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Review Article

Most Relevant Neuropathic Pain Treatment and Chronic Low Back Pain Management Guidelines: A Change Pain Latin America Advisory Panel Consensus

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Abstract

Objective. Chronic pain conditions profoundly affect the daily living of a significant number of people and are a major economic and social burden, particularly in developing countries. The Change Pain Latin America (CPLA) advisory panel aimed to identify the most appropriate guidelines for the treatment of neuropathic pain (NP) and chronic low back pain (CLBP) for use across Latin America.

Methods. Published systematic reviews or practice guidelines were identified by a systematic search of PubMed, the Guidelines Clearinghouse, and

Google. Articles were screened by an independent reviewer, and potential candidate guidelines were selected for more in-depth review. A shortlist of suitable guidelines was selected and critically evaluated by the CPLA advisory panel.

Results. Searches identified 674 and 604 guideline articles for NP and CLBP, respectively. Of these, 14 guidelines were shortlisted for consensus consideration, with the following final selections made:

- **"Recommendations for the pharmacological management of neuropathic pain from the Neuropathic Pain Special Interest Group in 2015—pharmacotherapy for neuropathic pain in adults: A systematic review and meta-analysis."**
- **"Diagnosis and treatment of low back pain: A joint clinical practice guideline from the American College of Physicians and the American Pain Society" (2007).**

Conclusions. The selected guidelines were endorsed by all members of the CPLA advisory board as the best fit for use across Latin America. In addition, regional considerations were discussed and recorded. We have included this expert local insight and advice to enhance the implementation of each guideline across all Latin American countries.

Key Words. Change Pain Latin America (CPLA); Neuropathic Pain; Chronic Low Back Pain; Latin America; Consensus Guidelines; Best Practice

Introduction

Chronic pain conditions affect a significant number of people, have a profound negative impact on quality of life (QoL), and markedly impair daily function. Globally, the direct and indirect economic cost of chronic pain is estimated to equal that of cancer and cardiovascular disease, and the social burden is particularly great in developing countries [1].

In Latin America, chronic pain is often undiagnosed and may be treated inappropriately or inadequately because of a wide range of barriers to best practice, such as limited access to medications and pain specialists in some countries [2]. In addition, there are gaps in the understanding of many pain conditions and widespread misconceptions regarding treatment [2]; therefore, there is a need for improved education and adoption of uniform management guidelines.

Neuropathic pain (NP) and chronic low back pain (CLBP) are two of the most common types of chronic pain, and there is a clear requirement for these conditions to be better managed across Latin America.

NP is defined as "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system" [3]. NP is characterized by abnormal somatosensory processing that occurs in the normal nociceptive system after injury [3] and can arise from a wide range of disorders, including painful diabetic neuropathy, postherpetic neuralgia, and trigeminal neuralgia [4].

In a Brazilian epidemiological study, the prevalence of chronic pain with neuropathic characteristics was 10% in the study population [5]. According to the Latin American Federation of Associations for the Study of Pain, the most frequent cause of NP in Latin America was lumbago with a neuropathic component (34% of patients) [6].

Due to the complexity of diagnosing and managing NP and its low prioritization in Latin American health care systems, it is associated with significant direct medical costs and a high overall economic and societal burden [7]. Of note, individuals reporting chronic pain with NP symptoms reported a higher prevalence of moderate or high pain intensity, disability resulting from pain, and depression than those with chronic pain without NP symptoms [5].

CLBP is defined as pain that has persisted for more than three months and is localized below the lower edge of the last rib and above the lower gluteal folds, with or without a neuropathic component [8]. CLBP is generally multifactorial, often including a neuropathic component [9], and is frequently under-recognized and undertreated [10,11]. Where there is neuropathic involvement, CLBP is associated with severe symptoms [11], comorbidities, and poor QoL.

Globally, CLBP causes more disability than any other condition [12] and is estimated to lead to direct and indirect costs of approximately 1.7% of the gross national product of a developed country [13]. In Latin America, the prevalence of CLBP has been estimated at 11% [8], accounting for 10% to 15% of all disability claims in Mexico [14], while CLBP is the third most common cause of employment-associated disability in Argentina [15]. In Brazil, back pain is the most common cause of permanent, pensionable disability, accounting for 97% of working days lost due to disability [16].

Change Pain Latin American (CPLA) is a new initiative committed to enhancing the QoL of chronic pain patients (Table 1) [2]. It was launched in response to a similar educational campaign that has improved chronic pain management throughout Europe.

Although many chronic pain management guidelines have been published, none completely satisfies the specific requirements of Latin America. Therefore, we set out to identify the most appropriate guidelines for NP and CLBP that are applicable to the Latin American region. This article summarizes the group's consensus and aims to provide a platform for the implementation and adoption of uniform management guidelines by

Table 1 Objectives of the Change Pain Latin America advisory panel [2]

- Identify factors influencing pain treatment and decision-makers across Latin America
- Understand factors/reasons behind the current pain treatment paradigm
- Identify levers that can be used to modify the situation
- Establish links between practice and theory in the management of chronic pain
- Establish real unmet needs in chronic pain treatment in Latin America
- Better understand the reality of chronic pain patients today
- Find consensus on managing chronic pain from a physician's perspective
- Evaluate the need to educate; raise awareness of best practice
- Assess the need to enhance communication between physicians and patients to improve the management of pain
- Develop solutions based on research data and experts' opinions, supporting more effective and efficient pain management
- Educate health care practitioners and patients about safe and responsible opioid therapy for chronic pain

health care practitioners across the Latin American region.

Methods

The CPLA advisory panel comprises 17 Latin American experts from Brazil, Chile, Colombia, Costa Rica, Ecuador, Mexico, Peru, Venezuela, and Spain who specialize in pain management across a range of clinical fields [2]. The panel convened at four meetings to discuss the need for a uniform set of management guidelines and to develop the methodology used to identify the guidelines most appropriate for the region.

Search Strategy

A systematic search for published guidelines was conducted using defined search terms (Table 2). For systematic reviews or practice guidelines, the PubMed search engine was employed using English and Spanish search terms. For evidence-based clinical practice guidelines, the National Guideline Clearinghouse database was searched, and additional searches were performed using the Google search engine in order to identify additional guidelines that were not indexed by other sources.

Preliminary Analysis

Extracted articles were screened by an independent reviewer according to a set of previously agreed-upon preliminary analysis criteria (Table 3). Guidelines considered to be potential candidates for adoption were identified based on this initial evaluation.

Guidelines were considered to be evidence based if their recommendations were based on published clinical trial data, as opposed to treatment recommendations based on physicians' experience or opinion. A source was considered to be well recognized if it was published in a peer-reviewed journal or on the website of a recognized physician association.

The reviewer's opinion on the applicability of guidelines was based on their clinical experience in pain management in Latin America and a range of objective factors, including whether a guideline recommended unavailable, infeasible, or costly treatments, therapies requiring resource-intensive administration or monitoring, or interventions requiring specialist skills.

Secondary Analysis

Candidate guidelines selected for further investigation during the initial screening were analyzed in depth, and a shortlist of guidelines suitable for consideration was selected based on a set of key selection criteria (Table 3).

Tertiary Analysis

As a final step in the selection process, shortlisted guidelines for NP and CLBP were assessed by the expert panel for relevance, validity, and practicality. The guidelines that best met these criteria were then presented at the CPLA advisory panel meeting, where each was considered at length in the context of current practice in Latin America.

Consensus Agreement

The CPLA advisory panel employed a process of consensus discussion and agreement in order to reach single guideline recommendations for NP and CLBP. At this meeting, all panelists formally ratified the recommendations, and each panelist was invited to add additional consideration points relevant to their country.

Results

The initial PubMed search identified 674 systematic reviews or practice guidelines for NP and 604 systematic reviews or practice guidelines for CLBP. Following the initial screening, 28 guidelines (18 NP, 10 CLBP) were selected as candidates for in-depth review by the CPLA expert panel.

Table 2 Search terms for identification of existing NP and CLBP guidelines

NP	Search Terms
PubMed English	MeSH terms: ("neuralgia"[MeSH Terms] OR "neuralgia"[All Fields] OR ("neuropathic"[All Fields] AND "pain"[All Fields]) OR "neuropathic pain"[All Fields]) AND ((Practice Guideline[ptyp] OR systematic[sb]) AND "2004/11/06"[PDat]: "2014/11/03"[PDat])
PubMed Spanish	MeSH terms: (("pain"[MeSH Terms] OR "pain"[All Fields] OR "dolor"[All Fields]) AND neuropathic[All Fields]) AND ((systematic[sb] OR Practice Guideline[ptyp]) AND "2004/11/07"[PDat]: "2014/11/04"[PDat] AND "humans"[MeSH Terms] AND Spanish[lang])
National Guidelines Clearing House	Neuropathic pain
Google	Neuropathic pain, guidelines OR review
CLBP	
PubMed English	MeSH terms: (chronic[All Fields] AND ("low back pain"[MeSH Terms] OR ("low"[All Fields] AND "back"[All Fields] AND "pain"[All Fields]) OR "low back pain"[All Fields])) AND ((Practice Guideline[ptyp] OR systematic[sb]) AND "2004/11/06"[PDat]: "2014/11/03"[PDat])
PubMed Spanish	MeSH terms: (("pain"[MeSH Terms] OR "pain"[All Fields] OR "dolor"[All Fields]) AND ("lumbosacral region"[MeSH Terms] OR ("lumbosacral"[All Fields] AND "region"[All Fields]) OR "lumbosacral region"[All Fields] OR "lumbar"[All Fields]) AND cronico[All Fields]) AND ((systematic[sb] OR Practice Guideline[ptyp]) AND "2004/11/07"[PDat]: "2014/11/04"[PDat] AND "humans"[MeSH Terms] AND Spanish[lang])
National Guidelines Clearing House	Chronic low back pain
Google	Chronic low back pain, guidelines OR review

CLBP = chronic low back pain; MeSH = medical subheading; NP = neuropathic pain.

Table 3 Key criteria for selection of guidelines

Preliminary Screening Criteria of Search Outputs	
Evidence based	
Comprehensive	
Derived from well-recognized source	
Current	
Based on best practice	
Applicable to Latin America	
Secondary Analysis of Candidate Guidelines for NP and CLBP	
Focused on CLBP	Focused on NP
Differentiates acute and CLBP	Provides accurate definition of NP and nociceptive painConsiders non-malignant NP
Adequate details of diagnostic methods relevant to Latin America	
Includes recommended treatments available in/relevant to Latin America	
Valid, clinically flexible, practical	
Easily implemented in Latin America	
Accessible by and relevant to primary care physicians	

CLBP = chronic low back pain; NP = neuropathic pain.

The candidate guidelines were narrowed down to a shortlist of eight NP and six CLBP management guidelines for further appraisal and consensus consideration (Table 4).

At the end of the final stage of discussion and debate, a single management guideline recommendation was identified for each condition, with seven of the shortlisted NP guidelines and five of the shortlisted CLBP guidelines considered to be unsuitable for adoption in the Latin American region (Supplementary Table S1).

By consensus agreement, we endorsed the following guidelines as the best fit for use across Latin America:

- "Recommendations for the pharmacological management of neuropathic pain: An overview and literature update: International Association for the Study of Pain Neuropathic Pain Special Interest Group (IASP NeuPSIG) 2010 guidelines" [19]. The 2015 revision of these recommendations, based on a recent systematic review and meta-analysis of NP pharmacotherapy, supersedes the original guidance and has been reviewed and endorsed by the CPLA panel members as the most up-to-date, appropriate guidance for implementation across Latin America [26].
- "Diagnosis and treatment of low back pain: A joint clinical practice guideline from the American College of Physicians (ACP) and the American Pain Society (APS)" (2007) [22].

Table 4 Guidelines for final analysis and CPLA advisory panel consensus

Author	Title	Published	Region
National Institute for Health and Clinical Excellence	Neuropathic pain: The pharmacological management of neuropathic pain in adults in non-specialist settings [4]	2010	England and Wales
Latin American Federation of Associations for the Study of Pain	Guidelines for the diagnosis and management of neuropathic pain: Consensus of a group of Latin American experts [6]	2009	Latin America
Guevara-Lopez et al.	Practice guidelines for neuropathic pain management [17]	2006	Mexico
Association Venezuela for the Study of Pain	Clinical practice guide for patients with neuropathic pain [18]	2012	Venezuela
International Association for the Study of Pain	Recommendations for the pharmacological management of neuropathic pain: An overview and literature update [19]	2010	International
British Society for Rheumatology and International Association for the Study of Pain	Guidelines for the integrated management of musculoskeletal pain symptoms [20]	2008	UK
Institute for Clinical Systems Improvement	Assessment and management of chronic pain [21]	2011	USA
American College of Physicians and the American Pain Society	Diagnosis and treatment of low back pain [22]	2007	USA
European Cooperation in Science and Technology	Management of chronic non-specific low back pain [23]	2005	Europe
National Institute for Health and Clinical Excellence	Low back pain: Early management of persistent non-specific low back pain [24]	2009	England and Wales
Guevara-Lopez et al.	Practice guidelines for the management of low back pain [25]	2011	Mexico

Although these guidelines were deemed the most appropriate, we felt it was important to make practitioners aware of regional issues that may need consideration. Therefore, we present additional advice that was collated as part of the consensus process to optimize guideline implementation (Tables 5 and 6). To highlight where regional issues are applicable, we have linked this information to the algorithms derived for each guideline (Figures 1 and 2).

It is beyond the scope of this article to discuss the content of each of these guidelines in detail.

Discussion

We reviewed all shortlisted guidelines at length. Reasons for or against final selection were based on the overriding consideration of finding the most appropriate and applicable guidelines from a Latin American perspective.

Our consensus recommendations for NP were the IASP (NeuPSIG) 2015 recommendations [26]; for CLBP, our recommendation was "Diagnosis and treatment of low back pain: A joint clinical practice guideline from the American College of Physicians (ACP) and the American Pain Society (APS)" (2007) [22].

The IASP (NeuPSIG) 2015 guidelines were considered the most relevant and practical NP guidelines as they are supported by excellent evidence-based sources and these recommendations have been included in other respected guidelines. Importantly, the IASP (NeuPSIG) recommendations are clear and concise, and therefore easy for primary care practitioners to adapt and adopt. The guidance on when to refer patients to specialists and the stepwise approach to therapy initiation, change of therapy, and therapy combination (Figure 1) is considered to be achievable in Latin America. Most of the therapies included in the guidelines are available in at least some Latin American countries, and the document incorporates some guidance on the rational use of analgesic combinations in the management of NP.

The ACP/ACS guidelines were selected because they are practical, evidence based, and include transparent inclusion and exclusion criteria. Although published in 2007, the consensus group agreed that the guidelines remained relevant in light of current treatment practices. The guidelines are concise and unambiguous and include seven key recommendations for the diagnosis

Table 5 CPLA panel observations, considerations, and regional issues regarding the implementation of the IASP (NeuPSIG) 2015 recommendations [26]

A. Some recommendations do not include diagnostic criteria
B. Not all recommended treatments are available in Latin America—in Chile, all drugs mentioned in the guidelines are available; in Peru, amitriptyline is available but desipramine is not; in Colombia, nortriptyline and desipramine are not available
C. As pharmacological treatments for NP are often prescribed long-term, physicians must balance pain relief against the risk of side effects
D. It is important to be aware of the cardiotoxicity of tricyclic antidepressant drugs when considering their use (e.g., nortriptyline [a standard treatment due to its low cost and relative efficacy], desipramine, and amitriptyline) [26,27], and they should not be used in patients age > 65 years with heart conduction disturbances or urinary retention
E. Tricyclic drugs are effective when prescribed at low doses and side effects are taken into account
F. Health care practitioners should consider use of analgesic combinations earlier to minimize the risk of side effects and manage NP more effectively
G. The guidelines do not focus in-depth on nonpharmacological management or management approaches using combination therapies
H. Pharmacological therapy may not always be sufficient, and interventional techniques should be considered for some patients
I. For practical use in Latin America, nonpharmacological multidisciplinary programs should be included
J. It was perceived that regional general practitioners may have become "desensitized" to prescribing treatments for NP and therefore tend to refer to a specialist rather than increase treatment intensity; education and policy change may be required to reverse this trend
K. Differences in health care systems and health care practitioners' access to treatments vary between Latin American countries and are partly determined by each country's economy
L. Guideline advice is particularly important in countries like Costa Rica, where there are no specialist pain clinics for noncancer pain management
M. The importance of ideal weight, exercising to strengthen the low back area, and reducing inactivity to help alleviate CLBP should be emphasized [28]

CLBP = chronic low back pain; NP = neuropathic pain.
A–N Latin American considerations linked to algorithm in Figure 1.

and treatment of CLBP. They are also sufficiently didactic, including treatment pathways for the initial evaluation and management of patients (Figure 2). We concluded

Table 6 CPLA panel observations, considerations, and regional issues regarding the implementation of ACP/APS 2007 guidelines [22]

A. The initial approach following a primary assessment may differ from those recommended in some Latin American countries
B. Evidence to guide optimal imaging strategies is not available for low back pain that persists for more than 1–2 months if there are no symptoms suggesting radiculopathy or spinal stenosis; plain radiography may be a reasonable initial option in these circumstances [29,30]
C. Imaging studies should only be performed if the patient has persistent low back pain or presents with signs of neurogenic claudication or radiculopathy [30]
D. Patients who are candidates for surgery or epidural steroids, i.e., with radiculopathy, should first undergo MRI (or, if MRI is not available or unsuitable, computed tomography) before making any treatment decisions [29]
E. The CPLA panel recommended that patients with red-flag symptoms should immediately be referred to a specialist [31]
F. Patients with subacute pain who demonstrate yellow-flag symptoms are at particular risk of developing CLBP and should be referred to a multidisciplinary treatment group to prevent them from progressing to chronic pain [31]
G. As yellow-flag cases may not be adequately defined in the guidelines, a range of affective, behavioral, belief-based, social, and occupational factors is proposed to help define/identify such cases in Latin America (Supplementary Figure S1) [32]
H. Primary care physicians can identify yellow-flag cases by reviewing the medical history and asking simple questions, including [33]:
   - Do you think you can recover from your lower back pain?
   - What activities do you avoid and why?
   - How has your mood been since you have had your lower back pain?
   - How is your relationship with your family and work colleagues/coworkers?
   - Which treatment do you think is the best?
   - What concerns you about your work?
   - When do you think you will return to work?
   - What do you think is the reason you have not improved?
I. The guideline recommendations for alternative therapies are not always responsibly regulated, and adequate training may not be available in some Latin American countries. For example, acupuncture and chiropractic therapy are not regulated in Colombia but are regulated in other countries; vocational spinal manipulation training is not available in most Latin

(continued)

American countries, and only a handful of health care practitioners are trained in these procedures in Colombia and Mexico

J. The guidelines do not include opioid analgesics, e.g., buprenorphine, or those recently approved by the FDA, e.g., dual μ-opioid agonist/norepinephrine reuptake inhibitor, tapentadol, and lidocaine 5% transdermal patch for low back pain with neuropathic pain in a defined area

K. The successful use of opioid therapy has been well demonstrated over the years, with weak opioids like tramadol and strong opioids like buprenorphine and tapentadol proven to be effective in the treatment of CLBP [34,35]

L. In Peru, the use of weak opioids in CLBP management has increased, and primary care practitioners need to make a careful risk assessment before initiating opioid therapy

M. The guidelines do not include some pharmacologic options available in certain countries, e.g., metamizol and gabapentin (particularly in cases of radiculopathy) [36]

N. The guidelines also omitted pregabalin and the antidepressants amitriptyline, imipramine, and duloxetine

O. Tricyclic antidepressants widely available in Europe and North America (e.g., nortriptyline and desipramine) may not be available across all Latin America and should be used with caution due to side effects, particularly cardiotoxicity [27]

P. Some treatments are prescribed in certain countries despite an absence of supporting trial-based evidence; e.g., in Colombia patients may receive steroids for radiculopathy [37]

Q. An interdisciplinary approach to CLBP management involving a neuropathic component is important, and there is a need to provide guidance on the use of simple tools to diagnose NP in subjects with CLBP

R. There are no specific interdisciplinary back rehabilitation centers and no regulated specialist back pain treatment centers in some Latin American countries (e.g., Colombia)

FDA = US Food and Drink Association; CLBP = chronic low back pain; CPLA = Change Pain Latin America; NP = neuropathic pain.
A–R Latin American considerations linked to algorithm in Figure 2.

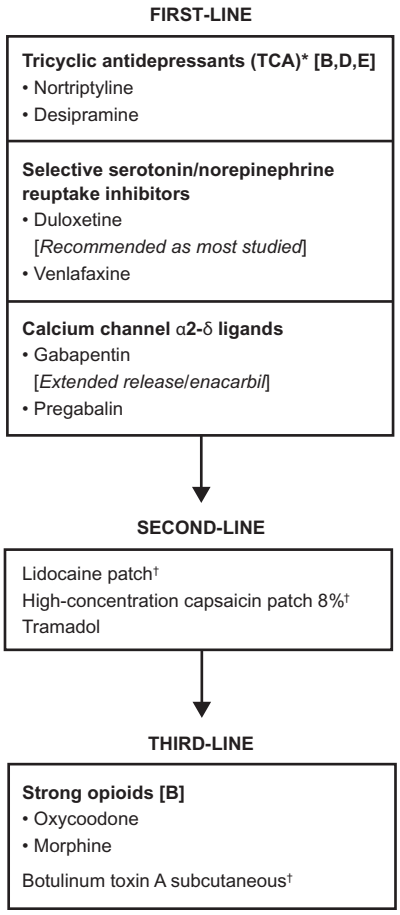

Figure 1 NP algorithm based on IASP (NeuPSIG) recommendations [22]. Consider combination therapy with TCA + calcium channel $\alpha 2$-δ ligand as an alternative to increased monotherapy dose in firstline therapy nonresponders. [B,D,E] refer to Latin America–specific considerations in Table 5. *Tertiary amine TCAs amitryptyline, imipramine, and clomipramine should be used with caution in patients older than age 65 years or with existing cardiovascular disease. †Recommended for peripheral neuropathic pain only. TCA = tricyclic antidepressant.

that the ACP/APS guidelines would be useful for primary care practitioners as they place sufficient emphasis on undertaking a thorough initial physical examination before performing imaging or other tests or starting treatment, thus avoiding unnecessary risks.

During our discussions, we identified a number of specific caveats and regional issues that should be considered when implementing these guidelines (Tables 5 and 6). These issues include significant variation in access to drug therapies—some regions have access to a limited range of drugs, some of which may be associated with unfavorable side effect profiles or other characteristics that may impact long-term use [38,26,27]. Other limitations can include a lack of specialist clinics, poor prescribing practices, and risk aversion by primary care practitioners.

Regional issues specific to CLBP include the need for initial assessment, imaging studies, and differential diagnosis. We also stress the need for immediate specialist referral for any patient exhibiting red-flag symptoms, and we have included practical guidance on the diagnosis for yellow-flag symptoms that may progress to chronic pain (Table 6; Supplementary Figure S1).

It should also be noted that the CLBP guidelines do not include guidance on opioid analgesics; thus, we

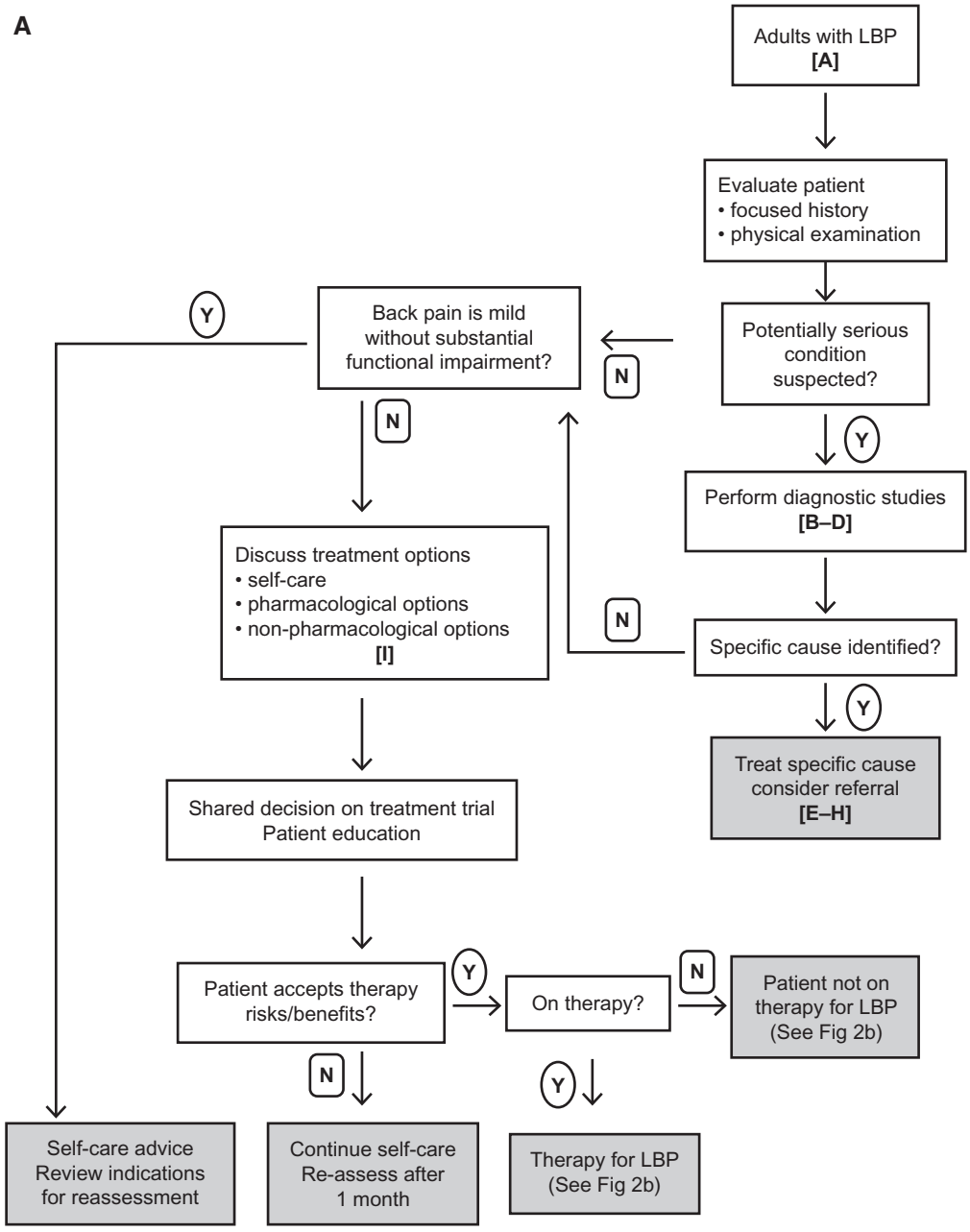

Figure 2 The ACP/APS guidelines' **(A)** initial evaluation of lumbar pain and **(B)** management of lumbar pain [26]. [A–R] refer to Latin America–specific considerations in Table 6. LBP = low back pain.

have included information on their use here based on our experience [39], US Food and Drug Administration recommendations, and regional trends. In addition, we draw attention to the use of treatments that lack consistent supporting evidence, such as steroids [40]; similarly, there is also wide variation in the availability of alternative therapies and considerable diversity in the level of regulation of practitioners and access to adequate training schemes across the region [41].

Because of these issues, there is a need for education and policy change to gain maximal benefit from the selected guideline recommendations, although we note that putting all of the recommendations into practice may be subject to the financial constraints of each local economy.

As an important first step, the guidelines must be made accessible and effectively disseminated to physicians in order to improve clinical practice. To do so, the IASP

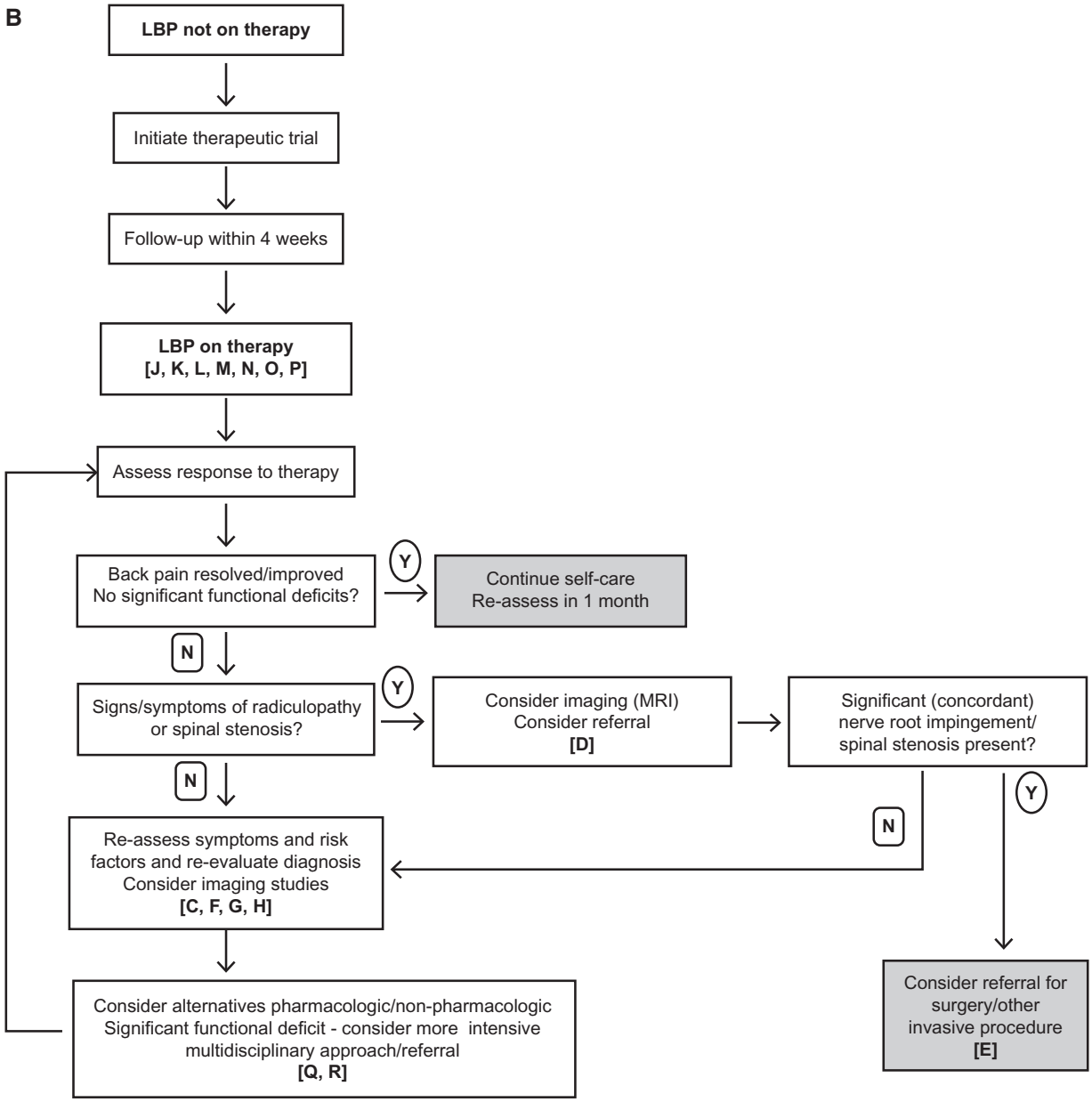

Figure 2 (continued)

(NeuPSIG) 2015 guidelines for NP and the ACP/APS 2007 guidelines for CLBP guidelines, as well as this consensus recommendation, will be translated into Spanish and Portuguese so they can be used by doctors throughout Latin America. Furthermore, CPLA plans to distribute the guidelines through multiple channels, including the CPLA online portal, which provides a repository of publications and educational materials relevant to the management of chronic pain, as well as through professional societies and centers of excellence. In addition, CPLA members and their colleagues will play a key role in fostering the uptake of these recommendations by health care professionals. Finally, CPLA also plans to collaborate with its sponsors to develop and implement a range of educational initiatives, such as preceptorships and workshops, in order to educate health care professionals on the importance of best practice treatment of chronic pain.

In summary, we recommend the implementation of the IASP (NeuPSIG) 2015 guidelines [26] for NP and the ACP/APS 2007 guidelines [22] for CLBP as these are considered the most relevant for Latin America and advise that attention is paid to the local factors that may

influence successful implementation of each guideline. We further propose that the current consensus guidelines should be translated into Spanish and Portuguese for ease of access.

Through practical strategies, such as the implementation of universal guidelines, it should be possible to overcome region-specific barriers to best practice and achieve the goal of effective management of patients with chronic pain.

Authors' Contributions

The authors were all involved in the design, methodology, analyses, interpretation, and achievement of the final guidelines consensus. Each author reviewed and contributed to the interpretation and regional perspectives contained in the manuscript.

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Supplementary Data

Supplementary Data may be found online at http://painmedicine.oxfordjournals.org.

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