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Pin-prick (Medipin) assessment for neuropathy in diabetes: Prospective screening study in primary care

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ABSTRACT

Aims: Diabetic patients are at elevated risk of neuropathy; early detection is desirable to minimise the risk of complications. The Medipin pin-prick device was appraised as a screening tool for diabetic neuropathy.
Methods: Prospective cross-sectional comparative screening study in primary care setting, involving 389 participants with type 2 diabetes mellitus. The Medipin pin-prick method, involving dorsal application on the hallux of both feet, was compared to 10 g monofilament testing.
Results: The ternary and semi-quantitative approach for scoring Medipin pin-prick sensation give very similar results (Spearman rho 0.67, $P < 0.001$). A total of 59 % patients had no signs of neuropathy (sharp sensation), 38 % reported impaired sensation (dull sensation), and an absence of sensation occurred in 3 % of patients. For the monofilament dorsal method, the figures were 79 % no neuropathy, 14 % elevated risk, and 7 % neuropathy respectively, and with the monofilament plantar method 87 % of patients had no neuropathy and 13 % did. Correlation analyses showed that taller patients and those with existing neuropathic pain are at very modest increased risk of neuropathy.
Conclusions: The Medipin pin-prick device can identify diabetic neuropathy and detects (first signs of) neuropathy in relatively more patients than 10 g monofilament testing. The differential targeting of nerve types, namely predominant small (Medipin) versus large (monofilament) fibre, likely underpins the difference in outcomes.

1. Introduction

Diabetes mellitus is a chronic condition that can lead to multiple complications affecting various organs, including diabetic neuropathy (DN) of the lower limbs. A reduced sensation in the feet increases the risk of developing ulcers and further morbidity [1]. The exact prevalence of diabetic neuropathy depends on the applied diagnostic method, but may be higher than 25 % amongst diabetic patients [2,3]. It is imperative to ensure DN is diagnosed early in patients with diabetes, and that patients are educated to look after their feet to minimise the risk of further complications.

In regular clinical practice in GP practices and the wider National Health Service (NHS) of the United Kingdom (UK), the use of a 10 g monofilament is the mainstay for DN screening. Two types of nerves are present in the skin, and diabetes-related damage can lead to both a) large fibre neuropathy, which manifests with the loss of joint position and vibration sense and sensory ataxia, and b) small fibre neuropathy, involving impairment of perception of pain, temperature and autonomic functions [4]. Monofilament application therefore tests predominantly for large fibre damage. There is evidence that small fibre damage develops before large fibre damage manifests, which may be of value if early intervention and prevention for DN is the goal [2,5–7]. Recently, Burgess and colleagues [4] stated "DN is diagnosed at a late, often pre-ulcerative stage due to a lack of early systematic screening and the endorsement of monofilament testing which identifies advanced neuropathy only".

A fit-for-purpose pin-prick test of the feet allows screening for predominantly small fibre function and should be a beneficial test since impairment in pain perception of the feet may risk injury [8,9]. The use of a pinprick has been utilized and reported on in the past [10,11]. It was

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shown that inability to perceive the pin-prick challenge is significantly associated with a risk of developing ulcers. However, this type of test does not feature in current the UK's National Health Service (NHS) guidance on screening for DN [12]. One reason may be that in the past very rudimentary or home-made pinprick device were utilized in the absence of a fit-for-purpose device. Taken together, there is a lack of evidence concerning the use of affordable and easily applicable pin-prick devices to diagnose DN in a real-world community and primary care setting. This study will determine the prevalence of DN using the Medipin pin-prick device and compare this to two methods using a 10 g monofilament device, to determine how DN detection rates compare between rapid screening devices that check chiefly for small fibre and large fibre damage, respectively.

2. Methods

2.1. Study design & patients

A prospective cross-sectional screening study was carried out between June 2023 and August 2024. After a postal invite, interested patients were seen at a one-off study visit. Patient enrolment was conducted at 11 GP practices in England. For each GP practice, the list of potentially eligible patients was randomised since a ~40 % sample of the total number of patients was screened and invited if indeed eligible. Patient inclusion criteria were adults aged $\geq$ 18 years with type II diabetes mellitus, diagnosed in accordance with national clinical guidelines [13]. Exclusions were lack of mental capacity, concurrent (medical) conditions that could compromise patient safety or study objectives (examples include receiving palliative care, active cancer treatment, patient immobile), amputation of a lower limb, confirmed and ongoing wound or ulcer located on the foot. The study was registered (ref ISRCTN11300898), and research governance clearance was obtained from UK ethics (ref 23/WM/0095), health research authority (reference 325532) and NHS sponsor. Written informed consent was obtained from all participating patients prior to any screening tests taking place.

2.2. Interventions and primary outcome measures

As part of the study visit, three DN screening tests were conducted in the same order: two different 10 g monofilament protocols and a Medipin pin-prick test.

- The 10 g monofilament plantar test.
  This concerns five applications in five different plantar areas of each foot. Presence (score of 1) or absence (score of 0) was recorded and therefore a maximum total score of 10 could be achieved. A total score of 8 or lower indicates presence of DN [14,15].
- The 10 g monofilament dorsal (hallux) test.
  First the monofilament was applied five times to the patient's forearm to obtain a reference sensation. Then the monofilament was applied four times to each large toe, above the nail bed. Per application to the dorsal hallux, either 1 (same or elevated sensation as to forearm), 0.5 (reduced sensation) or 0 (no sensation) can be scored A total score of between 5.5 to maximum score of 8 indicates normal nerve function. A score of between 3.5 and 5 indicates elevated risk of DN, whereas a total score of below 3 is deemed presence of DN [16].
- Medipin pin-prick test.

The Medipin pin-prick device (Medipin Ltd) is a UKCA-marked (UK, MHRA No. 1321) neuropathy test device. It was first applied five times to the patient's forearm to achieve a reference sensation. Subsequently, the Medipin device was applied once to the left and right hallux on the dorsal side adjacent to the nail bed (identical location to the 'dorsal' monofilament method). Two response elements were recorded for Medipin: a) a ternary outcome where the sensation on the toe can be sharp, dull or absent, and b) what the toe sensation score is compared to the forearm reference sensation using a 10-cm Likert visual display scale (with the forearm sensation being a score of 5 out of 10 cm). The ternary scoring system is an adoption of previous work [11]. In cases where no sensation was felt by the patient, the Medipin was applied once more to confirm the result.

A total of six practitioners applied the tests and all completed a collective training session to optimize correct and consistent methodology.

2.3. Secondary outcome measures and statistical analyses

Patient demographics, medical history, medicine use, and anthropometric measurements were obtained (from patient's medical records where available). Due to the vast number and types of medications in use, a dichotomous approach was taken to broadly determine if patients were prescribed: anti-hypertensives, non-insulin diabetes medication, and insulin medication. Two validated questionnaires were completed by patients, namely the quality of life survey EQ-5D-5L and the Michigan Neuropathy Screening Instrument (MNSI) symptom questionnaire [17, 18].

The aim was to have a sufficiently large sample to determine the prevalence of DN for each screening test with 95 % confidence interval and 5 % precision, assuming a theoretical conservative 10 % prevalence of DN. In this scenario a minimum 139 patients would have to recruited, and the aim was to exceed this number if possible. There is a wide variation in reported DN prevalence, with Burgess and colleagues mentioning a range of 10–50 % [4]. Data was collated on paper case report forms, transferred into Excel (Microsoft) and analysed using SPSS (v24, IBM) statistical analysis software. Correlation coefficient calculations, Kendall's tau concordance analysis, and binary logistic regression analysis were applied as indicated in the Results section (P of <0.05 deemed statistically significant). In order to have sufficient cases for regression analysis and to align with the binary outcome monofilament plantar method, for both Medipin and monofilament dorsal the 'elevated risk of neuropathy' and 'neuropathy' cases were combined and compared to 'no neuropathy'. The presented odds ratios (OR) express the risk of neuropathy for patients with the risk factors as compared with those without the risk factors.

3. Results

From list of potentially eligible patients, a random total of 2532 were screened in more detail for eligibility criteria and 1815 patients invited. An initial 466 patients expressed an interest and ultimately 399 patients gave consent and participated in the study (22 % accrual rate based on invites). Ten patients were excluded due to them not having T2DM upon further review, leaving 389 participants included for analyses. No adverse events related to the use of Medipin or monofilament were

Table 1,
Patient demographics, medical history, medicine use, and anthropometric measurements.

Variable	Value distribution
Sex	244 male (63 %) / 145 female (37 %)
Patient age, mean (95 % CI)	67 years (67−68)
Patient height, mean (95 % CI)	171 cm (170−172)
BMI, mean (95 % CI)	33 kg/m^2 (30−38)
Smoking status	36 current / 156 ex / 197 never
T2DM chronicity, mean (95 % CI)	17 years (6−27)
Pre-existing neuropathic pain	45 yes (12 %) / 344 no (88 %)
Anti-hypertension medication prescribed	297 yes (76 %) / 92 no (24 %)
Non-insulin diabetes medication prescribed	333 yes (86 %) / 56 no (14 %)
Insulin diabetes medication prescribed	61 yes (16 %) / 328 no (84 %)

95 % CI = 95 % confidence interval; BMI = body mass index; T2DM = type 2 diabetes mellitus.

observed. Table 1 provides a summary of the patient characteristics. The participants were a mean 67 years of age and predominantly male (63 %). On average they had been diagnosed with T2DM 17 years ago, 86 % were prescribed non-insulin diabetes medicines and 16 % were prescribed insulin medication Since the established monofilament tests - dorsal application and plantar application respectively – both apply a single outcome based on measurement of both patient's feet, an initial analyses involves comparing Medipin pin-prick results for the left and the right foot for each patient. Out of the 389 dual Medipin tests, a total of 291 (75 %) gave the same outcome for the left and right foot in terms of ternary feedback (sensation absent / dull sensation / sharp sensation), Spearman rho 0.45 ($P < 0.001$). The largest variation concerned the patient perceiving the sensation as sharp in one foot and dull in the other, or vice versa (89 out of 389 cases, 23 %). When the association strength between left and right foot sensation scores for the 10-cm Likert scale were compared, the Spearman rho value measured 0.54 ($P < 0.001$). The median score for the left foot was 5.0 (inter-quartile range [IQR] 3) and for the right foot the median was 5.0 (IQR 3.0) too. Therefore, for comparison analyses involving Medipin with the other neuropathy outcome measures, the 'worst' ternary score of the two feet and the average 10-cm Likert score for the two feet were used. There is a distinct distribution pattern when Medipin ternary and Likert scoring is compared, with a score of 5 seemingly the differentiator between a sharp and a dull (or absent) sensation; this is illustrated in Fig. 1. For those experiencing Medipin as sharp, n = 229, the median 10-cm Likert score was 6.0 (IQR 2.0); for those experiencing it as dull, n = 147, the median score was 4.0 (IQR 2.0); and for those with absent sensation, n = 13, the median score was 0 (IQR 1.8). The correlation between the two Medipin test scoring methods is strong; the Spearman rho value is 0.67 ($P < 0.001$). Distribution of test results between Medipin and monofilament tests is outlined in Table 2. Comparatively more patients report a dull sensation when the monofilament test result indicates that there is no neuropathy present (or elevated risk in case of dorsal monofilament test method). Conversely fewer patients report an absence of Medipin pin-prick sensation when compared to the rate of definitive neuropathy as measured with a monofilament method. Fig. 2 illustrates the observation that (a degree of) neuropathy is observed more often with Medipin testing versus 10 g monofilament testing. A dull sensation with Medipin is perceived by 107 out of 389 patients (28 %) in the population where the 10 g monofilament dorsal test result is normal. Conversely, only 27 patients (7 % of total sample) have an abnormal 10 g monofilament dorsal test result (risk of or total neuropathy) when the Medipin test is normal. The strength of the association between Medipin testing and the other screening methods used in the study is summarized in Table 3. Overall, the correlations between the two monofilament tests and also MNSI score are higher than associations with Medipin ternary outcomes. The concordance values, as determined through Kendall's tau, are virtually identical to the Spearman correlation coefficient values when the DN device test methods are compared: 0.32 ($P < 0.001$) for Medipin ternary versus monofilament dorsal, 0.28 ($P < 0.001$) for Medipin versus monofilament plantar, and 0.43 ($P < 0.001$) for monofilament dorsal versus monofilament plantar.

Binary logistic regression was conducted to deduce if any variables are significantly associated with impaired nerve function, see Table 4. In the regression models, patient height is associated with increased risk of neuropathy with both Medipin and monofilament methods, as is known

Table 2,
Distribution of neuropathy diagnoses for different screening methods.

Test method	Total n = 389		
	No neuropathy	Elevated risk#	Neuropathy
Medipin*, % (n)	59 % (229)	38 % (147)	3 % (13)
Monofilament dorsal, % (n)	79 % (309)	14 % (54)	7 % (26)
Monofilament plantar, % (n)	87 % (338)	n/a	13 % (51)

*As measured with ternary outcome method with sharp / dull / absent sensation options. # For Medipin, a dull sensation; for monofilament dorsal, score between 3.5 and 5; for monofilament plantar, not an outcome option.

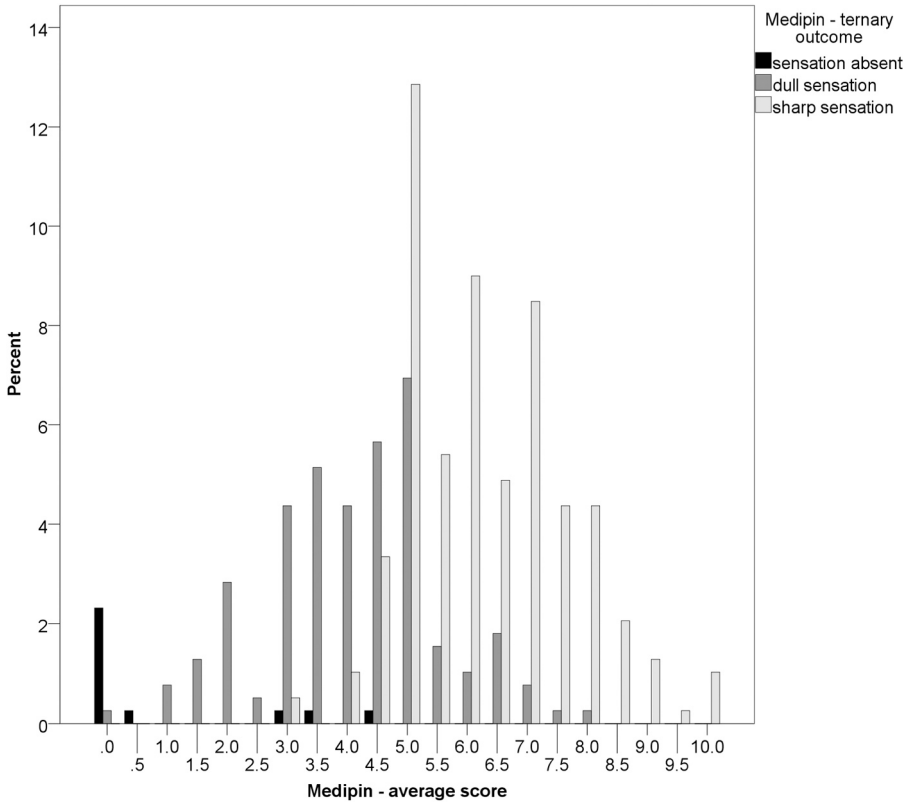

Fig. 1,. Comparison of Medipin ternary scoring and 10 cm visual display scale scoring.

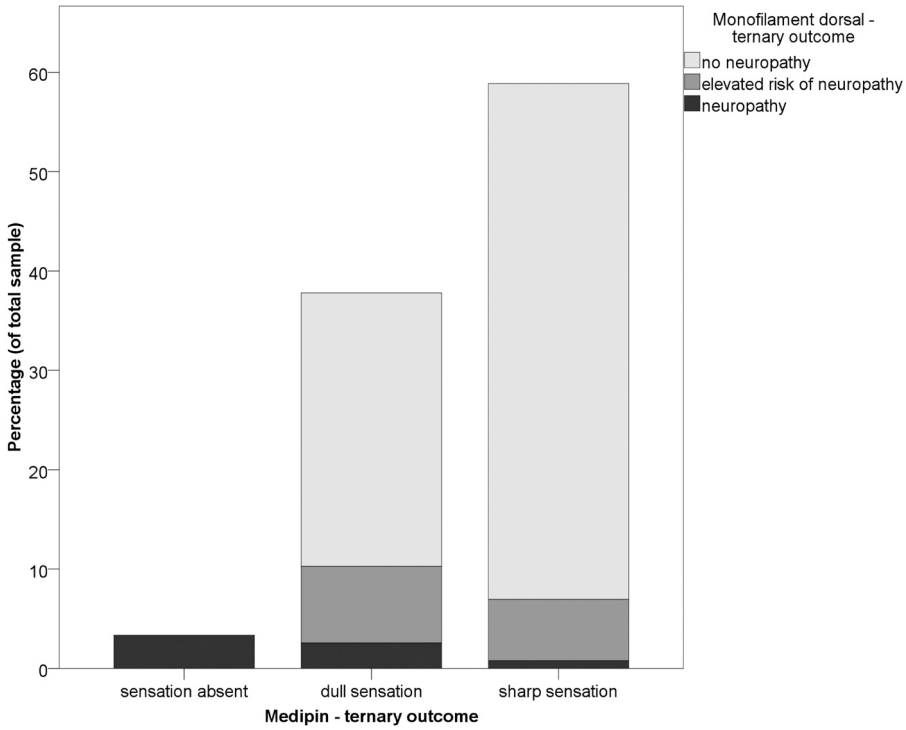

Fig. 2,. Comparison of outcomes with Medipin testing and 10 g monofilament dorsal testing.

Table 3,
Spearman rho correlation analyses of different test methods for diabetic neuropathy.

n = 389	Spearman rho [95 % confidence interval] (significance *P*)			
	Medipin – 10-cm Likert score	Medipin – ternary outcome	Monofilament dorsal – ternary outcome	Monofilament plantar – binary outcome
Medipin - ternary outcome	0.67 [0.61–0.73] ($P < 0.001$)			
Monofilament dorsal – ternary outcome	0.38 [0.28–0.47] ($P < 0.001$)	0.33, [0.22–0.44] ($P < 0.001$)		
Monofilament plantar – binary outcome	0.27 [0.15–0.37] ($P < 0.001$)	0.28 [0.16–0.37] ($P < 0.001$)	0.44 [0.31–0.56] ($P < 0.001$)	
MSNI total score	0.20 [0.10–0.30] ($P < 0.001$)	0.25 [0.15–0.34] ($P < 0.001$)	0.33 [0.24–0.42] ($P < 0.001$)	0.31 [0.22–0.39] ($P < 0.001$)

neuropathic pain for the monofilament methods. However, univariate Spearman association analysis between Medipin ternary outcome and pre-existing neuropathic pain does show a significant rho value of 0.17 ($P < 0.001$). All three regression models are statistically valid yet weak, with the Medipin model explaining merely 8 % of variance in outcome of the dependent.

4. Discussion

This study appraises the use of the healthcare-approved Medipin pin-prick device. Unlike with testing for mainly large fibre nerve damage using the reusable monofilament device, testing for small fibre damage by pin-prick testing requires more force and should therefore be conducted using a single use disposable device that does not penetrate through the skin. A pin-prick test has historically been part of quick and inexpensive testing for neuropathy. Before infection prevention and patient/staff safety became more prominent features of clinical practice, a pin-prick was performed with e.g. a push pin, a toothpick or another sharp implement [11]. One group devised a weighted pin-prick device using a hypodermic needle [19], and another took the following approach: “Pinprick sensation was tested with a sterile or unused safety pin” [20]. This highlights the need for a demonstrably safer and more practical solution. Medipin is a sharp device but due to its safety design, a very short sharp part directly followed by a wider annulus which acts as a limiter, the device does not push through the skin. Here an in-depth appraisal is presented for Medipin, involving two scoring modalities. Both a ternary (sharp, i.e. no neuropathy / dull, i.e. some loss of sensation and therefore elevated risk of neuropathy / absent sensation, i.e. neuropathy) scoring system and a semi-quantitative 10-cm Likert scale can be applied. Compared to monofilament testing, the Medipin device detects more at-risk patients. These results are in line with other published results showing that small nerve fibres are affected earlier than large nerve fibres [2,4,7].

The different target nerve fibre types for the two test devices for detection of neuropathy mean that an accuracy appraisal (i.e. sensitivity and specificity against a gold standard test) is not indicated in this present study. Pin-prick testing accuracy has previously been compared to skin biopsy as gold standard in a population of patients with carpal tunnel syndrome. The conclusion was that this is a cost-effective way to test for small nerve fibre damage; complementation with a cold/warm testing using e.g. a coin can give marginally improved performance [21]. It appears that 10 g monofilament testing has been a mainstay in clinics predominantly due to its affordability and the speed with which it can be applied. Systematic reviews that summarized the accuracy of

Table 4,
Binary logistic regression for each screening method, combined outcome of elevated risk of and presence of neuropathy versus no neuropathy.

	Dependent, and odds ratio (95 % CI) values		
Variable	Medipin[#]	Monofilament dorsal~	Monofilament plantar[$]
EQ−5D-5L total score	0.48 (0.15–1.51)	0.34 (0.09–1.33)	1.50 (0.28–8.05)
EQ−5D-5L health index value	1.00 (0.98–1.01)	0.98 (0.96–0.99) *	0.98 (0.96–1.00)
patient sex (male, female)	0.48 (0.25–0.93)*	1.15 (0.50–2.67)	0.51 (0.19–1.38)
patient age	1.01 (0.98–1.04)	0.99 (0.96–1.03)	1.01 (0.97–1.05)
patient height	1.05 (1.02–1.09)*	1.03 (0.99–1.08)	1.05 (1.00–1.11) *
BMI	0.97 (0.94–1.01)	0.99 (0.95–1.04)	1.01 (0.99–1.02)
T2DM chronicity (years)	1.00 (1.00–1.00)	1.00 (0.99–1.01)	1.00 (0.99–1.01)
smoking status (never, ex, current)	0.95 (0.68–1.32)	1.09 (0.72–1.66)	0.93 (0.56–1.56)
antihypertension medication	1.20 (0.70–2.05)	1.41 (0.68–2.94)	3.32 (1.09–10.14)*
pre-existing neuropathic pain	1.51 (0.77–2.95)	3.67 (1.77–7.61) *	5.18 (2.39–11.20)*
non-insulin T2DM medication	1.01 (0.54–1.86)	0.60 (0.28–1.29)	1.30 (0.45–3.77)
insulin medication	1.48 (0.82–2.65)	0.90 (0.42–1.91)	1.32 (0.57–3.07)
Model strength, Nagelkerke R^2	0.08	0.20	0.20

*Statistically significant, $P < 0.05$. #Ternary outcome combined into binary outcome: with sharp versus dull/absent sensation options. ~Ternary outcome combined into binary outcome: no neuropathy (score 5.5–8, out of 8) versus elevated risk (score 3.5–5)/neuropathy (score 0–3). $Existing binary outcome, no neuropathy (score 9 or 10, out of 10) versus neuropathy (score 8 or lower).

10 g monofilament testing with nerve conduction testing as gold standard concluded that monofilament testing is not particularly accurate (partly due to variety in application methodology) and should not be the sole method for neuropathy testing [22,23]. National clinical guidelines unfortunately do not settle the matter of number and exact locations for monofilament application either, with the UK's National Institute for Health and Care Excellence (NICE) not giving detailed guidance on how to assess for diabetic neuropathy [12]. The end result is that different NHS Trusts use different methods to determine if a patient has DN; hence two monofilament methods were compared to Medipin in this study. Of the two, the monofilament dorsal method appears to give the most similar results and it uses a ternary outcome scale. Furthermore, the monofilament plantar method does not discriminate for 'at risk' patients; neither does it use a reference sensation on the patient's forearm.

There are a number of study strengths and limitations to consider. A sufficiently large sample of only T2DM patients was used in this study, which proved necessary since the number of patient with complete absence of sensation in the Medipin test was very low at 3 %. Although patients from different GP practices were enrolled, all patients were white race and more males responded to the study invites. Type 1 diabetes mellitus patients were not included to keep the sample homogenous, and non-diabetic patients were excluded since diabetes is a major known risk factor for neuropathy and only diabetics are screened for it in standard clinical practice [1,24]. Repeat tests on the same patients were not conducted in this study for either monofilament or Medipin devices. For the latter, the vast majority of patients did report either a sharp or dull sensation and this was a) close to the reference sensation on the forearm, and b) very similar in both feet. Those with an absence of sensation tended to report this for both devices. There is an inherent and recognised risk of variation in patient response depending on the exact location where a monofilament or Medipin device is placed on the skin, and this alone makes performing accuracy studies challenging [25]. For this reason, and because the operator performs an initial test on the patient's forearm which creates an internal reference point for both patient and performer, inter-operator comparisons were not conducted either.

Two outcome options were appraised for Medipin, namely ternary and semi-quantitative. The former was applied since it has been devised and reported on previously for use with standard, unsafe, pin-prick [11]. The 10-cm visual analogue scale (with Likert points every 1-cm), taken from a standard validated scale used for generic pain [26], was appraised because it may potentially be practical for more precise monitoring of patients over time. Since the two scoring methods correlate well, future studies may utilise Medipin and the 10-cm visual analogue scale (with Likert points every 1-cm) to see how a patient's score changes over a longer time period of a few years. For both outcome scoring methods, an in-depth performance appraisal involving Bland-Altman analysis for paired test-retest measurements was not conducted. However, the pin-prick method has been utilised for decades and in case of absent sensation patients the test was repeated. To further validate either scoring system, establishing the prevailing Medipin test score can be achieved by applying it three times per foot. This could be applied in a follow-up study.

With the sample size and dataset of this study, no discernible difference could be observed in terms of any risk factors that may be associated with the presence of (elevated risk of) diabetic neuropathy. Although height and existing neuropathic pain were associated with abnormal Medipin and 10 g monofilament test results, observed by others before, other variables associated with diabetic neuropathy – and included in our analysis, such as patient age and BMI, and duration of diabetes – were not [27–29]. A challenge around the identification of risk factors for diabetic neuropathy is the multitude of different neuropathy test methods applied when looking at variables that may be associated with diabetic neuropathy. In this study, limitations were non-inclusion of some blood markers such as HbA1c, lipoproteins, triglycerides, and the cross-sectional study design. The progression rate of impaired protective sensation is relatively poorly understood; however, there is some evidence that progression of diabetic neuropathy develops over years and differs depending on the exact nature of the diabetes (type 1 versus type 2) [7,30]. Future studies involving the use of Medipin could further explore how diabetic neuropathy manifests itself over time and whether there is any benefit of using the ternary scoring method or the semi-quantitative method.

5. Conclusions

Making patients aware of any impaired pain perception they have in their feet may enable them to take evasive action to minimise damage to the feet (for example through compliance with wearing footwear). Medipin is an affordable and safe pin-prick device to screen for diabetic neuropathy, and appears to detect loss of protective sensation sooner than with monofilament testing. The device can be used as standalone test or complement 10 g monofilament testing since each respective test targets slightly different nerve types (small versus large fibre). Other more advanced and quantitative devices to detect small fibre nerves are available, but significant disadvantages with some of those are complexity and cost; for example, plantar thermography is technically relatively time-consuming and challenging to conduct and skin biopsy is invasive [31]. Further long-term monitoring of diabetic patients with Medipin may aid in obtaining evidence on the development and progression of impaired (small fibre) nerve function.

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional guidelines on human experimentation (Health Research

Authority, UK) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics approval was obtained via Health Research Authority (reference 325532) and Research Ethics Committee (reference 23/WM/0095). Participants consented to participating in the study in line with Declaration of Helsinki on Good Clinical Practice.

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Declaration of Competing Interest

None to declare.

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Author contribution

SF, conceptualisation, funding acquisition, chief investigator, study oversight, data collation, writing-reviewing & editing; HG/NK/DL, methodology, investigation, data collation; LJ, conceptualisation, investigation, methodology, formal analysis, writing-original draft.

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