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OXFORD

OPIOIDS, SUBSTANCE ABUSE & ADDICTIONS SECTION

Review Article

Use of Opioids in Latin America: The Need of an Evidence-Based Change

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Abstract

Objective. The subject of this publication has been focused on local considerations for facilitating regional best practice, including identifying and uniformly adopting the most relevant international guidelines on opioid use (OU) in chronic pain management.

Design and Setting. The *Change Pain Latin America* (CPLA) Advisory Panel conducted a comprehensive, robust, and critical analysis of published national and international reviews and guidelines of OU, considering those most appropriate for Latin America.

Methods. A PubMed search was conducted using the terms "opioid," "chronic," and "pain" and then refined using the filters "practice guidelines" and "within the last 5 years" (2007–2012). Once the publications were identified, they were selected using five key criteria: "Evidence based," "Comprehensive," "From a well-recognized source," "Current publications," and "Based on best practice" and then critically analyzed considering 10 key criteria for determining the most relevant guidelines to be applied in Latin America.

Results. The initial PubMed search identified 177 reviews and guidelines, which was reduced to 16 articles using the five preliminary criteria. After a secondary analysis according to the 10 key criteria specific to OU in Latin America, 10 publications were selected for critical review and discussion.

Conclusions. The CPLA advisory panel considered the "Safe and effective use of opioids for chronic non-cancer pain" (published in 2010 by the NOUGG of Canada) to be valid, relevant to Latin America, practical, evidence-based, concise, unambiguous, and sufficiently educational to provide clear instruction on OU and pain management and, thus, recommended for uniform adoption across the Latin America region.

Key Words. Chronic Pain; Latin America; Opioids Guidelines; Opioid Barriers

Introduction

The International Association for the Study of Pain (IASP) defines chronic pain as "pain which has persisted beyond normal tissue healing time," usually taken to be 3 months [1]. According to a recent systematic review [2], the prevalence of chronic pain worldwide is high, with a weighted mean ± standard deviation of about 30.3% ± 11.7. This prevalence seems to be significantly higher in countries with a Human Development Index (HDI) below 0.9 than in those with a HDI ≥ 0.9 (33.9$± 14.5 and 29.9% ± 12.7, respectively). However, differences in survey methodology and variability in the data make difficult to estimate with certainty the prevalence in countries with a HDI below 0.9. Therefore, there is a clear need for epidemiological studies, especially in Latin America, where the available data is scarce and variable among countries [3].

Chronic pain is an important public health issue. The Declaration of Montréal [4] states that access to pain management is a fundamental human right, addressing the right of all people with pain to have access to appropriate assessment and treatment without discrimination. Appropriate treatment includes access to pain medications, including opioids and other essential medications for pain control. However, in most of the world, there is an inadequate pain management due to various reasons including, but not limited to, severe restrictions on the availability of opioids and other essential medications considered critical for pain management [5].

Since the *United Nations Single Convention on Narcotic Drugs of 1961* [6], further revisions have been made with the aim of ensuring the availability of controlled medications for the relief of pain, while preventing recreational use and abuse [7]. In spite of these statements, the availability of opioid analgesics for the legitimate treatment of pain is still too low in many countries. While developed countries, including United States and Europe, account for 79% of global morphine consumption, developing countries, which account for 80% of the world's population, consumed just 6% [8]. Facing this skewed distribution, issues limiting the use and availability of opioids in Latin America have been addressed: *Declaration of Florianopolis* in 1995 [9], Santo Domingo report in 1997 [10], several reports from the United Nations *International Narcotics Control Board* [11], *Panama Proclamation* in 2008 [12], and so forth. However, significant challenges still need to be overcome, including opioid availability and prescribing barriers.

Many governments identify attitude and knowledge-related impediments (namely addiction concerns and insufficient training) among health care professionals (HCP) and patients as the main factors contributing to the underuse of opioids [13]. In Latin America, these impediments, together with regulatory barriers, are a key issue in restricting opioid availability and use, which result in the suboptimal management of chronic pain. As this is the subject of this publication, particular emphasis will be placed on local considerations for facilitating regional best practice, including identifying and uniformly adopting the most relevant international guidelines on opioid use (OU) in chronic pain management.

This review represents the view of the *Change Pain Latin America* (CPLA) Advisory Panel of Experts in the management of chronic pain, with the aim of dispelling the myths and stigma surrounding the OU. The CPLA initiative was launched in response to a similar campaign in Europe and aims to better understand the epidemiology of chronic pain in Latin America, identify and overcome barriers to regional best practice, and address the unmet needs of patients in the region.

In a meeting held in Guayaquil, Ecuador, 17–18 May 2013, the CPLA expert panel, composed of 16 experts in the field of pain belonging to eight countries in LA (Brazil, Chile, Colombia, Costa Rica, Ecuador, Mexico, Peru, and Venezuela) representing approximately 82% of the total population of the region (World Bank data), discussed and reached a consensus on the OU guidelines which better fit with the clinical practice across Latin America. Considering the CPLA objectives and the IASP's Montreal 2010 declaration [4], the panel discussed regulatory barriers to OU and drafted the framework for the CPLA campaign declaration. The ongoing CPLA initiatives aim to address the primary obstacles to the best practice in chronic pain management across Latin America.

Barriers to OU

Among the CPLA initiatives, the expert panel has extensively reviewed regulatory barriers in every country that restrict adequate access, distribution and prescription of opioids in the region. The results highlight the limited knowledge on OU among patients and HCP (opio-ignorance) [14], resulting in misconceptions about treatment

of chronic nonmalignant pain, mainly related to a fear of prescribing opioids due to their possible misuse and addiction (opiophobia), and a false perception of their lack of efficacy. Furthermore, there is not enough effective communication between HCP and institutions in relation to the benefits of OU in chronic non-cancer pain was noticed. All this considered, the CPLA strongly recommends a formal education of HCPs in Latin America focused on the appropriate OU and side-effect management, with the aim of overcoming negative attitudes toward the opioids and improve the insufficient knowledge regarding its risks and benefits in chronic pain management.

Among the regulatory barriers to OU in Latin America, the survey reported that laws controlling the storage and distribution of opioids are far more stringent than those laid down by international laws and the International Narcotics Control Board [11]. Moreover, local OU legislation in most countries is out of date and not reflective of current health care needs; for example, the last review of the legislation in Colombia was in 2006. Poor HCP education combined with a relative sparsity of epidemiological studies may have contributed to an out-of-date health care policy, and continued restrictions on OU.

The CPLA survey has also confirmed that, in Latin America, only few HCP—predominantly pain specialists—prescribe opioids. In some countries, HCP are required to obtain a licence to prescribe opioids and to maintain records of the patient's use. This complex and time-consuming process can deter HCP from prescribing opioids. In addition, due to these restrictions, patient prescriptions also have very short validity periods (typically ~5 days), and cover a limited treatment course (maximum of ~30 days' supply). The consequent need for patients to constantly obtain new prescriptions can also result in poor compliance.

The survey also highlighted the limited information on types and availability of opioid analgesics delivered to HCPs by the regulatory authorities. To obtain or produce controlled medicines, all Latin America countries are required to provide their estimated narcotic needs for the following year to the International Narcotic Control Board. Based on these estimates, the opioids storage is restocked, sometimes too conservatively and, thus, the stock is insufficient to cover the current needs, leading to drug shortage for the adequate care of patients and creating obstacles in the access to controlled medicines.

A further factor limiting opioid access is their cost, which varies markedly among geographic regions. Opioid cost is typically disproportionately higher in poorer countries, especially in Latin America, as compared with developed countries like the United States [15,16]. As regional health authorities have budgetary limitations, the high cost of opioids may explain why palliative care has been largely ignored in Latin America.

Pharmacists in Latin America also play an important role. On one side, they do not generally stock opioid analgesics, predominantly due to the cost and the restrictive legislation regulating their controlled storage and distribution. On the other side, they are not very willing to distribute opioids, mainly due to concerns related to their possible misuse by the patients. The rise of online pharmacy may also have contributed to inappropriate opioid self-prescribing. A study published in 2006 identified more than 300 Websites supplying opioid analgesics without prescription [17]. With an increase in prescribed opioids in the United States, Internet offers another vector into a market of unregulated OU. However, a decrease in availability of opioids via online pharmacies in the United States has been recently reported, probably related to an increased regulation of internet pharmacies [18].

Opiophobia stems from inadequate HCP education and a lack of clear uniform guidance. Misuse, abuse, unnecessary toxicities and deleterious outcomes can be attributed to inappropriate opioid management and prescribing. With appropriate education, and awareness and adherence to uniform guidelines, opioids are safe to use and represent effective treatment options for the management of chronic pain, including chronic lower back pain (CLBP). Thus, it is imperative that HCP and patients are better educated about the benefits and risks of opioid treatment [19]. Furthermore, HCPs should be provided with tools to promote confidence in opioids prescription, including patient risk assessment tools; patient agreement; improvements in patient screening (e.g., facilitating access to urine testing); and streamlined local regulations. New anti-tampering technologies, such as INTAC® formulation of oxymorphone, designed to resist crushing, and a novel opioid drug, tapentadol prolonged release, launched in the Latin American region in 2014, may improve the access to safer opioids [20,21].

Once detected the need for improving education on OU, the CPLA Expert Panel has conducted a review of the international guidelines, considering that Uniform OU Guides would help to provide a clear guidance on appropriately prescribing, managing, and monitoring opioids for treating patients with chronic pain.

CPLA International OU Guideline Review

Methodology: Search Strategy

This task was led by Dr. María Antonieta Rico and Dr. Durval Kraychete, who conducted a comprehensive, robust, and critical analysis of published national and international reviews and guidelines of OU, considering those most appropriate for Latin America. A search was conducted in PubMed using the search terms "opioid," "chronic," and "pain." Results were then further refined using the search filters "practice guidelines" and "within the last 5 years" (2007–2012). Once the publications

were identified, they were selected by the expert panel using the following five key criteria:

1) evidence based; 2) comprehensive; 3) from a well-recognized source; 4) current publications; and 5) based on best practice

The shortlisted guidelines were then critically analyzed by the CPLA expert panel, which considered 10 key criteria for determining the most relevant guidelines to be applied in Latin America:

1) focus on OU in nonmalignant pain; 2) relevance to Latin American circumstances; 3) generated by a well-recognized source or organization; 4) sufficiently up to date; 5) recommended adverse event management options; 6) advice on abuse screening and monitoring; 7) adequately define addiction, tolerance, and dependence; 8) accessibility to primary care physicians; 9) practicality; and 10) validity of guideline recommendations

The relevance of the 10 criteria were scored on a 1–5 scale (1 = low and 5 = high). A CPLA panel consensus was then reached on the set of guidelines considered to be the most relevant for OU in Latin America. The strengths and limitations of the chosen OU guidelines were noted by the panel, so that they could be addressed in future guideline updates, to further improve OU management and outcomes in the Latin American region.

Search Results

The initial PubMed search identified 177 reviews and guidelines, which was reduced to 16 articles following analysis using the five preliminary criteria. Following a secondary analysis according to the 10 key criteria specific to OU in Latin America, 10 publications were selected for critical review and discussion by the CPLA expert panel at the 3rd CPLA meeting, held in Guayaquil, Ecuador (May 2013) (Table 1) [16,22–31].

Outcome of the CPLA Expert Panel Review: Rejected Guidelines

Following discussion, the panel selected one of the 10 shortlisted OU guideline publications. The rest were considered unsuitable for the Latin American region due to different reasons:

- The 2012 Guidelines from the "*Asociación Latinoamericana de Cuidados Paliativos*" [22] (ALCP) were considered not sufficiently supported by clinical evidence. Moreover, the panel considered that they would not provide primary care physicians with sufficiently clear guidance on OU. However, the panel acknowledged that the ALCP guidance encompassed OU in general and specific populations (e.g., neuropathic pain), and had sections covering physiology and pharmacology issues.
- The 2010 *Updated Agency Medical Directors' Group* (AMDG) guidelines [23] were not considered appropriate for a Latin American audience for several reasons: they are designed to address United States-centric health care issues; to emphasize the risk associated with opioid prescriptions over their clinical benefit, which possibly potentiate opiophobia; and the screening and monitoring tools described in the AMDG publication (Opioid Risk Tool [ORT], CAGE-AID, and PHQ) have not been validated for the Latin American population.
- The rejection of the 2009 guidelines from the *American Pain Society* [24] (APS) was based on the fact that they are mainly tailored for the United States health care system. The panel acknowledged that the APS guidelines provide information and give strong recommendations on how to start and titrate chronic opioid therapy, the need to obtain an informed consent, and which risk stratification tools are to be used. However, these recommendations were only supported by low-quality evidence. Also the APS guidelines encourage the limitation of methadone use, based on United States opioid death rates, and contain information on opioid availability not suitable for Latin America. The APS guidelines also include tools for risk assessment of long-term opioid usage that have not been validated in Latin America, such as the Screener and Opioid Assessment for Patients with Pain (SOAPP). In addition, the panel noted that funding for the type of monitoring (urine screening by immunoassay and/or chromatography) recommended by the APS may not be available in Latin America.
- The 2012 guidelines from the *American Society of Interventional Pain Physicians* [25,26] (ASIPP) were rejected, predominantly because they are targeted at pain specialists. Despite a well-structured evidence-based treatment algorithm, the ASIPP guidelines overemphasize the risk of opioid-associated death, which could discourage prescribers from considering opioids for chronic pain management. The ASIPP guidelines also highlight issues associated with obtaining risk stratification and informed consent (informed decision-making) and included risk assessment tools that had not been validated in Latin America. These included the SOAPP; Pain Medication Questionnaire; Prescription Drug Use Questionnaire – Patient Version; Addiction Behaviors Checklist; and the Diagnosis, Intractability, Risk, Efficacy tool.
- The *British Society for Rheumatology and the IASP* [16] 2008 guidelines were rejected, as they were considered to be out of date and focused predominantly on the management of rheumatoid disease.
- The 2011 guidelines from the *Institute for Clinical Systems Improvement* [27] (ICSI) were also rejected, as they provide a general overview of concepts and definitions relating to chronic pain, but were not focused on OU.
- The 2012 guidelines from the *National Institute for Health and Care Excellence* [29] (NICE) were rejected because they are tailored toward the UK health care

Table 1 Most relevant international OU guidelines selected for further critical appraisal by the CPLA panel

	Opioid Use		
Authors	Guidelines Reviewed	Published	Region
ALCP (Bonilla et al.) [20]	Uso de opioides en tratamiento del Dolor: Manual para Latinoamérica	2012	Latin America
AMDG [21]	Inter-agency guidelines on opioid dosing for chronic non-cancer pain	2010	Washington State
APS (Chou et al.) [22]	Clinical guidelines for the use of chronic opioid therapy in chronic non-cancer pain	2009	United States
ASIPP (Manchikanti et al.) [23,24]	Guidelines for responsible opioid prescribing in chronic non-cancer pain	2012	United States
British Society for Rheumatology, and IASP [16]	Guidelines for the integrated management of musculoskeletal pain symptoms	2008	UK
ICSI [25]	Assessment and management of chronic pain	2011	United States
NOUGG [26]	Safe and effective use of opioids for chronic non-cancer pain	2010	Canada
NICE [27]	Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults	2012	England and Wales
HIS (Zacharoff et al.) [28]	Managing chronic pain with opioids in primary care	2010	United States
VA/DoD [29]	Clinical practice guideline for management of opioid therapy for chronic pain	2010	United States

system and focused on palliative care, particularly for chronic diseases (kidney, liver, and respiratory) and neurodegenerative disorders. In addition, the CPLA panel considered that the pharmacological options recommended by NICE were not relevant in Latin America.

- The Inflexion Health Series [30] (IHS) 2010 guidelines were rejected because they were not based on a systemic review, with a lack of evidence-based recommendations. In addition, the format was considered akin to textbook, rather than concise reference guidance. However, the panel acknowledged that the IHS guidelines did provide the necessary educational instruction on OU, patient monitoring, and treatment of adverse effects for a primary care audience.
- The Department of Veterans Affairs/Department of Defense (VA/DoD) [31] 2010 guidelines were also rejected for a number of reasons. These guidelines were specifically tailored to the United States Army Veterans population and, therefore, could not be representative of the Latin American population. Also, the panel believed that the guidelines would not be easy to implement in Latin America. In addition, the VA/DoD recommendations were based on weak evidence (i.e., physicians' clinical experience and a HCP working group consensus). Finally, the screening tests and informed consent described in the VA/DoD guidelines were not considered applicable to Latin America population.

Consensus on the OU Guideline for Adoption in Latin America

Following critical review and discussion, the panel agreeded that the international guidelines most relevant to Latin American practice were the "Safe and effective use of opioids for chronic non-cancer pain," guidelines published in 2010 by the National Opioid Use Guideline Group (NOUGG) of Canada [28]. The NOUGG guidelines were selected because they were considered to be valid, relevant, practical, evidence-based, clinically applicable, comprehensive, and unambiguous. The guidelines were considered valid because they highlighted opioids as useful tools in chronic pain treatment, outlining appropriate clinical outcomes. The negative effects of opioids (i.e., tolerance, dependence, and addiction) were also adequately defined and distinguished (Figure 1a). The guidelines were considered relevant because they sufficiently represented OU in current practice, having been compiled from strong supporting evidence/reference material, by a reliable and respected organization (Figure 1b). Also, the NOUGG guidelines constitute the basis of other local guidelines, including the forthcoming Brazilian guidelines on OU. The guidelines were considered practical because they recommend pharmacologic therapeutic options available in Latin America, including opioid rotation and equianalgesic dosing. The guidelines are also easy to implement in Latin America; they consider individualized therapy;

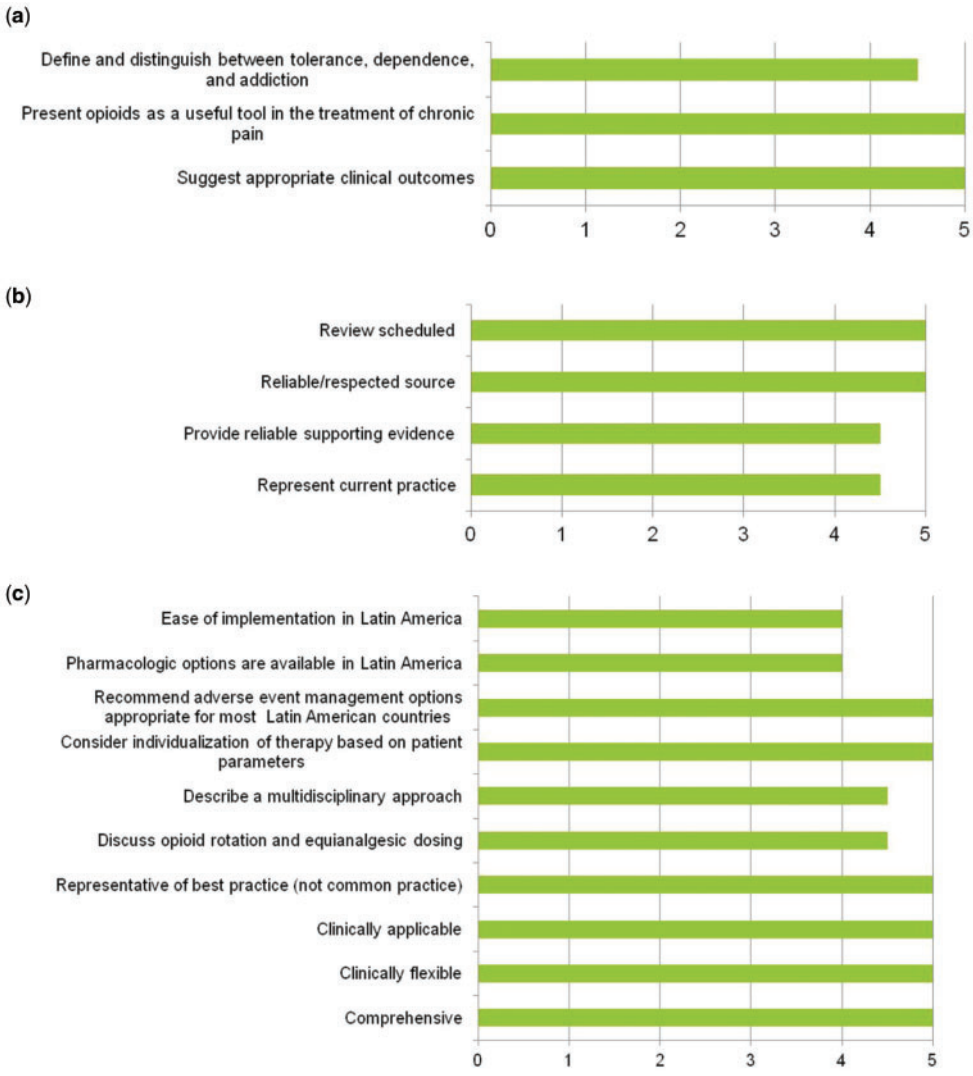

Figure 1 The CPLA panel considered the 2010 NOUGG guidelines to be: (a) valid,* (b) relevant,* and (c) practical.* *Ratings were defined as 1 = low and 5 = high.

recommend adverse event management options; describe multidisciplinary approaches; are representative of current best practice; and are clinically applicable and flexible, plus comprehensive (Figure 1c). The guidelines are evidence-based, as they are supported by a comprehensive revision of 87 first-level articles, and are based on clear inclusion and exclusion criteria, with graded evidence levels on a clear 0–5 scale, as determined using an instrument developed by Jadad et al. [32].The guidelines were considered clinically applicable (particularly recommendations R1–R24) because they included a treatment algorithm that comprised three drugs available in Latin America, and provide advice on dosing and titration (particularly on reducing benzodiazepine doses), and direction for the treatment of specific subpopulations (Figure 2). They were also considered comprehensive, as they are divided into clearly defined sections, which address the majority of challenges faced by physicians when treating patients with chronic pain in Latin America (Figure 3). Furthermore, the NOUGG guidelines were considered unambiguous due to the inclusion of a glossary that minimized the risk of misinterpretation by HCPs (particularly primary care physicians).

Latin American Perspectives on OU in Chronic Pain Management

When considering the consensus NOUGG guidelines [28] in the context of daily clinical practice in Latin America, some caveats were noted by the panel. The guidelines neither cover opiophobia nor provide guidance based on lessons that can be learned from opioid misuse in the United States. The CPLA panel noted that

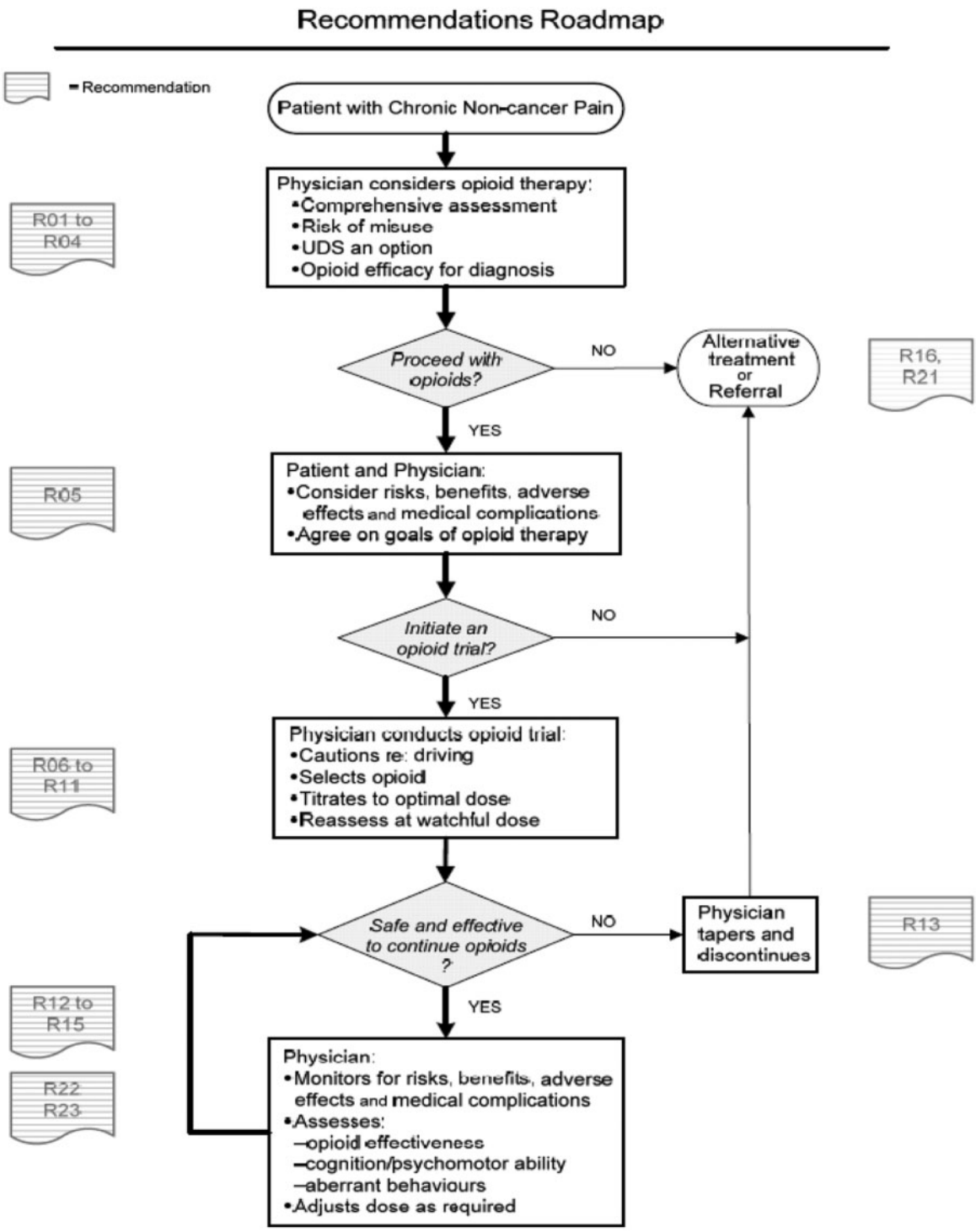

Figure 2 The CPLA panel considered the 2010 NOUGG guidelines to be clinically applicable, providing clear advice on treatment decisions, opioid dosing, and titration recommendations, and caveats for prescribing opioids to specific subpopulations. Reproduced from Ref. 28, *Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain*. © 2010 National Opioid Use Guideline Group (NOUGG). © 2015 McMaster University; *Physicians refer to prescribing tables at each appropriate stage of the algorithm.

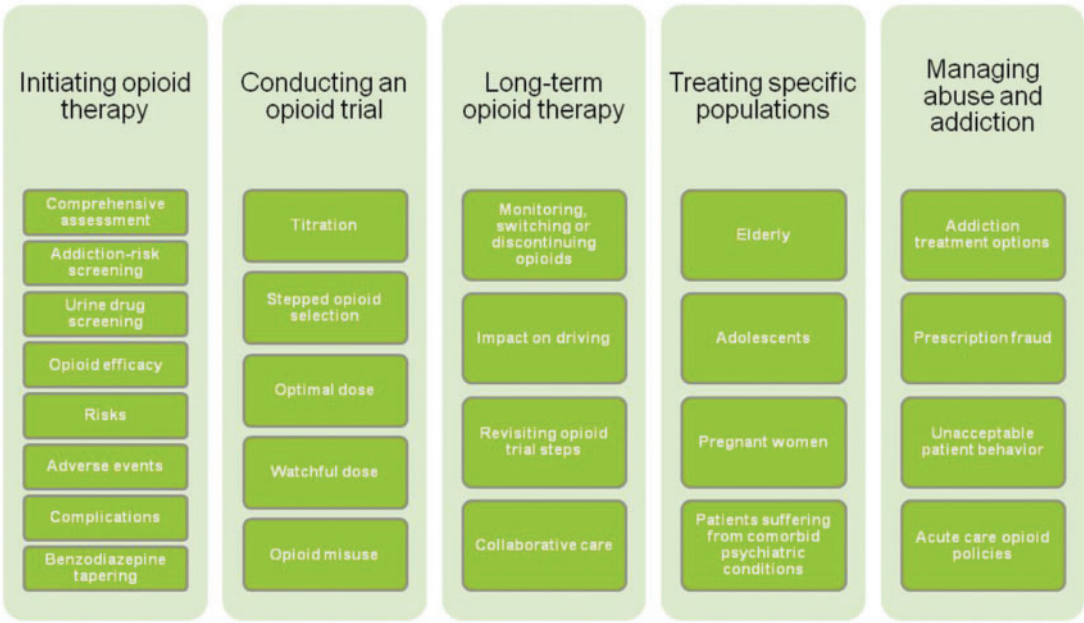

Figure 3 The CPLA panel considered the 2010 NOUGG guidelines to be comprehensive.

Latin Americans receiving opioids may exhibit marked differences in the opioid side effect profiles and perceived efficacy compared with other geographic regions. The panel perceived that Latin America does not have the high percentage of patients addicted to opioids, such as oxycodone, reported in North America. Interestingly, around 10–15% of Latin Americans have allelic cytochrome P450 variants associated with poor opioid metabolism that can lead to therapeutic failure with opioids like codeine that must be metabolized in vivo to an active form (i.e., morphine) [33]. However, despite the existence of this small subpopulation, HCP should not be deterred from prescribing opioids for chronic pain management.

The panel emphasizes that all analgesics listed in the Consensus NOUGG Guidelines are not available in all LA countries. Conversely, the document does not provide information about the use of buprenorphine metadone and hidrocodona, all of them widely used in our region. Therefore, the CLPA panel formulated a table of opioids currently available in Latin America (Table 2) [22].

In addition, the panelists noted that in Brazil, there is limited training in urine testing, but great experience in the use of methadone as an inexpensive treatment for chronic pain. In Chile, urine testing is rarely used partly due to its difficult access. The NOUGG guidelines do not cover the emerging opioid therapies in Latin America (including those exhibiting dual pharmacology, e.g., tapentadol) [34], informed consent forms to ensure patient understanding, treatment compliance, or how to prevent opioid redistribution.

Summary

The primary obstacles to best practice identified by the CLPA panel using the "regulatory barriers to OU" survey were: a) lack of HCPs training in chronic pain diagnosis and management; b) a lack of education of pharmacists and patients; and c) a sparsity of robust epidemiology on chronic pain to emphasize its importance as a major public health issue to policy-makers. Consequently, chronic pain management has remained as a low priority among health care policy-makers, resulting in poor access and distribution of opioids, and insufficient provision of trained pain management specialists.

Following a critical appraisal of international OU guidelines, the CPLA advisory panel recommended the "Safe and effective use of opioids for chronic non-cancer pain" (published in 2010 by the NOUGG of Canada) for uniform adoption by HCP across the Latin America region. The CPLA advisory panel considered these guidelines to be valid, relevant to Latin America, practical, evidence-based, concise, unambiguous, and sufficiently educational to provide clear instruction on OU and pain management in patients with chronic pain (in particular for primary care practitioners).

However, the panel noted that the NOUGG guidelines did not include advice on dosages and use of buprenorphine, methadone, and hydrocodone; therefore, they have developed a table which includes all available opioids in Latin America which can be a valuable source of reference for HCP in this region.

Table 2 Opioids availability in Latin America. Other possible formulations and doses not available in the Countries performing this study have not been included in this table

Formulation	Dose	Brazil	Chile	Colombia	Costa Rica	Ecuador	Mexico	Peru	Venezuela
Buprenorphine									
Tablets (sublingual)	0.2 mg					x	x		
Ampoules	0.3 mg/mL					x	x		
Transdermal patch (3 days)	35 μg/h		x	x		x	x	x	
	52.5 μg/h						x		
Transdermal patch (7 days)	5 μg/h	x					x		
	10 μg/h	x					x		
	20 μg/h	x							
Codeine									
Tablets	10 mg					x			
	30 mg	x			x				
	60 mg	x							
	100 mg							x	
Tablets (combination)	8 mg codeine/500 mg paracetamol			x					
	15 mg codeine/500 mg paracetamol			x					
	30 mg codeine/300 mg paracetamol				x	x			
	60 mg codeine/300 mg paracetamol							x	
	25 mg codeine/500 mg paracetamol								x
	30 mg codeine/500 mg paracetamol	x	x	x			x		
	60 mg codeine/500 mg paracetamol	x	x						
	12.5 mg codeine/200 mg ibuprofen								x
	20 mg codeine/300 mg ibuprofen								x
	50 mg codeine/50 mg diclofenac	x		x			x		x
Syrup	5 mg/5 mL					x		x	
	3 mg/mL	x							
	20 mg/mL		x						
	60 mg/mL		x					x	
	120 mg/mL		x						
Ampoules	60 mg/mL							x	
Fentanyl									
Transdermal patch	12.5 μg/h	x		x					
	25 μg/h	x	x	x	x		x	x	x
	50 μg/h	x	x	x	x		x	x	x
	75 μg/h	x		x					
	100 μg/h	x		x	x				

(continued)

Table 2 Continued

Formulation	Dose	Brazil	Chile	Colombia	Costa Rica	Ecuador	Mexico	Peru	Venezuela
Ampoules	25 μg/mL						x		
	50 μg/mL	x	x	x	x	x	x	x	x
	100 μg/mL				x				
Hydrocodone									
Tablets (combination)	5 mg hydrocodone/200mg ibuprofen			x					
	5 mg hydrocodone/500 mg paracetamol			x					
Hydromorphone HCl									
Tablets (immediate release)	2.5 mg			x					
	5 mg			x					
Tablets (extended release)	8 mg						x		
	16 mg						x		
Ampoules	2 mg/mL			x					
Methadone									
Tablets	5 mg	x			x		x		x
	10 mg	x	x	x			x		x
	40 mg			x			x		x
Oral solution	10 mg/1 mL						x		
Ampoules	10 mg/2 mL	x	x		x				
Morphine									
Tablets (immediate release)	5 mg								x
	10 mg	x					x		x
	15 mg						x		
	20 mg				x				
	30 mg	x					x	x	x
Oral solution	3 mg/mL		x						
	6 mg/mL		x						
	10 mg/mL	x							
	30 mg/mL			x[1]					
	10 mg/cc (syrup)		x						
Tablets (sustained release, bid)	10 mg		x			x			x
	30 mg	x	x		x	x		x	x
	60 mg	x	x					x	x
	100 mg	x				x			
Ampoules	1 mg	x					x		
	10 mg	x	x	x	x[2]	x	x	x	x
	15 mg				x[2]				
	20 mg		x			x		x	

(continued)

Table 2 Continued

Formulation	Dose	Brazil	Chile	Colombia	Costa Rica	Ecuador	Mexico	Peru	Venezuela
	25 mg						x		
Morphine parenteral solution 3%	30 mg/mL			x					
Oxicodona									
Tablets (immediate release)	5 mg							x	x
Tablets (sustained release)	10 mg			x			x	x	x
	20 mg		x	x			x	x	x
	40 mg		x	x			x	x	x
Tapentadol									
Tablets	50 mg		x	x			x		
	100 mg						x		
Sustained-release tablets	50 mg			x			x		
	100 mg			x			x		
Sustained-release capsules	50 mg		x						
	100 mg		x						
Tramadol HCl									
Tablets	25 mg						x[3]		
	50 mg	x	x	x	x	x	x	x	x
	100 mg	x			x		x		x
Sustained-release capsules	50 mg	x	x	x	x	x	x	x	
	100 mg	x	x	x	x	x	x	x	x
	150 mg		x	x		x	x		x
	200 mg		x	x		x	x	x	x
Drops	20 mg/mL			x					
	50 mg/mL		x					x	
	100 mg/mL		x	x	x		x		
Syrup	2.5 mg/mL			x					x
Ampoules	50 mg/mL	x	x	x	x	x	x	x	x
	100 mg/2 mL	x	x	x	x	x	x	x	x
Tablets (combination)	25 mg tramadol/25 mg diclofenac			x					
	37.5 mg tramadol/325 mg paracetamol	x	x	x	x	x	x[4]	x	x
Syrup (combination)	37.5 mg tramadol/325 mg paracetamol			x					

Notes: Colombia: Oxycodone ampoules will be available early 2015; x[1] = Morphine Oral Solution 3% (30 mg/mL). Costa Rica: x[2] = Morphine ampoules is available as 15 mg/mL and occasionally as 10 mg/mL, but never both at the same time. Mexico: x[3] = Tramadol 25 mg capsules; x[4] = Tramadol 37.5 mg/paracetamol 325 mg effervescent tablets.

The guidelines do not include a list of emerging therapies. Regional perspectives include a difficult access to urine testing in the region, the widespread use of methadone in Brazil for inexpensive chronic pain management, and a high proportion of poor opioid metabolizers in the region. Opiophobia, opioid ignorance, and learning from opioid misuse in the United States have also been highlighted in this manuscript.

Ongoing CPLA initiatives are seeking to provide robust epidemiological information on the regional burden of chronic pain in Latin America, and improve the management of CLBP with or without a neuropathic component.

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