Accuracy of neuropathic pain measurements in patients with symptoms of polyneuropathy: validation of painDETECT, Self-Completed Leeds Assessment of Neuropathic Symptoms and Signs, and Douleur Neuropathique 4

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Summary

Among patients referred to neurological outpatient clinics with symptoms of polyneuropathy, painDETECT, S-LANSS and DN4 demonstrated unsatisfactory predictive diagnostic accuracy.

Abstract

Pain is a common symptom in patients referred to polyneuropathy assessment. Diagnostic evaluation and choice of treatment may depend on whether the pain is likely to be neuropathic or not. The present study aimed to investigate the diagnostic accuracy of three tools commonly used to differentiate between neuropathic and non-neuropathic pain. To accomplish this, we included patients with bilateral distal lower extremity pain, referred to neurological outpatient clinics at five Norwegian University hospitals for polyneuropathy assessment. The patients filled in Norwegian versions of painDETECT, the Self-completed Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS), and the clinician-rated Douleur Neuropathique 4 (DN4). All patients underwent a clinical examination and nerve conduction measurements, and were classified according to the NeuPSIG neuropathic pain criteria (reference standard). In total, 729 patients were included, of which 63% had neuropathic pain by the reference standard. Only DN4 demonstrated high sensitivity (0.87), while all three tools had low specificity (≤0.65). Importantly, the tools' predictive ability was unsatisfactory; The probability of getting a correct test result was three quarters at best, and at worst, no better than two fifths. Consequently, we show that neither DN4, painDETECT nor S-LANSS can be confidently used to assess neuropathic pain in a neurological outpatient population with symptoms of polyneuropathy.

Introduction

Neuropathic pain represents a substantial part of the worldwide burden of pain, with an estimated population prevalence of 7-10% [66]. The prevalence of neuropathic pain is expected to increase, as an ageing population, improved cancer survival rates and rise in diabetes mellitus cases are likely to cause an upswing in painful polyneuropathies [13]. This increase imposes a need to identify patients with neuropathic pain in patient populations with likely polyneuropathy, in order to offer optimized care.

Patients with polyneuropathy often present with distal pain and a mixture of neurological signs and symptoms. This presentation is common in the neurological outpatient clinic, where clinicians need to determine whether the pain is likely to have a neurological cause or component. Discriminating between predominantly neuropathic and non-neuropathic pain is important because it can have direct consequences for further examination and choice of treatment.

Many clinical measurement tools have been developed to help clinicians distinguish between pain that is predominantly neuropathic and non-neuropathic. Amongst the most commonly used for both clinical– and research purposes are two questionnaires for self-assessment: painDETECT [18] and the Self-completed Leeds Assessment of Neuropathic Pain (S-LANSS) [5], and one structured clinical evaluation tool, the "Douleur Neuropathique 4" (DN4) [7]. All three are frequently used and have been cross-culturally adapted or translated to many languages. However, it's not clear whether they are adequately valid, or if the questionnaire items are sufficiently consistent and suitable for use in patients with polyneuropathy symptoms in an outpatient neurological setting [37].

The diagnostic accuracy of neuropathic pain tools depend upon the patient population in question (e.g. [2; 20; 24; 26; 28; 53]). Most of the knowledge about the diagnostic accuracy of painDETECT, S-LANSS and DN4 in patients with polyneuropathy is derived from studies of patients in pain clinics with mixed etiology, including e.g. arthritis, phantom pain, complex regional pain syndrome or back pain (e.g. [5; 14; 32; 41; 49]). This is problematic because different patient groups display diverse clinical presentations and degrees of co-morbidity that may affect the score of the clinical tools. For example, the score increases with pain severity [12; 18; 35; 43], anxiety [18; 54], depression [18; 54; 68] and reduced quality of life [11; 68]. In order to confidently apply painDETECT, S-LANSS and DN4 in patients with possible polyneuropathy, the validity of these tools should be evaluated in the target population.

Therefore, the general aim of this study was to assess the diagnostic accuracy of painDETECT, S-LANSS and DN4 in distinguishing between neuropathic and non-neuropathic pain in patients referred to polyneuropathy assessment. Specific objectives were to estimate the tools' discriminative and predictive abilities. Our secondary aim was to evaluate the tools' internal consistency, and explore which items

contributed the most to false positives and false negatives. This study is part of a large Norwegian multi-center study including five clinical neurophysiology departments at our University hospitals.

Methods

Overview

This study was carried out in two steps. First, the original version of painDETECT, S-LANSS and DN4 were translated and cross-culturally adapted into Norwegian. Next, diagnostic accuracy and internal consistency of the three tools were tested using a cross-sectional design. The NeuPSIG criteria [17] were treated as the reference standard for diagnosing neuropathic pain. We included patients with pain in the distal lower extremities that were referred to neurological outpatient clinics for polyneuropathy assessment. The study was approved by The Regional Committee for Medical Research Ethics, South-East Norway (ref no. 2017/1593), and all subjects gave informed consent prior to inclusion.

Translation and cross-cultural adaptation to Norwegian

The process of translation and cross-cultural adaptation of painDETECT, S-LANSS and DN4 was carried out according to international guidelines [3; 23] by Grotle, Nilsen and Killingmo (2015, Appendix 5-7). Two native Norwegian speakers (1 philologist and 1 clinician) independently translated the original tools from English into Norwegian. The two Norwegian versions were synthesized into one version before being back-translated into English. Two native English speakers (1 philologist and 1 clinician), both blinded to the original tools, independently performed the back-translation and synthesized the two English versions into one. An expert committee consisting of the translators and two researchers from our research group reviewed all translations. In a formal meeting, the committee discussed deviations until consensus on a pre-final version was reached. The goal was that the pre-final Norwegian tool should be as concise and easy to understand as possible. The pre-final version was tested on 10 patients from the neurological outpatient clinic at Oslo University Hospital. None of the patients had difficulties understanding the meaning of items or responses, and they found it easy to comprehend. No further changes were made, and the final versions of the Norwegian tools evaluated in this study is the same as the pre-final versions.

Study sample and recruitment procedure

Patients aged 18-70 years, referred to neurological hospital outpatient clinics for polyneuropathy

assessment, were consecutively asked to participate in the study. Five hospitals participated in the multi-center data collection between 05-2017 and 07-2021: Oslo University Hospital; Haukeland University Hospital, Bergen; Stavanger University Hospital; Trondheim University Hospital (St. Olavs Hospital); and The University Hospital of North Norway, Tromsø. The exclusion criteria were acute polyneuropathies (e.g., acute inflammatory demyelinating polyradiculopathy, acute motor axonal neuropathy), nerve entrapment without polyneuropathy, limited capacity to give informed consent (e.g., language barrier, dementia, psychiatric illness) and patients being too sick to participate (e.g., bed-ridden, high fever).

Measurement tools for neuropathic pain

The *painDETECT* questionnaire was originally developed by Freynhagen et al. [18] as a screening tool for neuropathic pain components in patients suffering from low back pain. The tool is self-completed and is made up of a pain drawing, three questions regarding current–, maximum– and average pain intensity (numerical rating scale and visual analogue scale (0-10), not scored), as well as three distinct main parts: gradation of pain, pain course pattern and answering whether the pain radiates. The gradation of pain consists of seven items for characterizing and grading pain and other sensations, from never experiencing them (0), to experiencing them very strongly (5). The questions cover pain sensation (e.g., burning, shooting pain), paresthesias (e.g., numbness, tingling) and allodynia (to light touch, pressure, heat or cold). Four different pain course patterns are illustrated and described, and the patient chooses the one that best describes their course of pain. Two patterns describe persistent pain with slight fluctuations or pain attacks – these are graded 0 or -1, i.e., principally persistent pain patterns do not contribute positively to the painDETECT score. The remaining two pain patterns describe pain attacks with or without baseline pain, and are both graded as +1. Lastly, the patient answers whether the pain radiates. A positive answer gives +2 while a negative answer is neutral (0). Maximum sum score is 38. The original painDETECT suggests two cutoffs: a sum score of <12 means it's unlikely that the pain has a neuropathic component (<15% chance), while a cut-off of >18 indicates that it's likely that the pain has a neuropathic component (>90% chance). In the present study, only the cut-off at >18 was used.

S-LANSS [5] is a revised version of the Leeds Assessment of Neuropathic Symptoms and Signs [4], intended to make self-completion possible. It is a 7-item tool for identifying pain that is predominantly neuropathic in origin. It was originally validated for a broad mix of chronic pain patients in pain clinics, day care wards and inpatient wards. The first five items are weighted descriptors of the patients' pain and other symptoms, to which the patient answers yes (graded as 1, 2, 3 or 5 depending on the item) or

no (0). The questions cover paresthesias (e.g., pins & needles, numbness), autonomic response (skin color change), hyperesthesia to touch, paroxysmal/shooting pain (e.g., electric, bursting), and burning sensations. For the last two items, the patients examine themselves with gentle pressing and rubbing of the painful area. If gentle rubbing leads to discomfort, pain or paresthesia, it is scored as +5, while tenderness or numbness following gentle pressing scores +3. Maximum sum score is 24. The original S-LANSS operates with a cut-off at ≥ 12, suggesting *pain of predominantly neuropathic origin*, and this cutoff was used in the present study.

DN4 was developed by Bouhassira et al. [7] and originally validated in patients with chronic pain of different etiologies and at least moderate pain severity (>40mm on a 100mm Visual Analogue Scale). It is intended to be a clinician-administered diagnostic tool for neuropathic pain. DN4 consists of two main subgroups of items: the 7-item interview (Q1 about pain characteristics and Q2 associated symptoms) and the 3-item clinical examination (Q3 about sensation loss and Q4 about allodynia). All items within questions are scored as yes (+1) or no (0). The first items cover whether the pain is characterized by burning, painful cold or electric shock-like sensations, and whether the pain is associated with tingling, "pins and needles", numbness or itching. Following this, the patient is examined for hypoesthesia to touch and pin-prick, and for mechanical brush allodynia. Maximum sum score is 10. The final 10-item tool was developed from an original 17-item-questionnaire, and a cut-off score at ≥4 for the diagnosis of neuropathic pain was determined by maximal Youden's index. The same cut-off score was used in the present study.

Reference standard

The reference standard for the diagnosis of neuropathic pain were the *NeuPSIG criteria* [17]. Published by the International Association for the Study of Pain's special interest group, these criteria are increasingly recognized as the gold standard for assessing neuropathic pain in clinical practice and for research purposes. The NeuPSIG criteria classifies patients by level of confidence that neuropathic pain is present: *unlikely, possible, probable* and *definite neuropathic pain. Possible neuropathic pain* requires a history of relevant neurological lesion or disease, as well as a pain distribution that is neuroanatomically plausible. Failure to meet these first criteria classifies the patient's pain as *unlikely* to be neuropathic. *Probable neuropathic pain* requires the former, in addition to an examination revealing that the pain is associated with sensory signs in the same distribution. *Definite neuropathic pain* requires all of the above, as well as a confirmatory diagnostic test for a lesion or disease of the somatosensory nervous system that can explain the pain.

In the present study, patients were dichotomized into two groups: neuropathic pain (*definite, probable*) and no neuropathic pain (*unlikely, possible*). Since all patients in the study were subject to sensitive confirmatory tests for a lesion or disease of the somatosensory nervous system, patients defined as having *probable neuropathic pain* all have negative electrodiagnostic tests. In order to ensure that any false positives in the reference standard did not change our results, a sensitivity analysis was performed where patients with *probable neuropathic pain* were also included as true negatives (no neuropathic pain) and excluded from the analysis. Furthermore, to reduce the chance of error in NeuPSIG classification, all data was reviewed and validated by a third party team from the research group. Any inconsistencies were flagged, and agreement was reached through discussion and assessment of the patient journal with a representative physician at the hospital in question.

Assessment procedure

Both painDETECT and S-LANSS were sent by traditional mail and filled out on paper by the patients preferably 0-14 days before their appointment. DN4 was administered by face-to-face interview by a physician clinical neurophysiologist as part of the routine assessment of polyneuropathy. History-taking, clinical examination and nerve conduction studies (NCS) were performed as part of routine assessments for polyneuropathy. All NCS were performed in concordance with the Norwegian national guidelines [34]. A minimum of two sensory nerves in the feet were tested (sural nerve and medial plantar nerve), as well as two motor nerves (tibial nerve and peroneal nerve), including F-responses. If the neurographic findings were not clear, one extra sensory nerve was tested (superficial peroneal nerve).

Of particular note, quantitative thermal testing was considered a confirmatory test for small-fiber lesions. This is not completely in line with the NeuPSIG classification, but consistent with clinical practice and recent guidelines for diagnosing small-fiber neuropathy [57; 69]. Detection– and pain thresholds for cold and heat were obtained in the lower extremities. Only detection thresholds (cold and/or warm) were used to define small-fiber abnormality – pain thresholds were used as supportive information. The method of limits was used, with a baseline temperature of 32°C, ramp-rate of 1°C/s and thermode size of 9-12cm^2, as per the national guidelines [34] and the hospitals' own protocol.

For both NCS and quantitative thermal testing, local reference values were applied when possible. Alternatively, references values from Powerpack^{tm} (Stefan Stålberg Software AB, Helsingborg, Sweden) [52], or the national guidelines (quantitative thermal testing) were used.

Polyneuropathy assessment

Polyneuropathy was defined in accordance with the criteria for diabetic polyneuropathy suggested by Tesfaye et al. [58], as these also fit general distal, symmetrical polyneuropathies. Patients were classified as having polyneuropathy if they fulfilled the criteria for *Confirmed DPSN.* The criteria for confirmed DPSN in myelinated nerve fibers require presence of an abnormal NCS or small-fiber test, and symptom(s) or sign(s) of neuropathy. In accordance with the Norwegian national guidelines for clinical neurophysiology [34], at least *two* nerves of different roots had to be abnormal to constitute a positive finding on NCS (three if abnormal medial plantar nerve). For small-fiber neuropathy, the Tesfaye criteria require the presence of length-dependent symptoms, clinical signs of small-fiber damage, normal (sural) NCS, and either altered intra-epidermal nerve fiber density or abnormal thermal detection thresholds in the feet [58]; In the present study, the latter was most commonly used.

Statistical analysis

Sample size

The current study is part of a large, multi-center study. Minimum sample size was conservatively calculated based on Buderer's recommendations [8]. With expected sensitivity and specificity of maximum 0.8, sample prevalence for neuropathic pain of 50%, and 95% confidence intervals with 5% precision, the study required a minimum of 492 patients included in the analyses.

Analyses of data quality

Descriptive statistics were conducted to explore distribution of the included tools; continuous variables with normal distribution are presented by mean values with standard deviations, while skewed variables are presented by their median with inter-quartile ranges. Categorical variables are presented as absolute and relative (percentage) frequencies.

Each participating hospital coded their own patients independently before data pooling. Item missingness was analyzed visually and by Little's MCAR test, and was found to be random. The missing percentage of clinical tool items ranged from 0–4.1%, with the exception of painDETECT's "pain pattern" (8%) and "radiating pain" (17.4%). Missing items were imputed by single imputation. The method of single imputation was based on fully conditional specification (chained equations) (SPSS v25). Twenty imputations (10 iterations) were run, and the rounded average value (discrete items) or mode

(categorical items) of these were used for the final calculations.

Floor– and ceiling effects (i.e., how many scored "never experiencing [item]" (0) and "experiencing [item] very strongly" (5)) for the pain gradation items in painDETECT were assessed through frequency tables, with a cut-off of >15%.

Main analyses of diagnostic accuracy and internal consistency

We assessed diagnostic accuracy in several ways. First, agreement between the neuropathic pain tools and the NeuPSIG criteria was determined by calculating Cohen's Kappa. Kappa scores indicating agreement between the tool and the NeuPSIG classification were interpreted as none to slight (0.01-0.20), fair (0.21-0.40), moderate (0.41-0.60), substantial (0.61-0.80) and almost perfect (0.81-1.00) [39].

Second, potential discriminative ability (to distinguish between neuropathic and non-neuropathic pain) was analyzed by Receiver Operating Curves (ROC) analysis, and presented by the area under the ROC curves (AUC). AUC values were considered non-discriminative (0.5-0.6), poor (0.6-0.7) acceptable (0.7-0.8), excellent (0.8-0.9) or outstanding (>0.9) [29]. However, since AUC values do incorporate cut-offs that are clinically nonsensical [36], the absolute discriminative ability was calculated for three different cut-offs: the original cut-off for each tool, a "best cut-off" (based on the highest Youden's Index, i.e., sensitivity + specificity – 1), as well as a cut-off weighted towards the highest possible sensitivity with specificity above 0.5. In the event of substantially better sensitivity and/or specificity at the additional cut-offs, predictive values would also be calculated.

Third, the tools' predictive ability (how well the tools can predict the presence of neuropathic pain in a real-life clinical setting) was assessed by positive predictive values (PPV), negative predictive values (NPV) and positive/negative likelihood ratios. Predictive values are clinically intuitive and important for the clinician interpreting actual results, i.e., "how likely is it that my patient has/doesn't have neuropathic pain, given the test result?" [36; 62]. With a sample prevalence of neuropathic pain close to 50%, likelihood ratios were understood as how much the result of each tool increased the probability of neuropathic pain (from pre-test to post-test). Specifically, the likelihood ratios were interpreted as s*mall, rarely important* (1-2 and 0.5-1), *small but sometimes important* (2-5 and 0.5-0.2), *moderate* (5-10 and 0.1-0.2) and *large, often conclusive* (>10 and < 0.01) [30].

Furthermore, we calculated Cronbach's alpha (α) to determine the internal consistency of the three tools in our particular study sample. Item-total-correlations (correlation between each item and the total score) were calculated as a complementary measure to interpret Cronbach α values and to assess each item's discriminative ability. Cronbach's alpha values between 70 and 95 were considered to imply

good internal consistency, and item-total-correlations between 0.3 and 0.5 were considered discriminative [15; 42].

Additional analyses

To examine which items contributed the most to false positives and false negatives, we explored item response frequency tables for each possible outcome.

Analyses were performed in SPSS v25 (IBM, Armonk, NY) and R v4.1.1 [55] with the packages *tidyverse v1.3.1* [70]*, table1 v1.4.2* [45]*, pROC v1.18* [46] and *epiR v2.0.33* [51].

Results

In total, 1498 patients were eligible for inclusion. We recruited 1163 patients, of which 729 were included in the main analysis (Figure 1). Patient demographics and clinical variables are presented for the entire sample, as well as stratified by presence of neuropathic pain (Table 1). The group with neuropathic pain were, on average, older, consisted of more males and diabetes patients, had a much higher prevalence of polyneuropathy, and higher use of pain medication. The prevalence of neuropathic pain and polyneuropathy was 63% and 53%. The mean (SD) scores for painDETECT, S-LANSS and DN4 were 17.85 (7.23), 13.03 (6.40) and 4.83 (2.04), respectively.

Diagnostic accuracy for distinguishing between neuropathic and non-neuropathic pain

There was none or slight, to fair agreement, between the three tools and the reference standard. Cohen's Kappa values for the NeuPSIG classification and painDETECT were $\kappa = 0.12$ (95% CI 0.05–0.19, $p = 0.002$); $\kappa = 0.13$ (95% CI 0.05–0.22, $p = 0.001$) for S-LANSS; and $\kappa = 0.38$ (95% CI 0.31–0.45, $p < 0.001$) for DN4.

Discriminative ability by AUC was acceptable for DN4 with an AUC of 0.77, poor for S-LANSS, and non-discriminative for painDETECT (Figure 2). Youden's index for the original cut-offs were 0.14 for painDETECT, 0.14 for S-LANSS and 0.37 for DN4, the latter largely driven by a sensitivity of 0.87. Changing the cut-offs to maximize Youden's Index or improve sensitivity did not improve discriminative ability to a clinically relevant degree (Figure 2).

Among patients with a positive result on either tool, the probability of having neuropathic pain was

71-75% (Table 2). On the flipside, among patients with a negative result on painDETECT or S-LANSS, the probability of not having neuropathic pain was 39-42%, rising to 68% for DN4.

None of the tools reached a positive likelihood ratio above 2, which means that a positive test result will rarely give the clinician important information, as it will not appreciably increase the post-test probability of neuropathic pain. Only DN4 had a somewhat promising negative likelihood of 0.27, meaning a negative test implies a small, but sometimes important decrease in the likelihood of the patient having neuropathic pain. Neither painDETECT nor S-LANSS reached a negative likelihood ratio of <0.5, showing poor ability for ruling out disease.

In the sensitivity analysis, excluding the "NeuPSIG *probable"* group had little effect on overall diagnostic accuracy, with the exception of an increase in DN4's NPV (0.68 to 0.75). Including the probable group as true negatives lead to a decrease in specificity for painDETECT (0.65-0.58) and DN4 (0.50 to 0.41). This also decreased PPV by 0.15 for all tools, and increased NPV by approximately 0.12 (Appendix 1).

Data quality and internal consistency

painDETECT had good internal consistency (Table 3), with a Cronbach's alpha score of $\alpha = 0.79$ and all items except *radiating* pain showed good item-total correlation (the item *pain pattern* was excluded from the analysis due to its -1 – 1 scoring). Neither S-LANSS nor DN4 reached good internal consistency. S-LANSS had a Cronbach's α of 0.61, with two items' item-total correlation below 0.3. DN4 had a Cronbach's α of 0.58, with six items below item-total correlation < 0.3. For painDETECT, a floor-effect was observed for the items *burning pain, light touch, electric shocks, painful temperature and light pressure*, while no ceiling-effects were present.

Item response frequency

The item response frequency tables for each tool showed that true positive and true negative patients had different item score distributions as compared to their wrongly classified counterparts (Appendix 2-4). However, several items may have contributed to the false positive and false negative results. All patients frequently reported *pins & needles*, *tingling*, *numbness*, and sometimes *burning– or electric/shooting pain,* in particular. Patients classified as false negatives rarely reported items related to itching, hypoesthesia to touch, temperature allodynia or mechanical allodynia. False positive patients commonly experienced all items, except for *changing color* (S-LANSS), *cold pain* (DN4*), itching* (DN4), *hypoesthesia to touch (DN4 exam), hypoesthesia to pinprick (DN4 exam)* and *brushing pain (DN4 exam)*.

Overall, items related to physical examination, small-fiber lesions, and mechanical allodynia contributed the least to false positives and negatives.

Discussion

The results from our large multicenter study on patients with suspected polyneuropathy showed acceptable discriminative ability for DN4. The discriminatory ability of S-LANSS was poor and non-discriminative for painDETECT. DN4 showed a promising negative likelihood value and the best predictive values of the three, although neither tool demonstrated good overall predictive ability. painDETECT demonstrated good internal consistency in our study sample, while S-LANSS and DN4 did not. Regardless of neuropathic pain classification, patients frequently reported *pins & needles, tingling* and *numbness*, which are common symptoms of polyneuropathy.

Due to the lack of published papers on polyneuropathy populations, it is difficult to compare our results directly with previous studies. We identified one study of DN4 in patients with diabetic polyneuropathy [50], that utilized an earlier version of the NeuPSIG criteria [61] as the reference standard, with both *probable* and *definite* reflecting neuropathic pain. The authors reported moderately good discriminative and predictive ability, concluding that the trade-off in diagnostic accuracy may be worthwhile due to its simplicity and user-friendliness. Aside from this, many studies report on the diagnostic accuracy of the three tools in other patient populations and across several languages, but with widely different results. For example, Youden's index for S-LANSS ranges from 0.06 in a study on cancer patients [28] to a near perfect 0.95 in patients with mixed etiology [63]. Likewise, studies on painDETECT and DN4 report Youden's indices from below 0.2 [16; 44] to 0.71 [22] and 0.92 [25], respectively. All three tools usually perform better in other patient populations than in the present study, with DN4 tending to outperform the other two.

It is not surprising that DN4 has shown acceptable diagnostic accuracy in a previous study and performs best in the present study, when one considers that it is the only tool administered by healthcare professionals (e.g., physicians). Such a healthcare professional could likely also employ the NeuPSIG guidelines to determine whether the patient is likely to have polyneuropathy. However, when compared with DN4, the NeuPSIG guideline requires a higher level of clinical judgment to establish *probable* (or *definite*) polyneuropathy. Since the time needed for clinical examination is only marginally longer for the NeuPSIG approach, the choice between the two may depend more on the clinical skills of the available personnel.

The nature of our sample likely contributes to the suboptimal predictive abilities in the present study. The tools were originally developed for use in patients with chronic low back pain (painDETECT), or in mixed groups of patients (S-LANSS, DN4), with painDETECT and DN4 primarily intended as screening tools. Singling out homogeneous groups, for which the tools were not originally intended, can be expected to impact their diagnostic accuracy. As screening tools, the results could also plausibly be expected to reflect a greater ability to pick up on neuropathic pain (e.g., higher sensitivity and positive likelihood ratios), although this was only true for DN4 in our sample. We found that *numbness*, *tingling* and *pins and needles* were amongst the most frequently reported items (cf. "easy" items in item-response theory [15]). This is in concordance with earlier studies on all three tools, across an array of different patient populations (e.g. [1; 6; 7; 11; 12; 16; 21; 25; 27; 32; 40; 48; 53; 56; 59; 60; 64; 65; 67; 68]). By themselves, "easy items" can be expected to be sensitive, with discriminative power in patients with few symptoms [15]. However, *numbness, tingling* and *pins and needles* are also cardinal symptoms of polyneuropathy, that is, hypoesthesia and paraesthesia in the feet. This entails that for patients with symptoms of polyneuropathy, these items can be expected to form a "baseline score" which artificially inflates sensitivity, reduces specificity, and consequently leads to an increase in false positives and worse predictive ability. While DN4 had the best predictive ability in our sample, it's still mediocre with likelihood ratios implying a small effect on post-test probability, and results only being correct 68-75% of the time. Thus, neither tool can be used confidently in patients with symptoms of polyneuropathy.

The multi-dimensional nature of pain makes it particularly difficult to create clinical tools that successfully isolates and measures certain elements or aspects. Earlier studies have shown that both painDETECT and DN4 scores may be associated with pain severity, pain catastrophizing, health-related quality of life, depression, anxiety, stress and disability [18; 54; 68]. The effect of these factors on scoring may help explain the low specificity, and the low PPV observed in spite of the high true prevalence in our sample. First, our study sample experienced high pain severity, which may inflate the scores of the clinical tools, leading to more false positives [9; 10; 12; 18; 35; 38; 43]. Second, a substantial portion of the patients included suffered from diabetic polyneuropathy – a group that often has a high burden of illness related to anxiety, depression, insomnia and disability [33; 47]. As such, instead of picking up on only neuropathic pain, the tools could be particularly sensitive to patients with co-morbidities and low health-related quality of life, making them incapable of ruling out neuropathic pain in patients with a high burden of disease.

The internal consistency of the three tools varied. painDETECT (pain pattern excluded) had good internal consistency, largely comparable with previous reports [9; 10; 14; 18; 22; 38]. In contrast, we

found poorer internal consistency for S-LANSS and DN4, for which earlier studies have been more conflicting (e.g. S-LANSS [2; 19; 48; 63]; DN4 [31; 49; 59; 65]). Although Cronbach's α can be expected to increase with number of items, the tools are comparable (7, 8 and 10 items) and the observed differences do not follow such a pattern in our data, nor in previous reports. Furthermore, neither Cronbach's α nor item-total correlation can discriminate between different constructs. This means that if the clinical tools do in fact also pick up on e.g., polyneuropathy in itself, health-related quality of life or psychosocial factors, Cronbach's α values make little sense, and we cannot deduce which constructs the items are actually correlating with, or even if they correlate with the same ones. This could help explain some of the lower item-total-correlation values found in S-LANSS and DN4, but does not resolve whether painDETECT is actually more consistent in measuring neuropathic pain, or if the items measure different constructs that correlate well with each other. Going forward, future studies may look to explore the construct validity of painDETECT, S-LANSS and DN4 in patients with polyneuropathy, in order to better understand which items have adequate discriminative ability for which constructs.

The present study is well-powered and has a number of strengths. First, it's a large multi-center study including five different Norwegian University hospitals. Second, we did not utilize inclusion– or exclusion criteria that is likely to impact scoring, e.g. pain severity. Third, the use of the recommended NeuPSIG criteria for diagnosis of neuropathic pain should improve the internal validity of our study. We included patients with *probable* neuropathic pain as true positives in the reference standard. However, we are aware that dichotomization practices varies between studies (e.g. [44; 56; 59; 65; 68]), and since patients with *probable* neuropathic pain could potentially increase the rate of false positives in the reference standard, we performed a sensitivity analysis that largely confirmed our findings.

Some limitations should be mentioned. Since an assessment of neuropathic pain must include descriptors of signs and symptoms to properly capture its subjective nature, it's unavoidable that there is some overlap between the tools, the clinical examination in DN4 (and to an extent, self-examination in S-LANSS), and the reference standard. In particular, both the clinical examination and lack of physician blinding may cause some bias, and could theoretically contribute specifically to why DN4 performs better. Although the NeuPSIG criteria makes it easier to standardize the diagnostic process in multi-center studies, it's possible that a different reference standard would be a better fit for patients with polyneuropathy.

Conclusion

The discriminative ability of DN4 was acceptable, while poorer results were observed for painDETECT and S-LANSS. The predictive ability of the three tools were poor to mediocre, with DN4 performing best. Applying any of the three tools had only a small effect on post-test probability of neuropathic pain. The probability of getting a correct test result was three-quarters at the very best, and only two fifths at worst. Hence, neither tool is appropriate when trying to distinguish between neuropathic and non-neuropathic pain in patients referred to polyneuropathy assessment at neurological outpatient clinics. The internal consistency of painDETECT was good, while that of S-LANSS and DN4 did not reach conventional limits for confirmatory studies. Crucially, common polyneuropathy symptoms likely form a baseline score for each clinical tool, reducing their diagnostic accuracy. The present study identifies a need for better supportive tools for differentiating between predominantly neuropathic and non-neuropathic pain in patients with symptoms of polyneuropathy.

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Figure legends

Figure 1. Flowchart of the recruitment process.

Figure 2. Area under the Receiver-Operating Curves (with 95% Confidence Intervals in the frame) for painDETECT, S-LANSS and DN4. Sensitivity and specificity for the following three cut-offs are included for each tool: 1) The original cut-off; 2) the cut-off maximizing Youden's Index (sensitivity + specificity – 1); and 3) the cut-off with the highest possible sensitivity while keeping specificity above 0.5.

Table 1. Patient demographics and clinical variables

	All patients (n=729)	Non-neuropathic pain[d] (n=264)	Neuropathic pain[d] (n=465)
Age, years, mean (SD)	55 (11)	52 (11)	57 (10)[a]
Sex, female, n (%)	405 (56)	169 (64)	236 (51)[a]
Pain medication, yes, n (%)	336 (46)	99 (38)	237 (51)[a]
Pain duration, n (%)			
1-3 months	12 (2)	6 (2)	6 (1)
3-12 months	124 (17)	48 (18)	76 (16)
1-5 years	289 (40)	102 (39)	187 (40)
> 5 years	0 (0)	0 (0)	0 (0)
Mean pain last 3 months, mean (SD)[b]	5.5 (2.1)	5.4 (2.2)	5.6 (2.1)
Diabetes, yes, n (%)	197 (27)	36 (14)	161 (35)[a]
Type 1	40 (6)	13 (5)	27 (6)[a]
Type 2	145 (20)	21 (8)	124 (27)[a]
Polyneuropathy etiology, n (%)			
Diabetes	153 (21)	11 (4)	142 (31)[a]
Idiopathic	154 (21)	13 (5)	141 (30)[a]
Chemotherapy-induced	26 (4)	1 (0)	25 (6)[a]
Small-fiber	112 (15)	14 (5)	98 (21)[a]
Hereditary	9 (1)	1 (0)	8 (2)
Post-traumatic nerve injury	2 (0.3)	1 (0)	1 (0)
Post-operative (iatrogenic)	1 (0.2)	0 (0)	1 (0)
Other[c]	103 (14)	65 (25)	38 (8)[a]
None/missing	169 (23)	158 (60)	11 (2)[a]
NeuPSIG grading, n (%)			
Unlikely	157 (21)	157 (59)	0 (0)
Possible	107 (15)	107 (41)	0 (0)
Probable	103 (14)	0 (0)	103 (22)
Definite	362 (50)	0 (0)	362 (78)

[a] Significant between the two NeuPSIG groups (neuropathic and non-neuropathic) at $p < 0.05$ after Bonferroni adjustment
[b] Numerical rating scale (0-10) where 0 = no pain, 10 = worst imaginable pain
[c] Chronic inflammatory neuropathies and neuropathies related to vitamin deficiency, Lyme disease and toxins (e.g., alcohol)
[d] Patients classified as having neuropathic pain (definite, probable) and no neuropathic pain (unlikely, possible) according to the NeuPSIG criteria for diagnosing neuropathic pain

Table 2. Discriminative and predictive ability of PainDETECT, S-LANSS and DN4

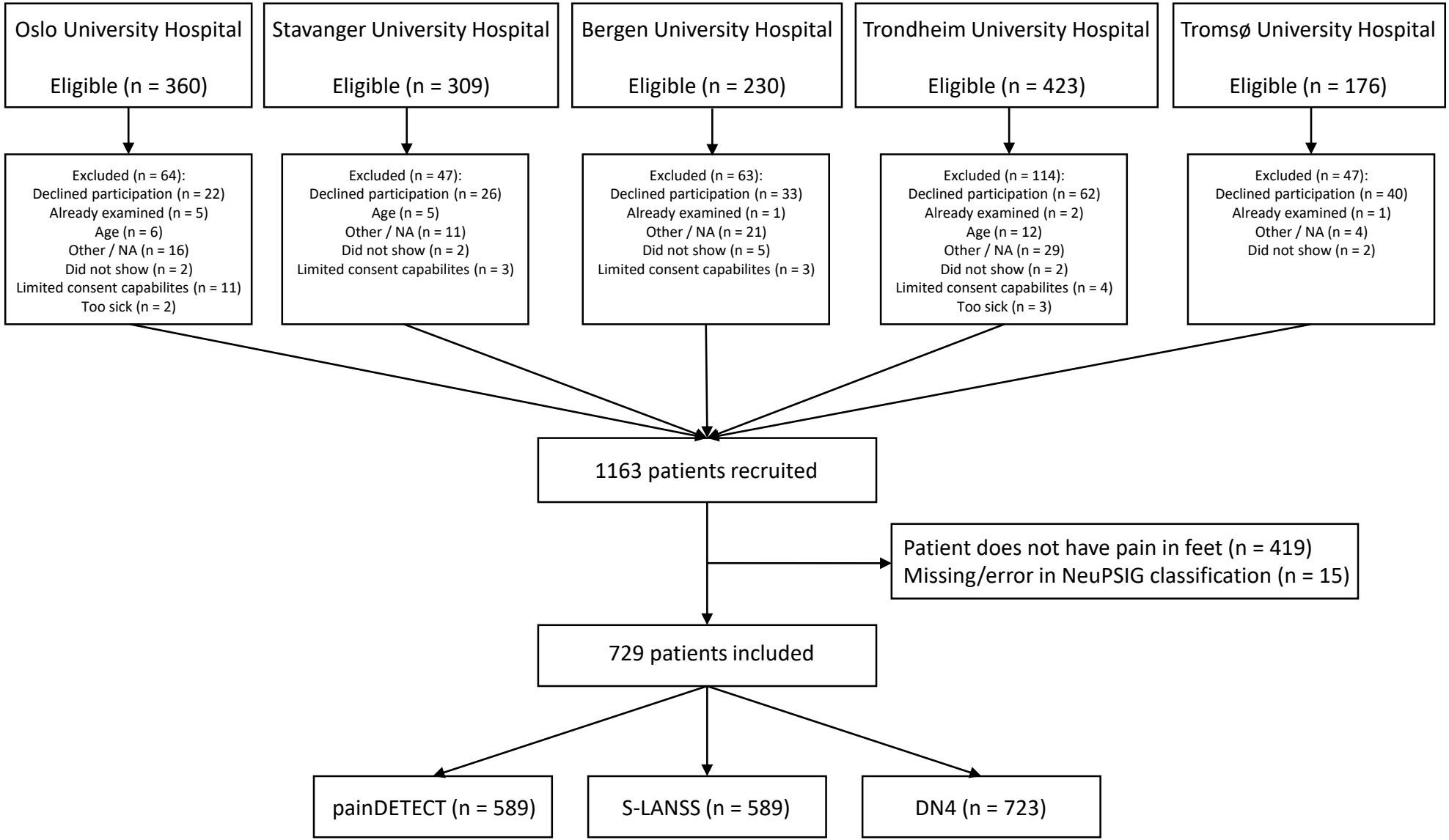
		Neuropathic pain (NeuPSIG)				Point estimate (95% CI)
		Positive	Negative	Total	Sensitivity	0.50 (0.45, 0.55)
PainDETECT	Positive	194	73	267	Specificity	0.64 (0.56, 0.70)
	Negative	195	127	322	Positive predictive value	0.73 (0.67, 0.78)
	Total	389	200	589	Negative predictive value	0.39 (0.34, 0.45)
					Positive likelihood ratio	1.37 (1.11, 1.68)
					Negative likelihood ratio	0.79 (0.68, 0.91)
		Positive	Negative	Total	Sensitivity	0.60 (0.55, 0.65)
S-LANSS	Positive	232	95	327	Specificity	0.54 (0.47, 0.61)
	Negative	152	110	262	Positive predictive value	0.71 (0.66, 0.76)
	Total	384	205	589	Negative predictive value	0.42 (0.36, 0.48)
					Positive likelihood ratio	1.30 (1.10, 1.54)
					Negative likelihood ratio	0.74 (0.62, 0.88)
		Positive	Negative	Total	Sensitivity	0.87 (0.83, 0.90)
DN4	Positive	399	132	531	Specificity	0.50 (0.43, 0.56)
	Negative	62	130	192	Positive predictive value	0.75 (0.71, 0.79)
	Total	461	262	723	Negative predictive value	0.68 (0.61, 0.74)
					Positive likelihood ratio	1.72 (1.52, 1.95)
					Negative likelihood ratio	0.27 (0.21, 0.35)

Cut-off value for neuropathic pains: painDETECT ≥ 19, S-LANSS ≥ 12 and DN4 ≥ 4
Abbreviations: S-LANSS = Self-Administered Leeds Assessment of Neuropathic Symptoms and Signs; DN4 = Douleur Neuropathique 4;
NeuPSIG: The NeuPSIG criteria for diagnosing neuropathic pain were used as the reference standard, with patients classified as having neuropathic pain (definite, probable) and no neuropathic pain (unlikely, possible).

Table 3. Item quality and internal consistency of painDETECT, S-LANSS and DN4

	Missing, %[e]	No, n (%)	Yes, n (%)	Item-total correlation[d]	Cronbach's α (if deleted [c])
DN4 (n = 723)					**0.58**
Burning pain	0.5	255 (35)	468 (65)	0.19	0.57
Cold pain	1.0	546 (76)	177 (25)	0.20	0.56
Electric shocks	0.7	377 (52)	346 (48)	0.22	0.56
Tingling	0.8	253 (35)	470 (65)	0.25	0.55
Pins and needles	0.4	149 (21)	574 (79)	0.33	0.53
Numbness	0.5	136 (19)	587 (81)	0.33	0.53
Itching	1.4	554 (77)	169 (23)	0.23	0.56
Hypoesthesia touch	1.4	453 (63)	270 (37)	0.35	0.52
Hypoestesia prick	1.8	407 (56)	316 (44)	0.31	0.53
Painful brush	1.9	623 (86)	100 (14)	0.17	0.57
S-LANSS (n = 589)					**0.61**
Tingling, pins and needles (0/5)	1.2	100 (17)	490 (83)	0.21	0.62
Color (0/5)	2.2	465 (79)	125 (21)	0.24	0.61
Sensitive to touch (0/3)	1.9	323 (55)	267 (45)	0.49	0.52
Electric shocks (0/2)	1.2	233 (40)	357 (61)	0.30	0.59
Burning pain (0/1)	2.2	253 (43)	337 (57)	0.36	0.60
Rubbing discomfort (0/5)	3.6	304 (52)	286 (49)	0.52	0.49
Numbness (0/3)	3.2	200 (34)	390 (66)	0.42	0.55
painDETECT (n = 589)		**Min score, n (%)**	**Max score, n (%)**		**0.79**
Pain pattern (-1 – 1)[a]	8.0	151 (25)	153 (26)		
Radiating pain (0/2)	17.4	316 (53)	280 (47)	0.23	0.80
Burning pain[b]	3.9	101 (17)	58 (10)	0.48	0.77
Tingling[b]	2.9	59 (10)	77 (13)	0.56	0.76
Light touch[b]	2.7	206 (34)	24 (4)	0.60	0.75
Electric shocks[b]	4.1	151 (25)	52 (9)	0.55	0.76
Painful temperature[b]	3.2	224 (38)	26 (4)	0.56	0.76
Numbness[b]	3.0	47 (8)	83 (14)	0.42	0.78
Light pressure[b]	3.4	160 (27)	39 (7)	0.57	0.76

[a] Pain pattern excluded from calculation of item-total-correlations
[b] Items are scored on a 0-5 point scale (5 represents more severe symptoms).
[c] Chronbach's α calculation without the item in question
[d] Correlation between each item and the total score
[e] Before imputation, results otherwise based on imputed dataset


Oslo University Hospital
Eligible (n = 360)
Stavanger University Hospital
Eligible (n = 309)
Bergen University Hospital
Eligible (n = 230)
Trondheim University Hospital
Eligible (n = 423)
Tromsø University Hospital
Eligible (n = 176)
Excluded (n = 64):
Declined participation (n = 22)
Already examined (n = 5)
Age (n = 6)
Other / NA (n = 16)
Did not show (n = 2)
Limited consent capabilites (n = 11)
Too sick (n = 2)
Excluded (n = 47):
Declined participation (n = 26)
Age (n = 5)
Other / NA (n = 11)
Did not show (n = 2)
Limited consent capabilites (n = 3)
Excluded (n = 63):
Declined participation (n = 33)
Already examined (n = 1)
Other / NA (n = 21)
Did not show (n = 5)
Limited consent capabilites (n = 3)
Excluded (n = 114):
Declined participation (n = 62)
Already examined (n = 2)
Age (n = 12)
Other / NA (n = 29)
Did not show (n = 2)
Limited consent capabilites (n = 4)
Too sick (n = 3)
Excluded (n = 47):
Declined participation (n = 40)
Already examined (n = 1)
Other / NA (n = 4)
Did not show (n = 2)
1163 patients recruited
Patient does not have pain in feet (n = 419)
Missing/error in NeuPSIG classification (n = 15)
729 patients included
painDETECT (n = 589)
S-LANSS (n = 589)
DN4 (n = 723)

Area Under the Receiver Operating Characteristic Curves

painDETECT *0.586 (0.538, 0.635)*
S-LANSS *0.612 (0.565, 0.660)*
DN4 *0.773 (0.738, 0.808)*

Sensitivity

1 − Specificity

		Original ⬢	*Max Youden's Index*	*Max sensitivity (specificity ≥ 0.5)*
painDETECT	Cut-off	19	21	17
	Sensitivity	0.50	0.43	0.58
	Specificity	0.64	0.72	0.55
S-LANSS	Cut-off	**12**	16	**12**
	Sensitivity	0.60	0.48	0.60
	Specificity	0.54	0.73	0.54
DN4	Cut-off	**4**	5	**4**
	Sensitivity	0.87	0.72	0.87
	Specificity	0.50	0.71	0.50

Appendix 1. Sensitivity analysis based on dichotomization of the NeuPSIG category *probable*: Excluded, included as true positives, or included as true negatives

	PainDETECT			S-LANSS			DN4		
	Excluded	Positive	Negative	Excluded	Positive	Negative	Excluded	Positive	Negative
Sensitivity	0.49	0.47	0.49	0.60	0.59	0.60	0.88	0.87	0.88
Specificity	0.64	0.65	0.58	0.54	0.54	0.49	0.50	0.50	0.41
Positive predictive value	0.67	0.72	0.57	0.66	0.70	0.55	0.70	0.75	0.60
Negative predictive value	0.44	0.39	0.51	0.48	0.41	0.54	0.75	0.68	0.77
Positive likelihood ratio	1.33	1.33	1.17	1.29	1.28	1.18	1.74	1.72	1.48
Negative likelihood ratio	0.81	0.82	0.88	0.75	0.76	0.82	0.25	0.27	0.30

Appendix 2. Item response frequency table for PainDETECT (n=589)

	Neuropathic pain (NeuPSIG positive)		No neuropathic pain (NeuPSIG negative)	
	Positive test, % n = 194	Negative test, % n = 195	Positive test, % n = 73	Negative test, % n = 127
Burning pain				
0	7	21	6	33
1	4	15	8	11
2	5	27	11	17
3	18	20	22	22
4	45	15	41	15
5	22	2	12	2
Tingling				
0	2	12	3	14
1	0	7	1	9
2	2	21	4	19
3	18	36	29	24
4	53	19	43	24
5	26	5	21	1
Light touch				
0	8	56	12	55
1	14	25	14	24
2	21	12	21	14
3	29	6	18	3
4	18	1	30	3
5	9	1	6	1
Electric shocks				
0	6	39	8	45
1	6	17	1	14
2	8	21	6	21
3	27	10	27	9
4	38	13	37	8
5	16	1	21	3
Painful temperature				
0	10	62	11	59
1	18	20	15	16
2	15	9	23	14
3	24	7	21	7
4	21	2	26	3
5	11	0	4	1
Numbness				
0	2	7	3	21
1	1	8	1	7
2	4	21	11	26
3	24	32	33	24
4	41	29	30	19
5	29	3	22	3
Light pressure				
0	6	46	8	42
1	12	26	10	23
2	17	13	8	21
3	25	11	29	9
4	26	5	32	4
5	14	1	14	1

NeuPSIG: The NeuPSIG criteria for diagnosing neuropathic pain were used as the reference standard, with patients classified as having neuropathic pain (definite, probable) and no neuropathic pain (unlikely, possible).

Appendix 3. Item response frequency table for S-LANSS (n=589)

	Neuropathic pain (NeuPSIG positive)		No neuropathic pain (NeuPSIG negative)	
	Positive test, % n = 232	Negative test, % n = 152	Positive test, % n = 95	Negative test, % n = 110
Pins & Needles				
Yes	95	76	90	62
No	4	24	10	38
Changes color				
Yes	62	5	25	4
No	38	95	75	96
Light touch				
Yes	71	12	73	14
No	29	88	27	86
Electric shocks				
Yes	73	43	75	45
No	27	57	25	55
Burning pain				
Yes	72	43	68	36
No	28	57	32	64
Rubbing discomfort				
Yes	84	7	80	4
No	16	93	20	96
Numbness				
Yes	90	40	86	34
No	10	60	14	66

NeuPSIG: The NeuPSIG criteria for diagnosing neuropathic pain were used as the reference standard, with patients classified as having neuropathic pain (definite, probable) and no neuropathic pain (unlikely, possible).

Appendix 4. Item response frequency table for DN4 (n=723)

	Neuropathic pain (NeuPSIG positive)		No neuropathic pain (NeuPSIG negative)	
	Positive test, % n = 399	Negative test, % n = 62	Positive test, % n = 132	Negative test, % n = 130
Burning pain				
Yes	75	32	73	41
No	25	67	27	59
Cold pain				
Yes	32	3	30	6
No	68	97	70	94
Electric shock				
Yes	58	27	52	22
No	42	73	48	78
Tingling				
Yes	78	40	76	26
No	22	60	24	74
Pins & Needles				
Yes	91	50	91	46
No	9	50	9	54
Numbness				
Yes	93	65	88	46
No	7	35	12	54
Itching				
Yes	30	0	33	5
No	70	100	67	95
Hypoesthesia touch (exam)				
Yes	58	8	19	5
No	42	92	81	95
Hypoesthesia prick (exam)				
Yes	63	29	27	8
No	37	71	73	92
Brushing pain (exam)				
Yes	18	6	14	2
No	82	94	86	98

NeuPSIG: The NeuPSIG criteria for diagnosing neuropathic pain were used as the reference standard, with patients classified as having neuropathic pain (definite, probable) and no neuropathic pain (unlikely, possible).

painDETECT

SPØRRESKJEMA OM SMERTE

Dato: ..... Pasient: Etternavn: ..... Fornavn: .....

Hvor sterke er smertene dine **nå**, i dette øyeblikk?

0 1 2 3 4 5 6 7 8 9 10

Ingen Maksimal

Hvor sterk var den **sterkeste** smerten i løpet av de siste 4 ukene?

0 1 2 3 4 5 6 7 8 9 10

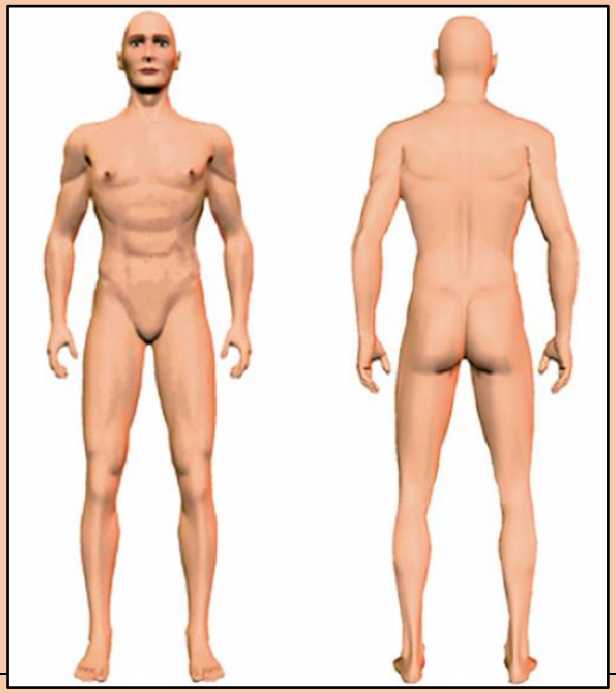
Ingen Maksimal

Hvor sterk har smerten vært i løpet av de siste 4 ukene **i gjennomsnitt**?

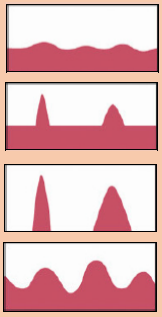
0 1 2 3 4 5 6 7 8 9 10

Ingen Maksimal

Vennligst marker **hovedområdet for smerte**



Marker det bildet som best beskriver forløpet av din smerte:



- Vedvarende smerter med små svingninger ☐
- Vedvarende smerter med smerteanfall ☐
- Smerteanfall uten smerter mellom ☐
- Smerteanfall med smerter mellom ☐

Stråler smertene dine ut til andre deler av kroppen? Ja ☐ Nei ☐

Hvis ja, tegn og vis med piler i hvilken retning smerten stråler ut

Plages du av en brennende følelse (f.eks som fra brennesle) i de markerte områdene?					
aldri ☐	nesten ikke ☐	litt ☐	moderat ☐	sterk ☐	veldig sterk ☐
Har du en prikkende eller stikkende følelse i smerteområdet (som følelsen av krypende maur eller elektriske prikkinger)?					
aldri ☐	nesten ikke ☐	litt ☐	moderat ☐	sterk ☐	veldig sterk ☐
Er lett berøring (klær, pledd) i dette området smertefullt?					
aldri ☐	nesten ikke ☐	litt ☐	moderat ☐	sterk ☐	veldig sterk ☐
Har du plutselige smerteanfall, som elektriske støt, i smerteområdet?					
aldri ☐	nesten ikke ☐	litt ☐	moderat ☐	sterk ☐	veldig sterk ☐
Er kulde eller varme (badevann) i dette området av og til smertefullt?					
aldri ☐	nesten ikke ☐	litt ☐	moderat ☐	sterk ☐	veldig sterk ☐
Plages du av en følelse av nummenhet i områdene som du har markert?					
aldri ☐	nesten ikke ☐	litt ☐	moderat ☐	sterk ☐	veldig sterk ☐
Kan lett trykk mot dette området, f.eks med en finger, utløse smerte?					
aldri ☐	nesten ikke ☐	litt ☐	moderat ☐	sterk ☐	veldig sterk ☐

(Skal fylles ut av legen)

aldri	nesten ikke	litt	moderat	sterk	veldig sterk
☐ x 0 = 0	☐ x 1 = ☐	☐ x 2 = ☐☐	☐ x 3 = ☐☐	☐ x 4 = ☐☐	☐ x 5 = ☐☐

Total skår ☐☐ av 35

PainDETECT etter Freynhagen R et al. PainDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. Curr Med Res Opin. 2006 Oct;22(10):1911-20. Oversatt av Grotle M, Nilsen KB og Munk R 2015, OUS/HiOA.

painDETECT

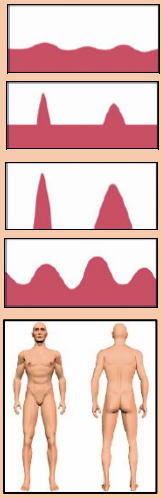
Skåring av smertespørreskjema

Dato: ..... Pasient: Etternavn: ..... Fornavn: .....

Vennligst overfør totalsummen fra smertespørreskjema

Total poengsum ☐☐

Vennligst summer de følgende tallene, avhengig av det angitte smerteatferdsmønster og smerteutstrålingen

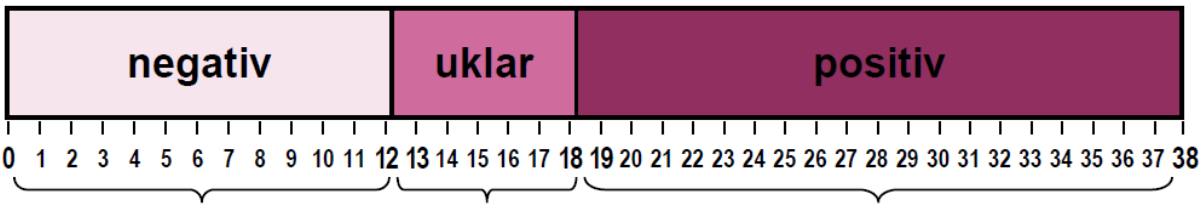


Vedvarende smerter med små svingninger	0	
Vedvarende smerter med smerteanfall	-1	hvis markert, eller
Smerteanfall uten smerter mellom	+1	hvis markert, eller
Smerteanfall med smerter mellom	+1	hvis markert, eller
Utstrålende smerter?	+2	hvis ja

Sluttresultat ☐☐

Screeningresultat

Vedrørende tilstedeværelse av en nevropatisk smertekomponent



En nevropatisk smertekomponent er usannsynlig (< 15 %)

Resultatet er tvetydig, men en nevropatisk smertekomponent kan være tilstede

En nevropatisk smertekomponent er sannsynlig (> 90 %)

Dette skjemaet erstatter ikke medisinsk utredning
Det brukes for screening av en nevropatisk smertekomponent

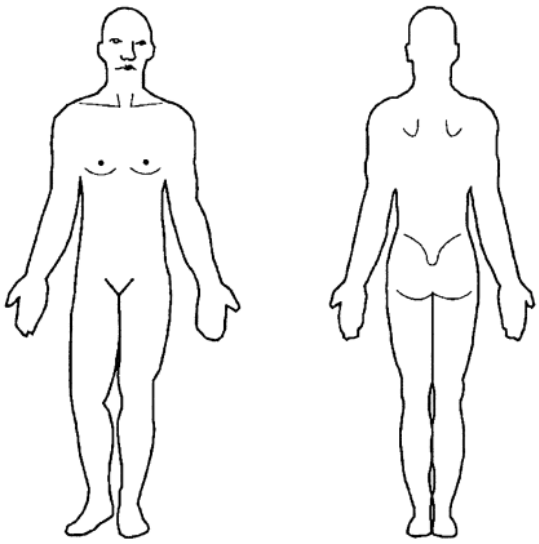
PainDETECT etter Freynhagen R et al. PainDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. Curr Med Res Opin. 2006 Oct;22(10):1911-20. Oversatt av Grotle M, Nilsen KB og Munk R 2015, OUS/HiOA.

S-LANSS SMERTESKÅR

Leeds Assessment of Neuropathic Symptoms and Signs (self-complete)

Navn: _____ **Dato:**_____

- Dette spørreskjemaet kan gi oss informasjon om hva slags type smerte du opplever. Dette kan hjelpe oss slik at vi kan finne den best mulige behandlingen for dine smerter
- Vennligst marker på tegningen nedenfor hvor du opplever smerter. Hvis du har smerter i mer enn ett område, **skal du kun skravere hovedområdet hvor smerten er verst**



- På skalaen nedenfor, vennligst kryss av for hvor sterke smertene har vært (som du har vist på tegningen ovenfor) i løpet av den siste uken: 0 betyr ingen smerte, og 10 betyr verst tenkelig smerte

INGEN 0 1 2 3 4 5 6 7 8 9 10 **VERST TENKELIG SMERTE**

- På den andre siden av arket er det 7 spørsmål om dine smerter (som du har vist på tegningen ovenfor). Tenk over hvordan du har opplevd smertene **i løpet av den sist uken**. Vennligst sett en ring rund de beskrivelsene som passer best for deg. Disse beskrivelsene kan passe bra eller dårlig uansett hvor sterke smertene oppleves

The S.LANSS etter Bennett MI et al. The S-LANSS Score for Identifying Pain of Predominantly Neuropathic Origin: Validation for Use in Clinical and Postal Research. The Journal of Pain, Vol 6, No 3 (March), 2005: pp 149-158. Oversatt av Grotle M, Nilsen KB og Munk R 2015, OUS/HiOA.

S-LANSS

1. **I det området hvor du har smerter, har du også en stikkende eller prikkende følelse?**
   a. NEI - Jeg har ikke denne type følelse (0)
   b. JA - Jeg har ofte denne type følelse (5)

2. **Endrer det smertefulle området farge (ser kanskje flekkete eller rødlig ut) når smertene er spesielt vonde?**
   a. NEI - Smertene mine påvirker ikke hudfargen (0)
   b. JA - Jeg får disse følelsene ganske ofte (5)

3. **Gjør smertene det affiserte hudområdet unormalt følsomt for berøring? Dette kan for eksempel være en ubehagelig følelse eller smerter når du stryker lett over huden**
   a. NEI - Smertene gjør ikke huden i dette området unormalt følsom for berøring (0)
   b. JA - Huden i dette området er særlig følsomt for berøring (3)

4. **Kommer smertene dine plutselig uten noen opplagt grunn når du er helt i ro? Ord som «elektriske støt», støkk og rykk kan gjerne brukes til å beskrive dette**
   a. NEI - Smertene mine føles ikke slik (0)
   b. JA - Jeg får ofte slik følelse (2)

5. **I det området hvor du har smerter, føles huden din uvanlig varm som en slags brennende smerte?**
   a. NEI - Jeg har ikke brennende smerter (0)
   b. JA - Jeg har ofte brennende smerter (1)

6. **Stryk over det smertefulle området med pekefingeren din og stryk deretter over et område uten smerter (for eksempel et hudområde lengre unna det smertefulle området, eller på motsatt side av det smertefulle området). Hvordan føles dette i det smertefulle området?**
   a. Det smertefulle området føles ikke annerledes enn området uten smerter (0)
   b. Jeg føler ubehag, som stikkende, prikkende eller brennende følelse som er annerledes enn i området uten smerter (5)

7. **Trykk forsiktig på det smertefulle området med fingertuppen din og trykk deretter på et område uten smerter (det samme smertefrie området som du valgte i det forrige spørsmålet). Hvordan føles dette i det smertefulle området?**
   a. Det smertefulle området føles ikke annerledes enn området uten smerter (0)
   b. Jeg føler nummenhet eller ømhet i det smertefulle området som er annerledes enn i området uten smerter (3)

Skåring: en poengsum på 12 eller mer antyder smerter med hovedsakelig nevropatisk opprinnelse

The S.LANSS etter Bennett MI et al. The S-LANSS Score for Identifying Pain of Predominantly Neuropathic Origin: Validation for Use in Clinical and Postal Research. The Journal of Pain, Vol 6, No 3 (March), 2005: pp 149-158. Oversatt av Grotle M, Nilsen KB og Munk R 2015, OUS/HiOA.

DN4 SPØRRESKJEMA

Vennligst fyll ut dette spørreskjemaet ved å krysse av for hvert punkt i de 4 spørsmålene nedenfor:

PASIENTINTERVJU

Spørsmål 1: Har smerten en eller flere av følgende karakteristikker?

	Ja	Nei
1. Brennende	□	□
2. Isende	□	□
3. Elektriske støt	□	□

Spørsmål 2: Er smerten forbundet med en eller flere av de følgende symptomene i det samme området?

	Ja	Nei
4. Kribling	□	□
5. Stikking/prikking	□	□
6. Nummenhet	□	□
7. Kløe	□	□

UNDERSØKELSE AV PASIENTEN

Spørsmål 3: Er smerten lokalisert til et område hvor den fysiske undersøkelsen avdekker en eller flere av de følgende funnene?

	Ja	Nei
8. Hypoestesi ved berøring	□	□
9. Hypoestesi ved stikk	□	□

Spørsmål 4: I det smertefulle området, kan smerten forårsakes av eller forsterkes ved:

	Ja	Nei
10. Strykende berøring	□	□

Det totale skåret regnes ut som summen av de 10 punktene, og med en grenseverdi på 4/10 for diagnosen nevropatisk smerte.

Total

DN4 Questionnaire etter Bouhassira D et al. Pain. 2005 Mar;114(1-2):29-36. Epub 2005 Jan 26: Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). Oversatt av Grotle M og Munk R 2014, HiOA.