

Screening, diagnosis and management of diabetic sensorimotor polyneuropathy in clinical practice: International expert consensus recommendations

INTERVIEW WITH PROFESSOR VINCENZA SPALLONE

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- I want young students and clinicians to be interested by the complexity of diabetic neuropathy while also recognizing the simplicity of checking for symptoms and indicators.
- Doctors should be aware that they can give efficacy to their work and well-being to their patients by following simple and accessible steps. **STOP ignoring, START caring.**
- From a global viewpoint, this Consensus meeting in November 2020 on the occasion of the World Diabetes Day aims to provide clear and practical guidelines and algorithms for screening, diagnosis, and treatment of diabetic polyneuropathy in clinical practice.

Why is diabetic neuropathy considered a “forgotten complication”?

Many studies from various countries show a significant underdiagnosis and undertreatment of diabetic neuropathy. This underscreening of diabetic neuropathy occurs in Italy as well. The Italian diabetes association, Associazione Medici Diabetologi, promoted a survey based on electronic medical records from 258 specialist diabetes centers, involving 34,705 patients with type 1 diabetes and 473,740 patients with type 2 diabetes. According to this survey,

only 23.1 percent of patients with type 1 diabetes and 21.4 percent of patients with type 2 diabetes were screened for the risk of diabetic foot complications in 2018.⁽¹⁾

Why do you engage for diabetic neuropathy?

My mentor first introduced me to diabetic neuropathy many years ago. In addition to clinical practice, I am still involved in this complication through research and education.

My observations of how disabling diabetic neuropathy can be, how it can disrupt quality of life, isolate patients, cause suffering, and interfere in so many aspects of their lives, arise from my experience caring for diabetic neuropathy patients. I became aware of the need to find solutions for them as well as the experience of being in an empathic relationship.

Taking care of these individuals exemplifies diabetes care, which should be comprehensive and open-minded about many aspects of the disease. A person who complains of feeling “like fire and ice under the feet” is more than treating his neuropathic pain. Taking care of his pain necessitates paying attention to and considering all of his other symptoms, including psychosocial ones.

Diabetic neuropathy care teaches multi-disciplinarity, the importance of the nervous system in many functions, and the ability to detect problems that aren't immediately apparent or aren't perceived as such (by patients and sometimes also by health care providers). The study of diabetic neuropathy allows for the discovery of how it is intriguing and interconnected including e.g. the link of:

- neuropathic pain with depression or sleep disturbance⁽²⁾, or
- the cornea that informs on the peripheral nerves^(3, 4)

Research also shows how diabetic neuropathy has a powerful influence on outcomes, e.g.:

- as with the predictive role of the symptom “numbness” on cardiovascular events⁽⁵⁾, or
- the fact that the beneficial effects of SGLT2 inhibitors may be mediated by the autonomic nervous system⁽⁶⁾

I would like young students and doctors to be fascinated by the complexity of diabetic neuropathy while also appreciating the simplicity of looking for symptoms and signs. It is also very important to recognize the benefits of being aware of diabetic neuropathy and acting accordingly, as well as the outcomes prevention and symptomatic forms treatment.

What are the main challenges regarding the symptomatic treatment of painful diabetic neuropathy?

The first challenge to overcome is a timely and accurate diagnosis of painful diabetic neuropathy. This symptomatic form of diabetic neuropathy is also susceptible to underdiagnosis due to pain misinterpretation and a lack of referral. The use of neuropathic pain screening questionnaires like the DN4 (very easy to use, available in many languages, and validated for painful diabetic neuropathy)⁽⁷⁾ can help to identify patients with neuropathic pain in the lower limbs. A correct clinical diagnosis of painful diabetic neuropathy, in my experience, allows you to begin with the right foot. Different analgesic drugs work for neuropathic and non-neuropathic pain.

Another challenge is adhering to neuropathic pain treatment guidelines. Undertreatment of painful diabetic neuropathy or nonadherence to recommendations regarding drug selection, titration, dosage, treatment length, and subsequent steps has been documented in studies from France⁽⁸⁾ and Germany^(9, 10).

Adherence to pain management guidelines, on the other hand, was found to be associated with significantly lower health care resource use and costs in a study from the United States, when compared to nonadherence to guidelines⁽¹¹⁾.

In addition to a clear definition of the neuropathic nature of the patient's pain and the selection of the recommended treatment, it is critical to assess treatment efficacy and safety and to consider the impact of pain and treatment on quality of life, mood, and sleep when making therapeutic decisions in the patients' follow-up. The Consensus report outlines a step-by-step approach to pain treatment, including drug titration, duration of treatment, response definition criteria, treatment combinations, and the role of other treatments and comorbidities in interfering with pain treatment.

Because pharmacological treatment is not always effective or well tolerated, a non-pharmacological approach should be considered in addition to or instead of drugs in some cases. In any stage of painful diabetic neuropathy, disease-modifying treatment with alpha-lipoic acid is possible, with the added benefit of a long-term favorable safety profile.

Neuropathic pain is a complex condition that necessitates a multidisciplinary approach for its treatment. GPs, diabetologists, neurologists, pain specialists, psychologists, psychiatrists, and podiatrists may all be involved in this integrative care. In many situations, however, it is not used or is not possible.

The greatest challenge and responsibility for the future is to educate patients and implement therapeutic pathways based on their needs and local resources.

“Therapeutic algorithms must be harmonized and constantly updated to foster appropriate and efficacious treatments in everyday routine,” the Consensus document concludes.

What differentiates the consensus report from other guideline documents or previous consensus reports?

A new feature of this Consensus document is a focus on how guidelines are implemented in clinical practice. The experts who spoke at this meeting authored the Toronto consensus report⁽¹²⁾, the American Diabetes Association position statement⁽¹³⁾, and other national guidelines on diabetic neuropathy. For both screening and treatment, however, there is a well-documented gap between guidelines and practical application. The consensus report fills in the gaps and makes ad hoc recommendations for putting diabetic polyneuropathy guidelines into practice, with key words like clarity, awareness, and education for a broad audience (including stakeholders), involvement of trained staff, diabetic neuropathy screening incorporated into routine procedures for other complications, and a risk-based approach for candidate selection.

As a result, the issue of translating guidelines from theory to practice is at the heart of this report.

Why would it be important for clinical practice to follow the consensus recommendations?

This document lays out a step-by-step approach to diabetic polyneuropathy screening, diagnosis, and differential diagnosis. It provides well-described modalities for the assessment of symptoms and signs with greater detail than previous guidelines and with a true attention to affordability of the procedures. It provides support information such as the choice of diagnostic tools, the site of examination, or the need for age-related normal reference, based on evidence from the literature and experts’ clinical experience in different countries. The document aims to translate evidence-based accuracy into a practical, informative approach that includes some pointers and tricks. Furthermore, it openly declares the areas where there was less unanimity in the degree of agreement.

The Consensus Report was published in the journal “Diabetes Research and Clinical Practice”. Why is this important?

The International Diabetes Federation’s official journal is Diabetes Research and Clinical Practice. This Consensus meeting, held on the 11th and 12th of November 2020 during World Diabetes Day, aimed to address its goal of providing clear and practical recommendations and algorithms for the screening, diagnosis, and treatment of diabetic neuropathy in clinical practice from a broad international perspective. As a result, the 15 experts represented the EU, the United Kingdom, Eastern Europe, Russia, the Middle East, Asia, and the United States. The goal was to use this composite panel to consider their experience in various regional realities and provide recommendations that would be appropriate in most clinical situations. The publication in Diabetes Research and Clinical Practice is in line with the Consensus’ goals and may help to make its findings more widely known.

What would you like to tell the audience? What is your appeal to your colleagues in clinical practice?

Neuropathic pain can be excruciating, limiting function, affecting quality of life and sleep, causing depression, and interfering with treatment adherence. Loss of sensation is silent and sneaky, but if ignored, it can lead to foot ulceration and a chain reaction that disrupts your life. In clinical practice, this significant burden on the lives of people with diabetes cannot be overlooked.

Be aware that diabetic neuropathy can be detected and treated more easily than is commonly assumed. You can give efficacy to your work and well-being to your patients by following simple and accessible steps.

STOP ignoring, START caring.

FOR ADDITIONAL INFORMATION, PLEASE SEE THE COMPLETE ARTICLE:

Ziegler D, Tesfaye S, Spallone V, Gurieva I, Al Kaabi J, Mankovsky B, Martinka E, Radulian G, Nguyen TK, Stirban AO, Tankova T, Varkonyi T, Freeman R, Kempler P, Boulton AJM. Screening, diagnosis and management of diabetic sensorimotor polyneuropathy in clinical practice: International expert consensus recommendations. *Diabetes Res Clin Pract*. 2021 Sep 18;109063. doi: 10.1016/j.diabres.2021.109063. Epub ahead of print.

Accessible online at: [https://www.diabetesresearchclinicalpractice.com/article/S0168-8227\(21\)00422-8/fulltext](https://www.diabetesresearchclinicalpractice.com/article/S0168-8227(21)00422-8/fulltext)

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REFERENCES

1. Candido R, Musacchio N, Manicardi V, Nicolucci A, Rossi MC, Di Cianni G, Mannino D, Di Bartolo P. Valutazione degli indicatori AMD di qualità dell'assistenza al diabete di tipo 1 e 2 in Italia. *Annali AMD* 2020. https://aemmedi.it/wp-content/uploads/2020/10/Annali-nuova-versione-2020_1-ok.pdf
2. D'Amato C, Morganti R, Greco C, Di Gennaro F, Cacciotti L, Longo S, Mataluni G, Lauro D, Marfia GA, Spallone V. Diabetic peripheral neuropathic pain is a stronger predictor of depression than other diabetic complications and comorbidities. *Diab Vasc Dis Res*. 2016 Nov;13(6):418-428.
3. Jin HY, Moon SS, Calcutt NA. Lost in Translation? Measuring Diabetic Neuropathy in Humans and Animals. *Diabetes Metab J*. 2021 Jan;45(1):27-42.
4. Petropoulos IN, Ponirakis G, Ferdousi M, Azmi S, Kalteniece A, Khan A, Gad H, Bashir B, Marshall A, Boulton AJM, Soran H, Malik RA. Corneal Confocal Microscopy: A Biomarker for Diabetic Peripheral Neuropathy. *Clin Ther*. 2021 May 5;S0149-2918(21)00197-1.
5. Seferovic JP, Pfeiffer MA, Claggett B, Desai AS, de Zeeuw D, Haffner SM, McMurray JJV, Parving HH, Solomon SD, Chaturvedi N. Three-question set from Michigan Neuropathy Screening Instrument adds independent prognostic information on cardiovascular outcomes: analysis of ALTITUDE trial. *Diabetologia*. 2018 Mar;61(3):581-588.
6. Spallone V, Valensi P. SGLT2 inhibitors and the autonomic nervous system in diabetes: A promising challenge to better understand multiple target improvement. *Diabetes Metab*. 2021 Jul;47(4):101224.
7. Spallone V, Morganti R, D'Amato C, Greco C, Cacciotti L, Marfia GA. Validation of DN4 as a screening tool for neuropathic pain in painful diabetic polyneuropathy. *Diabet Med*. 2012 May;29(5):578-85.
8. Bouhassira D, Letanoux M, Hartemann A. Chronic pain with neuropathic characteristics in diabetic patients: a French cross-sectional study. *PLoS One*. 2013 Sep 13;8(9):e74195.
9. Meisinger C, Bongaerts BWC, Heier M, Amann U, Kowall B, Herder C, Rückert-Eheberg IM, Rathmann W, Ziegler D. Neuropathic pain is not adequately treated in the older general population: Results from the KORA F4 survey. *Pharmacoepidemiol Drug Saf*. 2018 Jul;27(7):806-814.
10. Happich M, Schneider E, Boess FG, Wilhelm S, Schacht A, Birklein F, Ziegler D. Effectiveness of duloxetine compared with pregabalin and gabapentin in diabetic peripheral neuropathic pain: results from a German observational study. *Clin J Pain*. 2014 Oct;30(10):875-85.
11. Margolis JM, Princic N, Smith DM, Abraham L, Cappelleri JC, Shah SN, Park PW. Economic Impact of Adherence to Pain Treatment Guidelines in Chronic Pain Patients. *Pain Med*. 2019 Oct 1;20(10):1907-1918.
12. Tesfaye S, Boulton AJ, Dyck PJ, Freeman R, Horowitz M, Kempler P, Lauria G, Malik RA, Spallone V, Vinik A, Bernardi L, Valensi P; Toronto Diabetic Neuropathy Expert Group. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. *Diabetes Care*. 2010 Oct;33(10):2285-93.
13. Pop-Busui R, Boulton AJ, Feldman EL, Bril V, Freeman R, Malik RA, Sosenko JM, Ziegler D. Diabetic Neuropathy: A Position Statement by the American Diabetes Association. *Diabetes Care*. 2017 Jan;40(1):136-154.