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## DM

# Symptom scoring systems to diagnose distal polyneuropathy in diabetes: the Diabetic Neuropathy Symptom score

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#### Abstract

**Aims** To provide one of the diagnostic categories for distal diabetic polyneuropathy, several symptom scoring systems are available, which are often extensive and lack in validation. We validated a new four-item Diabetic Neuropathy Symptom (DNS) score for diagnosing distal diabetic polyneuropathy.

**Methods** We compared score characteristics of the generally accepted Neuropathy Symptom Score (NSS) with the DNS score, and tested construct validity, predictive value and reproducibility with the Diabetic Neuropathy Examination score, Semmes–Weinstein monofilaments and Vibration Perception Threshold (clinical standards) in 73 patients with diabetes (24 Type 1, 49 Type 2; 43 male/30 female; mean age 57 years (19–90); mean diabetes duration 15 years (1–43)).

**Results** Correlation between NSS and DNS score was high (Spearman r = 0.88). Patient scores were more differentiated on the DNS score. The relation of the NSS and DNS scores, respectively, with clinical standards was good (Spearman r = 0.21-0.60). Reproducibility of the DNS score was high (Cohen weighted  $\kappa 0.78-0.95$ ). The DNS score was easier to perform in clinical practice.

**Conclusions** The DNS is validated, fast and easy to perform, with a high predictive value when screening for diabetic polyneuropathy.

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**Keywords** diabetic neuropathy, symptom score, polyneuropathy, DNS score, DNE score

#### Introduction

Distal symmetric polyneuropathy is a common complication of diabetes and a major cause of diabetic foot ulcers [1,2]. When diagnosing neuropathy, the San Antonio Consensus recommended at least one measurement in five different diagnostic categories [3], including symptoms. Symptom scores should fulfil the criteria as described by Jaeschke, including validation (independent reference standard, adequate spectrum and number of patients, standardization, soundly based item selection), predictive value and practicality (reproducibility, performance in clinical practice) [4].

Several symptom scores have been developed to assess symptoms of diabetic neuropathy, including the Neuropathy Symptom Score (NSS) [5–8]. The latter has been widely studied and is known to be valid and sensitive. It is extensively used in clinical practice. Several adaptations are available such as the Neuropathy Symptom Profile, the Michigan Neuropathy Screening Instrument (MNSI) and the modified NSS scores of Veves and Young [9–12]. However, none of these scoring systems fulfils all Jaeschke's diagnostic criteria. Our aim was to validate a new, four-item Diabetic Neuropathy Symptom (DNS) score for diagnosing distal neuropathy in diabetes, and compare it with the NSS.

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#### Table 1 Patient characteristics

n	73
Mean age (years) (SD)	56.9 (16.1)
Minmax. (years)	19–90
Mean duration DM (years) (SD)	14.9 (9.9)
Minmax. (years)	1-43
Sex, male-female	43-30
Type DM 1–2	24-49
Mean HbA <sub>1c</sub> (%) (sD)	8.7 (1.4)
Minmax.	6.6-13.5
Retinopathy, %	40
Nephropathy, %	42
Peripheral vascular disease, %	38
Present or former ulcer, %	20

#### **Patients and methods**

#### Patients

We studied 73 patients with diabetes, covering the entire spectrum of secondary complications. Informed consent was obtained. Exclusion criteria were factors which may have interfered with the neurological condition other than neuropathy. Fifty patients were randomly selected from the diabetes out-patient clinic of the University Hospital Groningen. The other 23 all had obvious diabetic foot complications or clinical neuropathy, and attended the Rehabilitation Centre Beatrixord. Patient characteristics are shown in Table 1.

#### Methods

The same researcher (J.W.G.M.) examined all 73 individuals. The symptom scores were obtained first, followed by clinical standards: a physical examination score (the Diabetic Neuropathy Examination (DNE) score) and quantitative sensory tests (Semmes–Weinstein Monofilaments (SW-MF) and Vibration Perception Thresholds (VPT)), respectively.

#### Symptom scores

NSS The NSS consists of 17 items, eight focusing on muscle weakness, five on sensory disturbances and four on autonomic symptoms [5,6]. Items that are answered negative/absent are scored 0, presence scored as 1 point. The maximum score is 17 [5–8].

DNS score An expert panel developed a four-item symptom score for diabetic neuropathy, consisting of a diabetologist, a vascular internist, a neurologist and a physician for rehabilitation medicine. The DNS score has the following items: (i) unsteadiness in walking, (ii) pain, burning or aching at legs or feet, (iii) prickling sensations in legs or feet, and (iv) numbness in legs or feet. Presence is scored 1, absence 0, maximum score 4 points. Guidelines to use with the score are shown in the Appendix.

#### Clinical standards

The DNE score, SW-MF and VPT were chosen as clinical standards to study the construct validity of the symptom scores for neuropathy.

DNE score This is a validated, hierarchical physical examination score, identifying distal symmetric polyneuropathy [13]. It exists of eight items, two testing muscle strength, one a tendon reflex, and five sensation. The maximum score is 16. A score > 3 points is considered abnormal.

Semmes–Weinstein monofilaments These were tested on the plantar surface of the hallux and centrally at the heel (when necessary after removal of excessive callus), using standard guidelines [14–17]. We used the 'yes–no' method, meaning that the patient says yes each time he/she senses the application of a monofilament. Six trials were taken; when the patient was unable to respond correctly in more than one trial, a heavier monofilament was taken. The 1, 10 and 75-g monofilaments were used [14–17]. Insensitivity to the 10-g monofilament was defined as abnormal.

Vibration Perception Threshold VPT was tested using a hand-held biothesiometer at the dorsum of the hallux on the interphalangeal joint and at the lateral malleolus [18–20]. The voltage of vibration was increased until the patient could perceive vibration on three occasions. The mean of these was used to determine the VPT. Age-adjusted reference values were used [18–20], with values higher than the mean +  $2 \times sD$  (reference value) considered abnormal.

#### Reproducibility

To test reproducibility of the DNS score, inter- and intra-rater agreement was assessed in a separate study on 10 patients. The six women and four men, with a mean age of 50.0 years (sD 15.9) had a wide range of neuropathy severity. The mean duration of diabetes mellitus (DM) was 11.5 years (sD 10.5); three participants had Type 1, and seven Type 2 DM. Two doctors rated these on two occasions at 1-week intervals.

#### **Statistical analysis**

Internal consistency of the symptom scores was assessed by calculating Cronbach's  $\alpha$ , and reliability coefficient  $\rho$ , which is comparable to  $\alpha$ . The statistical package SPSS-PC was used to compute the descriptive statistics, reliability coefficient Cronbach's  $\alpha$ , Spearman's correlation coefficient *r*, Student's *t*-test and ROC curves [21].

Inter- and intra-rater agreement was assessed using Cohen's weighted  $\kappa$  [22,23].

#### Results

The NSS and DNS scores, scored a mean (sD) of 1.9 (2.0), and 1.1 (1.3), respectively. The reliability of the DNS score (0.64) was somewhat lower than of the NSS (0.74). Correlation (Spearman *r*) between these two symptom scores was 0.88 (P < 0.001).

#### Relationship of NSS and DNS with the clinical standards

Spearman's correlation coefficient *r* for the DNE score with NSS and DNS score was similar at 0.56 and 0.60 (both P < 0.001), respectively. Scores between the monofilament, NSS and DNS scores were 0.21 (NS) and 0.25 (P < 0.05), respectively; and for VPT, 0.46 and 0.56 (both P < 0.001), respectively.

Table 2	The relation	n of clinica	l standard	s to symptoi	n scores
DNE sco	ore				

	n	Mean NSS (sd)	Mean DNS (SD)	
0	24	0.92 (1.47)	0.42 (0.93)	
1 48		2.42 (2.07)	1.52 (1.24)	
		P = 0.002	P = 0.000	
SW-MI	F hallux			
	п	Mean NSS (sd)	Mean DNS (SD)	
0	45	1.42 (1.42)	0.84 (1.04)	
1	25	2.64 (2.63)	1.56 (1.41)	
		P = 0.014	P = 0.019	
VPT ha	llux			
	n	Mean NSS (sd)	Mean DNS (SD)	
0	39	1.28 (1.47)	0.67 (0.98)	
1	32	2.63 (2.34)	1.69 (1.30)	
		P = 0.004	P = 0.000	

Group 0, Normal on clinical standard; group 1, disturbed on clinical standard.

The NSS and DNS scores predicted the clinical standards adequately (Table 2).

#### Sensitivity/specificity and reproducibility

Figure 1 shows the ROC curves of the NSS and DNS, respectively, compared with the DNE. The areas under the curve are 0.75 and 0.78 for NSS and DNS, respectively. Using the monofilament at the hallux these values were 0.62 and 0.65, respectively; and using VPT 0.68 and 0.73.



Figure 1 ROC curves of NSS and DNS scores in relation to the DNE score.

At a cut-off point of 0 vs. 1–4 for the DNS, sensitivity was 79% and specificity 78%, using the DNE. With the monofilament, sensitivity was 81% and specificity 56%, and VPT 81% and 58%, respectively.

The intra-rater agreement showed a Cohen's weighted  $\kappa$  for both raters of 0.89 and 0.78, the inter-rater agreement on two occasions was 0.95 and 0.83, respectively, indicating a good to very good level of agreement [22,23].

#### Discussion

The DNS and NSS scored similarly and both fulfil the Jaeschke criteria for diagnostic tests. Although the NSS has been validated previously and is widely accepted, it is probably too extensive to be used in every day clinical practice to diagnose neuropathy. Other, shorter scoring systems and modifications do not appear to fulfil the criteria for diagnostic tests. Thus, we propose the four-item DNS score as a fast and easy to perform symptom score with high reproducibility. The DNS has been validated using standard clinical methods, but might be too short to provide reliable follow-up when used alone.

Sensitivity and specificity of the DNS score were high when defined using other standard methods for evaluating neuropathy. Because the DNS score will be used for screening purposes, a high sensitivity is to be preferred. A score of 1 or more points on the DNS score is sensitive when identifying neuropathy. In combination with the results of the other diagnostic categories, classified by the San Antonio Consensus, the type and severity of neuropathy can be estimated. Unfortunately, the relative importance of different categories of the San Antonio Consensus in diagnosing diabetic neuropathy and predicting diabetic foot complications is unknown.

Controversy exists about the use of symptom scoring in diagnosing diabetic neuropathy [7,24–27]. In our report, significant and clinically relevant correlations were shown between the symptom scores and other methods which can predict diabetic foot complications. We believe that symptom scoring should complement other diagnostic categories for diabetic neuropathy [3].

However, symptom scores may be less reliable [3,4,8], due to their subjectivity. Using dichotomous scores may improve reproducibility [3], a feature of the DNS.

In conclusion, the DNS has been validated for cases of diabetic polyneuropathy, and is fast and easy to perform in clinical practice. However, it should be used in combination with other methods.

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### **Appendix 1 DNS score**

The questions should be answered 'yes' (positive: 1 point) if a symptom occurred more times a week during the last 2 weeks or 'no' (negative: no point) if it did not

#### DNS-score and guidelines

1 Are you suffering of unsteadiness in walking?
need for visual control, increase in the dark, walk like a drunk man, lack of contact with floor
2 Do you have a burning, aching pain or tenderness at your legs or feet?
occurring at rest or at night, not related to exercise, exclude claudicatio intermittens
3 Do you have prickling sensations at your legs and feet?
occurring at rest or at night, distal>proximal, stocking glove distribution
4 Do you have places of numbness on your legs or feet?
distal>proximal, stocking glove distribution

Maximum score: 4 points; 0 points, PNP absent; 1-4 points, PNP present.

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