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REVIEW

WILEY

Earlier diagnosis of peripheral neuropathy in primary care: A call to action

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Abstract

Peripheral neuropathy (PN) often remains undiagnosed (~80%). Earlier diagnosis of PN may reduce morbidity and enable earlier risk factor reduction to limit disease progression. Diabetic peripheral neuropathy (DPN) is the most common PN and the 10 g monofilament is endorsed as an inexpensive and easily performed test for DPN. However, it only detects patients with advanced neuropathy at high risk of foot ulceration. There are many validated questionnaires to diagnose PN, but they can be time-consuming and have complex scoring systems. Primary care physicians (PCPs) have busy clinics and lack access to a readily available screening method to diagnose PN. They would prefer a short, simple, and accurate tool to screen for PN. Involving the patient in the screening process would not only reduce the time a physician requires to make a diagnosis but would also empower the patient. Following an expert meeting of diabetologists and neurologists from the Middle East, South East Asia and Latin America, a consensus was formulated to help improve the diagnosis of PN in primary care using a simple tool for patients to screen themselves for PN followed by a consultation with the physician to confirm the diagnosis.

KEYWORDS
early-diagnosis, peripheral neuropathy, primary care

1 | INTRODUCTION

Peripheral neuropathy (PN) has a heterogeneous etiology and clinical presentation and often remains undiagnosed or may be misdiagnosed for other painful conditions.[1,2] Indeed, neuropathic pain (NeP) is associated with three times higher healthcare expenditure,[3] due to anxiety, depression, and sleep disturbance.[4] The patient is often unaware of a loss of sensation[5] and will only present to the physician with advanced disease leading to falls and foot ulceration.[6]

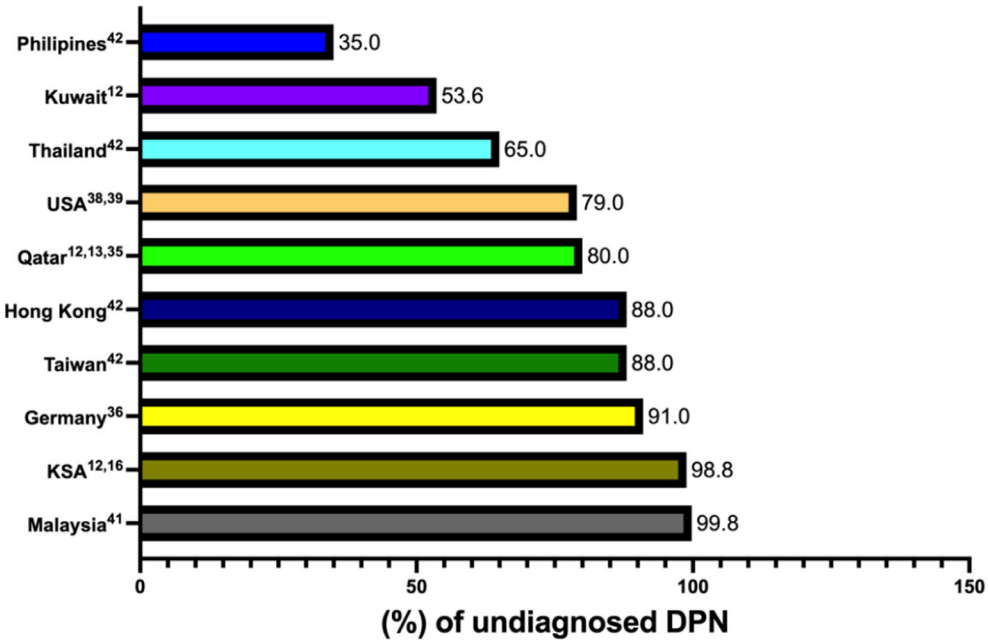

FIGURE 1 Percentage of undiagnosed diabetic peripheral neuropathy (DPN) globally.

The International association for the study of pain (IASP) defines NeP as "Pain initiated or caused by a primary lesion or dysfunction in the peripheral or central nervous system".[7] Pain, including NeP is one of the most common reasons for primary care physician (PCP) visits, and impaired sensation is one of the five most frequent reasons for consultation with a neurologist.[8] The prevalence of PN in the general population is substantial and ranges from 2.4% to 8%.[9] PN has multiple etiologies and whilst the commonest cause is diabetes[10] it also develops in patients with vitamin B_{12} deficiency,[11] pre-diabetes[12] and metabolic syndrome[13] and there is an increasing body of evidence implicating obesity[14] and vitamin D deficiency,[15] especially in the development of painful diabetic neuropathy.

The primary goal of screening is to identify early sub-clinical disease within a recognizable latent or early stage of a disease with a test that can be easily administered and is acceptable to a broad population. Diabetic peripheral neuropathy (DPN) is highly prevalent affecting 20%–90% of patients with diabetes[16,17] and timely treatment of risk factors[18,19] can limit disease progression.[20,21] Screening for DPN has relied primarily on identifying loss of sensation to the 10-g monofilament and assessment of touch/vibration and ankle reflexes.[22–25] However, these tests identify large fiber abnormalities which miss the majority of people with early diabetic neuropathy,[26,27] especially those with NeP, mediated by small fiber abnormalities. These screening techniques are not fit for purpose as they detect advanced neuropathy.[28]

PN is a common neurological condition encountered by family physicians, characterized by numbness, pain or burning sensation in the feet.[29] The diagnosis of PN requires a comprehensive history, neurological examination, and relevant laboratory testing.[29–31] Despite extensive investigations ~20% will be diagnosed with idiopathic PN.[32] Genetic testing targeting peripheral ion channel and transient receptor potential (TRP) genes has recently shown promise in the evaluation of painful neuropathies,[33–35] but is not widely available. There are limited rapid and objective measures of early neurodegeneration[36,37] and DPN may be undiagnosed in 35%–99.8% of patients in Saudi Arabia,[18,22] Qatar,[18,19,38] Kuwait,[18] Germany,[39] United Kingdom,[40] USA,[41,42] Japan,[43] Malaysia,[44] Hong Kong, Philippines, Taiwan and Thailand[45] (Figure 1).

1.1 | The gap

A lack of awareness of the symptoms among patients may lead to an ~5 year delay in the diagnosis and treatment of PN.[46] Patients tend to only report symptoms that have a substantial impact on their daily activities, work, mobility, and sleep with milder neuropathic symptoms being perceived as a normal sign of aging or they simply do not complain about pain, as it may be seen as a sign of weakness in some cultures. Physicians do not proactively ask patients for symptoms of PN as they prioritize other complications of diabetes, for example, retinopathy, nephropathy, and cardiovascular disease, which are of course highly prevalent and a cause of significant morbidity and mortality.[47] Even if patients complain of neuropathic symptoms, there are no readily available diagnostic tools in the clinic.[19,48] Indeed, neuropathy screening is underutilized in primary care,[42] ranging from 12% to 65% and both patients and physicians lack awareness of painful DPN (pDPN).[45] PCPs, especially have busy clinics and they perceive the diagnosis of PN as time-consuming and complex, with limited benefit of treatment.[16]

1.2 | Questionnaires for PN

Whilst there are many validated questionnaires for diagnosing PN, they have limited diagnostic accuracy, require considerable time to complete[49] and have complex and variable scoring systems

TABLE 1 Summary of scoring systems for peripheral neuropathy/neuropathic pain questionnaires.

Tool	Scoring system
NTSS-6[73,74]	A 6-item questionnaire for DPN. Scoring is based on a combined value of frequency and severity of symptoms: • 1 = mild and occasional (1/3 of the time) • 1.33 = mild and often (1/3 to 2/3 of the time) • 1.66 = mild and almost continuous (2/3 of the time) The increment of thirds repeats with moderate symptoms at 2, 2.33, 2.66 and severe symptoms at 3, 3.33, 3.66.
NTSS-6-6A (self-administered)[75]	Scoring is based on the frequency and intensity of six DPN symptoms: numbness, allodynia, pricking and three types of pain: aching, burning, and sharp. Scores are classified based on: • 0 = None • Mild >0 to ≤3.33 • Moderate >3.33 and ≤7.64 • Severe >7.64
SF-MPQ-2[76]	A 22-item questionnaire to assess the quality of painful symptoms and a score based on a 0–10 rating scale.
DN4 and LANSS[64,77,78]	The DN4 is a 10-item questionnaire, where the first 7 items are related to pain characteristics and the remaining 3 items are related to neurological examination with a score of 1 to each answer of "yes: and 0 for "no". A score of ≥4 indicates neuropathic pain. The LANSS pain scale is a 7-item questionnaire, where the first 5 questions refer to symptoms and type of pain and the last 2 questions are based on sensory testing of the painful area to assess allodynia and pinprick threshold. Scoring is based on a binary response and positive responses are scored as 1,2,3, or 5 based on the item and negative items are scored as 0. The maximum score is 24, and a cut-off score of ≥12 indicates neuropathic pain.
NeuroQol[79]	The NeuroQoL is a 27-item questionnaire, divided into 6 subscales to assess painful symptoms and paresthesia; loss of sensation on the feet; unsteadiness while standing or walking; limitations to daily activities; physical/emotional dependance; and emotional distress. It also includes 2 separate questions to assess the overall impact of neuropathy on QoL. The score is based on a Likert scale of 1–5 for each question, where 1 = never and 5 = all the time.
NDS[80,81]	NDS requires examination of vibration sensation (128 Hz tuning fork), temperature sensation, pinprick and ankle reflexes in both feet and is scored as: • Vibration sensation: 0 = present, 1 = reduced /absent • Temperature sensation: 0 = present, 1 = reduced /absent • Pin-prick sensation: 0 = present, 1 = reduced /absent • Ankle reflex: 0 = present, 1 = reduced /absent The NDS scoring system ranges from 0 to 10 and the severity of neuropathy can be graded as follows: mild,[3–5] moderate,[6–8] and severe.[9,10]
MNSI[81]	This is a 15-item questionnaire with a foot examination section. The questionnaire assesses positive (pain, temperature, sensation, tingling) and negative sensory symptoms (numbness), cramps, muscle weakness, foot ulcers/cracks and amputation. Neuropathy is based on a score of ≥7 for the first section and ≥2 for the MNSI examination. MNSI examination is scored as: • Appearance of feet: 0 = normal, 1 = abnormal • Ulceration: 0 = normal, 1 = abnormal • Ankle reflexes: 0 = present, 0.5 = present with reinforcement, 1 = absent • Vibration perception: 0 = present, 0.5 = reduced, 1 = absent

Abbreviations: DN4, Douleur Neuropathique 4; LANSS, Leeds assessment of neuropathic symptoms and signs; MNSI, Michigan neuropathy screening instrument; NDS, neuropathy disability score; NeuroQol, neuropathy specific quality of life; NTSS, neuropathy total symptom score-6; SF-MPQ-2, short-form McGill Pain Questionnaire.

(Table 1).[50] Because questionnaires are subjective, they can generate a wide range of prevalence for PN[51] (Figure 2A–F) and they lack agreement on sensitivity and specificity (Figure 3). Questionnaire accessibility and language barriers are additional challenges faced by the PCP.

The MNSI questionnaire is widely used in clinical trials,[52] but it is a lengthy tool validated only for DPN[52] and has a highly variable sensitivity and specificity.[53] The NTSS-6 questionnaire has only been validated for DPN[54] with limited validation of the translated versions and is subject to considerable misunderstanding when self-administered. The SF-NPQ has relatively poor and highly variable sensitivity and specificity. Whilst, LANSS has high sensitivity, it is time-consuming (20–30 min to complete) which is not feasible in a busy primary care clinic. The DN4 questionnaire has been more widely used but is subject to misunderstanding when self-administered. Validated questionnaires assessing the impact of PN on quality of life such as NeuroQoL[55] and Norfolk QOL-DN[56] have proven to be useful, but are time-consuming and not readily available in multiple languages.

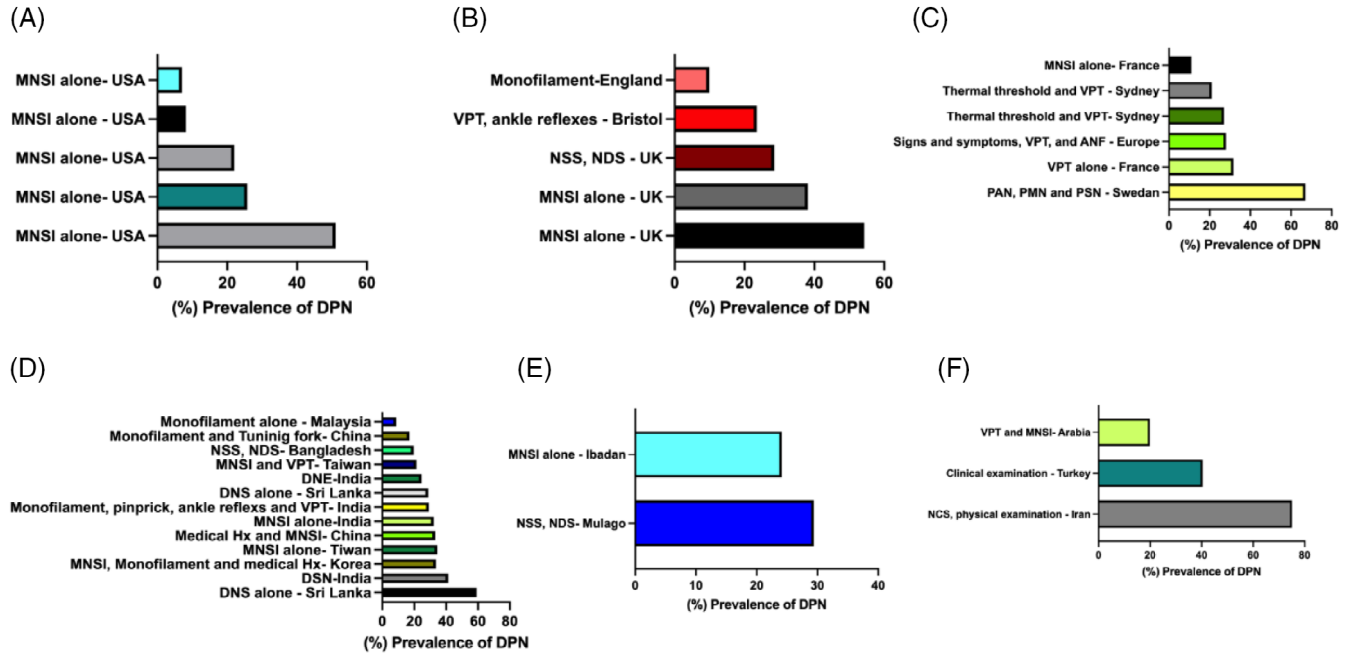

FIGURE 2 Prevalence of diabetic peripheral neuropathy (DPN) using different screening tools in different geographical areas.

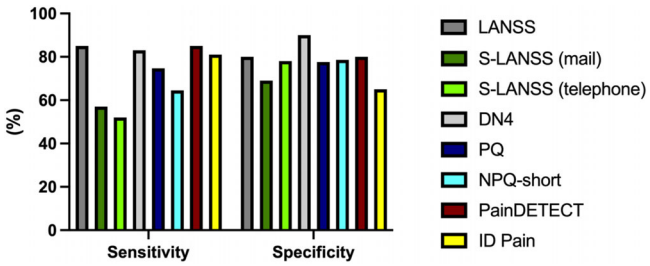

FIGURE 3 Varying sensitivity and specificity of different neuropathic pain questionnaires.

1.3 | Bridging the gap

Physicians favor the use of objective measures to diagnose and quantify the severity of disease. This is a challenge in the area of PN as objective tools are not widely accessible in primary care. Whilst objective measures of small fiber damage such as corneal nerve or intraepidermal nerve fiber loss can identify patients with painful diabetic neuropathy[57–59] and idiopathic small fiber neuropathy[2] they are not widely available. Patient self-report instruments are critical for raising patient awareness[60] and can identify other conditions, for example, rheumatological disease, leading to an earlier consultation with the healthcare provider.[61] Proactive self-screening may therefore help to diagnose early PN.[62]

Self-screening and diagnosis including the use of artificial intelligence platforms have recently gained in popularity, especially to address a lack of access to healthcare services.[63] PCPs would prefer a short, simple, and accurate tool to screen for pDPN.[64] Important considerations when developing self-administered tools for patients are the time and the level of literacy required to complete the questionnaire. Thus, tools longer than 15 questions with a complex scoring system would be unacceptable in primary care.[65]

Following a meeting of diabetologists and neurologists from the Middle East, South East Asia, and Latin America a consensus was formulated to help improve the diagnosis of PN:

- "*Community awareness*" is critical in raising awareness and increasing understanding of the importance of nerve health and potential risk factors for PN among the general population.
- "*Group education*" may improve patients' knowledge, health behavior, and quality of life. Group education has been shown to be effective in improving HbA1c, BMI, and lipids.[66] Additionally, physicians spent less time seeing the 9–10 patients/group rather than individually and patients had a chance to interact longer with healthcare providers.[67]
- "*Physician education*" regarding when and how to treat and when to refer to a neurologist or pain specialist is needed.
- "*TeleNeuropathy screening*" Teleophthalmology screening in an urban primary care setting showed a high level of satisfaction and enabled patient education.[68] Telemedicine has become very popular since the COVID-19 pandemic and is well-accepted by patients, providing access to physicians for patients, especially in rural and geographically isolated areas.[69] Implementing a similar approach with PN screening utilizing telemedicine services could help to identify those who need further investigations and referrals.
- "*Implementing dual screening programs*" Implementing a national screening program for PN like the English NHS Diabetic Eye Screening Program (DESP)[70] would enable earlier identification of undiagnosed PN. The NHS DESP reduced the prevalence of blindness in England by screening 82.8% of people with diabetes and

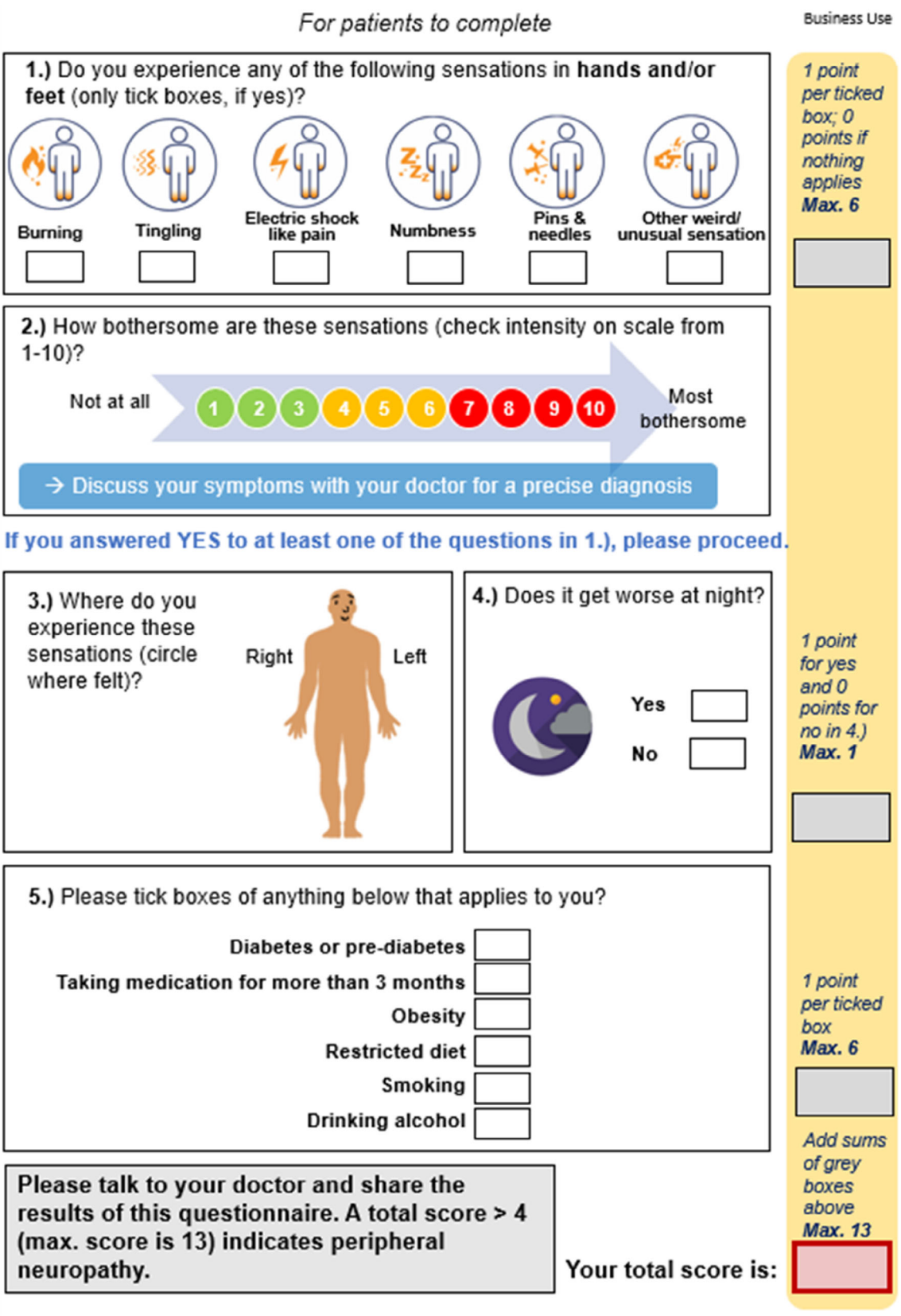

FIGURE 4 Patient-led questionnaire-screening for peripheral neuropathy (PN).

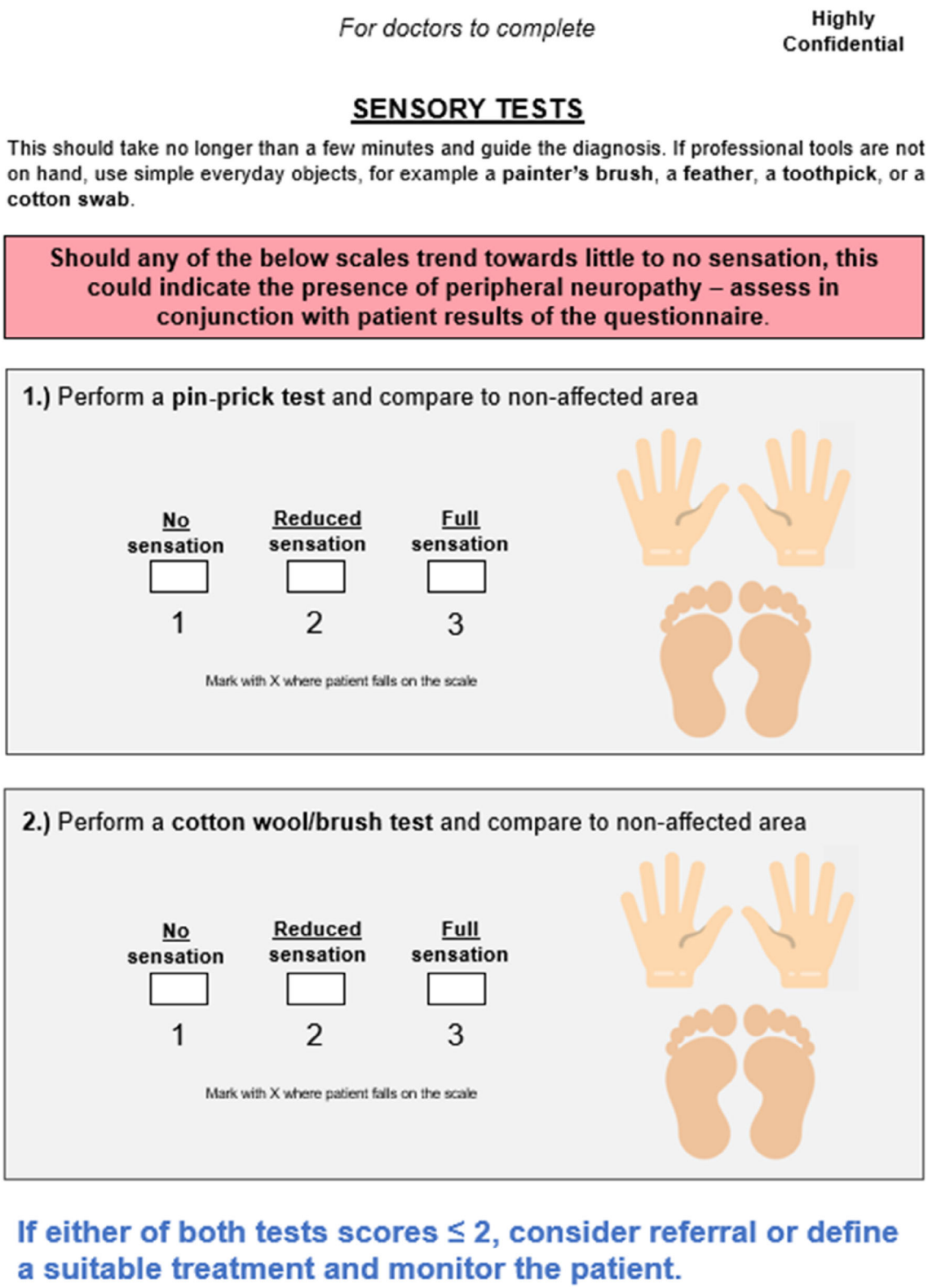

FIGURE 5 Physician-led questionnaire-confirmation of peripheral neuropathy (PN) diagnosis.

urgently referring people with proliferative DR and pre-proliferative DR to ophthalmology clinics for timely intravitreal VEGF and or surgery[70] as well as improvement of glycemia and blood pressure.[71] PN screening alongside DR screening in an optometry setting is feasible to identify both DPN and DR at the same time. In a community optometry setting in Manchester, 95% of patients underwent corneal confocal microscopy (CCM) to assess DPN, alongside DR screening.[72]

- *"Shift the focus of control"* by providing a simple self-administered screening tool to make a presumptive risk assessment based on the symptoms of PN to alert the physician to undertake a neurological examination and further investigations and if appropriate referral to secondary care to diagnose PN and its etiology.

1.4 | Patient-led questionnaire– screening for PN (Figure 4)

- A 5-item questionnaire was developed for patients to complete.
- *Question 1* consists of 5 typical symptoms of PN in the feet and hands. Pain is not listed among these symptoms as patients are often not able to differentiate various types of pain. Only typical symptoms such as tingling, numbness, and burning are listed with one additional option of "weird or unusual sensation" as patients may not always be able to describe their symptoms.
- *Question 2* provides a scale to rate the severity of symptoms from 1 to 10, to enable monitoring of the severity of pain and effect of therapy.
  If the patient answers YES to one of the first questions (one symptom) they proceed to question three otherwise, they can stop.
- *Question 3* provides an option to localize the symptoms on a body cartoon.
- *Question* 4 identifies if the patients' symptoms get worse at night. This is a critical question, as worsening at night is typical for PN, as opposed to mechanical pain which worsens when patients get out of bed and move.
- *Question 5* provides a list of the main risk factors for PN.

The patient will share the results of the questionnaire with their physician who will derive a score to make a quick decision regarding the need for further evaluation and management. If two symptoms, getting worse at night and one risk factor have been selected to achieve a score of 4 points, the likelihood for PN is high. The same for 2 risk factors and 2 symptoms, and so forth.

1.5 | Physician-led questionnaire–confirmation of PN diagnosis (Figure 5)

- The physician section is a 2-item assessment of sensation to pinprick and a cotton wool/brush test on precise locations on the foot where 1 = no sensation, 2 = reduced sensation, 3 = full sensation. A score ≤2 for each sensory test should prompt referral to a specialist.

This tool empowers patients to self-refer to their PCP for further assessment of PN. Validation of this tool against established diagnostic questionnaires including DN4 is being undertaken in 2024.

2 | CONCLUSION

PN is markedly underdiagnosed or misdiagnosed across the world, especially in resource-constrained healthcare settings. Healthcare providers are overburdened, addressing multiple comorbidities in a short consultation time, especially in patients with diabetes. There are no simple readily available rapid objective tests that can be deployed, especially in primary care. Whilst a number of questionnaires have been validated for the diagnosis of PN, most are time-consuming and have limited sensitivity and specificity. A consensus was formulated amongst experts in diabetes and neurology from the Middle East, South East Asia, and Latin America that identified and bridged the gap for improving the diagnosis of PN in a primary care setting. A quick questionnaire-based tool initiated by the patient and completed by the physician is proposed to screen for PN.

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CONFLICT OF INTEREST STATEMENT

H.G. received Honoraria from P&G. S.K. received Honoraria from P&G. R.P. received grants and/or Honoraria for consultancy or giving lectures from P&G, Eisai, Abbott, Pfizer, Otsuka, and Bayer Pharmaceutical. R.N.G. received Honoraria from P&G. K.Y. received Honoraria from P&G. A.C. consultant, speaker, Honoraria: AstraZeneca, Boehringer Ingelheim, Eli Lilly, Merck, Novartis, Novo Nordisk, Proctor& Gamble, Sanofi. Grant/research support from: Africa Health, Shareholder and executive board member Unrelated. J.N. received Honoraria from Novo Nordisk, Eli Lilly, Aventis Sanofi, Servier, Pfizer, Boehringer Ingelheim, Merck, Merck Serono, astra Zeneca, P&G. L.L. received grants and/or Honoraria for consultancy or giving lectures from Abbott, Amgen, AstraZeneca, Boehringer Ingelheim, Merck Sharp & Dohme, Novo Nordisk, Roche, Sanofi, Servier, Viatris Pharmaceutical, and Zuellig Pharma. P.E.F. received Honoraria from P&G, Servier, Novo Nordisk, Abbott, Astra Zeneca and Asofarma. V.L. received Honoraria from P&G, Sanofi, Novo Nordisk, Amgen, Zuellig Pharma, AstraZeneca, Abbott, BI, Merck, BD, and Pfizer. R.A.M received Honoraria for lectures: Novo Nordisk, Lilly, Sanofi, P&G, Viatris, Novo Nordisk, and was on the DSMB for the PACT-MEA study.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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REFERENCES

1. Marchettini P, Lacerenza M, Mauri E, Marangoni C. Painful peripheral neuropathies. *Curr Neuropharmacol*. 2006;4(3):175-181.

2. Egenolf N, Zu Altenschildesche CM, Kreß L, et al. Diagnosing small fiber neuropathy in clinical practice: a deep phenotyping study. *Ther Adv Neurol Disord*. 2021;14:17562864211004318.
3. Berger A, Dukes EM, Oster G. Clinical characteristics and economic costs of patients with painful neuropathic disorders. *J Pain*. 2004;5(3):143-149.
4. Sadosky A, Schaefer C, Mann R, et al. Burden of illness associated with painful diabetic peripheral neuropathy among adults seeking treatment in the US: results from a retrospective chart review and cross-sectional survey. *Diabetes Metab Syndr Obes*. 2013;6:79-92.
5. Hicks CW, Wang D, Windham BG, Matsushita K, Selvin E. Prevalence of peripheral neuropathy defined by monofilament insensitivity in middle-aged and older adults in two US cohorts. *Sci Rep*. 2021;11(1):19159.
6. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. *N Engl J Med*. 2017;376(24):2367-2375.
7. (IASP). IAFTSoP. Part II: Detailed Descriptions of Pain Syndromes. *Classification of Chronic Pain: Description of Chronic Pain Syndromes and Definitions of Pain Terms [Internet]*. International Association for the Study of Pain (IASP); 2012. https://www.iasp-pain.org/publications/free-ebooks/classification-of-chronic-pain-second-edition-revised/
8. Prevention. CfDCa. National Ambulatory Medical Care Survey Factsheet: Neurology. Centers for Disease Control and Prevention website. https://www.cdc.gov/nchs/data/ahcd/NAMCS_2010_factsheet_neurology.pdf
9. Chronic symmetric symptomatic polyneuropathy in the elderly: a field screening investigation in two Italian regions. I. Prevalence and general characteristics of the sample. Italian General Practitioner Study Group (IGPSG). *Neurology*. 1995;45(10):1832-1836.
10. Kirthi V, Perumbalath A, Brown E, et al. Prevalence of peripheral neuropathy in pre-diabetes: a systematic review. *BMJ Open Diabetes Res Care*. 2021;9(1):e002040.
11. Miyan Z, Waris N. Association of vitamin B(12) deficiency in people with type 2 diabetes on metformin and without metformin: a multicenter study, Karachi, Pakistan. *BMJ Open Diabetes Res Care*. 2020;8(1):e001151.
12. Asghar O, Petropoulos IN, Alam U, et al. Corneal confocal microscopy detects neuropathy in subjects with impaired glucose tolerance. *Diabetes Care*. 2014;37(9):2643-2646.
13. D'Onofrio L, Ferdousi M, Kalteniece A, et al. Corneal confocal microscopy identifies small nerve fibre damage in patients with hypertriglyceridemia. *J Clin Lipidol*. 2022;16(4):463-471.
14. Azmi S, Ferdousi M, Liu Y, et al. Bariatric surgery leads to an improvement in small nerve fibre damage in subjects with obesity. *Int J Obes*. 2021;45(3):631-638.
15. Alam U, Petropoulos IN, Ponirakis G, et al. Vitamin D deficiency is associated with painful diabetic neuropathy. *Diabetes Metab Res Rev*. 2021;37(1):e3361.
16. Watson JC, Dyck PJ. Peripheral neuropathy: a practical approach to diagnosis and symptom management. *Mayo Clin Proc*. 2015;90(7):940-951.
17. Ferdousi M, Kalteniece A, Azmi S, et al. Diagnosis of neuropathy and risk factors for corneal nerve loss in type 1 and type 2 diabetes: a corneal confocal microscopy study. *Diabetes Care*. 2021;44(1):150-156.
18. Ponirakis G, Elhadd T, Al Ozairi E, et al. Prevalence and risk factors for diabetic peripheral neuropathy, neuropathic pain and foot ulceration in the Arabian gulf region. *J Diabetes Invest*. 2022;13(9):1551-1559.
19. Ponirakis G, Elhadd T, Chinnaiyan S, et al. Prevalence and risk factors for diabetic neuropathy and painful diabetic neuropathy in primary and secondary healthcare in Qatar. *J Diabetes Invest*. 2021;12(4):592-600.
20. Iqbal Z, Bashir B, Ferdousi M, et al. Lipids and peripheral neuropathy. *Curr Opin Lipidol*. 2021;32(4):249-257.
21. Liu G, Li Y, Pan A, et al. Adherence to a healthy lifestyle in association with microvascular complications among adults with type 2 diabetes. *JAMA Netw Open*. 2023;6(1):e2252239.
22. Algeffari MA. Painful diabetic peripheral neuropathy among Saudi diabetic patients is common but under-recognized: multicenter cross-sectional study at primary health care setting. *J Family Community Med*. 2018;25(1):43-47.
23. Armstrong DG, Lavery LA, Vela SA, Quebedeaux TL, Fleischli JG. Choosing a practical screening instrument to identify patients at risk for diabetic foot ulceration. *Arch Intern Med*. 1998;158(3):289-292.
24. Olaleye D, Perkins BA, Bril V. Evaluation of three screening tests and a risk assessment model for diagnosing peripheral neuropathy in the diabetes clinic. *Diabetes Res Clin Pract*. 2001;54(2):115-128.
25. Perkins BA, Olaleye D, Zinman B, Bril V. Simple screening tests for peripheral neuropathy in the diabetes clinic. *Diabetes Care*. 2001;24(2):250-256.
26. Breiner A, Lovblom LE, Perkins BA, Bril V. Does the prevailing hypothesis that small-fiber dysfunction precedes large-fiber dysfunction apply to type 1 diabetic patients? *Diabetes Care*. 2014;37(5):1418-1424.
27. McIlhatton A, Lanting S, Lambkin D, Leigh L, Casey S, Chuter V. Reliability of recommended non-invasive chairside screening tests for diabetes-related peripheral neuropathy: a systematic review with meta-analyses. *BMJ Open Diabetes Res Care*. 2021;9(2):e002528.
28. Dube S, Hulke SM, Wakode SL, et al. Effectiveness of Semmes Weinstein 10 gm monofilament in diabetic peripheral neuropathy taking nerve conduction and autonomic function study as reference tests. *J Family Med Prim Care*. 2022;11(10):6204-6208.
29. Castelli G, Desai KM, Cantone RE. Peripheral neuropathy: evaluation and differential diagnosis. *Am Fam Physician*. 2020;102(12):732-739.
30. Malik RA, Andag-Silva A, Dejthevaporn C, et al. Diagnosing peripheral neuropathy in South-East Asia: a focus on diabetic neuropathy. *J Diabetes Invest*. 2020;11(5):1097-1103.
31. Verdugo RJ, Matamala JM, Inui K, et al. Review of techniques useful for the assessment of sensory small fiber neuropathies: report from an IFCN expert group. *Clin Neurophysiol*. 2022;136:13-38.
32. Freeman R, Gewandter JS, Faber CG, et al. Idiopathic distal sensory polyneuropathy: ACTTION diagnostic criteria. *Neurology*. 2020;95(22):1005-1014.
33. Almomani R, Sopacua M, Marchi M, et al. Genetic profiling of sodium channels in diabetic painful and painless and idiopathic painful and painless neuropathies. *Int J Mol Sci*. 2023;24(9):8278.
34. Marchi M, Salvi E, Andelic M, et al. TRPA1 rare variants in chronic neuropathic and nociplastic pain patients. *Pain*. 2023;164:2048-2059.
35. Ślęczkowska M, Almomani R, Marchi M, et al. Peripheral Ion Channel gene screening in painful- and painless-diabetic neuropathy. *Int J Mol Sci*. 2022;23(13):7190.
36. Devigili G, Di Stefano G, Donadio V, et al. Clinical criteria and diagnostic assessment of fibromyalgia: position statement of the Italian Society of Neurology-Neuropathic Pain Study Group. *Neurol Sci*. 2023;44(7):2561-2574.
37. Truini A, Aleksovska K, Anderson CC, et al. Joint European academy of neurology-European pain federation-neuropathic pain special Interest Group of the International Association for the study of pain guidelines on neuropathic pain assessment. *Eur J Neurol*. 2023;30:2177-2196.
38. Ponirakis G, Elhadd T, Chinnaiyan S, et al. Prevalence and risk factors for painful diabetic neuropathy in secondary healthcare in Qatar. *J Diabetes Invest*. 2019;10(6):1558-1564.
39. Bongaerts BW, Rathmann W, Heier M, et al. Older subjects with diabetes and prediabetes are frequently unaware of having distal sensorimotor polyneuropathy: the KORA F4 study. *Diabetes Care*. 2013;36(5):1141-1146.
40. Daousi C, MacFarlane IA, Woodward A, Nurmikko TJ, Bundred PE, Benbow SJ. Chronic painful peripheral neuropathy in an urban

community: a controlled comparison of people with and without diabetes. *Diabet Med*. 2004;21(9):976-982.
41. Wang W, Balamurugan A, Biddle J, Rollins KM. Diabetic neuropathy status and the concerns in underserved rural communities: challenges and opportunities for diabetes educators. *Diabetes Educ*. 2011;37(4):536-548.
42. Herman WH, Kennedy L. Underdiagnosis of peripheral neuropathy in type 2 diabetes. *Diabetes Care*. 2005;28(6):1480-1481.
43. Tsuji M, Yasuda T, Kaneto H, et al. Painful diabetic neuropathy in Japanese diabetic patients is common but underrecognized. *Pain Res Treat*. 2013;2013:318352.
44. Lee PY, Hani SS, Cheng YG, Zainuddin Z, Singh H, Loh KW. The proportion of undiagnosed diabetic peripheral neuropathy and its associated factors among patients with T2DM attending urban health clinics in Selangor. *Malays Fam Physician*. 2022;17(1):36-43.
45. Malik RA, Aldinc E, Chan SP, et al. Perceptions of painful diabetic peripheral neuropathy in South-East Asia: results from patient and physician surveys. *Adv Ther*. 2017;34(6):1426-1437.
46. Srinivasan AVPS, Bhattacharyya KB, Maji D, Hazra K, Talwalkar P, et al. Consensus recommendations for the management of peripheral neuropathy in India. *J Indian Med Assoc*. 2018;116(10):45-55.
47. Verma S, Alamuddin N, Alawadi F, et al. Prevalence of diabetes and cardiovascular risk in the Middle East and Africa: primary results of the PACT-MEA study. *Circulation*. 2023;147(16):1251-1255.
48. Ponirakis G, Elhadd T, Al Ozairi E, et al. Prevalence and risk factors for diabetic peripheral neuropathy, neuropathic pain and foot ulceration in the Persian Gulf region. *J Diabetes Invest*. 2022;13:1551-1559.
49. Bouhassira D, Attal N. Diagnosis and assessment of neuropathic pain: the saga of clinical tools. *Pain*. 2011;152(3 Suppl):S74-S83.
50. Unluturk Z, Oztekin SNS, Alkan H, Senol H, Betas S, Erdogan C. Which scale is more useful to detect diabetic neuropathic pain?: a cross-sectional study. *BMC Endocr Disord*. 2022;22(1):56.
51. Sun J, Wang Y, Zhang X, Zhu S, He H. Prevalence of peripheral neuropathy in patients with diabetes: a systematic review and meta-analysis. *Prim Care Diabetes*. 2020;14(5):435-444.
52. Herman WH, Pop-Busui R, Braffett BH, et al. Use of the Michigan neuropathy screening instrument as a measure of distal symmetrical peripheral neuropathy in type 1 diabetes: results from the diabetes control and complications trial/epidemiology of diabetes interventions and complications. *Diabet Med*. 2012;29(7):937-944.
53. Moghtaderi A, Bakhshipour A, Rashidi H. Validation of Michigan neuropathy screening instrument for diabetic peripheral neuropathy. *Clin Neurol Neurosurg*. 2006;108(5):477-481.
54. Bastyr EJ, Price KL, Bril V, Group MS. Development and validity testing of the neuropathy total symptom score-6: questionnaire for the study of sensory symptoms of diabetic peripheral neuropathy. *Clin Ther*. 2005;27(8):1278-1294.
55. Vileikyte L, Peyrot M, Bundy C, et al. The development and validation of a neuropathy- and foot ulcer-specific quality of life instrument. *Diabetes Care*. 2003;26(9):2549-2555.
56. Coelho T, Marques W Jr, Dasgupta NR, et al. Eplontersen for hereditary transthyretin amyloidosis with polyneuropathy. *JAMA*. 2023;330(15):1448-1458.
57. Püttgen S, Bönhof GJ, Strom A, et al. Augmented corneal nerve fiber branching in painful compared with painless diabetic neuropathy. *J Clin Endocrinol Metab*. 2019;104(12):6220-6228.
58. Kalteniece A, Ferdousi M, Azmi S, et al. Corneal confocal microscopy detects small nerve fibre damage in patients with painful diabetic neuropathy. *Sci Rep*. 2020;10(1):3371.
59. Kalteniece A, Ferdousi M, Azmi S, et al. Corneal nerve loss is related to the severity of painful diabetic neuropathy. *Eur J Neurol*. 2022;29(1):286-294.
60. Wolf FPT. Data collection in the CLINIC. *Rheum Dis Clin North Am*. 1995;21(2):321-358.
61. Pincus T. Documenting quality management in rheumatic disease: are patient questionnaires the best (and only) method? *Arthritis Care Res*. 1996;9(5):339-348.
62. Gavan NA, Veresiu IA, Vinik EJ, Vinik AI, Florea B, Bondor CI. Delay between onset of symptoms and seeking physician intervention increases risk of diabetic foot complications: results of a cross-sectional population-based survey. *J Diabetes Res*. 2016;2016:1567405.
63. Aboueid S, Liu RH, Desta BN, Chaurasia A, Ebrahim S. The use of artificially intelligent self-diagnosing digital platforms by the general public: scoping review. *JMIR Med Inform*. 2019;7(2):e13445.
64. Unal-Cevik I, Sarioglu-Ay S, Evcik D. A comparison of the DN4 and LANSS questionnaires in the assessment of neuropathic pain: validity and reliability of the Turkish version of DN4. *J Pain*. 2010;11(11):1129-1135.
65. Miller PNS, Walkom E, Schneider J, Li S, Evans T. The performance and accuracy of depression screening tools capable of self-administration in primary care: a systematic review and meta-analysis. The. *Eur J Psychiatry*. 2021;35(1):1-18.
66. Owen C, Woodward S. Effectiveness of dose adjustment for normal eating (DAFNE). *Br J Nurs*. 2012;21(4):224 6-28, 30-2.
67. Trento M, Passera P, Tomalino M, et al. Group visits improve metabolic control in type 2 diabetes: a 2-year follow-up. *Diabetes Care*. 2001;24(6):995-1000.
68. Nguyen M, Stamenova V, Onabajo N, et al. Perceptions of a Teleophthalmology screening program for diabetic retinopathy in adults with type 1 and type 2 diabetes in urban primary care settings. *Can J Diabetes*. 2022;46:649-654.
69. Haleem A, Javaid M, Singh RP, Suman R. Telemedicine for healthcare: capabilities, features, barriers, and applications. *Sens Int*. 2021;2:100117.
70. Scanlon PH. The English National Screening Programme for diabetic retinopathy 2003-2016. *Acta Diabetol*. 2017;54(6):515-525.
71. Scanlon PH. The contribution of the English NHS diabetic eye screening Programme to reductions in diabetes-related blindness, comparisons within Europe, and future challenges. *Acta Diabetol*. 2021;58(4):521-530.
72. Carmichael J, Fadavi H, Ishibashi F, et al. Implementation of corneal confocal microscopy for screening and early detection of diabetic neuropathy in primary care alongside retinopathy screening: results from a feasibility study. *Front Endocrinol*. 2022;13:891575.
73. Moors VJ, Graveran KD, Shahsavari D, Parkman HP. A cross-sectional study describing peripheral neuropathy in patients with symptoms of gastroparesis: associations with etiology, gastrointestinal symptoms, and gastric emptying. *BMC Gastroenterol*. 2022;22(1):315.
74. Lawal-Bello AT. Diabetic neuropathy: an evaluation using the ntss-6 questionnaire and biothesiometry in type 2 DM patients. Presented at Society for Endocrinology BES 2015, Edinburgh, UK: Endocrine Abstracts 2015.
75. Currie CJ, Poole CD, Woehl A, et al. The health-related utility and health-related quality of life of hospital-treated subjects with type 1 or type 2 diabetes with particular reference to differing severity of peripheral neuropathy. *Diabetologia*. 2006;49(10):2272-2280.
76. Dworkin RH, Turk DC, Revicki DA, et al. Development and initial validation of an expanded and revised version of the short-form McGill pain questionnaire (SF-MPQ-2). *Pain*. 2009;144(1–2):35-42.
77. Hamdan A, Luna JD, Del Pozo E, Galvez R. Diagnostic accuracy of two questionnaires for the detection of neuropathic pain in the Spanish population. *Eur J Pain*. 2014;18(1):101-109.
78. Bennett MI, Smith BH, Torrance N, Potter J. The S-LANSS score for identifying pain of predominantly neuropathic origin: validation for use in clinical and postal research. *J Pain*. 2005;6(3):149-158.
79. Alam U, Fawwad A, Shaheen F, Tahir B, Basit A, Malik RA. Improvement in neuropathy specific quality of life in patients with diabetes after vitamin D supplementation. *J Diabetes Res*. 2017;2017:7928083.

80. Kisozi T, Mutebi E, Kisekka M, et al. Prevalence, severity and factors associated with peripheral neuropathy among newly diagnosed diabetic patients attending Mulago hospital: a cross-sectional study. *Afr Health Sci*. 2017;17(2):463-473.
81. Yang ZCR, Zhang Y, Huang Y, et al. Scoring systems to screen for diabetic peripheral neuropathy. *Cochrane Database Syst Rev*. 2018; 2018(7):CD010974.

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