Formulary availability and regulatory barriers to accessibility of opioids for cancer pain in Latin America and the Caribbean: a report from the Global Opioid Policy Initiative (GOPI)

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The nations of the Caribbean, Central America and South America form a heterogeneous region with substantial variability in economic, social and palliative care development. Palliative care provision is at varied stages of development throughout the region. The consumption of opioids in Latin America and the Caribbean is variable with moderate levels of consumption by international standards (1–10 mg morphine equivalents/capita/year) observed in Argentina, Brazil, Chile, Colombia, Cuba, Mexico, Costa Rica, Uruguay and most of the Caribbean but relatively low levels of consumption in other countries particularly Guatemala, Honduras and Bolivia. Data for Latin American and Caribbean is reported on the availability and accessibility of opioids for the management of cancer pain in 24 of the 33 countries surveyed. The results of this survey are relevant to 560 million of the region’s 595 million people (94%). Opioid availability continues to be low throughout most of Latin America and the Caribbean. While formularies in this region generally include all recommended morphine formulations, access is significantly impaired by widespread over-regulation that continues to be pervasive across the region.

introduction

The nations of the Caribbean, Central America and South America form a heterogeneous region with substantial variability in economic, social and palliative care development. Spanish is the most prevalent language with English, Portuguese and ethnic languages also being spoken as primary languages in the area. While the Latin American countries of Central and South America are more similar culturally, together with the Caribbean Islands, there is great diversity based on historical ties. The region has the highest income gap in the world and includes some of the fastest growing economies (e.g. Brazil) and some of the poorest countries in the world. Over the past century the region has been characterized by economic and social instability and frequent changes in government, with a history of dictatorships and centrally controlled governments \(^1\). In many countries in the region, health care systems operate and function with inadequate infrastructures, poor administrative systems, poverty, limited educational opportunities, and other challenges.

A recent report on cancer care in Latin America and the Caribbean \(^2\) highlighted that cancer is a rapidly growing and increasingly deadly epidemic in the region. It is estimated that by 2030, 1.7 million cases of cancer will be diagnosed in the region, and more than a million people will die from cancer each year. Cervical cancer is the leading cause of cancer in 10 of 25 Latin American countries, and is a major cause of cancer mortality among women, with 68 220 new cases and 31 712 deaths reported annually. Cancer mortality rates are substantially higher than those seen in North America, Europe and Japan for all cancer types. Most patients present with advanced disease (e.g. Brazil, 80% of breast cancer patients; Mexico 90% of breast cancer patients). Overall, the report concluded that Latin America and the Caribbean are poorly equipped to deal with the alarming rise in cancer incidence and disproportionately high mortality rates.

The Latin American Association for Palliative Care (ALCP for its Spanish acronym) has been active in the region with growth in palliative care services in some of the regions of the middle- and high-income countries. A recent survey of palliative care services by the ALCP \(^3\) identified a total of 922 palliative care services and nearly 600 palliative care accredited physicians. There is a major concentration of services and manpower in Chile, Mexico and Argentina with very limited resources for palliative care outside of those countries. Palliative care provision is at varied stages of
development throughout the region [4]. Few countries in the region have palliative care policies and in many parts of the region, pain management has been surrounded by myths, cultural bias and attitudes.

The consumption of opioids in Latin America and the Caribbean is variable (Figure 1) with moderate levels of consumption by international standards (1–10 mg morphine equivalents/capita/year) observed in Argentina, Brazil, Chile,

![Figure 1](image1.png)

**Figure 1.** Rank order of opioid consumption (mg/capita in morphine equivalence without methadone) for surveyed Latin American and Caribbean countries.

![Figure 2](image2.png)

**Figure 2.** Comparison of opioid consumption (mg/capita in morphine equivalence without methadone) the World, the WHO Regional Offices for the Americas (AMRO), without North America from 1980 to 2010.
Colombia, Cuba, Mexico, Costa Rica, Uruguay and most of the Caribbean, but relatively low levels of consumption in other countries, particularly Guatemala, Honduras and Bolivia. Overall, regional opioid consumption has increased even in countries with relatively low levels of opioid consumption (Figure 2).

This report provides further details on opioid availability and accessibility beyond those previously reported in the Atlas of Palliative Care in Latin America [3], and this is the first time this data has been evaluated systematically.

**methodology**

See Cherny et al. [5].

**results**

Data for Latin America and the Caribbean are reported on the availability and accessibility of opioids for the management of cancer pain in 24 of 33 countries. The reported data is relevant to 560 million of the region’s 595 million people (94%). Surveys were received from Anguilla, Argentina, Barbados, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Dominica, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Jamaica, Mexico, Panama, Paraguay, Peru, St Lucia, Trinidad and Tobago, Uruguay and Venezuela.

**formulary availability and cost of opioids for cancer pain**

The availability of opioids and their cost to consumers are summarized in Figure 3. All countries but Anguilla had injectable morphine. Dominica had only injectable morphine and was one of the six countries that did not have immediate release (IR) morphine (Dominica, Ecuador, El Salvador, Honduras, Paraguay and Trinidad and Tobago). Significantly, despite having no IR morphine, Ecuador, El Salvador and Trinidad and Tobago had controlled release morphine, while Honduras and Paraguay had transdermal (TD) fentanyl on formulary. Seventeen of 24 countries had TD fentanyl. There was little IR oxycodone available, and oral methadone was primarily available in Central America and the Caribbean.

Data were mixed as to cost of the medications. Generally the cost was consistent within each country, and in most cases medications were either free or at full cost to the patient. When medications were on formulary, they were usually available. Significantly, five countries with IR morphine on the formulary stated that it was only available half the time (Chile) or...
occasionally (Anguilla, Bolivia, Colombia and Guatemala) (Figure 4).

regulatory restrictions to accessibility

Regulatory restrictions limiting accessibility to opioids were widely reported. They are detailed below and summarized in Table 12.

requirement for permission/registration of a patient to render them eligible to receive an opioid prescription

In Latin America and the Caribbean when countries required patient authority or registration to receive opioids this was usually applied in all settings. Most restrictions applied to outpatients across the region and Anguilla did not allow outpatient prescribing of opioids (Figure 5).

requirement for physicians and other clinicians to receive a special authority/license to prescribe opioids

Generally, prescriptive authorities were consistent across countries for oncologists, family doctors and surgeons and were most permissive for oncologists. In 18 of 24 countries, oncologists are always allowed to prescribe opioids. Family

Figure 4. Actual availability of the seven essential opioid formulations of the International Association for Hospice and Palliative Care (IAHPC) in Latin American and Caribbean countries. MoIR, immediate release oral morphine; MoCR, controlled release oral morphine; MoINJ, injectable morphine; OcIR, oral immediate release oxycodone; FentTD, transdermal fentanyl; MethPO, oral methadone.

Eligibility restrictions for cancer patients in Latin American and Caribbean countries.
doctors require special authority in Anguilla and Belize, while surgeons in Anguilla are only allowed to prescribe in an emergency. Very few countries allowed nurse or pharmacist prescribing, although Uruguay does allow nurse prescribing in an emergency and Anguilla, Jamaica and St Lucia allow nurse prescribing with special permit. The same is true for pharmacists in Anguilla and Argentina (Figure 6).

requirement for duplicate prescriptions and special prescription forms
Almost all the countries reported the need for special prescription forms. These are generally readily available, however in most counties they must be purchased by the prescribing physician (Figure 7).

prescription limits
Most commonly, 30 days was the allowable maximum number of days for the duration of a prescription. However, in some countries there were shorter periods: Ecuador three days, and in five countries (Argentina, Costa Rica, Dominican Republic, Jamaica and Peru) between 10 and 15 days. The quantity prescribed in Bolivia was limited by dose (Figure 8).

limitations on dispensing privileges
While 9 of 24 countries allow dispensing from any pharmacy, most countries have some restrictions, i.e. hospital pharmacies (six), a single-designated pharmacy (two) and other designated location (six) (Figure 9).

provision for opioid prescribing in emergency situations
An emergency situation is defined as one when there is an immediate need to relieve strong cancer pain but the physician is not able to physically provide a prescription. Examples include a pain crisis at night, on a public holiday or in a remote region. Few countries allowed pharmacists the ability to accept emergency prescriptions (Figure 10).

pharmacist privileges to correct a technical error on a prescription
In the situation of a patient presenting a prescription that contains a technical error (no address, misspelling, missing value, etc.), few countries allowed pharmacists to correct the error and dispense the medication.
use of stigmatizing terminology for opioid analgesics in regulations

Opioid regulations incorporated negative language such as ‘drugs of addiction’ or ‘dangerous drugs’ in 13 of the 24 countries (Figure 11).

discussion

Cancer continues to be an increasing problem throughout the world with an increase in cancer incidence in low- and middle-income countries. Cancer mortality rates in Latin America and the Caribbean are high by international standards and, in particular, there is a very high prevalence of cervical cancer and mortality and morbidity associated with this disease in the Caribbean countries [2].

For comparative purposes, and to maintain the consistency with the analysis done with the data from the other regions, methadone was not included in the consumption reports for Latin America. However, reports indicate that most of the methadone consumed in the region is for analgesic purposes, while very limited amounts are used for the treatment of dependency syndrome. Therefore, the data in the graphs may not be reflective of the actual consumption of opioids for analgesic purposes.

Despite increases in opioid consumption observed in the Latin America and the Caribbean, many countries have very low and ‘concerning’ levels of opioid consumption as defined by the INCB with an S-DDD (statistical defined daily dose) of <200 mg/day/100,000 people [6]. The exceptions to this were Argentina (430), Chile (390), Colombia (290), Barbados (260) and Brazil (215). Latin American and Caribbean data including S-DDD and Adequacy of Consumption Measure (ACM) for opioids with in the region are shown in Table 1. All surveyed countries in the region have <10% of the anticipated ACM for opioids (Table 1).

The approach to improving opioid consumption is guided by the World Health Organization (WHO) policy guidelines, Ensuring Balance in National Policies on Controlled Substances, Guidance for availability and accessibility of controlled medicines. Moreover, the WHO Palliative Care Strategy states that medication availability, education and government policy must all be addressed and implemented if adequate pain relief and palliative care are to be provided.
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<th>Country</th>
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Figure 9. Dispensing pharmacy sites and their accessibility for Latin American and Caribbean countries.

**medication availability**

Opioid formulary deficiencies do not seem to be a major issue in Latin American and the Caribbean. Over half the countries (15 of 24) surveyed had five or more essential opioids as outlined by the IAHPC [9]. A small number of countries (Ecuador, Honduras, Paraguay and Dominica) had limited access with three or less opioids available. Six countries did not have oral immediate release morphine (Dominica, Ecuador, El Salvador, Honduras, Paraguay and Trinidad and Tobago), but half of these countries had transdermal fentanyl, which was actually available in 17 of the 24 countries of the region. Interestingly, the Caribbean countries were less likely to have transdermal fentanyl. It is widely recognized that pharmaceutical companies and importers are reluctant to invest in the registration and promotion of products, such as oral immediate release morphine or oxycodone that do not generate significant profit. In contrast, where there is room for profit from the promotion and marketing of proprietary products, such as transdermal fentanyl, there is greater commercial motivation.

A particular difficulty noted in Colombia regarding opioid availability was the limited number of hours for which pharmacies dispensed medication. However, a particular effort was made to ensure that each district always had a pharmacy open to dispense opioids around the clock [13].

**education**

Medical education for end-of-life care in Latin America is not standardized or well developed. Most specialists and general practitioners who provide palliative care have had little formal training. Although most clinicians are adept at providing analgesia according to the WHO three-step Pain Relief Ladder many providers are not comfortable treating other cancer-related symptoms. Similar to the historical development of palliative care in other regions of the world, palliative care for
cancer patients in Latin America is distributed between different subspecialties, although largely focused on oncologists.

In Cuba and Uruguay all medical schools offer palliative care training. In Colombia the Universidad de la Sabana teaches a Pain and Palliative Care Course and several medical schools in Bogota teach interns Good Prescription Practices for opioid analgesics, however, it has been a challenge to have this sort of educational initiatives adopted by all medical schools in Colombia [10]. Medical schools in Bolivia, El Salvador, Honduras and Nicaragua do not have any formal teaching in palliative care.

government policies and regulations

Regulatory barriers appear to be major issue with access to opioids in Latin America and the Caribbean. With the exception of St Lucia, Trinidad and Tobago and Jamaica (in the Caribbean) and Chile, Costa Rica, Paraguay and Uruguay (in Latin America) all other countries have four or more restrictive regulations that impaired access to opioids for pain relief (Figure 12). This is despite efforts since the 1990’s to bring about changes with the Declaration of Florianopolis in 1997 [11] and the on opioid availability in Latin America 1997 [12].

The role of policy makers and regulators is critical in opioid availability. A report from Colombia included a survey of competent authorities within the states. The identified barriers for the availability of opioids were insufficient human resources (46.9%), deficiencies in filling out official forms (46.9%), fear of expiration of the medication (43.7%), not enough safety conditions to store the medications (40.6%), administrative procedures (37.5%), transportation of medication (21.9%), and communication difficulties (21.9%). Interestingly the regulations themselves were not perceived as barriers by the regulators [13].

Multiple workshops regarding opioid accessibility and the need and process for regulatory reform have been undertaken in the region. For Example workshops in Quito, Ecuador with Bolivia, Chile, Colombia, Ecuador, Panama and Venezuela were reported on in 2001 [14] and more recently in 2011 and 2012 workshops have involved Panama, Guatemala, Colombia, El Salvador, Honduras, Nicaragua and Costa Rica (in 2011) and Bolivia, Ecuador and Venezuela (in 2012). The region has been a focus of Pain and Policy Studies Group International Pain Policy Fellowships Program [15]. Fellows from the region have come from Argentina, Colombia [10, 13], Guatemala, Jamaica [16] and Panama, with all of these countries showing an increase in opioid consumption in the last 15 years.

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**Figure 10.** Pharmacy restrictions for Latin American and Caribbean countries.

**Figure 11.** Negative laws regarding opioids in Latin American and Caribbean countries.
Conclusion

Opioid availability continues to be low throughout most of the Latin America and the Caribbean countries. While formularies in this region generally include all recommended morphine formulations, access is significantly impaired by widespread over-regulation that continues to be pervasive across the region.

There are substantial needs for educational initiatives, and regulatory review and reform in most of the participating countries in this region.

Further strategies for improvement are given in the 'Next steps in access and availability of opioids for the treatment of cancer pain: reaching the tipping point?', the final chapter of this supplement [17].

Funding

Self-funded by the coordinating partner organizations.

disclosure

The authors declared no conflicts of interest.

References


Table 1.

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*Calculated from INCB graphs.

S-DDD, defined daily doses consumed per million inhabitants per day; ACM, Adequacy of Consumption Measure.

Figure 12. Summary for Latin American and Caribbean countries of regulatory barriers to opioid access for cancer pain relief.


