing her skills in the area of diabetic foot disease, behavioural change and clinical gait analysis.

PORTFOLIO

PhD student: Renske Keukenkamp
Research Period: Part-time (1 day/week) from June 2010 – July 2020*
*PhD trajectory formally started in January 2018
PhD supervisors: Prof. dr. S.A. Bus, Prof. dr. F. Nollet, and dr. S.J.J. van Netten

PhD Training	Year	Workload (Hours/ ECTS)
General courses		
Pubmed. AMC Graduate school.	2012	2.5/0.1
Basic course in legislation and organization for clinical researchers (BROK). AMC Graduate school.	2012 2015 2019	28/1.0 4/0.1 4/0.1
Practical Biostatistics E-learning. AMC Graduate school.	2013	28/1.0
Writing a Scientific Paper. Amsterdam UMC Graduate school.	2020	42/1.5
Specific courses		
Motivational interviewing basic and advanced course, plus individual training (external).	2013	26/1.0
Presentations		
The value and feasibility of the use of motivational interviewing as educational tool to improve adherence to wearing prescribed footwear in diabetic foot patients. Research meeting, Amsterdam UMC, Amsterdam, The Netherlands (Oral presentation).	2012	14/0.5
The value and feasibility of the use of motivational interviewing as educational tool to improve adherence to wearing prescribed footwear in diabetic foot patients. Research meeting, Amsterdam UMC, Amsterdam, The Netherlands (Oral presentation).	2013	14/0.5
The effect of motivational interviewing on adherence to wearing protective shoes in diabetic foot patients. Research meeting, Amsterdam UMC, Amsterdam, The Netherlands (Oral presentation).	2014	14/0.5
The effect of motivational interviewing on adherence to wearing protective shoes in diabetic foot patients. International Conference on Motivational Interviewing, Amsterdam, The Netherlands (Oral presentation).	2014	14/0.5
The effect of motivational interviewing on adherence to wearing protective shoes in diabetic foot patients. Annual Dutch Diabetes Research Meeting; Nederlandse Vereniging voor Diabetes Onderzoek, Oosterbeek, The Netherlands (Oral presentation).	2014	14/0.5
The effect of motivational interviewing on adherence to wearing prescribed shoes in diabetic foot patients. Research meeting, Amsterdam UMC, Amsterdam, The Netherlands (Oral presentation).	2015	14/0.5
Motivational interviewing to improve footwear adherence in diabetic patients: a pilot RCT. International Symposium on the Diabetic Foot, The Hague, The Netherlands (Poster presentation).	2015	14/0.5
Het effect van motiverende gespreksvoering op therapietrouw van het dragen van orthopedisch schoeisel bij patiënten met diabetes. Congres Motiverende Gespreksvoering, Zwolle, The Netherlands (Oral presentation).	2015	14/0.5

Plantar foot pressures, footwear adherence and ulcer recurrence in diabetic patients with a Charcot foot deformity. Annual Dutch Diabetes Research Meeting, Oosterbeek, The Netherlands (Oral presentation).	2016	14/0.5
Plantar foot pressures, footwear adherence and ulcer recurrence in diabetic patients with a Charcot foot deformity. 7th Annual MOVE research meeting, ACTA, Amsterdam, The Netherlands (Poster presentation).	2016	14/0.5
Plantar foot pressures, footwear adherence and ulcer recurrence in diabetic patients with a Charcot foot deformity. Conference of the Diabetic Foot Study Group, Porto, Portugal (Poster presentation).	2017	14/0.5
Plantar foot pressures, footwear adherence and ulcer recurrence in diabetic patients with a Charcot foot deformity. Dutch Congress of Rehabilitation Medicine. Maastricht, The Netherlands (Pitch & Poster presentation).	2017	14/0.5
Plantar foot pressures, footwear adherence and ulcer recurrence in diabetic patients with a Charcot foot deformity. 2nd AMS Annual Research meeting, Amsterdam, The Netherlands (Poster presentation).	2018	14/0.5
Een orthopedische huisschoen ter bevordering van de therapietrouw bij hoog-risico diabetespatiënten. Research meeting, Amsterdam UMC, Amsterdam, The Netherlands (Oral presentation).	2018	14/0.5
Custom-made footwear for indoor use increases adherence in people at high risk for ulceration. International Symposium on the Diabetic Foot. The Hague, The Netherlands (Oral presentation).	2019	14/0.5
Custom-made footwear for indoor use increases adherence in people at high risk for ulceration. Annual Dutch Diabetes Research Meeting. Wageningen, The Netherlands (Oral presentation).	2019	14/0.5
Custom-made footwear for indoor use increases adherence in people at high risk for ulceration. Dutch Congress of Rehabilitation Medicine, Utrecht, the Netherlands (Pitch & Poster presentation).	2019	14/0.5
Custom-made footwear for indoor use increases adherence in people at high risk for ulceration. XVIIe Diabetische voet symposium Almelo, Almelo, The Netherlands (Oral presentation).	2020	14/0.5
Custom-made indoor footwear increases short and long-term adherence in people with diabetes at high ulcer risk. Dutch Congress of Rehabilitation Medicine, Utrecht, The Netherlands, online (Poster presentation).	2020	14/0.5
Een orthopedische huisschoen ter bevordering van de therapietrouw bij hoog-risico diabetespatiënten. Research meeting, Amsterdam UMC, Amsterdam, The Netherlands (Oral presentation).	2021	14/0.5
Footwear adherence in persons with diabetic foot disease. Research meeting, Amsterdam UMC, Amsterdam, The Netherlands (Oral presentation).	2022	14/0.5
Footwear adherence in persons with diabetic foot disease. Thesis presentation. XIXe Diabetische voet symposium Almelo, Almelo, the Netherlands (Oral presentation).	2022	14/0.5
Custom-made indoor footwear for people with diabetes: from design to use in daily practice. AMS P5 symposium, Amsterdam, The Netherlands (Oral presentation).	2023	14/0.5

Attended (inter)national conferences

International Conference on Motivational Interviewing. Amsterdam, The Netherlands.	2014	8/0.3
Annual Dutch Diabetes Research Meeting; Nederlandse Vereniging voor Diabetes Onderzoek. Oosterbeek, The Netherlands.	2014	8/0.3
International Symposium on the Diabetic Foot. The Hague, The Netherlands.	2015	24/0.8

Congres Motiverende Gespreksvoering, Zwolle, The Netherlands.	2015	8/0.3
Annual Dutch Diabetes Research Meeting. Oosterbeek, The Netherlands	2016	8/0.3
7th Annual MOVE research meeting, ACTA, Amsterdam, The Netherlands.	2016	4/0.1
XVIIe Diabetische voet symposium Almelo, Almelo, The Netherlands.	2017	8/0.3
Congress of the Diabetic Foot Study Group of the European Association for the study of Diabetes, Porto, Portugal	2017	24/0.8
Dutch Congress of Rehabilitation Medicine, Maastricht, The Netherlands.	2017	16/0.5
7th Annual MOVE research meeting, ACTA, Amsterdam, The Netherlands.	2018	8/0.3
9th International Symposium on the Diabetic Foot. The Hague, the Netherlands.	2019	24/0.8
Annual Dutch Diabetes Research Meeting, Wageningen, The Netherlands.	2019	8/0.3
Dutch Congress of Rehabilitation Medicine, Utrecht, The Netherlands.	2019	16/0.5
XVIIIe Diabetische voet symposium Almelo, Almelo, The Netherlands.	2020	12/0.4
Dutch Congress of Rehabilitation Medicine, Utrecht, The Netherlands.	2020	12/0.4
XIXe Diabetische voet symposium Almelo, Almelo, The Netherlands.	2022	16/0.5

Teaching

Lecturing

Guest lecture 'Gangbeeldanalyse en voetdrukmetingen'. Oefentherapie Mensendieck, Amsterdam, University of Applied Sciences, Amsterdam, The Netherlands.	2015 2016 2017	4/0.1 4/0.1 4/0.1
Teaching in the course 'Metingen in Beweging', keuzeonderwijs Geneeskunde, Faculty of Medicine, University of Amsterdam, Amsterdam, The Netherlands.	2013 2014 2015 2016	16/0.6 16/0.6 16/0.6 16/0.6
Teaching in the course 'Hulpmiddelen in de Revalidatie', keuzeonderwijs Geneeskunde, Faculty of Medicine, University of Amsterdam, Amsterdam, The Netherlands.	2016 2017	16/0.6 16/0.6
Teaching in the course 'Revalidatie: Optimaal bewegen, leven en werken met een beperking. Meten is weten!', keuzeonderwijs Geneeskunde. Faculty of Medicine, University of Amsterdam, Amsterdam, The Netherlands.	2019	16/0.6
Teaching in the postacademic course '(Knie) Enkel Voet Orthesen ter correctie van het looppatroon'. Amsterdam UMC, Amsterdam, The Netherlands.	2021	16/0.6

Supervision

Scientific internship supervision. Faculty of Medicine, University of Amsterdam, Amsterdam, the Netherlands.	2015 2016	20/0.8 20/0.8

List of publications

Peer-reviewed research publications

Keukenkamp R, Van Netten JJ, Busch-Westbroek TE, Bus SA. Custom-made footwear designed for indoor use increases short-term and long-term adherence in people with diabetes at high ulcer risk. BMJ Open Diab Care 2022;10:e002593.

Keukenkamp R, Van Netten JJ, Busch-Westbroek TE, Nollet F, Bus SA. Users' needs and expectations and the design of a new custom-made indoor footwear solution for people with diabetes at risk of foot ulceration. Disabil Rehabil. 2022;44(26):8493-500.

Keukenkamp R, Busch-Westbroek TE, Barn R, Woodburn J, Bus SA. Foot ulcer recurrence, plantar pressure and footwear adherence in persons with diabetes and Charcot midfoot deformity: A cohort analysis. Diabet Med. 2020;00:e14438.

Keukenkamp R, Merkx MJM, Busch-Westbroek TE, Bus SA. An explorative study on the efficacy and feasibility of the use of motivational interviewing to improve footwear adherence in persons with diabetes at high risk for foot ulceration. J Am Podiatr Med Assoc. 2018;108(2):90-99.

Waaijman R, *Keukenkamp R*, de Haart M, Polomski WP, Nollet F, Bus SA. Adherence to wearing prescription custom-made footwear in patients with diabetes at high risk for plantar foot ulceration. Diabetes Care. 2013;36(6):1613-8.

Van Schie CH, Slim FJ, *Keukenkamp R*, Faber WR, Nollet F. Plantar pressure and daily cumulative stress in persons affected by leprosy with current, previous and no previous foot ulceration. Gait Posture. 2013;37(3):326-30.

Arts ML, Waaijman R, de Haart M, *Keukenkamp R*, Nollet F, Bus SA. Offloading effect of therapeutic footwear in patients with diabetic neuropathy at high risk for plantar foot ulceration. Diabet Med. 2012;29(12):1534-41.

Slim FJ, Van Schie CH, *Keukenkamp R*, Faber WR, Nollet F. Increased plantar foot pressure in persons affected by leprosy. Gait Posture. 2012;35(2):218-24.

Slim FJ, Van Schie CH, *Keukenkamp R*, Faber WR, Nollet F. Foot impairments and limitations in walking activities in people affected by leprosy. J Rehabil Med. 2011;43(1):32-8.

Slim FJ, Van Schie CH, *Keukenkamp R*, Faber WR, Nollet F. Effects of impairments on activities and participation in people affected by leprosy in The Netherlands. J Rehabil Med. 2010;42(6):536-43.

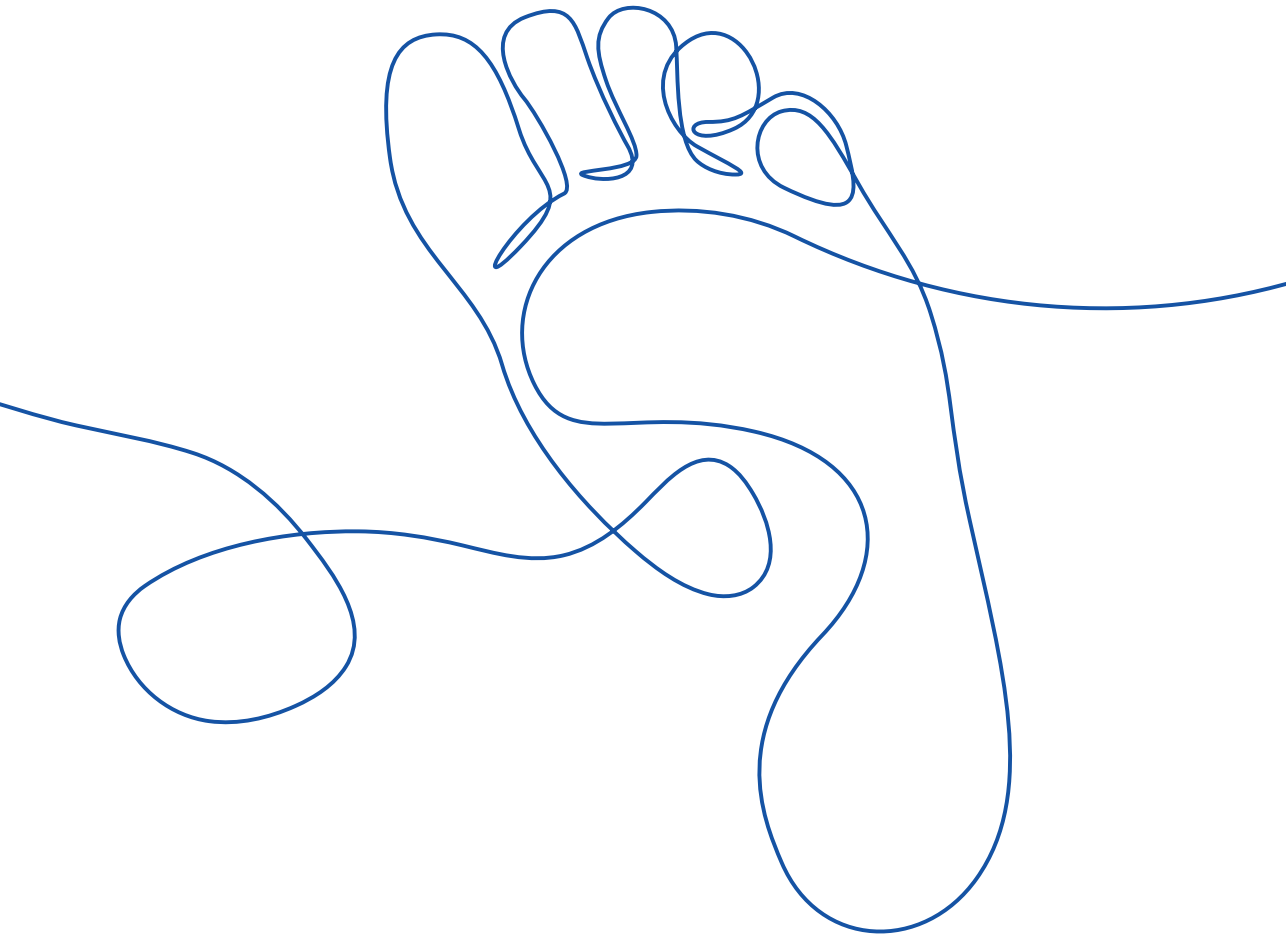
Other publications

Hulshof CM, *Keukenkamp R*, Bus SA, van Netten JJ. Response to: Effects of wear and tear of therapeutic footwear in patients remission. A 5-year follow-up study. Diabetes Res Clin Pract. 2023;196,110243.

Van Netten J, *Keukenkamp R*, Busch-Westbroek TE, Bus SA. Lange-termijn uitkomsten in gebruik van de orthopedische huisschoen door mensen met diabetes. Orthopedische Techniek, NVOS Orthobanda. Editie januari 2021.

Van Netten J, *Keukenkamp R*, Busch-Westbroek TE, Bus SA. Orthopedische huisschoen ter bevordering van de therapietrouw bij patiënten met een hoog risico op diabetische voetulcera. Orthopedische Techniek, NVOS Orthobanda. Editie december 2018.

Keukenkamp R, Busch-Westbroek TE, Bus SA. De diabetes patiënt met een Charcot voet: voetdrukken, gebruik van orthopedische schoenen en recidive voetulcera. Orthopedische Techniek, NVOS Orthobanda. Editie december 2017.



Author contributions

AUTHOR CONTRIBUTIONS

Chapter 2 Waaijman R, Keukenkamp R, de Haart M, Polomski WP, Nollet F, Bus SA. Adherence to wearing prescription custom-made footwear in patients with diabetes at high risk for plantar foot ulceration. Diabetes Care. 2013;36:1613-8.

RW, RK and WPP researched data. RW, RK, MdH, FN and SAB contributed to discussion. RK, MdH, WPP, FN and SAB reviewed and edited the manuscript. RW and SAB wrote the manuscript. All authors approved for the final version of the manuscript.

Chapter 3 Keukenkamp R, Busch-Westbroek TE, Barn R, Woodburn J, Bus SA. Foot ulcer recurrence, plantar pressure and footwear adherence in people with diabetes and Charcot midfoot deformity: A cohort analysis. Diabetic Medicine. 2020;00:e14438.

RK performed the data analysis, interpreted the data, prepared and wrote the manuscript. RB contributed to the data interpretation, writing and revising of the manuscript. TEB-W and JW revised the manuscript. SAB interpreted the data, wrote and revised the manuscript. All authors approved for the final version of the manuscript.

Chapter 4 Keukenkamp R, Merkx MJM, Busch-Westbroek TE, Bus SA. An explorative study on the efficacy and feasibility of the use of motivational interviewing to improve footwear adherence in persons with diabetes at high risk for foot ulceration. J Am Podiatr Med Assoc. 2018;108(2):90-99.

RK collected the data, conducted the motivational interviewing sessions, analysed and interpreted the data, prepared and wrote the manuscript. SAB conducted the motivational interviewing sessions, interpreted the data and revised the manuscript. TEB-W revised the manuscript. MJMM trained RK and SAB in motivational interviewing, analysed their motivational interviewing skills, and revised the manuscript. All authors approved for the final version of the manuscript.

Chapter 5 Keukenkamp R, van Netten JJ, Busch-Westbroek TE, Nollet F, Bus SA. Users' needs and expectations and the design of a new custom-made indoor footwear solution for people with diabetes at risk of foot ulceration. Disability and Rehabilitation. 2022;44(26) 8493-500.

RK collected, analysed and interpreted the data, prepared and wrote the manuscript. JJvN interpreted the data and wrote the manuscript. TEB-W, FN and SAB revised the manuscript. All authors approved for the final version of the manuscript.

Chapter 6 Keukenkamp R, van Netten JJ, Busch-Westbroek TE, Bus SA. Custom-made footwear designed for indoor use increases short and long-term adherence in people with diabetes at high ulcer risk. BMJ Open Diabetes Res Care. 2022;10(1):e002593.

RK collected the data, conducted the statistical analysis, interpreted the data, prepared and wrote the manuscript. JJvN contributed to data collection and statistical analysis. JJvN, TEB-W and SAB interpreted the data, reviewed and edited the manuscript. All authors approved the final manuscript.