**Can a combination of lifestyle and clinical characteristics explain the presence of foot ulcer in patients with diabetes?**

**Running Title:**

**Common characteristics of patients with and without active diabetic foot ulcer**

**Authors:**

Roozbeh Naemi[1]*, Nachiappan Chockalingam[1], Janet K. Lutale[2], Zulfiqarali G. Abbas [2,3]

[1]School of Life Sciences and Education, Staffordshire University, Science Centre, Leek Road, Stoke on Trent, ST4 2DF United Kingdom,

[2]Muhimbili University of Health and Allied Sciences, P.O. Box 65015, Dar es Salaam, Tanzania,

[3]Abbas Medical Centre, 27 Cnr Ndovu & Swahili Street, Kariakoo, Dar es Salaam, Tanzania,

*Corresponding Author Dr Roozbeh Naemi

Corresponding Author's email: r.naemi@staffs.ac.uk

Corresponding Author's Address: Science Centre, Leek Road, Stoke on Trent, ST4 2DF, UK

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**Abstract**

**Aims:**

The aim of this study was to identify the biomechanical, neurological and clinical parameters along with other demographics and life style risk factors that could explain the presence of foot ulcer in patients with diabetes in Africa.

**Methods:**

A total of 1270 (M/F:696/574) patients; 77(M/F:53/24) with ulcerated vs 1193 (M/F: 643/550) with non-ulcerated feet; participated in this study. A set of 28 parameters were collected and compared between the participants with and without active foot ulcers. Multivariate logistic regression was utilised to develop an explanatory model for foot ulceration.

**Results:**

Foot swelling ($\chi 2(1,n=1270)=265.9,P=0.000,Phi=0.464$) and impaired sensation to monofilament ($\chi 2(2,n=1270)=114.2,P=0.000,Cramer'sV=0.300$) showed strong association with presence of ulceration. A lower Temperature sensitivity to cold stimuli and limited ankle joint mobility were observed to be significant ($P<0.05$) contributors to ulceration. The logistic regression model can justify the presence of foot ulceration with 95.3% diagnostic accuracy, 99.1 % specificity and 37.3% sensitivity.

**Conclusion:**

Participants with ulcerated foot show distinct characteristics in few foot related parameters. Swollen foot, limited ankle mobility, and peripheral sensory neuropathy were significant characteristics of patients with diabetic foot ulcer. One out of three patients with ulcerated foot showed common characteristics that could be justified by the model.

**Key words,**

**Diabetic Foot, Diabetic Neuropathy, Biomechanics, Vascular disease, Diagnosis, plantar soft tissue**

**Highlights:**

- 28 parameters were used to explain foot ulcer in 77 of 1270 diabetic patients.
- Patients with swollen foot were more than 16 times more likely to have DFU.
- Impaired sensation was significantly associated with presence of DFU
- Patients with normal ankle mobility were less than half likely to have DFU.

## 1. Introduction:

The life time incidence rate of Diabetic Foot Ulcers was estimated to be between 15 to 25 % [1] and has been recently reported to be between 19 to 34% for persons with diabetes [2]. The rate of ulcer recurrence is approximated to be 65% in 5 years [2], with more than 50% of diabetic ulcers becoming infected [3]. Approximately 20% of moderate or severe diabetic foot infections lead to some level of amputation [4 5]. Diabetic Foot Ulcer (DFU) is the main cause of lower limb amputation in patients with diabetes worldwide[1]. The presence of diabetic foot ulcers in patient increase the risk of death at 5 years by 2.5 times [6]. In order to decrease the socioeconomic cost associated with diabetic foot ulcers, a specific management protocol needs to be developed for patients with ulcerated foot. For developing such protocols, a thorough knowledge of the clinical characteristics of individuals with diabetic foot ulcer is necessary.

There has been an abundance of studies on the predictive factors for diabetic foot ulceration [7]. A recent systematic review of literature and meta-analysis reported that insensitivity to a 10-g monofilament or one absent pedal pulse as established prognostic factors that identify patients with moderate or intermediate risk of foot ulceration[8]. While history of DFUs or lower-extremity amputations were reported to be sufficient to identify those at high risk of developing DFU [8], the studies of patients with active DFU in large cohort ( >200 participants) have been much less frequent [9 10 11 12 13].

Previous study of patients with active DFU in Australian population have identified that the duration of diabetes, neuropathy and vascular insufficiencies are associated with DFU [9]; while in a study on Asian population age and cigarette smoking were identified as characteristics of patients with DFU [10]. Another study in North Europe found that age, male gender and macrovascular complications were associated factors for participants with a previous or current DFU. People with DFU were reported to be significantly taller than those who never had DFU [11]. In a study conducted on South American population male gender, smoking, neuroischmeic foot and absence of vibration perception were found to be associated with participants with previously healed or current DFU [12]. In another study on North American population loss of protective sensation, history of amputation, elevated plantar pressure, foot deformities, poor diabetes control, duration of diabetes and male sex were found to be associated with participants with current or recently healed DFU [13]. Despite these, there is a scarcity of studies in which characteristics of patients with current DFU is considered in a large cohort in Africa.

While poor glycaemic control was commonly reported as a risk factors for diabetic foot ulceration [14], in study involving smaller cohort of patients alcohol consumption was found to be significantly higher in patients with active DFU compared to those with no DFU [15].

Impaired thermal sensation, associated with small fibre neuropathy has also been associated with presence of neuropathic DFU in small patient population [16]. Despite this, the differences in thermal sensation between ulcerated and non-ulcerated and the association between thermal sensitivity and DFU has not been previously investigated in a large cohort of patients. In addition, although recent study on smaller groups pf patients have shown that the plantar pressure is significantly higher in patients with DFU, compared to their non-ulcerated counterparts [17], with the exception of few studies i.e. [13] this has not been confirmed in other large cohort of patients.

The aim of this study was to identify the biomechanical, neurological and clinical parameters along with other demographics and life style risk factors that could explain the presence of DFU in patients with diabetes from African population.

The first objective of this study is to identify the differences in biomechanical, neurological, clinical, demographics and life style between patients with DFU against other patients without DFU. The second objective of this study was to propose an explanatory model that can justify the presence of DFU in this group of patients based on their common characteristics.

## 2. Material and Method

### 2.1. Participants:

Patients who attended the diabetic foot clinic in Tanzania between Jan 2011 and Dec 2015 were recruited to participate in this study. Ethical approval was sought and granted by the local ethics committee and informed consent was obtained from all participants. DFU was defined as a full-thickness wound involving the foot or the ankle, distal to and including the malleoli. The sample size was calculated as 1128 participants based on the prevalence of foot ulceration rate of 10%, in the studied group and DFU prevalence OF 7 % in diabetes population in Africa [18] with Alpha level of 5% and power of 95%. Assuming a missing data in 1 out 8 participants, an additional 142 participants were needed to be recruited to the study to ensure that the calculated sample size is used in every statistical analysis.

### 2.2. Data Collection

A combination of categorical and continuous parameters (as follows) were collected from the patients during a single visit.

#### 2.2.1. Categorical parameters

The general categorical parameters were: Smoking (Current smoker, Never smoked, Previous smoker), Alcohol habits (Currently drinks, Never drunk, in the past), Previous amputation, and History of Ulceration according to protocols set by IWGDF [19].

The foot-specific categorical parameters included: Neuropathy (using 10-g monofilament loss of sensation [20] was assessed on both feet at 10 sites including Hallux, 3rd Toe, 5th Toe, 1st Met head, 3rd Met head, 5th Met head, lateral midfoot, medial midfoot, centre of the hindfoot, and dorsum of the foot [21]. For sensitivity to monofilament each patient was categorised into 3 levels as Normal (sensation present in >8 sited), Decreased (sensation present in 4-7 sites) and Absent (sensation is felt in < 3 sites).

Foot deformity was assessed as structural abnormalities in the foot such as Claw/Hammer Toe and Hallux Valgus or prominent metatarsal heads, status after Charcot foot, amputations and other foot surgery were considered as having foot deformity [22].

Skin status was considered as: Dry when Epidermis that lacks moisture or sebum; Fissures: characterized by a pattern of fine lines, scaling, and fissures; and Normal: well-balanced skin eudermic that is neither too oily nor too dry [23] [24]. Mycosis was considered as fungal infection in between the toes and macerated skin [23].

Nail ingrowth was considered as in-growing toe nail (also known as onychocryptosis) and it was considered as present when the nail grows so that it cuts into one or both sides of the paronychium or nail bed [23]. Swelling was considered as present when swelling of foot sufficiently pronounced to leave a clear imprint of the pressure by a finger[23]. Presence of callus was also considered to be present based on the protocol proposed in IWGFD guidelines[23].

Specific categorical parameters for each participant were defined as if these occurred on either or both feet for each participant.

2.2.2. Continuous parameters:

The general continuous parameters included: Age, Body mass, Height, Shoe size (UK), Duration of Diabetes, Body Mass Index. The foot-specific continuous parameters were: Ankle Brachial Pressure Index (ABPI), Vibration Perception Threshold, Temperature Sensation and Tolerance Thresholds and plantar pressure.

Vibration Perception Threshold was measured using a clinically accepted device (Neuropathy Analyser – Vibrotherm – Dx (Diabetik Foot Care India Pvt Ltd, Chennai, India) at the wrist, knee, ankle and big toe according to the previous protocol [25]. This device was also used to measure the Temperature Sensation and Temperature Tolerance Thresholds to cold/warm at: Hallux, 3rd Toe, 5th Toe, underneath the arch and Heel according to the previous protocol [26].

A plantar pressure platform (EMED, Novel, Munich, Germany) was utilised to measure average plantar pressure during the stance phase of walking were measured at 16 sites (Hallux, 2nd Toe, 3rd Toe, 4th Toe, 5th Toe, 1st Met head, 2nd Met head, 3rd Met head, 4th Met head, 5th Met head, lateral midfoot, central midfoot, medial midfoot, lateral hindfoot, medical hindfoot, centre of the hindfoot), based on previous protocol [27] where the toes, heel and midfoot regions were further divided into more specific regions to allow further in-depth analyses of the plantar pressure . The participants were asked to walk over the platform using a two-step protocol [28] after completing a number of familiarisation trials. The mean of average pressures from 3 stance phases from each foot were calculated based on which the overall and regional pressures were reported [29]. All specific continuous parameters were averaged between the left and right feet.

## 2.3. Data analyses

All statistical tests were performed using IBM® SPSS®v.25.

2.3.1. Test of differences

Chi-square test for independence with Yates Continuity Correction was utilized to identify significant ($p<0.05$) association between categorical parameters and the prevalence of DFU.

Furthermore, given the non-normal distribution of the data which was established through the test of normality (Kolmogorov-Smirnov, $p< 0.05$), Mann-Whitney U-Test was utilized to assess significant ($p<0.05$) differences in continuous parameters between the patients with and without ulceration.

### 2.3.2. Explanatory model for foot ulceration

Multivariate logistic regression was utilised to develop the explanatory model for foot ulceration based on the risk factors. Logistic regression was used to justify the presence or absence of ulceration based on values of a set of predictor variables (covariates).

To identify the effect of each set of parameters on the explanatory accuracy of the model, the covariates were entered through 9 blocks of covariates as shown in (Table 1).

These blocks were decided based a hierarchical fashion in which clinically plausible set of similar parameters were included in each consecutive block of parameters that were sorted based on increase in the complexity level. Furthermore, for set of parameters across different blocks, diagnostic test of multicollinearity (with tolerance value of 0.1 or $R^2$ >0.9) was performed and ensured no independent parameters (covariate) existed across blocks.

In each block of parameters, an automated backward stepwise selection algorithm (retaining variables with $p<0.05$ Removal testing is based on the probability of the Wald statistic) was used to arrive at the multiple regression model. The collinearity between independent parameters in the same block was taken care of by the automated backward stepwise selection algorithm.

*Table 1: Blocks representing each set of covariates that were added to reach the final explanatory model.*

Logistic regression coefficients were also used to estimate odds ratios for each of the independent variables in the model along with the significance of the parameters in the model. Chi-square and significance level based on Hosmer-Lemeshow goodness of fit was used to indicate how worthwhile the model was in explaining the presence of ulceration. Furthermore Cox & Snell and Nagelkerke R Square values provided an indication of a pseudo R square value that indicates the upper and lower range of variability in ulceration status that can be explained by the model.

The sensitivity (as the percentage of participants with DFU incidence that are identified as having DFU) and specificity (as the percentage on of participants with no ulceration incidence that are identified as not having DFU) along with the overall explanatory accuracy (as the percentage of the entire cases that are explained correctly) of the method were reported when the consecutive blocks (1 to 9) were added. Furthermore, using the area under the receiver operating characteristic (ROC) curve with 95% confidence Ievels were calculated and referred to as the diagnosis strength of the model.

## 3. Results:

A total of 1270 (M/F: 696/574) participants as 77 (M/F: 53/24) with ulcerated vs 1193 (M/F: 643/550) with non-ulcerated feet were recruited to the study. Table 2, and 3 represent the results related to the test of differences along with the bivariate and multivariate logistic regression for the categorical and continuous parameters respectively. While there was no missing data for the categorical and for the majority of continuous parameters, the TST and TTT data were missing for 16-19 participants, and the VPT at knee and Blood Glucose level data were missing for 1 and 3 participants respectively. The missing data was accounted for in all statistical analyses, as indicated in Table 2 and Table 3.

*Table 2: shows the categorical parameters for all participants and for each group of with and with no ulceration. a- P values based on Chi-square test of independence (with Yates continuity correction) P <0.5 indicates significant association between ulcerated and non-ulcerated group on the parameter. b- Effect size as the Phi coefficient, with small =0.01, Medium = 0.30, Large = 0.50; c- Effect size as Cramer's V coefficient (three categories), where small = 0.07, Medium = 0.21, Large = 0.35; d – Effect size as Cramer's V coefficient (four categories), where small = 0.06, Medium = 0.17, Large = 0.29*

*Table 3: shows the continuous parameters for all participants and for the groups with and with no ulceration. a- Mann-Whitney; r = z / (N1 + N2 )0.5 where 0.1 small effect, 0.3 medium effect, 0.5 large effect ; Note that the selection of parameters in the logistic regression model was based on the univariate analyses in which parameters with P<0.2 were selected. The P values for these selected parameters are underlined in the table.*

### 3.1. Differences in Categorical parameters

In comparing the general categorical parameters between the two groups, it was found that male gender, was significantly (P=0.010) associated (with presence of ulceration with a small effect size. Significant associations for foot swelling (P= 0.000) and impaired sensation to monofilament (P= 0.000) were observed with presence of ulceration (both with large effect size). Also, amputation, foot deformity (P=0.000), Ankle joint limited mobility (P= 0.000) and MTP

joint limited mobility (P= 0.000) were all significantly associated with ulcerated group (medium effect size). It should also be mentioned that previous ulceration (P= 0.046), nail ingrowth (P= 0.008) and skin dryness level (P= 0.002) were all associated significantly with ulcerated group (small effect size).

### 3.2. Differences in Continuous parameters

Whilst comparing general continuous parameters between the two groups, the results of this study indicate that the ulcerated group were significantly (P= 0.020) taller (small effect size) and had significantly (P= 0.000) longer duration of diabetes (medium effect size).

Furthermore, in comparison of foot specific continuous parameters between the two groups, the ulcerated group showed a significantly (P= 0.000) higher vibration perception threshold (Medium effect size).

While the plantar pressure were significantly lower at Hallux (P= 0.007); $2^{nd}$ toe (P= 0.006); $3^{rd}$ toe (P= 0.000); $4^{th}$ Toes (P= 0.002); and 5th Toe (P= 0.000) in ulcerated patients the plantar pressure at the $1^{st}$ (P= 0.004) and 5th MTH (P= 0.042) showed to be significantly higher in ulcerated patients compared to non-ulcerated patients (all with small effect size).

The average, total, and all the site-specific TTT and TST to cold probe was significantly (P= 0.000) lower for the ulcerated group, while the corresponding values for TTT and TST to hot probe at all tested sites were significantly (P= 0.000) higher in ulcerated group (all with Medium effect size).

The VPT at wrist, knee, ankle and Hallux was significantly (P= 0.000) higher in ulcerated group (all with medium effect size), while Blood Glucose level showed to be significantly (P= 0.002) lower in ulcerated patients (small effect size).

### 3.3. Explanatory model for DFU

Hosmer-Lemeshow goodness of fit indicated that the model was worthwhile indicated by the goodness of fit test results ($\chi^2$=4.882, P=0.770) that indicated that the hypothesis of a good fit is not rejected (P>0.05).

The result of multiple regression analyses with backward stepwise selection algorithm (retaining variables with p<0.05) indicated that only 15 (6 categorical and 9 continuous) parameters stayed in the final model. From categorical parameters, only the presence of foot swelling (OR= 16.456; 95%CI=8.199-33.028; P= 0.000) and normal ankle mobility (OR=0.438; 95%CI=0.231-0.834; P= 0.012) contributed significantly to justification of presence of DFU (Table 2 and Figure 1).

From continuous parameters only four parameters including lower blood sugar level (OR= 0.938; 95%CI=0.885-0.995; P= 0.032), lower average TST to cold (OR=0.630; 95%CI=0.445-0.891; P=0.009), higher Average TTT to cold (OR=1.399; 95%CI=1.096-1.786; P=0.007), and lower plantar pressure at the fifth toe (OR= 0.977; 95%CI=0.862-0.992; P= 0.003) were shown to be significant identifiers of ulcerated patients.

*Figure 1: The Sensitivity ( percentage of the group with ulceration occurrence that is correctly identified by the model) , Specificity ( percentage of the group with No ulceration occurrence that is correctly identified by the model), Identification Accuracy ( percentage of the overall group that is correctly identified by the model), along with the Diagnosis Strength ( the areas below the Receiver Operation Curve) of the model when the covariates are added in sequential order from left to right. Block 1: The model includes covariate A, B & C; Block 2: The model includes covariates: A, B, C, D, E & F; Block 3: The model includes covariates: A, B, C, D, E, F & G; Block 4: The model includes covariates: A, B, C, D, E, F, G & H; Block 5: The model includes covariates: A, B, C, D, E, F, G & H; Block 6: The model includes covariates: A, B, C, D, E, F, G, H, I, J & K; Block 7: The model includes covariates: A, B, C, D, E, F, G, H, I, J, K, L, and M; Block 7: The model includes covariates: A, B, C, D, E, F, G, H, I, J & K; Block 8: The model includes covariates: A, B, C, D, E, F, G, H, I, J, K, L, M and N; Block 9: The model includes covariates: A, B, C, D, E, F, G, H, I, J, K, L, M, N and O.*

*Where A: Sex (Female:0; Male:1); B: Duration of Diabetes (in days); C: Blood Glucose level (mmol/L); D: Amputation (0:without, 1:with); E: Foot deformity (0 without, 1 with); F: Foot swelling (0:without, 1:with); G: Ankle Mobility ( 0:without, 1:with); H: Sensitivity to monofilament ( 0: Absent, Decreased: 1, Normal: 2); I: Sum of Temperature Sensitivity Threshold to cold probe(°c); J: : Average Temperature Sensitivity Threshold to cold probe(°c); K: Average Temperature Tolerance Threshold to cold probe(°c); L: Temperature Tolerance Threshold to hot probe underneath the arch(°c); M: Sum of Temperature Tolerance Threshold to hot probe (°c); N: Plantar pressure at the centre of the Heel ( kPa); O: Plantar pressure at the Fifth Toe ( kPa).*

Figure 1 shows the effect of each set of parameters on the explanatory accuracy of the model, where the covariates were entered through 9 blocks.

As indicated in figure 1, while the sensitivity shows a significant increase from Block 1 (0%) to Block 9 (37.3%), the specificity of the model dropped only marginally by 0.8% from Block 1 (@ 99.9 %) to Block 9 (99.1%). This has led to the identification accuracy of the model to improve only marginally by 1.5% (from 93.8% to 95.3 %). It was also observed that the diagnosis strength of the model was also increased from 70.5% in Block 1 to 73.7% in Block 9.

The model as a whole could justify between 17.4 % (Cox and Snell R Square) and 47.1 % (Nagelkerke R Square) of the variation in ulceration status.

## 4. Discussion:

### 4.1. Difference in Categorical parameters

When, comparing the general categorical parameters between the two groups, it was found that male gender, was associated with presence of DFU with a small effect size. This has been in line with the previous studies in which significantly higher proportion of patients with DFU reported to be male in western population in the North America [13], North Europe [11]. However these findings are contrary to the study in Australian population where no significant difference in the proportion of male sex in the ulcerated vs non-ulcerated population was reported [9].

In this study previous amputation was found to be significantly higher in the ulcerated group which is in line with the results of previous studies on North European [11] population.

From the specific categorical parameter, impaired sensation to monofilament show significant association with presence of ulceration with a large effect size (Cramer's V coefficient = 0.3), indicates the relationship between sensory neuropathy and DFU and is in line with previous studies on Australian [9] population.

The results of the current study in which a significantly higher number of participants with swollen feet that was observed in the ulcerated (vs non ulcerated) group with a large effect size (Phi coefficient = 0.464) was never reported in previous studies where the group of ulcerated and non-ulcerated participants were compared. While the difference cannot indicate a causal relationship between ulcer and presence of foot swelling, the finding can have implications in designing footwear interventions for this group of patients.

Foot deformity has been associated with a medium effect size in the current study. Although there is no study with comparable population size against which the results of this study can be compared, our findings are in line with the results by Fernando and co-workers [17] who reported significantly higher proportion of patients with Hammer toe deformity in the ulcerated group compared to the group with diabetic neuropathy.

The inconclusive results of this study re the contribution of Alcohol ingestion to justifying the risk of diabetic foot ulceration are in line with previous findings on Australian [9], North American [13] and Asian [10] population. Furthermore the inconclusive results of the current study regarding smoking as a contributing factor to justify the presence of DFU are in line with the previous study in North European [11], North American [13] and Australian [9] population, while it contradicted the results on South American [12] and Asian [10] populations where smoking was reported as a contributing factor to justify diabetic foot ulceration.

Ankle and MTP joint limited mobilities were all associated with ulcerated group (medium effect size), that is in contrary to the findings by Fernando and co-workers [17] in which no significant difference was found between either of the parameters and ulceration.

### 4.2. Difference in Continuous parameters

The results of this study are in line with the previous literature in which patients with ulcers have shown to have higher duration of diabetes compared to their non-ulcerated counterparts in studies of South American [12], North European [11] and Australian [9] population.

While the results of the current study indicated that the ulcerated group were significantly taller that is in line with findings on North European population [11], the results of the current study are contrary to the findings reported for Australian population [9], who found no significant difference in height of ulcerated and non-ulcerated group.

The results of the current study on the plantar pressure at the toes also contradict the results by Fernando and co-workers [17] who reported a significantly higher pressure at these sites in patients with DFU. Although the difference may be due to the fact that the previous study [17] measured pressure at the entire area under the lesser toes, the current study measured the pressure under toes separately.

Furthermore, the results of the current study that indicate that the plantar pressure at the 1st and 5th MTH are significantly higher in ulcerated patients when compared to non-ulcerated patients (all with small effect size). However no such significant differences were reported by Fernando and co-workers [17].

As opposed to the previous study [17], the current study found no significant difference in the plantar pressure at the midfoot between the ulcerated and non-ulcerated group. This may also be related to the fact that in the current study 3 different zones of midfoot were considered separately.

The average, total, and all the site-specific TTT and TST to cold probe was significantly lower for the ulcerated group, while the corresponding values for TTT and TST to hot probe at all tested sites were significantly higher in ulcerated group (all with Medium effect size). This distinct feature of ulcerated patients indicate presence of small fibre neuropathy that is in line with the previous findings [16].

The values of average VPT at foot and VPT at wrist, knee, ankle and Hallux was significantly higher in ulcerated group (medium effect size) are in line with our earlier the findings that significantly higher number of participants with ulcerated foot showed neuropathy.

While the finding of this study that indicated that the Blood Glucose level showed to be significantly lower in ulcerated patients (small effect size) seem to be contradictory to previous studies in North Europe [11] , Australian [9] and South America [12] where Glycated Haemoglobin ( HbA1c) was reported to be significantly higher in ulcerated vs nonulcerated group. However the reduced blood sugar level in ulcerated group in the current study may be the effect of trauma rather than on blood sugar level rather than being an existing condition before the ulceration.

### 4.3. The explanatory model

The model was adequately specific in identifying the factors that protect the patients against ulceration. However, the ability of model in justifying the characteristics of patients with ulcerated foot is currently relatively limited. With just over 1 out of three patients with ulcerated foot showing common characteristics based on the parameters that were investigated in this study. However comparison between this model that is proposed in the current study against what was proposed for other patient populations in North America [13], South America [12], North Europe [11] , Asia [10] and Australia [9] is not possible as these have not reported the accuracy of the model in terms of sensitivity, specificity and diagnosis power.

Only six parameters (foot swelling, ankle joint mobility, blood Glucose Level, Average TTT and TST to cold probe and plantar pressure at the fifth toe) were found to be significantly ($p<0.05$) contributed to the model in the current study.

In essence the findings indicate that a patient with swollen foot is more than 16 times (OR= 16.456) more likely to have DFU and that a patients with normal ankle mobility is less than half likely (OR=0.438) to have DFU.

It is interesting to observe that none of the parameters that were found in the explanatory model of the current study are among parameters that were reported to be significant risk factor for diabetic foot ulceration in previous studies on different patient populations in North America[13], South America[12], North Europe[11] , Asia[10] and Australia [9].

It is also worth mentioning that with the exception of Blood Glucose Level all other parameters that significantly contributed to justify the presence of DFU in this study were found to be foot specific.

Furthermore, in the current study plantar pressure at the fifth toe was the only plantar pressure parameter that was found to be a significant contributor to the explanatory model of ulceration. In the current study an increase in the plantar pressure at the fifth toe has been affiliated to decreased risk of foot ulceration with the Odd Ratio of 0.977. This is contrary to the previous study where excessive plantar pressure (>650 kPa) had been found to be significantly (OR=5.9, P<0.001) contributing to the explanatory model for foot ulcer [13]. This can be related to the fact that an increase in the plantar pressure at the fifth toe could decrease the pressure at other plantar sites of the foot by offloading the critical areas of the foot.

Although from the demographic parameters male sex (OR= 1.44) were also included in the final model contrary to previous studies in South American (OR=1.71) [12] population and North American ( OR=2.7) [13] population, the contribution of sex to diagnosis power of the model was not significant (p>0.05).

Similarly in line with the previous study on North American population [13], previous amputation was included in the final ulceration risk diagnostic model, however the contribution was not significant ( P>0.05)

Overall the discrepancy of the results of the diagnostic model in this study could be the result of the differences in the selected parameters and the participants population that were investigated in this study compared to other studies [13] [12] [11] [10] [9].

### 4.4. **Strength and Limitations**

This study is unique in a sense that it reports a wide range of foot-specific parameters in a big cohort of Diabetic patients in Africa. In addition, this is the first study to report on a wide range of foot-related characteristics along with the clinical and life style factors which are being investigated in patients with DFU is compared against those without. This will have implications for clinical practice and have an impact on future research as previous studies did not include adequate foot-specific parameter in their model [11] [10] [9] or when they include the foot specific parameters the ulcerated group contained the participants with previous[12] or recently healed [13] ulcers or in addition to those with active foot ulcers which could have affected the results of these studies. It should be

mentioned that the results of the current study indicate that the model could justify the lack of DFU with specificity of 99.1 %. Despite the inclusion of number of foot-specific parameters in this study, the final model can only justify the presence of foot ulcer with 37.3% sensitivity.

### 4.5. Clinical implications and Future directions

The results of this study can indicate a trend toward considering more foot-specific parameters in identifying the risk of diabetic foot ulceration in patients. Additionally, the results can be used to develop specific intervention for diabetic patients with active DFU that is suitable to the distinct characteristics of these patients against their non-ulcerated counterparts. These characteristic include the presence of swelling, limited ankle range of motion and distinct small fibre neuropathy.

It worth mentioning that the group of parameters related to the temperature tolerance and sensitivity thresholds to hot and cold stimuli have shown to be significantly contributing to explaining foot ulceration.

Although a vast range of parameters were collected from each participant and the inclusion of further parameters to reflect the micro circulatory [30], and mechanical properties of the plantar soft tissue [31] could have resulted in a more comprehensive model of diabetic foot ulceration risk that can achieve higher sensitivity in justifying the presence of DFU, however at these were considered to be beyond the scope of this work.

While few studies have reported severe abnormalities the temperature tolerance and sensitivity thresholds in ulcerated foot [16] [32] and have indicated that small fibres to be more vulnerable in diabetes, these parameter have not been previously investigated in large cohort studies of this nature. The results of the current study justifies the need to assess small fibre neuropathy as a risk factor for foot ulceration in diabetic patients. As outlined in a recent critical evaluation of the diabetic foot screening guidelines there is a clear need for more structured data that can provide evidence for the development of screening guidelines[33].

## 5. Conclusion:

Overall, the participants with ulcerated foot show distinct characteristics in a number of clinical parameters including the pronounced impaired sensation and foot swelling.

The combination of parameters collected in this study can explain the common characteristics of patients that can be protective against foot ulceration. However only 1 out of three patients with ulcerated foot show common characteristics that can are considered as risk factors for ulceration in this study.

**References**


1. Singh N, Armstrong DG, Lipsky BA. Preventing Foot Ulcers in Patients With Diabetes. *JAMA*. 2005;293(2):217. doi:10.1001/jama.293.2.217

2. Armstrong DG, Boulton AJM, Bus SA. Diabetic Foot Ulcers and Their Recurrence. Ingelfinger JR, ed. *N Engl J Med*. 2017;376(24):2367-2375. doi:10.1056/NEJMra1615439

3. Prompers L, Huijberts M, Apelqvist J, et al. High prevalence of ischaemia, infection and serious comorbidity in patients with diabetic foot disease in Europe. Baseline results from the Eurodiale study. *Diabetologia*. 2007;50(1):18-25. doi:10.1007/s00125-006-0491-1

4. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections. *Clin Infect Dis*. 2012;54(12):e132-e173. doi:10.1093/cid/cis346

5. Lavery LA, Armstrong DG, Wunderlich RP, Tredwell J, Boulton AJM. Predictive Value of Foot Pressure Assessment as Part of a Population-Based Diabetes Disease Management Program. *Diabetes Care*. 2003;26(4):1069-1073. doi:10.2337/diacare.26.4.1069

6. Walsh JW, Hoffstad OJ, Sullivan MO, Margolis DJ. Association of diabetic foot ulcer and death in a population-based cohort from the United Kingdom. *Diabet Med*. 2016;33(11):1493-1498. doi:10.1111/dme.13054

7. Monteiro-Soares M, Boyko EJ, Ribeiro J, Ribeiro I, Dinis-Ribeiro M. Predictive factors for diabetic foot ulceration: a systematic review. *Diabetes Metab Res Rev*. 2012;28(7):574-600. doi:10.1002/dmrr.2319

8. Crawford F, Cezard G, Chappell FM, et al. A systematic review and individual patient data meta-analysis of prognostic factors for foot ulceration in people with diabetes: the international research collaboration for the prediction of diabetic foot ulcerations (PODUS). *Health Technol Assess*. 2015;19(57):1-210. doi:10.3310/hta19570

9. Baba M, Davis WA, Davis TME. A longitudinal study of foot ulceration and its risk factors in community-based patients with type 2 diabetes: The Fremantle Diabetes Study. *Diabetes Res Clin Pract*. 2014;106(1):42-49. doi:10.1016/J.DIABRES.2014.07.021

10. S MA and MA. SOCIODEMOGRAPHIC AND LIFESTYLE FACTORS AS THE RISK OF DIABETIC FOOT ULCER IN THE UNIVERSITY OF MALAYA MEDICAL CENTRE. *J Heal Transl Med*. 2009;12(1):15-21. https://ejournal.um.edu.my/index.php/jummec/article/view/4613.

11. Molvær AK, Graue M, Espehaug B, Østbye T, Midthjell K, Iversen MM. Diabetes-related foot ulcers and associated factors: Results from the Nord-Trøndelag Health Survey (HUNT3) (2006–2008). *J Diabetes Complications*. 2014;28(2):156-161. doi:10.1016/J.JDIACOMP.2013.10.010

12. Parisi MCR, Moura Neto A, Menezes FH, et al. Baseline characteristics and risk factors for ulcer, amputation and severe neuropathy in diabetic foot

at risk: the BRAZUPA study. *Diabetol {&} Metab Syndr*. 2016;8(1):25. doi:10.1186/s13098-016-0126-8

13. Lavery LA, Armstrong DG, Vela SA, Quebedeaux TL, Fleischli JG. Practical criteria for screening patients at high risk for diabetic foot ulceration. *Arch Intern Med*. 1998;158(2):157-162. http://www.ncbi.nlm.nih.gov/pubmed/9448554. Accessed December 1, 2016.

14. Boulton AJM, Armstrong DG, Albert SF, et al. Comprehensive foot examination and risk assessment: a report of the task force of the foot care interest group of the American Diabetes Association, with endorsement by the American Association of Clinical Endocrinologists. *Diabetes Care*. 2008;31(8):1679-1685. doi:10.2337/dc08-9021

15. Altenburg N, Joraschky P, Barthel A, et al. Alcohol consumption and other psycho-social conditions as important factors in the development of diabetic foot ulcers. *Diabet Med*. 2011;28(2):168-174. doi:10.1111/j.1464-5491.2010.03151.x

16. Guy RJC, Clark CA, Malcolm PN, Watkins PJ. Evaluation of thermal and vibration sensation in diabetic neuropathy. *Diabetologia*. 1985;28(3):131-137. doi:10.1007/BF00273859

17. Fernando ME, Crowther RG, Lazzarini PA, et al. Plantar pressures are higher in cases with diabetic foot ulcers compared to controls despite a longer stance phase duration. *BMC Endocr Disord*. 2016;16(1). doi:10.1186/s12902-016-0131-9

18. Zhang P, Lu J, Jing Y, Tang S, Zhu D, Bi Y. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis. *Ann Med*. 2017;49(2):106-116. doi:10.1080/07853890.2016.1231932

19. Jeffcoate WJ, Bus SA, Game FL, Hinchliffe RJ, Price PE, Schaper NC. Reporting standards of studies and papers on the prevention and management of foot ulcers in diabetes: required details and markers of good quality. *Lancet Diabetes Endocrinol*. 2016;4(9):781-788. doi:10.1016/S2213-8587(16)30012-2

20. Feng Y, Schlösser FJ, Sumpio BE. The Semmes Weinstein monofilament examination as a screening tool for diabetic peripheral neuropathy. *J Vasc Surg*. 2009;50(3):675-682.e1. doi:10.1016/J.JVS.2009.05.017

21. Frykberg RG, Zgonis T, Armstrong DG, et al. Diabetic foot disorders. A clinical practice guideline (2006 revision). *J Foot Ankle Surg*. 2006;45(5 Suppl):S1-66. doi:10.1016/S1067-2516(07)60001-5

22. Ledoux W, Shofer J, … DS-J of, 2005 undefined. Relationship between foot type, foot deformity, and ulcer occurrence in the high-risk diabetic foot. *archive-ouverte.unige.ch*. https://archive-ouverte.unige.ch/unige:39927/ATTACHMENT01. Accessed July 11, 2018.

23. Schaper NC, Van Netten JJ, Apelqvist J, Lipsky BA, Bakker K. Prevention and management of foot problems in diabetes: A Summary Guidance for Daily Practice 2015, based on the IWGDF Guidance Documents. *Diabetes Metab Res Rev*. 2016;32. doi:10.1002/dmrr.2695

24. Bus SA, van Netten JJ, Lavery LA, et al. IWGDF guidance on the prevention of foot ulcers in at-risk patients with diabetes. *Diabetes Metab Res Rev*.

2016;32. doi:10.1002/dmrr.2696

25. Jayaprakash P, Bhansali A, Bhansali S, et al. Validation of bedside methods in evaluation of diabetic peripheral neuropathy. *Indian J Med Res*. 2011;133(6):645-649. http://www.ncbi.nlm.nih.gov/pubmed/21727664. Accessed July 12, 2018.

26. Ziegler D, Mayer P, Gries FA. Evaluation of thermal, pain, and vibration sensation thresholds in newly diagnosed type 1 diabetic patients. *J Neurol Neurosurg Psychiatry*. 1988;51(11):1420-1424. doi:10.1136/JNNP.51.11.1420

27. Fernando M, Crowther RG, Cunningham M, et al. The reproducibility of acquiring three dimensional gait and plantar pressure data using established protocols in participants with and without type 2 diabetes and foot ulcers. *J Foot Ankle Res*. 2016;9(1):4. doi:10.1186/s13047-016-0135-8

28. Bus SA, Lange A de. A comparison of the 1-step, 2-step, and 3-step protocols for obtaining barefoot plantar pressure data in the diabetic neuropathic foot. *Clin Biomech*. 2005;20(9):892-899. doi:10.1016/j.clinbiomech.2005.05.004

29. Naemi R, Chevalier TL, Healy A, Chockalingam N. The effect of the use of a walkway and the choice of the foot on plantar pressure assessment when using pressure platforms. *Foot*. 2012;22(2):100-104. doi:10.1016/j.foot.2012.01.004

30. Körei AE, Istenes I, Papanas N, Kempler P. Small-Fiber Neuropathy. *Angiology*. 2016;67(1):49-57. doi:10.1177/0003319715583595

31. Naemi R, Chatzistergos P, Sundar L, Chockalingam N, Ramachandran A. Differences in the mechanical characteristics of plantar soft tissue between ulcerated and non-ulcerated foot. *J Diabetes Complications*. 2016;30(7):1293-1299. doi:10.1016/j.jdiacomp.2016.06.003

32. Ali Z, Carroll M, Robertson KP, Fowler CJ. The extent of small fibre sensory neuropathy in diabetics with plantar foot ulceration. *J Neurol Neurosurg Psychiatry*. 1989;52(1):94-98. doi:10.1136/JNNP.52.1.94

33. Formosa C, Gatt A, Chockalingam N. A Critical Evaluation of Existing Diabetic Foot Screening Guidelines. *Rev Diabet Stud*. 2016;13(2-3):158-186. doi:10.1900/RDS.2016.13.158

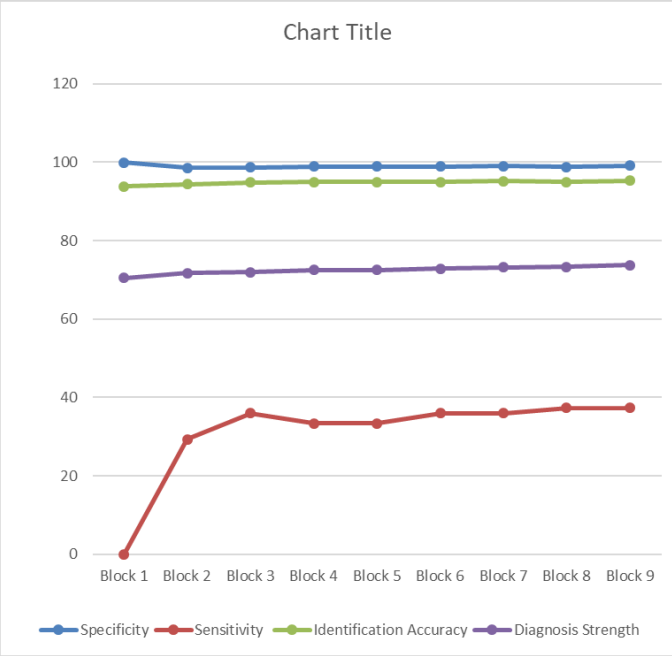


Figure 1: The Sensitivity ( percentage of the group with ulceration occurrence that is correctly identified by the model) , Specificity ( percentage of the group with No ulceration occurrence that is correctly identified by the model), Identification Accuracy ( percentage of the overall group that is correctly identified by the model), along with the Diagnosis Strength ( the areas below the Receiver Operation Curve) of the model when the covariates are added in sequential order from left to right. Block 1: The model includes covariate A, B & C; Block 2: The model includes covariates: A, B, C, D, E & F; Block 3: The model includes covariates: A, B, C, D, E, F & G; Block 4: The model includes covariates: A, B, C, D, E, F, G & H; Block 5: The model includes covariates: A, B, C, D, E, F, G & H; Block 6: The model includes covariates: A, B, C, D, E, F, G, H, I, J & K; Block 7: The model includes covariates: A, B, C, D, E, F, G, H, I, J, K, L, and M; Block 7: The model includes covariates: A, B, C, D, E, F, G, H, I, J & K; Block 8: The model includes covariates: A, B, C, D, E, F, G, H, I, J, K, L, M and N; Block 9: The model includes covariates: A, B, C, D, E, F, G, H, I, J, K, L, M, N and O.

Where A: Sex (Male:1, Female:2); B: Duration of Diabetes (in days); C: Blood Glucose level (mmol/L); D: Amputation (0:without, 1:with); E: Foot deformity (0 without, 1 with); F: Foot swelling (0:without, 1:with); G: Ankle Mobility ( 0:without, 1:with); H: Sensitivity to monofilament ( 0: Absent, Decreased: 1, Normal: 2); I: Sum of Temperature Sensitivity Threshold to cold probe(°c); J: : Average Temperature Sensitivity Threshold to cold probe(°c); K: : Average Temperature Tolerance Threshold to cold probe(°c); L: Temperature Tolerance Threshold to hot probe underneath the arch(°c); M: Sum of Temperature Tolerance Threshold to hot probe (°c); N: Plantar pressure at the centre of the Heel ( kPa); O: Plantar pressure at the Fifth Toe ( kPa).

| Block | Parameters |
|---|---|
| 1 | Age, Sex, Weight, Height, Body Mass Index (BMI), Shoe size, Diabetes duration, Smoking habit, Alcohol Consumption, and Fasting Blood Sugar Level. |
| 2 | History of amputation, Previous ulceration, presence of Callus, Foot deformity, Swelling, and Nail ingrowth. |
| 3 | Ankle Brachial Index, MTP Joint mobility and Ankle Joint Mobility |
| 4 | Vibration Perception Threshold, and sensitivity to Monofilament. |
| 5 | Vibration Perception Thresholds at Wrist, Knee, Ankle and Hallux. |
| 6 | Temperature Sensation and Tolerance Thresholds to Cold probe at Hallux, 1$^{st}$ Toe, 3$^{rd}$ Toe, 5th Toe, underneath the arch, Heel and the average and the total corresponding values for these sites. |
| 7 | Temperature Sensation and Tolerance Thresholds to Hot probe at Hallux, 1st Toe, 3rd Toe, 5th Toe, underneath the arch, Heel and the average and the total corresponding values for these sites. |
| 8 | Plantar Pressure at the lateral midfoot, central midfoot, medial midfoot, lateral hindfoot, medical hindfoot, and centre of the hindfoot. |
| 9 | Plantar Pressure at the Lateral Hallux, 2nd Toe, 3rd Toe, 4th Toe, 5th Toe, 1st Met head, 2nd Met head, 3rd Met head, 4th Met head, and 5th Met head |

Table 1: Blocks representing each set of covariates that were added to reach the final explanatory model.

| | All (1270) | | No Ulceration (1193-93.9%) | | With Ulceration (77- 6.1%) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Categorical Variable | No | % | No | % | No | % | Odd Ratio (CI at 95%) | P Value Multi-variate Analyses | P Value for differences [a] | Effect size for difference | Effect size classification |
| Male sex (1) | 696 | 54.8 | 643 | 53.9 | 53 | 68.8 | 1.488 (0.784-2.825) | 0.224 | 0.010 | -0.072 [b] | small |
| Previous Ulceration | 13 | 1.0% | 10 | 0.8% | 3 | 3.9% | | | 0.046 | 0.072 [b] | small |
| Amputation | 4 | 0.3% | 0 | 0.0% | 4 | 5.2% | $2.932 * 10^{9}$ (0- ∞) | 0.999 | 0.000 | 0.221 [b] | med |
| Presence of Callus | 209 | 16.5% | 199 | 16.7% | 10 | 13.0% | | | 0.491 | -0.024 [b] | |
| Foot deformity | 26 | 2.0% | 19 | 1.6% | 7 | 9.1% | 3.816 (0.826-17.632) | 0.086 | 0.000 | 0.126 [b] | Small/med |
| Mycosis | 34 | 2.7% | 31 | 2.6% | 3 | 3.9% | | | 0.794 | 0.019 [b] | |
| Nail Ingrowth | 4 | 0.3% | 2 | 0.2% | 2 | 2.6% | | | 0.008 | 0.103 [b] | small |
| Foot swelling | 76 | 6.0% | 38 | 3.2% | 38 | 49.4% | 16.456 (8.199-33.028) | 0.000 | 0.000 | 0.464 [b] | large |
| No Smoking (1,0) | 984 | 77.5% | 930 | 78.0% | 54 | 70.1% | | | | | |
| Past smoker (0,1) | 216 | 17.0% | 199 | 16.7% | 17 | 22.1% | | | 0.298 | 0.045 [c] | |
| Current smoker (0,0) | 70 | 5.5% | 64 | 5.4% | 6 | 7.8% | | | | | |
| No Alcohol cons. (Ref) | 721 | 56.8% | 681 | 57.1% | 40 | 51.9% | | | | | |
| Past Alcohol cons. | 392 | 30.9% | 362 | 30.3% | 30 | 39.0% | | | 0.255 | 0.047 [c] | |
| Current Alcohol cons. | 157 | 12.4% | 150 | 12.6% | 7 | 9.1% | | | | | |
| Ankle joint Normal Mobility | 1051 | 82.8% | 1013 | 84.9% | 38 | 49.4% | 0.438 (0.231-0.834) | 0.012 | 0.000 | -0.225 [b] | medium |
| MTP joint Normal Mobility | 1049 | 82.6% | 1011 | 84.7% | 38 | 49.4% | | | 0.000 | -0.223 [b] | medium |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Skin viability normal | 125 | 9.8% | 124 | 10.4% | 1 | 1.3% | | | 0.002 | 0.089 [c] | small |
| Skin viability Dry | 1127 | 88.7% | 1054 | 88.3% | 73 | 94.8% | | | | | |
| Skin Viability Dry with fissures | 18 | 1.4% | 15 | 1.3% | 3 | 3.9% | | | | | |
| Sensitivity to Monofilament - Absent (Ref) | 45 | 3.5% | 28 | 2.3% | 17 | 22.1% | | 0.177 | 0.000 | 0.300 [c] | large |
| Sensitivity to Monofilament- Impaired | 329 | 25.9% | 292 | 24.5% | 37 | 48.1% | 0.652 (0.229-1.861) | 0.424 | | | |
| Sensitivity to Monofilament - Normal | 896 | 70.6% | 873 | 73.2% | 23 | 29.9% | 0.337 (0.096-1.180) | 0.089 | | | |

Table 2: shows the categorical parameters for all participants and for each group of with and with no ulceration. [a]- P values based on Chi-square test of independence (with Yates continuity correction) P <0.5 indicates significant association between ulcerated and non-ulcerated group on the parameter. [b]- Effect size as the Phi coefficient, with small =0.01, Medium = 0.30, Large = 0.50; [c]- Effect size as Cramer's V coefficient (three categories), where small = 0.07, Medium = 0.21, Large = 0.35; [d] – Effect size as Cramer's V coefficient (four categories), where small = 0.06, Medium = 0.17, Large = 0.29

| Continuous Parameter | All | | | No-Ulceration | | | With Ulceration | | | OR (CI at 95%) | P- Multi-variate | P - Differences | Effect size[a] Difference | Effect size category |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Median | IQR | N | Median | IQR | N | Median | IQR | N | | | | | |
| Age (year) | 52 | 17.0 | 1270 | 52 | 12.5 | 1193 | 53 | 17.0 | 77 | | | .177 | -.038 | |
| Height (m) | 1.60 | 0.1 | 1270 | 1.60 | 0.1 | 1193 | 1.60 | 0.1 | 77 | | | .020 | -.065 | Small |
| Weight (Kg) | 73.7 | 20.7 | 1268 | 73.6 | 18.1 | 1191 | 74.0 | 20.8 | 77 | | | .752 | -.009 | |
| Body Mass Index (Kg/m$^2$) | 29.4 | 7.5 | 1270 | 29.4 | 5.5 | 1193 | 29.1 | 7.9 | 77 | | | .143 | -.041 | |
| Shoe size | 8 | 2.0 | 1268 | 7 | 2.0 | 1191 | 8 | 2.0 | 77 | | | .117 | -.044 | |
| Ankle Brachial Index (ABI) | 1.1 | 0.1 | 1270 | 1.1 | 0.1 | 1193 | 1.1 | 0.1 | 77 | | | .864 | -.005 | |
| Vibration Perception Threshold Average (V) | 20 | 14.3 | 1270 | 20 | 15.5 | 1193 | 35 | 15.0 | 77 | | | .000 | -.221 | Med |
| Duration of Diabetes (days) | 1095 | 2747.5 | 1270 | 1095 | 4380.0 | 1193 | 2920 | 2770.0 | 77 | 1.017 (0.973-1.064) | .453 | .000 | -.167 | Med |
| Plantar pressure at Hallux (KPa) | 253 | 155.0 | 1270 | 255 | 171.3 | 1193 | 215 | 152.9 | 77 | | | .007 | -.075 | Small |
| Plantar pressure at 2$^{nd}$ Toe (KPa) | 133 | 88.0 | 1270 | 135 | 78.8 | 1193 | 115 | 87.5 | 77 | | | .006 | -.078 | Small |
| Plantar pressure at 3$^{rd}$ Toe (KPa) | 88 | 67.5 | 1270 | 90 | 57.5 | 1193 | 68 | 65.0 | 77 | | | .000 | -.102 | Small |
| Plantar pressure at 4$^{th}$ Toe (KPa) | 58 | 50.0 | 1270 | 60 | 30.0 | 1193 | 48 | 52.5 | 77 | | | .002 | -.086 | Small |
| Plantar pressure at 5$^{th}$ Toe (KPa) | 30 | 37.5 | 1270 | 30 | 25.0 | 1193 | 18 | 37.5 | 77 | 0.977 (0.862-0.992) | .003 | .000 | -.105 | Small |
| Plantar Pressure 1$^{st}$ MTH (KPa) | 160 | 80.0 | 1270 | 158 | 83.8 | 1193 | 193 | 79.0 | 77 | | | .004 | -.081 | Small |
| Plantar Pressure at 2$^{nd}$ MTH(KPa) | 205 | 90.0 | 1270 | 205 | 86.3 | 1193 | 215 | 90.0 | 77 | | | .239 | -.033 | |
| Plantar Pressure at 3$^{rd}$ MTH (KPa) | 228 | 90.0 | 1270 | 228 | 86.3 | 1193 | 223 | 90.0 | 77 | | | .421 | -.023 | |
| Plantar Pressure at 4$^{th}$ MTH (KPa) | 213 | 82.5 | 1270 | 213 | 97.5 | 1193 | 220 | 82.5 | 77 | | | .214 | -.035 | |
| Plantar Pressure at 5$^{th}$ MTH (KPa) | 180 | 95.0 | 1270 | 180 | 121.3 | 1193 | 198 | 95.0 | 77 | | | .042 | -.057 | Small |
| Plantar Pressure at lateral midfoot (KPa) | 78 | 40.0 | 1270 | 78 | 37.5 | 1193 | 78 | 40.0 | 77 | | | .630 | -.014 | |
| Plantar Pressure at centre of midfoot (KPa) | 101 | 57.5 | 1270 | 101 | 65.0 | 1193 | 98 | 57.5 | 77 | | | .604 | -.015 | |
| Plantar Pressure at medial midfoot (KPa) | 68 | 35.0 | 1270 | 68 | 31.3 | 1193 | 68 | 35.0 | 77 | | | .670 | -.012 | |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Plantar Pressure at lateral hindfoot (KPa) | 115 | 50.0 | 1270 | 115 | 56.8 | 1193 | 110 | 50.0 | 77 | | | .604 | -.015 | |
| Plantar Pressure at medical hind foot (KPa) | 170 | 52.5 | 1270 | 170 | 50.0 | 1193 | 173 | 52.5 | 77 | | | .915 | -.003 | |
| Plantar Pressure at centre of hindfoot (KPa) | 122 | 62.5 | 1270 | 123 | 68.8 | 1193 | 118 | 62.5 | 77 | 1.004 (0.998-1.010) | .178 | .595 | -.015 | |
| TST to Cold probe at Hallux (°C) | 29 | 3.0 | 1254 | 29 | 0.5 | 1178 | 27 | 3.0 | 76 | | | .000 | -.207 | Med |
| TST to Hot probe at Hallux (°C) | 38 | 6.0 | 1253 | 38 | 1.0 | 1177 | 40 | 6.0 | 76 | | | .000 | -.197 | Med |
| TTT to Cold probe at Hallux (°C) | 21 | 3.0 | 1254 | 21 | 0.8 | 1178 | 19 | 3.0 | 76 | | | .000 | -.188 | Med |
| TTT to Hot probe at Hallux (°C) | 45 | 3.5 | 1254 | 45 | 1.3 | 1178 | 47 | 3.5 | 76 | | | .000 | -.219 | Med |
| TST to Cold probe at 3rd Toe (°C) | 29 | 2.5 | 1254 | 29 | 0.5 | 1178 | 27 | 2.5 | 76 | | | .000 | -.205 | Med |
| TST to Hot probe at 3rd Toe (°C) | 37 | 5.0 | 1254 | 37 | 0.5 | 1178 | 40 | 5.0 | 76 | | | .000 | -.191 | Med |
| TTT to Cold probe at 3rd Toe (°C) | 21 | 2.5 | 1253 | 21 | 1.0 | 1177 | 19 | 2.5 | 76 | | | .000 | -.173 | Med |
| TTT to Hot probe at 3rd Toe (°C) | 45 | 3.5 | 1254 | 44 | 1.5 | 1178 | 47 | 3.5 | 76 | | | .000 | -.198 | Med |
| TST to Cold probe at 5th Toe (°C) | 29 | 2.0 | 1253 | 29 | 1.0 | 1177 | 27 | 2.0 | 76 | | | .000 | -.196 | Med |
| TST to Hot probe at 5th Toe (°C) | 38 | 5.0 | 1254 | 38 | 1.0 | 1178 | 40 | 5.5 | 76 | | | .000 | -.192 | Med |
| TTT to Cold probe at 5th Toe (°C) | 21 | 3.0 | 1254 | 21 | 1.5 | 1178 | 19 | 3.0 | 76 | | | .000 | -.191 | Med |
| TTT to Hot probe at 5th Toe (°C) | 44 | 3.5 | 1254 | 44 | 1.3 | 1178 | 47 | 3.5 | 76 | | | .000 | -.219 | Med |
| TST to Cold probe underneath the arch (°C) | 28 | 3.0 | 1254 | 29 | 0.5 | 1178 | 27 | 3.0 | 76 | | | .000 | -.192 | Med |
| TST to Hot probe underneath the arch (°C) | 38 | 4.0 | 1254 | 38 | 0.5 | 1178 | 40 | 4.0 | 76 | | | .000 | -.189 | Med |
| TTT to Cold probe underneath the arch (°C) | 20 | 3.0 | 1254 | 21 | 1.3 | 1178 | 19 | 3.0 | 76 | | | .000 | -.174 | Med |
| TTT to Hot probe underneath the arch (°C) | 45 | 3.0 | 1254 | 45 | 1.0 | 1178 | 47 | 3.0 | 76 | 1.423 (0.999-2.028) | .051 | .000 | -.215 | Med |
| TST to Cold probe at Heel (°C) | 29 | 3.0 | 1254 | 29 | 0.3 | 1178 | 27 | 3.0 | 76 | | | .000 | -.179 | Med |
| TST to Hot probe at Heel (°C) | 38 | 3.0 | 1254 | 38 | 1.0 | 1178 | 40 | 3.0 | 76 | | | .000 | -.168 | Med |
| TTT to Cold probe at Heel (°C) | 21 | 3.0 | 1254 | 21 | 2.0 | 1178 | 19 | 3.0 | 76 | | | .000 | -.159 | Med |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| TTT to Hot probe at Heel (°C) | 45 | 3.0 | 1254 | 45 | 1.5 | 1178 | 48 | 3.0 | 76 | | | .000 | -.203 | Med |
| TST to Cold probe Total (°C) | 144 | 12.5 | 1254 | 144 | 4.3 | 1178 | 133 | 12.0 | 76 | 0.998 (0.927-1.074) | .955 | .000 | -.236 | Med |
| TST to Hot probe Total (°C) | 185 | 23.5 | 1254 | 185 | 16.5 | 1178 | 198 | 24.0 | 76 | | | .027 | -.062 | Small |
| TTT to Cold probe Total (°C) | 104 | 13.5 | 1254 | 104 | 7.5 | 1178 | 93 | 13.5 | 76 | | | .000 | -.174 | Med |
| TTT to Hot probe Total (°C) | 221 | 17.0 | 1254 | 220 | 19.5 | 1178 | 233 | 16.5 | 76 | 0.975 (0.948-1.003) | .080 | .170 | -.039 | |
| TST to Cold probe Average (°C) | 29 | 2.5 | 1248 | 29 | 0.4 | 1173 | 27 | 2.4 | 75 | 0.630 (0.445-0.891) | .009 | .000 | -.218 | Med |
| TST to Hot probe Average (°C) | 37 | 4.7 | 1254 | 37 | 1.0 | 1178 | 40 | 4.9 | 76 | | | .000 | -.154 | Med |
| TTT to Cold probe Average (°C) | 21 | 2.7 | 1251 | 21 | 0.9 | 1175 | 19 | 2.7 | 76 | 1.399 (1.096-1.786) | .007 | .000 | -.167 | Med |
| TTT to Hot probe Average (°C) | 44 | 3.3 | 1251 | 44 | 0.8 | 1175 | 47 | 3.3 | 76 | | | .000 | -.195 | Med |
| Vibration Perception Threshold Wrist (V) | 11 | 4.0 | 1270 | 11 | 3.5 | 1193 | 14 | 3.5 | 77 | | | .000 | -.178 | Med |
| Vibration Perception Threshold Knee (V) | 22 | 12.0 | 1267 | 22 | 10.0 | 1190 | 30 | 11.5 | 77 | | | .000 | -.193 | Med |
| Vibration Perception Threshold Ankle (V) | 21 | 13.5 | 1270 | 20 | 13.3 | 1193 | 34 | 13.0 | 77 | | | .000 | -.222 | Med |
| Vibration Perception Threshold Hallux (V) | 21 | 15.0 | 1270 | 21 | 16.5 | 1193 | 36 | 15.0 | 77 | | | .000 | -.231 | Med |
| Blood Glucose Level (mmol/L) | 12 | 7.9 | 1269 | 12 | 7.0 | 1192 | 10 | 7.9 | 77 | 0.938 (0.885-0.995) | .032 | .002 | -.085 | Small |

Table 3: shows the continuous parameters for all participants and for the groups with and with no ulceration. [a]- Mann-Whitney; $r = z / (N_1 + N_2)^{0.5}$ where 0.1 small effect, 0.3 medium effect, 0.5 large effect; Note that the selection of parameters in the logistic regression model was based on the univariate analyses in which parameters with P<0.2 were selected. The P values for these selected parameters are underlined in the table.