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ORIGINAL ARTICLE

Management of neuropathic pain: a survey of the Italian Association for the Study of Pain

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ABSTRACT

BACKGROUND: Neuropathic pain significantly impacts the quality of life. This study explores neuropathic pain management practices among members of the Italian Association for the Study of Pain (AISD).

METHODS: During the 46th National Congress, 240 physicians affiliated with AISD were surveyed. The data included demographics, clinical settings, diagnostic procedures, treatment approaches, and preferences. The analysis utilized descriptive statistics, treatment rankings, and consensus evaluations.

RESULTS: Respondents practicing in pain medicine reported the numbers of cases managed monthly. Neuropathic pain diagnoses relied on clinical findings corroborated by diagnostic tools. Treatment typically commenced within one to two weeks, emphasizing pharmacological interventions, which were often combined with invasive procedures. The leading pharmacological choices included gabapentinoids, tricyclic antidepressants, and serotonin-norepinephrine reuptake inhibitors. Varied rankings were noted for invasive procedures, with nerve and neuraxial blocks particularly favored. Nutraceuticals such as palmitoylethanolamide, alpha-lipoic acid, and vitamin B complex were commonly prescribed, reflecting differences based on the physician's age and specialty.

CONCLUSIONS: Generally, practices aligned with guidelines, showing a strong consensus on specific pharmacological treatments. Discrepancies in the rankings of invasive procedures, particularly among specialists, have led to questions regarding their perceived efficacy. These inconsistencies may indicate varying levels of expertise in interventional management, differences in the availability of these techniques, or different views on the current evidence supporting these procedures. The use of nutraceuticals indicated potential gaps in the guidelines.

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KEY WORDS: Neuralgia; Chronic pain; Surveys and questionnaires; Gabapentin; Antidepressive agents.

The International Association for the Study of Pain (IASP) taxonomy defines neuropathic pain as pain that arises as a direct consequence of a lesion or disease affecting the somatosensory system.[1] Neuropathic pain is a significant health issue in the general population because of its high prevalence (6.9-10%) and its impact on the quality of life.[2] A survey with around 3000 respondents found that patients with predominantly neuropathic chronic pain reported more severe pain, and even after correcting for pain intensity, age, and sex, they still scored considerably lower on health than the chronic pain group across all dimensions of the SF-36 general health questionnaire.[3]

Patients with neuropathic pain may experience inadequate pain relief from prescribed medications or need multiple adjustments to their treatment due to low efficacy or adverse reactions. In a nationwide observational study of primary care, including almost 26 thousand patients spanning over a decade (1992-2002), treatment was initiated at diagnosis for different neuropathic pain conditions, with percentages ranging from 45.5% to 65.8%.[4] Most initial prescriptions included one to four items, with antidepressants (30.1%), anticonvulsants (20.4%), and opioid analgesics (20.1%) being the most common choices.[4] A total of 951 different initial treatment regimens were identified across conditions. A minority of patients (29-49%) maintained stable treatment regimens for one year.[4]

No large-scale observational studies have been conducted on the actual clinical management of neuropathic pain in Italy. Therefore, we designed an exploratory survey among the members of the Italian Association for the Study of Pain (AISD), a multidisciplinary scientific society affiliated as the Italian Chapter to the European Pain Federation - EFIC and the International Association for the Study of Pain (IASP).

We aimed to investigate the current practice of pain diagnosis, treatment, and expectations regarding outcomes using a survey of AISD members participating at the National Congress.

Materials and methods

We designed an electronic survey form on a secure web-based electronic data capture system hosted and managed by Polistudium (Supplementary Digital Material 1: Supplementary Text File 1). The survey aimed to assess the relative frequency of patients affected by neuropathic pain managed by pain physicians and establish current clinical practices and preferences in diagnosing and managing neuropathic pain.

The first section described the respondents' demographic characteristics, current practice in pain medicine, educational background, and clinical setting. The second section investigated the diagnostic process of neuropathic pain in the respondents' clinical setting and the first steps after the provisional diagnosis. The third section investigated preferences, expressed as ordered rankings, attributed to different therapeutic measures divided into pharmacological and interventional or invasive procedures. The questions in this third section were structured to allow the assignment of only one rank to each treatment or group of similar therapies.

The invitation to the survey was disseminated *via* a mailing list to the members of the Italian Chapter of the International Association for the Study of Pain (Associazione Italiana per lo Studio del Dolore, AISD) registered to attend the 46th National Congress held in Bari, Italy (September 28-30, 2023). No personal data or any identifier for the respondents was collected.

Statistical analysis

Data were analyzed with descriptive statistics using mean and standard deviation or median and interquartile range (IQR), as appropriate, using R (4.3.1) and JASP (0.17.2.1).[5, 6] Pie and bar plots were generated with the Matplotlib package version 3.7.1 in Python 3.10.9 using the integrated development environment PyCharm 2023.1.3.[7] Treatment rankings were analyzed using a branch-and-bound algorithm to find the median ranking according to Kemeny's axiomatic approach, and consensus was measured with the item-weighted TauX rank correlation coefficient, as implemented in the R Package ConsRank version 2.1.3, using the integrated development environment Rstudio version 2023.06.0.[8, 9]

This alternative approach was chosen over Kendall's tau to address the challenges associated with ties and missing data.[10]

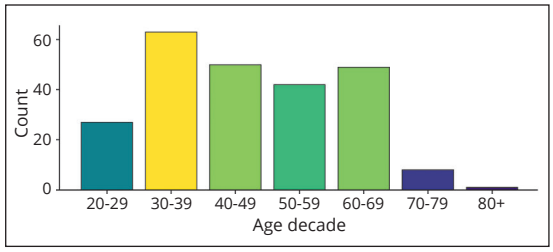

Figure 1.—Histogram representing the age distribution of the sample of respondents.

Results

Respondents

Two hundred and forty physicians completed the survey form, resulting in a 48% response rate. Gender representation was quite balanced (male 53%, female 45%, unreported 2%). The mean age was 46.7±13.7 years (Figure 1), with most respondents in Italy (southern Italy and islands, 47%; northern Italy, 31%; central Italy, 21%) and only two respondents working abroad.

The most reported specialties or subspecialties were anesthesiology-pain medicine (49.6%), anesthesiology and critical care medicine (11.7%), residency training in anesthesiology and critical care medicine (7.9%), physical medicine and rehabilitation (5.8%), and general practice (4.6%, Figure 2A). Most respondents reported receiving their training in anesthesiology, highlighting the position of pain medicine as a subspecialty within the field of anesthesiology in Italy.

Slightly more than half (55.4%) of respondents managed ≤20 chronic pain patients per month, while a fifth (22.5%) of participants treated ≥40 patients per month (Figure 2B).

Over 53% of our respondents reported managing neuropathic pain syndromes in more than 20% of their patients (Figure 2C). Most clinicians reported that central neuropathic pain syndromes affected only a small proportion of their patients.

The diagnostic process and first steps after diagnosis

Most respondents reported relying on history and clinical findings to classify neuropathic pain as follows: etiology (67.1%), distribution of pain (81.7%), and presence of positive and negative signs (55.8%). The use of radiological or neurophysiological examinations (37.9%), the painDETECT questionnaire (18.7%), the Neuropathic Pain Symptom Inventory (NPSI, 23.3%), and the Douleur Neuropathique en 4 Questions (DN4, 45.4%) were less frequently reported. Over a third of the participants (37.9%) viewed the lack of a satisfactory clinical response to common pain medications as a significant hint to the neuropathic pain diagnosis.

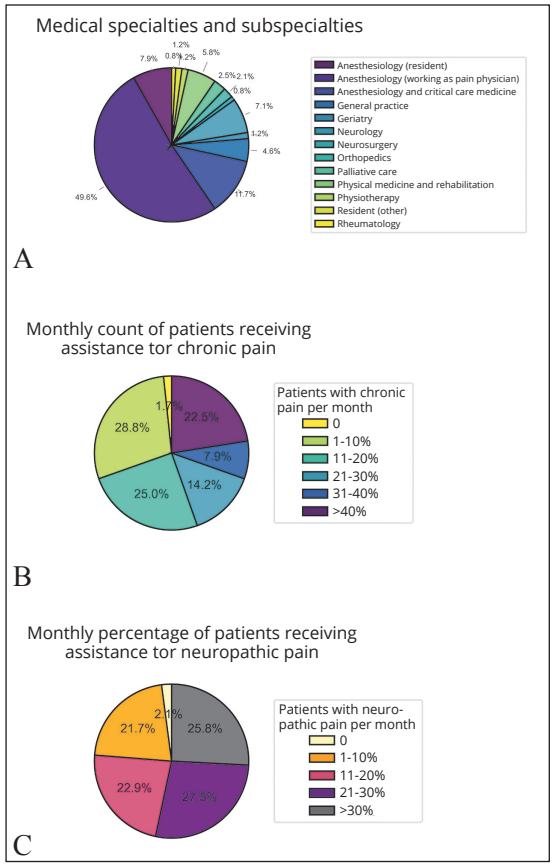

Figure 2.—A) The pie chart displays the distribution of survey respondents based on their medical specialty; B) the pie chart displays the volume of clinical activity in pain medicine, expressed as the number of chronic pain patients assisted per month; C) the pie chart shows the average proportion of patients with neuropathic pain in their clinical practice.

Therapeutic approaches

With a prevalence rate of 63.7%, most medical practitioners reported a rapid prescription of therapeutic intervention focused on managing neuropathic pain within one-week timeframe fol-

lowing the initial diagnosis. Eighty-nine percent of respondents prescribed therapy within two weeks.

Most respondents reported pharmacological treatment in more than 30% of cases (62.9%), whereas invasive treatments were less frequently reported (Table I).

Among the surveyed respondents, 44.4% indicated that they do not use invasive treatments to patients with neuropathic pain (Table I). On the other hand (34.6%) of the respondents reported using such treatments for a limited portion of their patients, specifically within the range of 1-10% (Table I).

Interestingly, a relatively smaller percentage (45.1%) reported using invasive treatments for a significant proportion of their patients, accounting for 20% or more (Table I).

Most respondents (97.9%) reported administering a combination or multimodal therapy, whereas few physicians reported prescribing or administering single treatments (Table I).

Drug therapy and combination therapy, including drugs and supplements, are the strategies most commonly adopted by physicians for managing more than half of the patients (Table I).

The prescription for physical therapy was more uniform among the different options (Table I). Psychotherapy was prescribed to up to 10% of patients by 53.3% of the respondents.

Most respondents (92%) reported prescribing dietary supplements and nutraceutical products. The most prescribed nutraceutical products were palmitoylethanolamide (71.7%), alpha-lipoic acid (64.2%), L-acetylcarnitine (61.7%), and vitamin B complex (59.2%), curcumin (28.3%).

Treatment ranking

Complete rankings were available for 239 participants. The median ranking for pharmacological treatments was gabapentinoids, tricyclic antidepressants, SNRI, weak opioids, lidocaine patch, paracetamol, strong opioids, NSAIDs, corticosteroids, capsaicin patch, and cannabinoids, with a moderate to strong degree of consensus (averaged TauX rank correlation coefficient 0.42, Table II).

Gabapentinoids emerged as the most favored option, receiving a total of 148 Rank 1 votes,

TABLE I.—*Overview of the clinical management strategies prescribed by our respondents to manage neuropathic pain.*

Treatment	Votes collected from respondents					
	0	1-10%	11-20%	20-30%	30-50%	>50%
Drug therapy	9	13	32	35	42	109
Invasive techniques	67	67	20	36	28	22
Drugs combined with invasive techniques	60	54	31	24	32	39
Physical therapy	26	39	48	53	27	47
Psychotherapy	60	68	37	35	21	19
Supplement only	69	61	39	27	20	24
Multimodal therapy with supplements	27	34	42	39	48	50

TABLE II.—*Distribution of votes among 11 pharmacological classes.*

Treatment	N. votes per rank										
	Rank 1	Rank 2	Rank 3	Rank 4	Rank 5	Rank 6	Rank 7	Rank 8	Rank 9	Rank 10	Rank 11
Gabapentinoids	148	29	21	21	10	1	2	2	1	2	2
Tricyclic antidepressants	14	68	34	25	20	14	21	15	13	8	7
SNRIs	10	34	49	30	21	26	16	20	13	11	9
Weak opioids	11	23	30	39	45	36	24	6	17	5	3
Strong opioids	5	14	15	17	33	28	30	34	19	19	25
Lidocaine patch	1	14	23	44	29	31	30	23	26	17	1
Capsaicin patch	1	3	5	9	16	19	25	37	33	44	47
Cannabinoids	5	1	5	2	9	12	28	39	35	37	66
NSAIDS	14	28	10	11	20	21	21	31	42	28	13
Paracetamol	24	15	21	21	22	19	24	19	17	38	19
Corticosteroids	6	10	26	20	14	32	18	13	23	30	47

NSAIDs: nonsteroidal anti-inflammatory drugs; SNRIs: serotonin epinephrine reuptake inhibitors.

indicating its designation as the top treatment choice among participants. Following closely, tricyclic antidepressants garnered 68 Rank 1 votes, reflecting significant regard within the treatment spectrum. When considering combined rankings for Rank 1, Rank 2, and Rank 3, gabapentinoids accumulated a total of 198 votes, while tricyclic antidepressants and SNRIs received 116 and 93 votes, respectively. In contrast, mid-ranked treatments, including weak opioids, strong opioids, lidocaine patches, and NSAIDs, exhibited a distribution of rankings across the middle tiers (Ranks 4-7), highlighting a range of opinions regarding their effectiveness. Similarly, paracetamol and corticosteroids demonstrated comparable patterns, frequently appearing in mid to lower rankings. Conversely, the least preferred treatments, such as the capsaicin patch, cannabinoids, and corticosteroids, garnered the highest counts in the lowest ranks (Ranks 9-11), with the capsaicin patch receiving 47 Rank 11 votes, thus reflecting its status as the least effective option according to participant evaluations. Cannabinoids and corticosteroids also featured prominently in the lowest rankings, suggesting their limited acceptance among respondents. Overall, while specific treatments like gabapentinoids and tricyclic antidepressants exhibited a strong preference at the higher ranks, others, particularly the capsaicin patch, cannabinoids, and corticosteroids, trended toward the lower tiers, with treatments like NSAIDs and paracetamol displaying more variability in perceived effectiveness.

The median ranking for invasive treatments was nerve blocks, neuraxial blocks, radiofrequency, sympathetic blocks, intrathecal drug delivery, spinal cord stimulation, peripheral nerve neurostimulation, and ozone therapy, with a moderate degree of consensus (TauX coefficient 0.35, Table III). The survey results indicate a clear preference hierarchy among various interventional treatments for pain management. Nerve blocks emerged as the most preferred option, garnering the highest total of Rank 1 votes (86) along with notable support in Ranks 2 (58) and 3 (25), which suggests a strong consensus on their effectiveness. Neuraxial blocks followed closely in preference, with significant representation in Rank 1 (45) and Rank 2 (59). In contrast, sympathetic blocks, while receiving a total of 73 votes across the top three ranks, demonstrated a more dispersed pattern of preference, indicating mixed opinions among respondents. Treatments such as spinal cord stimulation and peripheral neurostimulation were predominantly ranked lower, frequently appearing in Ranks 6 to 8, highlighting their less favorable status. Ozone therapy stood out as the least preferred treatment, with a marked majority of Rank 8 votes (107). Overall, the findings underscore that nerve blocks and neuraxial blocks are favored interventions, while the lower rankings for ozone therapy and certain neurostimulation techniques reflect less enthusiasm within the surveyed population.

Considering only rankings from self-reported pain physicians, both median rankings were confirmed with a higher consensus (TauX coefficients 0.48 and 0.43). The other specialists provided a slightly different ranking: gabapentinoids, tricyclic antidepressants, weak opioids, SNRIs, NSAIDs, paracetamol, corticosteroids, strong opioids, lidocaine patch, capsaicin patch, cannabinoids (TauX coefficient 0.37), and nerve blocks, neuraxial blocks, sympathetic blocks, intrathecal drug delivery, radiofrequency, pe-

TABLE III.—*Distribution of votes among the eight interventional therapies.*

Treatment	N. votes per rank							
	Rank 1	Rank 2	Rank 3	Rank 4	Rank 5	Rank 6	Rank 7	Rank 8
Nerve blocks	86	58	25	19	19	13	11	8
Neuraxial blocks	45	59	52	25	20	19	11	8
Sympathetic blocks	7	18	48	42	30	40	33	21
Intrathecal drug delivery	16	18	21	50	46	33	32	23
Radiofrequency	28	30	30	39	60	26	16	10
Spinal cord stimulation	3	13	19	20	32	65	50	37
Peripheral neurostimulation	15	18	26	28	22	32	73	25
Ozone therapy	39	25	18	16	10	11	13	107

ripheral neurostimulation, ozone therapy, and spinal cord stimulation (TauX coefficient 0.28). The other specialists penalized SNRIs and spinal cord stimulation and presented a higher degree of disagreement.

Respondents with the highest volume of patients per month, *i.e.*, >40 patients per month, when compared with the entire sample, favored lidocaine patch over weak opioids (ranks 4 and 5, respectively) and capsaicin over corticosteroids (ranks 9 and 10, respectively, TauX coefficient 0.46), while there was no difference in the median ranking of the invasive treatments (TauX coefficient 0.34).

Comparing the two groups of respondents according to age, younger or older than 50 years, minor differences emerged concerning the rankings of strong opioids (rank 7 *vs*. 8), NSAIDs (rank 8 *vs*. 9), and corticosteroids (rank 9 *vs*. 7). More significant differences were found in the invasive treatments' rankings: sympathetic blocks (rank 4 *vs*. 3), intrathecal drug delivery (rank 5 *vs*. 4), radiofrequency ranking (rank 3 *vs*. 5), SCS (rank 6 *vs*. 7), peripheral neurostimulation (rank 7 *vs*. 6).

Clinicians' impressions regarding the efficacy of neuropathic pain management

Few respondents reported improved pain and quality of life, which is estimated at more than 50% for their neuropathic pain patients (20% and 25.8%, respectively). Most respondents reported an improvement of 20-50% in their patients' pain (70.4%) and quality of life (65.8%, Figure 3).

Discussion

A survey of 240 physicians participating in the 46th National Congress of the Italian Association for the Study of Pain (AISD) yielded a 48% response rate, with a balanced gender representation. Most practitioners managed ≤20 chronic pain patients monthly (55.4%), and over half reported treating neuropathic pain syndromes in more than 20% of their patients. The majority relied on clinical history for diagnosis and prescribed therapies within one week for 63.7% of new cases. Most physicians perceived suboptimal (<50%) improvements in patient pain and quality of life following treatment, with gabapentinoids ranked as the most favored pharmacological option and nerve blocks as the most favored invasive treatment. Notably, 97.9% of physicians used multimodal therapies, and 92% reported prescribing dietary supplements, with palmitoylethanolamide being the most common at 71.7%.

In 2015, the Neuropathic Pain IASP Special Interest Group (NeuPSIG) published a systematic review on pharmacologic therapy for neuropathic pain. Tricyclic antidepressants, duloxetine and venlafaxine, pregabalin, and gabapentin showed the best efficacy for a 50% decrease in pain intensity.[11] According to the 2018 Japanese Society of Pain Clinicians guidelines, pregabalin or gabapentin, TCAs, and SNRIs are the first line of treatment.[12] The 2020 French recommendations included SNRIs, gabapentin, and TCAs as first-line treatments, while pregabalin and tramadol were reported as second-line treatments.[13]

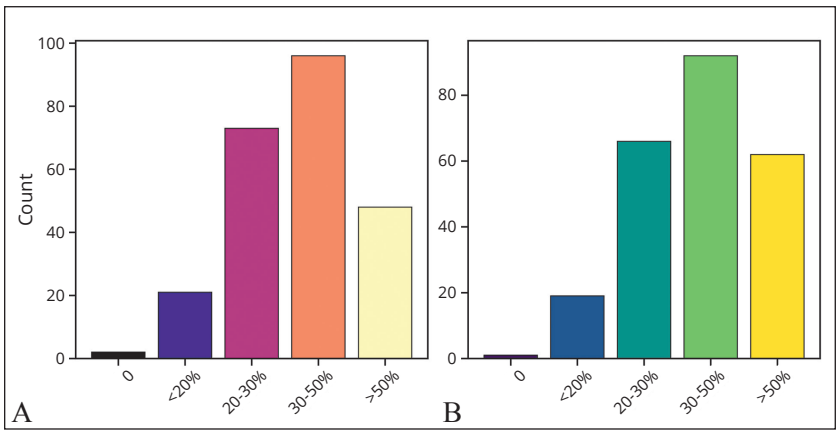

Figure 3.—A) The bar plot illustrates physicians' perceptions of pain intensity improvement due to therapeutic care expressed as a percentage change from the baseline; B) the bar graph illustrates physicians' perceptions of an improvement in the quality of life expressed as a percentage change from the baseline due to their clinical management.

The participants in our survey identified gabapentinoids, TCAs, and SNRIs as the three most preferred treatment options.

These findings indicate that guidelines on pharmacologic management are actively applied in the practice of pain medicine in Italy.

The 2013 NeuPSIG recommendations support epidural injections for herpes zoster, steroid injections for radiculopathy, spinal cord stimulation for failed back surgery syndrome, and complex regional pain syndrome type 1. However, they advise against sympathetic blocks for postherpetic neuralgia and radiofrequency lesions for radiculopathy.[14] In our sample, the highest rankings were attributed to nerve blocks, neuraxial blocks, radiofrequency modulation, lesions, and sympathetic blocks. These findings were confirmed in the subset of pain physicians and are in contrast with the current guidelines.[14]

Furthermore, most specialists prescribe nutraceuticals. This choice may arise from clinicians' view of the low effectiveness of recommended pharmacological therapies or from patients' requests for a more "natural" approach to chronic pain that does not adequately respond to established therapies.[15] Our results show that 80% of practicing physicians reported a pain reduction of ≤50%, and 74% reported a quality-of-life improvement of ≤50%.

The lack of solid evidence, the complexity of neuropathic pain, and significant knowledge gaps may make applying these guidelines difficult, or the results of our management disappointing.[13]

Combination therapies, the effect of nutraceuticals, and the effect of treatments on quality of life are considerable gaps in our knowledge that can leave the practicing clinician without proper guidance in the management of actual patients.[16-18]

The specialist training for pain physicians in Italy lacks a dedicated residency program. Anesthesiology residencies allocate varying portions of the curriculum to chronic pain. In 2020, the Italian Republic established a Palliative Medicine residency program, with a core curriculum overlapping some fields of pain medicine.[19] This contrasts with Anglo-Saxon Countries, where aspiring consultants in chronic pain undergo a mandatory subspecialty or fellowship training.[20]

Violini *et al.* discussed the urgent need for a profound reform of chronic pain training curricula in a recent opinion paper.[21] Pain management specialists should undergo structured training courses designed in agreement with the international standards set by international scientific organizations such as the IASP and the European Federation of IASP Chapters (EFIC).[21]

Our study is the first to investigate the perspectives of Italian pain physicians on neuropathic pain management, with only a French survey focusing on a similar topic. This previous work reports the results of an electronic survey of 319 general practitioners (GPs) evaluating adherence to the 2010 French Pain Society guidelines for neuropathic pain management.[22] This study, which used direct questions and clinical vignettes, showed that half of the GPs were aware of the guidelines, more than 40% declared to follow them, and 34% used a standardized neuropathic pain questionnaire (DN4).[22]

Recognition of neuropathic pain was excellent for diabetic neuropathy or cancer, but postoperative neuropathic pain was often mistaken for persistent nociceptive pain.[22] When the physicians recognized neuropathic pain correctly, the likelihood of prescribing an appropriate first-line treatment was around 90%.[22]

Limitations of the study

The limitations of our study pertain to the general definition of neuropathic pain in our questionnaire. Neuropathic pain syndromes may share pathophysiological mechanisms; however, within the same diagnostic category, manifestations can vary among individuals due to the prevalence of specific mechanisms.[23]

Another possible limitation could be related to the sampling of our respondents. The response rate was below 50%. Additionally, this survey took place during the 46th AISD National Congress, attracting respondents who likely have a strong interest in pain medicine, possibly reflecting their primary clinical focus. Therefore, our results cannot be generalized to a broader population, including different cultures and clinical settings. The French survey was conducted on a more homogenous sample of physicians in the

general practice setting and assessed clinical management using case vignettes.[22] This methodology may better reflect actual practice than simple multiple-choice questions, but it did not explore the use of nonpharmacological or complementary treatments. However, since AISD is the main scientific society in pain medicine in Italy, our results could represent neuropathic pain management practices by specialists in our country setting.

Conclusions

Our results provide a snapshot of medical practice patterns regarding neuropathic pain in Italy and highlight significant gaps in knowledge, especially concerning supplements and nutraceuticals, which are commonly prescribed therapies. The survey showed that responding physicians referred to the NeuPSIG recommendations for diagnosis and pharmacologic treatment in their clinical practice.[14, 24]

Discrepancies in the rankings of invasive procedures, particularly among specialists, have led to questions regarding their perceived efficacy. These inconsistencies may indicate varying levels of expertise in interventional management, differences in the availability of these techniques, or different views on the current evidence supporting these procedures.[14]

It could be helpful to undertake studies that analyze the reasons that lead pain physicians to extensively use nutraceuticals in neuropathic pain because there is still no robust evidence of their effectiveness in this type of pain.

What is known

• Patients with neuropathic pain experience a significant reduction in their quality of life, and healthcare providers often face challenges in treating it.

What is new

• A survey conducted by the Italian Chapter of the International Association for the Study of Pain, involving two hundred forty physicians, revealed that their pharmacological management aligns with current international guidelines.

• Patients' perceived improvement in pain intensity and quality of life often remains unsatisfactory.

• This frequently results in the prescription of nutraceuticals, often lacking robust supporting evidence.

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Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions
All authors read and approved the final version of the manuscript.

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