



# Annals of Oncology

Official Journal of the European Society  
for Medical Oncology and the Japanese  
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Volume 24, 2013 Supplement 11

Opioid availability and accessibility for the relief of  
cancer pain in Africa, Asia, India, the Middle East,  
Latin America and the Caribbean: Final Report of the  
International Collaborative Project

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# The Global Opioid Policy Initiative (GOPI) project to evaluate the availability and accessibility of opioids for the management of cancer pain in Africa, Asia, Latin America and the Caribbean, and the Middle East: introduction and methodology

N. I. Cherny<sup>1,2\*</sup>, J. Cleary<sup>3,4</sup>, W. Scholten<sup>5,†</sup>, L. Radbruch<sup>6,7</sup> & J. Torode<sup>8</sup>

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Opioid analgesics are critical to the effective relief of cancer pain. Effective treatment is predicated on sound assessments, individually tailored analgesic therapy, and the availability and accessibility of the required medications. In some countries, pain relief is hampered by the lack of availability or barriers to the accessibility of opioid analgesics. As the follow-up to a successful project to evaluate the availability and accessibility of opioids and regulatory barriers in Europe, the European Society for Medical Oncology (ESMO) and the European Association for Palliative Care (EAPC) undertook to expand their research to those parts of the world where data were lacking regarding these aspects of care, in particular Africa, Asia, the Middle East, Latin America and the Caribbean, and the states of India. This project has been undertaken in collaboration with the Union for International Cancer Control (UICC), the Pain and Policy Studies Group (PPSG) of the University of Wisconsin, and the World Health Organization (WHO), together with a consortium of 17 international oncology and palliative care societies. This article describes the study methodology.

## introduction

For patients with cancer, and especially those with advanced and incurable cancer, adequate relief of pain is a central goal of care [1, 2]. Indeed, adequate relief of cancer pain is considered to be a human right by many organizations of health care professionals [3–10], but is not yet enshrined in human right conventions. This right implies duties; the duties of clinicians to assess pain and to treat it in accordance with the best of contemporaneous practices (that prevailing resources will enable), and that of governments and healthcare regulatory authorities to ensure that patients can access the medications needed to relieve pain.

There is a fundamental need to ensure that opioid analgesics are available to the patients who need them and to prevent these medications from becoming a source of harm or abuse. Drug abuse is a significant global problem. Although most of the opioids abused on a worldwide scale are obtained from illicit channels [11], a proportion are prescription medications that have been diverted through fraud, theft, forged prescriptions,

illegal pharmacies [11, 12], and via unscrupulous health professionals [13] or poor clinical practice. These considerations demand that the parties involved in the legal manufacture, distribution, prescription and dispensing of opioid medications for medical purposes be mindful of their substantial abuse potential.

Ideally, international and local regulations of opioid manufacture, distribution, storage prescription, and dispensing should aim to maintain a balance between good patient care and diversion prevention. Preventing drug abuse is important, but it should not hinder patients' ability to receive the care they need and deserve. This is the approach of the World Health Organization (WHO) and the International Narcotics Control Board (INCB) [11, 14–17]. Both recommend that opioids should be available for all patients with moderate to severe pain at hospital and community levels, and that physicians should be able to prescribe opioids according to the individual needs of each patient.

Opioid analgesics are critical to the effective relief of cancer pain. Effective treatment is predicated on sound assessments, individually tailored analgesic therapy, and the availability and accessibility of the required medications. In some countries, pain relief is hindered by the lack of availability or barriers to the accessibility of opioid analgesics. In many countries,

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excessively zealous drug controllers or policy makers, or poorly considered laws and regulations to restrict the diversion of medicinal opioids into illicit markets, profoundly interfere with the medical availability of opioids for the relief of pain. Often, the logistics of the treatment of pain with opioids is so burdensome or complex for physicians, nurses, and pharmacists as to be a major disincentive to the use of opioids in the treatment of pain.

This burden is compounded for patients, their families, and carers, who in many situations must cajole doctors, chase after permits, wait excessively in inconveniently located pharmacies, and return for frequent refills of prescriptions or any correction on a prescription that may not have been written with adequate attention to required details. In some countries, the degree of legal intimidation is such that fear of criminal prosecution contributes to deliberate under-treatment by clinicians to avoid risk of persecution or prosecution.

The problem of over-regulation has been highlighted by the INCB [15, 16, 18, 19], the WHO [14, 20], the Council of Europe [21], and by Human Right Watch [3]. The consequences for health care professionals, patients, and their families are manifold and profound. Excessive regulatory restrictions make it nearly impossible for many patients to achieve relief of moderate and severe cancer pain that undermines their own quality of life and that of their family and carers.

A research initiative by WHO found that, in 2010, countries corresponding to 66% of the world population had virtually no consumption of strong opioids, 10% very low, 3% low, and 4% moderate. In fact, only 7.5% of the world's population resides in countries considered to have adequate consumption levels. In addition, the level of adequacy of access for a country has been shown to highly correlate with its Human Development Index ( $R^2 = 0.7583$ ) [22].

In 2006, the European Society for Medical Oncology (ESMO) launched a campaign to improve the availability and accessibility of opioids for the management of cancer pain [23]. Partnering with the European Association for Palliative Care (EAPC), they produced in 2010 the first comprehensive survey of the formulary availability and cost of opioid medications in Europe and of the regulatory barriers that were possibly impeding access for cancer patients in need [24]. This study provided graphic evidence of the widespread problems that existed in much of Eastern Europe and the Baltic states and helped provide substrate data for intervention programs that are currently underway to address these shortcomings.

The countries of Africa, Asia, the Middle East, Latin America and the Caribbean, and the states of India are diverse with a wide range in the level of social and economic developments ranging from extreme wealth to extreme deprivation. This variability is reflected in the available data regarding the level of development of palliative care services and the degree to which they are integrated into the health care sector, and in per capita opioid consumption data [25]. To date, there have been no systematic studies to evaluate the availability and accessibility of opioids for the management of cancer pain or to evaluate the regulatory barriers that impede patient access to opioids for the relief of cancer pain.

## conceptualization and development of the project

As a follow up to the successful project to evaluate the availability and accessibility of opioids and regulatory barriers in Europe, ESMO and EAPC undertook to expand their research to those parts of the world where data were lacking regarding of these aspects of care. Given that good data were available regarding North America, Australia, and New Zealand, the identified geographic areas with inadequate data included Africa, Asia, and the Middle East, Latin America and the Caribbean, and the states of India. (The Indian states were surveyed separately because of their large populations and the complexity of the situation, which is different for each state.) The total population of these areas constitutes more than 5.7 billion people.

In view of the global scope of this project ESMO and EAPC invited three other important international organizations which have demonstrated pre-existing activity and commitment to these issues on a global scale to evaluate these issues. ESMO and EAPC together with the three other partners: the Union for International Cancer Control (UICC), the Pain and Policies Study Group (PPSG) of the University of Wisconsin, and the WHO constitute the five coordinating partners for this project. Within ESMO, the study activities were coordinated between the ESMO Executive Board, the Palliative Care Working Group, and the Emerging Countries Committee.

The aims of this study were to evaluate the formulary availability and cost to the consumer of the seven opioid formulations that have been deemed essential by the WHO and the International Association for Hospice and Palliative Care (IAHPC). In addition, the study aimed to evaluate the actual availability of these medicines for patients and the regulatory barriers that impede accessibility. A credible and comprehensive data set is essential for identifying shortcomings in the formulary and the actual availability, excessive costs to the consumer, and excessive regulatory barriers.

The adequacy of formulary availability was evaluated relative to the IAHPC list of essential medicines for palliative care and the WHO Model List of Essential Medicines, 17th Edition, [26] which was current at the start of this project. In 2007, the IAHPC developed an expert-generated essential medicines list for palliative care based on criteria of efficacy and safety. This list of recommendations, published in 2007 [27–30], is endorsed by the WHO Cancer Control Program [2]. The IAHPC lists all the formulations on the WHO Model List of Essential Medicines, 17th Edition, along with three others: transdermal fentanyl, oral methadone, and oral immediate release oxycodone (Table 1). Over-regulation was evaluated according to the principles derived from the WHO guidelines for the assessment of national opioid policies and regulations [14, 20].

This dataset provides a valuable foundation for global, regional, and national policy initiatives in individual countries that wish to take the right steps to truly improve the availability and accessibility of opioids for the management of cancer pain.

The five coordinating partner organizations have a shared responsibility for survey design, identification of collaborating partner organizations, identification of credible field reporters, data collection, and analysis. To ensure the widest possible

**Table 1.** Opioid analgesics on essential medicines lists used in this survey

Formulation	Abbreviation	WHO 2007	IAHPC 2007
Codeine	Codeine	X	X
Morphine PO immediate release (tablet or liquid)	MoIR	X	X
Morphine PO controlled release	MoCR	X	X
Injectable morphine	MoINJ	X	X
Oxycodone PO immediate release	OcIR		X
Fentanyl TD	FentTD		X
Methadone PO immediate release	MethPO		X

PO, by mouth; TD, transdermal.

**Table 2.** Collaborating partner organizations

1 African Organisation for Research and Training in Cancer (AORTIC)
2 African Palliative Care Association (APCA)
3 Asia Pacific Hospice Palliative Care Network (APHN)
4 Chinese Society of Clinical Oncology (CSCO)
5 Foundation Akbaraly, Madagascar
6 Help the Hospices
7 Indian Association of Palliative Care (IAPC)
8 International Association for Hospice & Palliative Care (IAHPC)
9 Japanese Society of Medical Oncology (JSMO)
10 Latin American and Caribbean Society of Medical Oncology (SLACOM)
11 Latin American Association for Palliative Care (ALCP)
12 Malaysian Oncology Society (MOS)
13 Middle East Cancer Consortium (MECC)
14 Multinational Association of Supportive Care in Cancer (MASCC)
15 Myanmar Oncology Society
16 Open Society Foundations (OSF)
17 Worldwide Palliative Care Alliance (WPCA)

coverage of the collection of data by field reporters, the coordinating partners invited the collaboration from palliative care and oncology organizations working in these regions. Seventeen organizations agreed to be ‘collaborating partners’ (Table 2). The key roles for the collaborating partner organizations were in the identification of field reporters, encouraging compliance with data submission requirements and deadlines, and in the process of open peer review of the preliminary data.

## methodology

The survey tool was based on the questionnaire developed and implemented in a study of opioid availability and accessibility in Europe [24]. The European questionnaire was modified by the coordinating partner organizations to collect additional data regarding the inclusion of opioids in a national essential medicines list, the presence or absence of a national palliative care association, cultural or social barriers to the use of opioids, changes in opioid regulation over the last 5 years, the actual availability of opioids to a patient holding a valid prescription, and the accessibility of sites able to dispense opioids for the management of cancer pain.

The survey was developed in English and was translated into Spanish and French. English and Spanish versions of the survey were prepared in a Form Master 2008 platform for electronic data collection via the EAPC website. The French version was distributed in electronic form by email and the data was manually entered into the online EAPC survey collection tool.

Data submitted by the two or more field reporters from each country/state were crosschecked by the Principle Investigator Nathan Cherny. When discrepancies between reporters were identified, clarifications were requested. When discrepancies persisted, priority was given to the response provided by the most highly credentialed reporter and where supportive data were presented. The principle investigator tabulated and graphically presented the data in the same format used in the European Survey.

A preliminary report of the findings was presented at the ESMO Congress in Vienna in September 2012. Between November 2012 and January 2013, the preliminary data was posted on the websites of ESMO, EAPC, and the PPSG. Invitations were sent to all members of the coordinating and collaborating partner organizations to review the data and to submit any corrections or amendments. Amendments were collated, crosschecked, and incorporated into the final report that was completed in May 2013.

## results

One hundred and fifty-six complete reports were submitted from 104 countries and states (Table 3a and b). This figure represents 67% of the target countries and states. On a population basis, the dataset is relevant to 5.03 billion people, which represent 87.3% of the target population consisting of 5.76 billion people.

**Table 3.** Surveyed countries and response rate: (a) by population and (b) by country

(a)	Population (Mil)	Population countries reported	% Population
Africa	1127	744	66
Asia	2612	2515	96
Middle East	436	408	93
Latin America and the Caribbean	595	560	94
Indian States	1189	1061	89
	5757 <sup>a</sup>	5027 <sup>a</sup>	87.30
(b)	No countries or states	Countries reported	% Countries
Africa	52	25	48
Asia	27	20	74
Middle East	21	16	76
Latin America and the Caribbean	33	24	72
Indian States	28	25	89
	155 <sup>a</sup>	104 <sup>a</sup>	67.09

<sup>a</sup>Afghanistan, Algeria, Egypt, Morocco, Libya, and Tunisia are listed in more than one continent.

In the open peer review process after presentation of the preliminary data, feedback was submitted by 49 persons via ESMO and EAPC, and by an additional 10 through the PPSG. Of these, 18 confirmed the veracity of the report for their country or state, and the remainder suggested corrections.

The specific findings relative to each region are presented in the subsequent papers in this supplement of *Annals of Oncology*.

## disclaimers

The information presented in this survey was derived from practicing clinicians working in the field of palliative and/or cancer care and not from state authorities or statutory bodies. In circumstances in which the reporting physicians were unsure of a regulation or formulary issue they were requested to consult with regulatory authorities. The accuracy of the data is dependent on the accuracy of field reporters and their due diligence of verification of facts and regulations with any relevant authority. Field reporters were nominated on the basis of recognized involvement in practice and, in many cases, in leadership of cancer pain management in their country or state. We have no information regarding the extent to which field reporters verified their reporting. Although the methodology incorporated is designed to minimize error, including multiple reporters and crosschecks between reporters, this was not possible for 40 countries and most of the Indian states where submissions were received by a single reporter only. The study leadership considers the relatively small number of corrections submitted after the 60-day open peer review process as an indirect indicator of the integrity of the collated dataset.

The degree to which one specific regulatory restriction on opioid accessibility actually reduces patient access is variable and is influenced by specific procedural requirements and logistic arrangements. The authors also acknowledge that other documented factors besides the regulatory issues highlighted in this report may contribute to the under-treatment of cancer pain. These include the attitudes of patients and their families towards opioid medications, the knowledge and attitudes of the prescriber with respect to opioid use and the management of moderate and severe pain, and the availability and accessibility of other modalities for the treatment of cancer pain, such as radiotherapy.

## discussion

Any national program for the relief of cancer pain must ensure both the availability of opioid medications and a regulatory environment that does not impede accessibility of opioids to patients with medical need. Addressing these issues requires a broad strategy involving policy reform, securing supply, cooperation of regulatory authorities, education of providers and consumers, and the development of a culture, emphasizing the importance of palliative care and pain relief. The data that have been collected and collated in this international collaboration provide valuable insights into common barriers to adequate pain management. This dataset should be used by governments and stakeholders in the fields of palliative care and cancer management as the basis for regulatory and policy

reforms and to initiate essential measures to correct these shortcomings.

This international collaboration is the largest and most comprehensive that has ever been undertaken in the study of opioid availability and accessibility. It involved an unprecedented collection of resources and organizations cooperating together to derive a dataset that is relevant to more than two-thirds of the population of the world. It provides a graphic overview of the extent of the problem in the counties under evaluation that is unparalleled in its scope and detail. The study demonstrated the power of a shared commitment to the importance of pain relief for cancer patients, effective united leadership, highly skilled administrative support, and a strategic research agenda.

Major international efforts are underway to address the pandemic lack of availability and accessibility of opioids for the benefit of cancer patients (and other patients) in pain that affects the majority of the emerging economies and the developing world. The authors applaud recent progress on the global stage through inclusion of a specific target on access to essential medicines for cancer and other non-communicable diseases (NCDs) in the WHO Global NCD Action Plan 2013–2020. In addition, the WHO plan includes a specific indicator on morphine consumption in the associated Global Monitoring Framework (<http://www.who.int/nmh/en/>). Clearly, factors such as economic and social development are contributory; however, pilot projects in Uganda and Vietnam have demonstrated robustly that economic development is not an insurmountable barrier to the routine provision of pain medication for cancer patients suffering with severe pain.

The Global Opioid Policy Initiative (GOPI) members are partnering with other key civil society and intergovernmental agency players in the global efforts that are underway to improve accessibility to opioids for patients with cancer pain. The EAPC, the WHO, and Help the Hospices are key partners in the Access to Opioid Medication in Europe (ATOME) project ([www.atome-project.eu](http://www.atome-project.eu)). The ATOME project is a multiyear collaborative project involving 10 organizations to improve access to opioids across Europe by identifying and removing barriers that prevent people from accessing medicines that could improve end-of-life care, to alleviate debilitating pain, and to treat heroin dependence. It focuses on 12 target countries: Bulgaria, Cyprus, Estonia, Greece, Hungary, Latvia, Lithuania, Poland, Serbia, Slovakia, Slovenia, and Turkey. Based on individual country assessments, ATOME plans to formulate and disseminate tailor-made recommendations to each country for improving the accessibility, availability, and affordability of controlled medicines, and to disseminate these to governments, health care professionals, other key decision-making bodies, as well as to the general public. Early outputs of this initiative include the revision of the WHO publication '*Ensuring balance in national policies on controlled substances: guidance for the availability and accessibility of controlled medicines*' [31]. This revised policy guide has been published in English and 14 other languages.

The 'Global Access to Pain Relief Initiative' (GAPRI) is another major international effort led by the UICC ([www.uicc.org/programmes/gapri](http://www.uicc.org/programmes/gapri)). This ambitious collaborative project

aims to contribute to the World Cancer Declaration target of universal access to essential pain medications by the year 2020. GAPRI will achieve this through synergies between civil society organizations in the field of global and regional advocacy that include both public health and regulatory bodies, national capacity building through workshops, and country-based projects supported by UICC member organizations and partners, in order to embed pain and palliative care services into comprehensive approaches to cancer control. For example, GAPRI is partnering with The Pain and Policy Studies Group at the University of Wisconsin to support and train clinical leaders in tandem with regulatory representatives from the same country through an International Pain Policy Fellowship Program [32]. The graduates of these programs constitute an important part of the local leadership needed to champion the changes identified by this research.

Further, the American Cancer Society's 'Treat the Pain' campaign is implementing projects in Nigeria, Kenya, Uganda, India, and Haiti that are providing 2.8 million additional days of pain treatment.

In addition to these three major multinational programs, critical contributions have been made by the International Palliative Care Initiative of the Open Society Foundation (OSF) led by Kathleen Foley and Mary Callaway ([www.opensocietyfoundations.org](http://www.opensocietyfoundations.org)), the Worldwide Palliative Care Alliance (WPCA) led by Stephen Connor ([www.thewpca.org](http://www.thewpca.org)), the International Association for Hospice and Palliative Care (IAHPC) led by Liliana De Lima (<http://hospicecare.com/home/>), the Human Rights Watch Palliative Care Project led by Diederik Lohman ([www.hrw.org/topic/health/palliative-care](http://www.hrw.org/topic/health/palliative-care)), Help the Hospices ([www.helpthehospices.org.uk](http://www.helpthehospices.org.uk)), and the National Institutes of Health (NIH) through the Center for Global Health of the National Cancer Institute (NCI) ([www.cancer.gov/aboutnci/globalhealth](http://www.cancer.gov/aboutnci/globalhealth)) and the World Health Organization (WHO) ([www.who.int](http://www.who.int)). All these organizations, often working collaboratively and in coordination with local palliative care and oncology organizations, have been deeply involved in projects in Africa, Asia, Eastern Europe, Latin America, and the Middle East.

These international efforts are paying dividends. Through the process of advocacy, education, regulatory reform, and the engagement of suppliers, meaningful progress has been documented in many countries, including Romania, Hungary, the Czech Republic, Serbia, Armenia, Georgia, Columbia, Guatemala, Uganda, Kenya, Vietnam, and most recently, the Ukraine [33–40]. This progress is incremental but real, and it exemplifies the potential for reform through concerted and sustained efforts [32].

The data provided by the GOPI highlight, on a country-by-country basis, issues in formulary inadequacy, problems with cost to consumer and actual availability of medication, and the extent of regulatory barriers that may be impeding accessibility of opioids to patients in need. Beyond the publication of the survey results, the data will be incorporated in targeted advocacy efforts across the membership of the international collaborating partners to achieve a worldwide outreach, aimed at sensitizing key decision-making bodies about the urgent need for policy reform and action at the country level.

## acknowledgements

The authors wish to acknowledge the feedback and input of representatives of the collaborating partner organizations who critically reviewed earlier versions of this manuscript. This study could not have been brought to fruition without the logistic support of Gracemarie Bricalli of ESMO, Heidi Blumhuber, Amelia Giordano, and Silvana Gori of EAPC and the wonderful field reporters (see Appendix 1) who submitted and peer reviewed field reports.

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**appendix 1: field reporters and peer reviewers**

Country	Field reporters and peer reviewers
Afghanistan	Muhammad Shafiq Anonymous
Algeria	Bensalem Assia

*Continued*

**appendix 1. Continued**

Country	Field reporters and peer reviewers
Argentina	Graciela Jacob Gustavo De Simone Maria Viniegra
Bangladesh	Arunangshu Das Rumana Dowla Nezamuddin Ahmad
Barbados	Cheryl Alexis
Belize	Beatriz Maria Thompson
Bhutan	Jampel Tshering
Bolivia	Elizabeth Justiniano
Botswana	Joseph Kasese Howard Moffat
Brazil	Roberto Bettega
Cambodia	Marion Rejeaunier ONG Douleurs Sans Frontieres
Chile	Marisol Ahumada Olea Maritza Velasco
China	Ke Magsar Li Jinxiang Haibo Mou Im Meng Kuoc Beili Gao Yongqin Jiang Qi Mei
China-Hong Kong	Rico Liu
Colombia	Carlos Castro
Costa Rica	Marco Ferrandino Carballo
Côte D'Ivoire	Beugre Kouassi
Dominica	Errol Thomas
Dominican Republic	Gloria Altagracia Castillo Pichardo
Ecuador	Maria Cristina Cervantes
Egypt	Khaled Mostafa Maged El Ansary
El Salvador	Marvin Colorado Castellanos Rolando Arturo Larin Lovo
Ethiopia	Yoseph Mamo
Ghana	Mathew Kyei Beatrice Wiafe Addai Verna Vanderpuye Ama Nkansah
Guatemala	Eva Rossina Duarte Juarez William Campbell Eva Rossina Duarte
Honduras	Tulio Enrique Velasquez Castellanos
India	Abhijit Dam Gladstone D'costa Nagesh Simha Jaichand Singh Mohmad Ashraf Teli
Indonesia	Maria Witjaksono
Iran	Mamak Tahmasebi Maryam Karbasi Motlagh Hadi Zamanian
Iraq	Mazin Al-Jadiry Salma Al-Hadad
Israel	Nathan Cherny Michael Silbermann

*Continued*

## appendix 1. Continued

Country	Field reporters and peer reviewers
Jamaica	Dingle Spence Verna Edwards
Japan	Takashi Higashiguchi Tsatsuya Morita Kazuhiko Koike Yoshiko Asano Hiroshige Yoshioka Yuji Tada Takahiro Tsushima Yasuhiko Yamamura Tetsuya Hamaguchi Kenji Tamura Hidehito Horinouchi Takaaki Tokito Takahiro Mikawa Hideki Ueno Hiroaki Goto Naoto Morikawa Yoshitaka Seki Kyota Oda Nobuyuki Katakami Keisuke Aoe Narikazu Boku Eishi Baba Yoshito Takahashi Kazuhiro Yanagihara Kazuo Tamura Toshinori Kanemura
Kazakhstan	Valentina Sirota
Kenya	Zipporah Ali John Weru Michelle Muhanda Catherine Ajuoga Nicholas Anthony Othieno Abinya
Korea, South	Daegyun Kim
Laos	Keo Phommarat
Lebanon	Michel Daher Hibah Osman
Liberia	Christian Maembe
Libya	Muftah Alshiban
Madagascar	Rakototiana Auberlin Felantsoa Dieu Donna Randrianiaina
Malawi	Jane Bates Lameck Thambo
Malaysia	Hayati Yaakup
Mauritius	Devi Tanooja Hemoo Swaran Bala Poorun
Mexico	Beatriz Montes De Oca
Mongolia	Navchaa Gombodorj Gantuya Tserendorj
Morocco	Mati Nejmi

Continued

## appendix 1. Continued

Country	Field reporters and peer reviewers
Mozambique	Tawfiq Nezha Madalena Oliveira-Dias
Myanmar	Kyaw Min Htay Aung
Namibia	Chris Ntege
Nepal	Bishnu Dutta Paudel
Nigeria	Emmanuel Ezeome Simbo Daisy Amanor-Boadu Adeniyii Adenipekun Tonia Onyeka
Oman	Essam Abdul Monem
Pakistan	Syed Ahmer Hamid
Palestine	Hani Ayyash Amal Dweib Khleif
Panama	Rosa Buitrago Del Rosal Carlina Santana
Paraguay	Roberto Reichert Duarte
Peru	Maria Del Rosario Berenguel Cook Fernando Alberto Calderon-Higginson
Philippines	Rhodora Ocampo Agnes Bausa-Claudio Maria Fidelis Manalo
Qatar	Azza Hassan
Rwanda	Grace Mukankuranga
Saudi Arabia	Margaret Robinson Waleed Bokhari
Sierra Leone	Gabriel Madiye
South Africa	Daniel Vorobiof Sarah Fakroodeen Charmaine Blanchard
Sri Lanka	Prasad Abeysinghe Allison Jean David Bristol
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Tanzania	Paul Z. Mmbando Twalib A. Ngoma
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Trinidad & Tobago	Pat Stollmeyer
Tunisia	Rais Henda
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Vietnam	Yen Nguyen
Yemen	Munef Mohammed Saleh Ali
Zimbabwe	Stephen Williams Anna Mary Nyakabau

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

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With nearly 1.1 billion inhabitants living in more than 50 countries, Africa is the world's poorest and most socioeconomically underdeveloped continent. Despite some advances for individual states, many African countries have very low opioid consumption and, overall, the continent has the lowest consumption per capita of any in the world. This article presents the findings of the first systematic study of the availability and accessibility of opioids for the management of cancer pain across the continent. Data are reported on the availability and accessibility of opioids for the management of cancer pain in 25 of 52 countries, with 744 million of the region's 1127 million people (66%) covered by the survey. Many countries had severely restricted formularies of opioids and only 15 of 25 had morphine available in oral IR, CR and injectable formulations. Even when opioids are on formulary they are often unavailable, and access is significantly impaired by widespread over-regulation that is pervasive across the region.

## introduction

With nearly 1.1 billion inhabitants living in more than 50 countries, Africa is the world's poorest and most socioeconomically underdeveloped continent. Despite the relatively young demographic profile of the population of Africa, cancer is an emerging public health problem [1]. In 2008, there were 715 000 new cases and 542 000 cancer deaths in Africa, projected to nearly double (1.28 million new cases and 970 000 deaths) by 2030 due to population growth and aging [2]. Not only do the cancer incidence and mortality patterns vary remarkably across the region [1], 36% of cancers are infection-related, twice the global average [3].

Despite advances over the last decade, including an increased number of service providers [4], provision of palliative care on the continent remains inconsistent—especially in rural areas [5, 6]—primarily provided from isolated centers among nongovernmental faith- and secular-based community agencies with restricted geographic and population coverage and minimal in-built sustainability, rather than being integrated into mainstream healthcare structures. In 2011, only four African countries had palliative care integrated into either their health or cancer strategic plans (Kenya, South Africa, Tanzania and

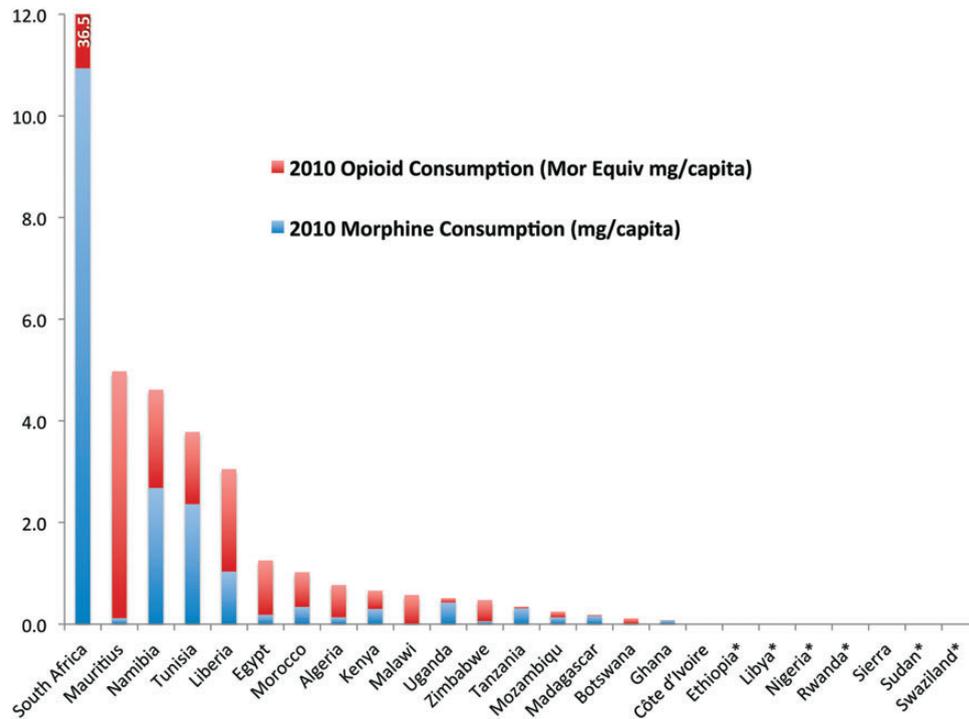
Uganda), and only two (Rwanda and Swaziland) had developed stand-alone national palliative care policies [7]. Additionally, only five countries have palliative care integrated in the training curriculum of health professionals, of which only four (Kenya, Malawi, South Africa and Uganda) have recognized palliative care as an examinable subject, resulting in a significant skills training deficit [7]. These challenges are exacerbated by poor health and social care infrastructures and inadequate health financing in many countries on the continent.

Moreover, in multiple African countries, access to even the simplest pain-relieving medication is limited, while strong painkillers—e.g. opioids—are legally restricted. Widespread deficiencies in the supply chain [8] are compounded by a lack of pharmacists in public health services and widespread restriction of prescriptive authority [9].

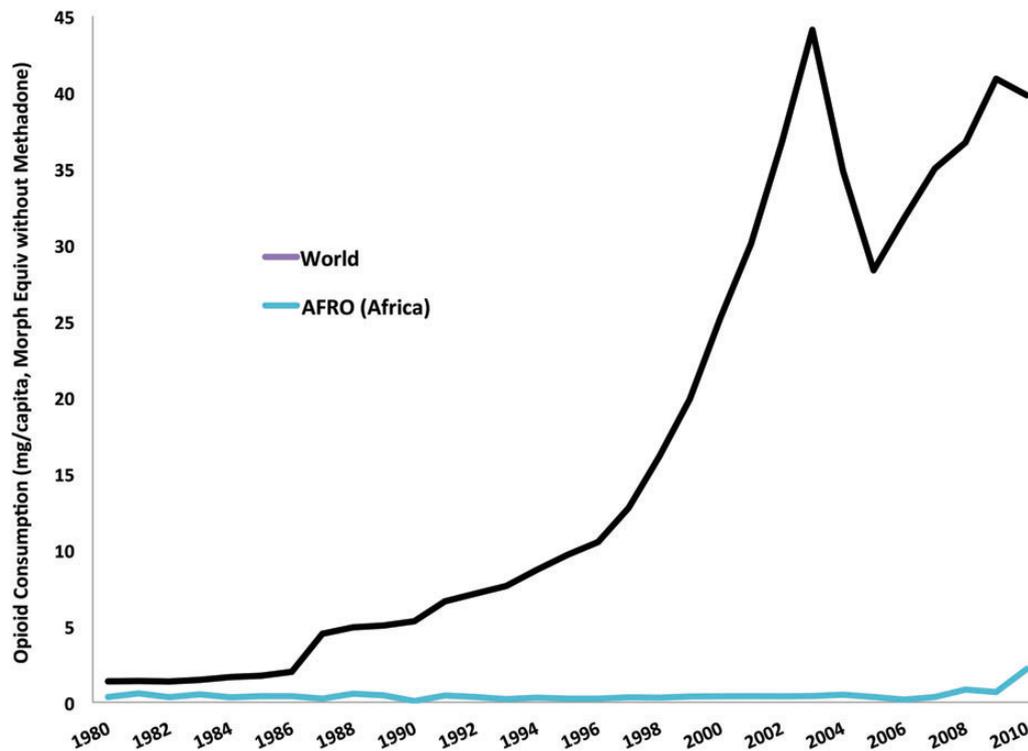
Additionally, and despite some advances for individual states, many African countries have very low opioid consumption (Figure 1); overall, the continent has the lowest consumption per capita of any in the world [10]. While global opioid consumption has increased throughout the last 30 years, there has been negligible increase in opioid consumption in Africa (Figure 2), and especially minimal increase in morphine. The lack of opioids has been particularly challenging in the face of the HIV/AIDS epidemic in Africa—with sub-Saharan Africa accounting for 69% of the global disease burden in 2011 [11]—and the increasing burden faced from non-communicable diseases, especially cancer.

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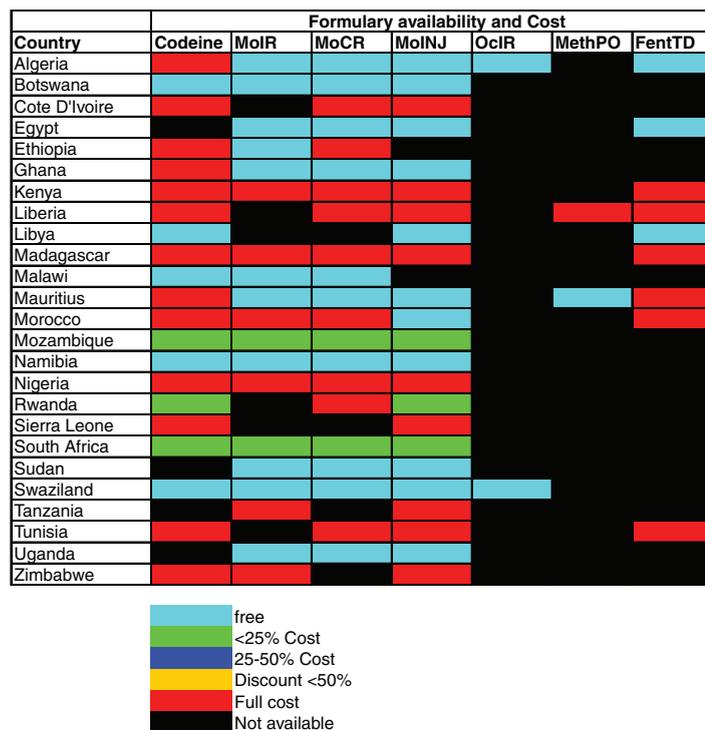
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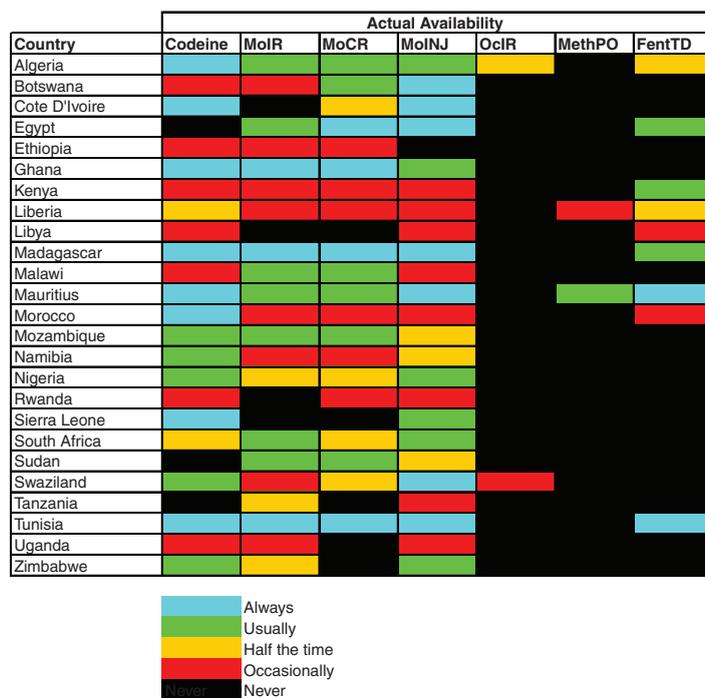
**Figure 1.** Rank order of 2010 opioid consumption (mg/capita in morphine equivalence without methadone) for surveyed African countries.



**Figure 2.** Comparison of opioid consumption (mg/capita in morphine equivalence without methadone) between the World and the WHO African Region (AFRO) from 1980 to 2010.



**Figure 3.** Formulary availability and cost to patients of the seven essential opioid formulations of the International Association for Hospice and Palliative Care (IAHPC) in African 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.



**Figure 4.** Actual availability of the seven essential opioid formulations of the IAHPC in African 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.

Country	Eligibility Restriction		
	Outpatients	Inpatients	Hospice
Algeria			
Botswana			
Cote D'Ivoire			
Egypt			
Ethiopia			
Ghana			
Kenya			
Liberia			
Libya			
Madagascar			
Malawi			
Mauritius			
Morocco			
Mozambique			
Namibia			
Nigeria			
Rwanda			
Sierra Leone			
South Africa			
Sudan			
Swaziland			
Tanzania			
Tunisia			
Uganda			
Zimbabwe			

	Always
	Only with special authorization
	Never
	No submitted data

Figure 5. Eligibility restrictions for cancer patients in African countries.

The impact of this inaccessibility was demonstrated among over 500 patients attending HIV clinics in rural and urban areas of South Africa [12]. Approximately 40% of patients had moderate-to-severe pain during interviews and pharmacological pain management was poor, with 29% of rural and 55% of metropolitan participants in pain not receiving any treatment. No HIV patients were receiving strong opioids, and only 3% of metropolitan participants were receiving a weak opioid.

The benefits of effective pain management were shown in a study of 182 patients in severe pain, with the most common cancer diagnoses being breast and uterine cervix, attending a Nigerian radiotherapy clinic [13]. From a pretreatment pain intensity score mean of 8.09 on a 0–10 scale, following access to oral morphine elixir [immediate release (IR) form] almost 85% achieved a 3-point reduction in intensity after 1 week's treatment, which was maintained throughout a 3-month follow-up period.

To date, however, there has been no systematic study of the availability and accessibility of opioids for the management of cancer pain across the continent.

**methods**

See Cherny et al. [14].

Country	Prescriber privileges				
	Oncologist	FamilyDoc	Surgeon	Nurse	Pharmacist
Algeria					
Botswana					
Cote D'Ivoire					
Egypt					
Ethiopia					
Ghana					
Kenya					
Liberia					
Libya					
Madagascar					
Malawi					
Mauritius					
Morocco					
Mozambique					
Namibia					
Nigeria					
Rwanda					
Sierra Leone					
South Africa					
Sudan					
Swaziland					
Tanzania					
Tunisia					
Uganda					
Zimbabwe					

	Always
	Only with special permit or authorization
	Only in emergency
	Never

Figure 6. Opioid prescriber privileges for cancer patients in African countries.

**results**

Data is reported on the availability and accessibility of opioids for the management of cancer pain in 25/52 African countries, representing 744 million of the region’s 1,127 million people (66%). Algeria, Egypt, Libya, Morocco and Tunisia are presented here and in the Middle East report [15].

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

The availability of opioids and their cost to consumers are summarized in Figure 3 and show minimal variability throughout the region. Codeine and morphine were the primary medicines on formulary. No country had all seven essential opioids available, and only three North African countries (Algeria, Mauritius and Morocco) had six of the seven opioids available. While six countries (Côte d’Ivoire, Liberia, Libya, Rwanda, Sierra Leone and Tunisia) reported no oral immediate release (IR) morphine, four had no controlled release (CR) morphine (Libya, Sierra Leone, Tanzania and Zimbabwe), and two had no injectable morphine (Ethiopia and Malawi). Only fifteen countries had oral IR, oral CR and injectable morphine

available. Transdermal (TD) fentanyl was on formulary in six countries, while IR oxycodone and oral methadone were only available in two countries. Sierra Leone and Tanzania had the most limited formulary, with only two medications on formulary. Libya had codeine, injectable morphine and TD fentanyl available.

In approximately half the countries, the medicines were free. Otherwise the full cost of medications was borne by patients with a few exceptions, where a payment of <25% of the medication cost was charged.

Availability of these formulations for a patient presenting with a valid prescription (Figure 4) was very inconsistent and in 10 countries (Botswana, Ethiopia, Kenya, Liberia, Malawi, Morocco, Namibia, Rwanda, Swaziland and Uganda) several of the medications on formulary were only occasionally available. Only three countries (Ghana, Madagascar and Tunisia) had IR morphine always available.

**regulatory restrictions to accessibility**

Countries used a range of regulatory restrictions to limit accessibility of opioids. Most countries had considerable restrictions to the accessibility of opioids as described below and as summarized in Figure 12.

Prescription forms				
Country	Duplicate or Triplicate	Special Prescr Forms	ready access to forms	Pay for forms
Algeria	restrictive	restrictive	restrictive	restrictive
Botswana	restrictive	restrictive	restrictive	restrictive
Cote D'Ivoire	restrictive	restrictive	restrictive	restrictive
Egypt	restrictive	restrictive	restrictive	restrictive
Ethiopia	restrictive	restrictive	restrictive	restrictive
Ghana	not restrictive	not restrictive	not restrictive	not restrictive
Kenya	restrictive	restrictive	restrictive	restrictive
Liberia	not restrictive	not restrictive	not restrictive	not restrictive
Libya	restrictive	restrictive	restrictive	restrictive
Madagascar	restrictive	restrictive	restrictive	restrictive
Malawi	restrictive	restrictive	restrictive	restrictive
Mauritius	restrictive	restrictive	restrictive	restrictive
Morocco	not restrictive	not restrictive	not restrictive	not restrictive
Mozambique	restrictive	not restrictive	restrictive	restrictive
Namibia	restrictive	restrictive	restrictive	restrictive
Nigeria	restrictive	not restrictive	restrictive	restrictive
Rwanda	restrictive	not restrictive	restrictive	restrictive
Sierra Leone	not restrictive	restrictive	restrictive	restrictive
South Africa	not restrictive	not restrictive	not restrictive	not restrictive
Sudan	not restrictive	restrictive	restrictive	restrictive
Swaziland	restrictive	not restrictive	restrictive	restrictive
Tanzania	restrictive	restrictive	restrictive	restrictive
Tunisia	restrictive	restrictive	restrictive	restrictive
Uganda	restrictive	not restrictive	restrictive	restrictive
Zimbabwe	not restrictive	restrictive	restrictive	restrictive

	restrictive
	not restrictive
	Not relevant

**Figure 7.** Prescription restrictions in African countries.

Country	Max Days Opioids Supplied
Algeria	30
Botswana	30
Côte d'Ivoire	7
Egypt	14
Ethiopia	Physician discretion
Ghana	2
Kenya	14
Liberia	7
Libya	7
Madagascar	7
Malawi	14
Mauritius	10
Morocco	7
Mozambique	30
Namibia	
Nigeria	30
Rwanda	
Sierra Leone	Physician discretion
South Africa	30
Sudan	15
Swaziland	30
Tanzania	10
Tunisia	28
Uganda	30
Zimbabwe	30

	28+ days
	15-28 days
	1-2 weeks
	< 1 week
	No submitted data

**Figure 8.** Maximum number of days opioid supplied on single prescription.

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

The majority of countries (16 of 25) required special authorization for outpatients, 15 of 25 for inpatients and 11 of 21 for hospice patients (Figure 5). There were no restrictions on cancer patient eligibility in six countries (Côte d'Ivoire, Malawi, Mauritius, Nigeria, Tanzania and Zimbabwe).

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

Overall, African countries had few restrictions limiting physician prescribing (Figure 6). Three countries (Egypt, Liberia and Morocco) required a special permit even for oncologists, also requiring similar authority for family doctors and surgeons. Algeria, Libya and Mauritius limited prescribing to family doctors and surgeons in emergencies. Seven countries allowed nurse prescribing—four with special permit or authorization—

and six countries allowed pharmacist prescribing with special authorization or in emergencies.

#### requirement for duplicate prescriptions and special prescription forms

Most countries had restrictive laws for opioid prescription writing (15 of 25), with special prescription forms needed in 16 of 25. In most countries in which such forms were required there were problems in readily accessing them (Figure 7). In Mauritius, Morocco, Sierra Leone and Tunisia, physicians must pay for prescription forms.

#### prescription limits

Ten countries do not allow physicians to prescribe an amount of opioid analgesics to a patient for more than 2 weeks at a time (Figure 8). These limits ranged from 2 days in Ghana, to a week in Côte d'Ivoire, Liberia, Libya, Madagascar and Morocco, to 10 days in Mauritius and Tanzania and 2 weeks in Egypt, Kenya and Malawi.

#### limitations on dispensing privileges

In 11 of 25 African countries, opioids are dispensed at hospital pharmacies, with few local pharmacies being able to dispense (Figure 9). The ability to access pharmacies was limited in all but six countries. Major problems in accessing the dispensing pharmacies were reported in many countries, including Algeria, Botswana, Côte d'Ivoire, Ethiopia, Ghana, Kenya, Liberia, Malawi, Morocco, Mozambique, Namibia, Rwanda, Sudan, Tanzania, Uganda and Zimbabwe.

#### provision for opioid prescribing in emergency situations

An emergency situation is defined as one where there is an immediate need to relieve strong pain but where the physician is unable to physically provide a prescription (e.g. a pain crisis at night, on a public holiday or in a remote region). Only Botswana, Namibia and South Africa allowed faxing/calling of emergency situation prescriptions (Figure 10).

#### pharmacist privileges to correct a technical error on a prescription

In the situation of a patient presenting with a prescription that contains a technical error (e.g., no address, misspelling, missing value), in 12/25 countries the pharmacist had no discretionary authority to correct or accept the prescription.

#### use of stigmatizing terminology for opioid analgesics in regulations

The majority of African countries have negative language in drug laws, while 40% of countries precluded patients taking opioids from driving even if they have no cognitive or attention impairment (Figure 11).

## discussion

Cancer continues to be an increasing problem throughout the world, with an increase in cancer incidence in low- and middle-



Figure 9. Dispensing pharmacy sites and their accessibility for African countries.

income countries. Many adult patients in Africa present with advanced disease, with significant pain associated with late presentations.

Opioid consumption has been documented in various formats for Africa [16–18]. While many countries show an increase in consumption since 2000, all African countries had very low consumption levels, as defined by the INCB, with a S-defined daily dose (DDD) of <200 mg/day/100 000 people [16]. Indeed, all of the surveyed countries in Africa have <10% of the anticipated Adequacy of Consumption Measure (ACM) for opioids (Table 1).

This is in marked contrast to the approach to improving opioid consumption described in the World Health Organization (WHO) policy guidelines, *Ensuring Balance in National Policies on Controlled Substances, Guidance for availability and accessibility of controlled medicines* [19]. Moreover, the enhanced 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.

**medication availability**

The majority of African countries surveyed had limited access to the essential opioids outlined by the IAHPC [20]. Codeine and

morphine are clearly the primary medicines used in the region but consumption evidence indicates they are used very infrequently (Figure 2).

Harding et al. [21] investigated the challenges to opioid availability when they examined 62 HIV treatment facilities from multiple locations in Kenya, Nigeria, South Africa, Tanzania, Uganda and Zambia and single institutions in Botswana, Cote d'Ivoire, Ethiopia, Mozambique, Namibia and Rwanda. Thirty-six of the 62 sites were dispensing opioids, primarily in the liquid form. While WHO Pain Relief Ladder Step I (non-opioid) and II analgesics were available 100% of the time, only 28 of 62 facilities had a Step III analgesic available 100% of the time. Moreover, despite the overall very low consumption data in their countries, most of the reporting Competent National Authority representatives interviewed were satisfied with the functioning of the current regulatory system. The authorities were skeptical as to their ability to adequately regulate and monitor increased numbers of providers in every country. Furthermore, these authorities cited specific opioids they believed to be available that were never reported by any facility within the respective country.

A further study of 120 health facilities in Kenya and Uganda [22] showed only 7% of facilities had access to morphine. Importantly, only 1 of 14 referral hospitals had morphine and 2

Country	Pharmacist restrictions	
	Pharmacists accept emergency telephone/fax prescriptions	Pharmacists may correct tech errors
Algeria	Yes	Yes
Botswana	Yes	Yes
Cote D'Ivoire	Yes	Yes
Egypt	Yes	Yes
Ethiopia	Yes	Yes
Ghana	Yes	Yes
Kenya	Yes	Yes
Liberia	Yes	Yes
Libya	Yes	Yes
Madagascar	Yes	Yes
Malawi	Yes	Yes
Mauritius	Yes	Yes
Morocco	Yes	Yes
Mozambique	Yes	Yes
Namibia	Yes	Yes
Nigeria	Yes	Yes
Rwanda	Yes	Yes
Sierra Leone	Yes	Yes
South Africa	Yes	Yes
Sudan	Yes	Yes
Swaziland	Yes	Yes
Tanzania	Yes	Yes
Tunisia	Yes	Yes
Uganda	Yes	Yes
Zimbabwe	Yes	Yes

Yes
  No
  No submitted data

**Figure 10.** Pharmacy restrictions for African countries.

of 19 district hospitals. It was also found far more common for those facilities stocking opioids to have 'stock-outs' (i.e. no medicines available) than it was to have expired medications. Among the African nations, Uganda is the example most widely applauded for improved availability of morphine [23]. However, even in Uganda there has been major difficulty in ensuring the availability of morphine. Systems of ensuring availability need to be identified and implemented.

### education

There is a substantial need to educate both patients and clinicians in Africa regarding the role of opioids in cancer pain. Only 50% of surveyed health workers in Rwanda could define palliative care accurately [24]. The prescribing pattern of doctors in an 850-bedded tertiary institution pioneering oral morphine in Nigeria was essentially limited to radiation oncologists (50%) and those working in a new hospice day care (30%); oral opioids were not prescribed by general medicine physicians in the hospital [25]. A further study in Nigeria evaluated the knowledge of cancer pain management among teaching hospital physicians [26], and found 90% had no formal education on the topic. Only 20% used strong opioids and only

Country	Laws	
	Negative language in drug laws	Driving forbidden
Algeria	Yes	Yes
Botswana	Yes	Yes
Cote D'Ivoire	Yes	Yes
Egypt	Yes	Yes
Ethiopia	Yes	Yes
Ghana	Yes	Yes
Kenya	Yes	Yes
Liberia	Yes	Yes
Libya	Yes	Yes
Madagascar	Yes	Yes
Malawi	Yes	Yes
Mauritius	Yes	Yes
Morocco	Yes	Yes
Mozambique	Yes	Yes
Namibia	Yes	Yes
Nigeria	Yes	Yes
Rwanda	Yes	Yes
Sierra Leone	Yes	Yes
South Africa	Yes	Yes
Sudan	Yes	Yes
Swaziland	Yes	Yes
Tanzania	Yes	Yes
Tunisia	Yes	Yes
Uganda	Yes	Yes
Zimbabwe	Yes	Yes

No
  Yes
  No submitted data

**Figure 11.** Negative laws regarding opioids in African countries.

50% would consider using opioids even if patients reported strong cancer pain.

The Namibian public appears aware of the natural history of cancer, with a quarter fearing pain as the most concerning symptom with advanced cancer [27]. However, a study in Ghana highlighted the problems of patient reluctance to use opioids, either because of an exaggerated fear of patient dependency or the implication that the use of opioids implied death was very near [28]. Studies conducted by the WHO have also demonstrated that negative attitudes and fears regarding opioid use are widespread in Africa [29].

### government policies and regulations

WHO palliative care projects in Africa have initiated workshops to change opioid prescribing policies in Eastern, Southern and Western Africa [30]. These workshops, conducted with the African Palliative Care Association, have addressed the knowledge base of opioid availability policies, evaluating country-specific policies and legislation on opioid availability and developing advocacy action plans to facilitate accessibility to, and availability of, opioids.

National governments across the continent are starting to recognize the dire need to include palliative care in their health

**Table 1.** Comparison of S-DDD and %ACM [16–18]

	S-DDD <sup>a</sup> (1997–1999)	%ACM (2006)	S-DDD (2007–2009)	%ACM (2010)
Algeria	60	0.33	162	0.63
Botswana	40	0.44	21	0.07
Côte d'Ivoire	1	0.01	2	0.01
Egypt	45	0.76	49	1.29
Ethiopia	0	0.01	2	ND
Ghana	ND	1.42	15	0.04
Kenya	5	0.48	16	0.42
Liberia	ND	ND	ND	ND
Libya	10	4.85	86	2.43
Madagascar	0	0.03	13	0.09
Malawi	4	0	13	0.44
Mauritius	40	5.8	75	ND
Morocco	20	0.54	33	0.82
Mozambique	1	0.04	7	0.07
Namibia	75	0.19	57	1.81
Nigeria	0	ND	<1	ND
Rwanda	3	0.01	<1	ND
Sierra Leone	12	ND	2	ND
South Africa	460	0.76	600	4.69
Sudan	ND	0.13	1	ND
Swaziland	ND	ND	ND	ND
Tanzania	4	ND	<1	0.14
Tunisia	60	3.46	123	1.64
Uganda	5	0.19	19	0.18
Zimbabwe	50	ND	18	0.19

<sup>a</sup>Calculated from INCB graphs [16].

S-DDD, defined daily doses consumed per million inhabitants per day [16]; ACM, Adequacy of Consumption Measure [17, 18].

care plans and budgets. For example, in October 2012 in Addis Ababa, Ethiopia, the African Union issued a common position statement on controlled substances and access to pain management medicines [31]. Subsequently, in September 2013, at the 4th conference of the African Palliative Care Association, delegations from the Ministries of Health of 17 African countries issued a consensus statement on the integration of palliative care into healthcare systems. These are most promising initiatives that will hopefully provide sufficient political momentum to improve the status quo, so patients suffering with cancer pain will be able to access opioids in all African countries.

Further strategies for improvement arising from this study are outlined 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 [32].

### conclusion

Opioid availability continues to be critically low in most African countries. This is a humanitarian crisis that will need concerted efforts involving suppliers, regulators, medical and public educators, palliative care and oncology organizations and, given the poverty in the region, philanthropic bodies. Governments and their Competent Authorities need to work with international bodies and NGOs to bring about improved access to opioids as essential medicines for the relief of suffering across Africa.

### funding

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Country	Eligibility Restriction	Physician Precrifer Restrictions	No emergency prescriptions by Fx/Phone or non medical prescribing	Limited prescription duration	No pharmacist authority to correct prescription	Increase bureaucratic burden of prescriptions	Restricted dispensing sites	Negative language in laws	Number of restrictive domains (N/8)
Botswana							Yes	Yes	2
Namibia						Yes	Yes		2
South Africa	Yes				Yes				2
Ethiopia	Yes					Yes		Yes	3
Zimbabwe			Yes			Yes		Yes	3
Swaziland	Yes		Yes			Yes			3
Malawi				Yes		Yes	Yes	Yes	4
Mozambique			Yes		Yes	Yes	Yes		4
Nigeria			Yes			Yes	Yes	Yes	4
Uganda	Yes					Yes	Yes	Yes	4
Tunisia	Yes		Yes		Yes	Yes			4
Algeria	Yes	Yes	Yes			Yes	Yes		5
Cote D'Ivoire			Yes	Yes	Yes	Yes	Yes	Yes	5
Ghana	Yes			Yes	Yes	Yes	Yes	Yes	5
Kenya	Yes			Yes	Yes	Yes		Yes	5
Liberia	Yes	Yes	Yes	Yes		Yes	Yes		5
Sudan	Yes	Yes				Yes	Yes	Yes	5
Tanzania				Yes	Yes	Yes	Yes	Yes	5
Libya	Yes	Yes	Yes	Yes		Yes	Yes		6
Madagascar	Yes	Yes		Yes	Yes	Yes	Yes		6
Morocco	Yes	Yes	Yes	Yes		Yes	Yes		6
Rwanda	Yes	Yes	Yes		Yes	Yes		Yes	6
Sierra Leone	Yes	Yes			Yes	Yes	Yes	Yes	6
Egypt	Yes	Yes	Yes	Yes	Yes	Yes	Yes		7
Mauritius		Yes	Yes	Yes	Yes	Yes	Yes	Yes	7

**Figure 12.** Summary for African countries of regulatory barriers to opioid access for cancer pain relief.

**disclosure**

The authors have declared no conflicts of interest.

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

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Asia is a heterogeneous region with substantial variability in economic, social and palliative care development. While the global consumption of opioids has increased, the consumption in most Asian countries has not increased at the same rate. This is the first comprehensive study of opioid availability and accessibility for cancer patients in Asia. Data are reported on the availability and accessibility of opioids for the management of cancer pain in 20 of 28 countries. The countries in the report represent 2515 million of the region's 2612 million people (96%). With the exception of Japan and South Korea, opioid availability continues to be low throughout most of Asia. Formulary deficiencies are severe in several countries, in particular Bangladesh, Myanmar, Afghanistan, Kazakhstan and Laos. Even when opioids are on formulary, they are often unavailable, particularly in the same countries. Access is significantly impaired by widespread over-regulation that continues to be pervasive across the region.

## Introduction

Asia is a heterogeneous region with substantial variability in economic, social and palliative care development. The region has diverse governance within its nations and is of diverse cultural origins and religious affiliations. Some of the region's countries have undergone significant political and social change over the last two decades. Palliative care provision is at varied stages of development throughout the region [1]. 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 formed from historical experiences with opioids.

Asia carries a disproportionate part of the global burden of liver, esophageal and stomach cancer; with 50–70% of new cases worldwide occurring in Asia [2]. The incidence of lung and breast cancers is rising dramatically. The majority of patients with cancer are diagnosed with advanced-stage disease, and often the only realistic treatment options are pain relief and palliative care. Registry data from the region indicate that the regional burden of cancer continues to increase largely because of an aging and growing local population coupled with an increasing adoption of cancer-causing behaviors, particularly smoking.

Palliative care services throughout the region vary in their development. Singapore, and China-Hong Kong have very

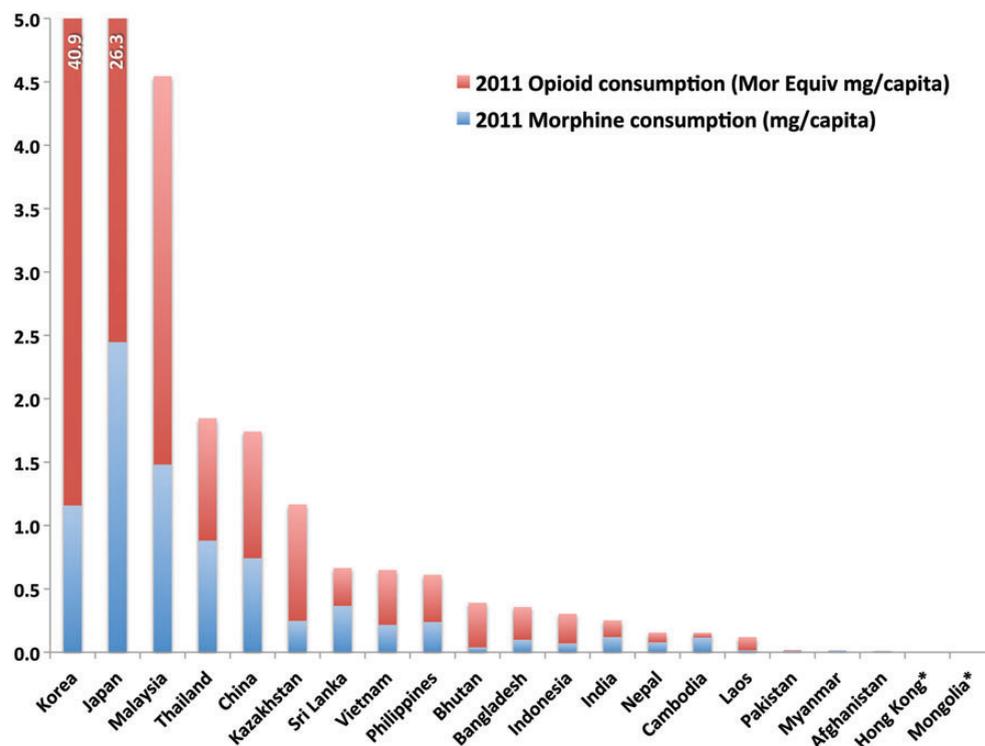
developed palliative care programs and have been rated highly in global surveys [3]. Other countries such as Afghanistan, Pakistan, Laos and Cambodia have poorly developed palliative care [1]. But even in some of those nations with well-developed palliative care, opioid consumption has often remained low (Figure 1).

While the global consumption of opioids has increased, the consumption in most Asian countries has not increased at the same rate. The area included in this report includes countries from two World Health Organization (WHO) regions namely the South East Asian Regional Organization (SEARO) and the Western Pacific Region Organization (WPRO). The morphine consumption in each region is compared with the increase in global consumption over the last 30 years (Figure 2). The WPRO increase has largely been due to an increase in opioid consumption in Australia, Japan and South Korea. There has been little increase in opioid consumption in SEARO, a region that includes India, which is considered independently in another report in this supplement [4].

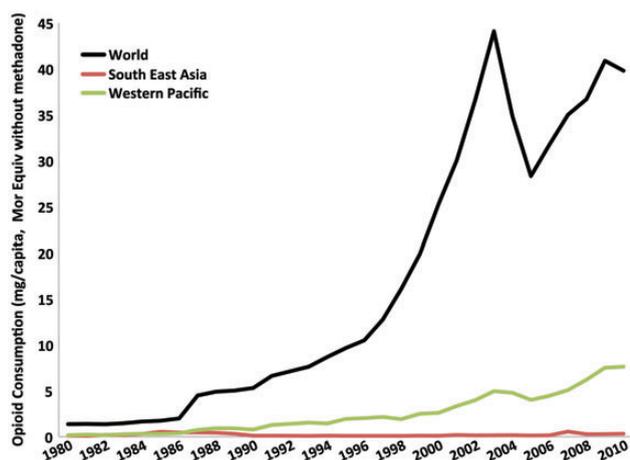
The Asian Pacific Hospice and Palliative Care Network (APHN) has been active in the region with growth in palliative care in some of the regions of middle- and high-income countries. AHPN and the International Association for the Study of Pain have been working to start national palliative care associations and pain chapters within low-income countries of the region. But many impediments remain throughout the region in making opioids available to cancer patients.

This is the first comprehensive study of opioid availability and accessibility for cancer patients in Asia.

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**Figure 1.** Rank order of opioid consumption (mg/capita in morphine equivalence without methadone) for surveyed Asian countries. Countries marked with \* did not report.



**Figure 2.** Comparison of opioid consumption (mg/capita in morphine equivalence without methadone) between the World, WHO South East Asia Region (SEARO), and WHO Western Pacific Region (WPRO) from 1980–2010.

## methodology

Asia is defined for the purposes of these studies as countries extending from Japan in the East to Pakistan in the West, and from Mongolia and Kazakhstan in the North to Indonesia in South. Representatives from 20 countries submitted reports: Afghanistan, Bangladesh, Bhutan, Cambodia, China, China-Hong Kong, Indonesia, Japan, Kazakhstan, The Republic of Korea (South Korea), Laos, Malaysia, Mongolia, Myanmar, Nepal, Pakistan, Philippines, Sri Lanka, Thailand and Vietnam (see Cherny et al. [5]).

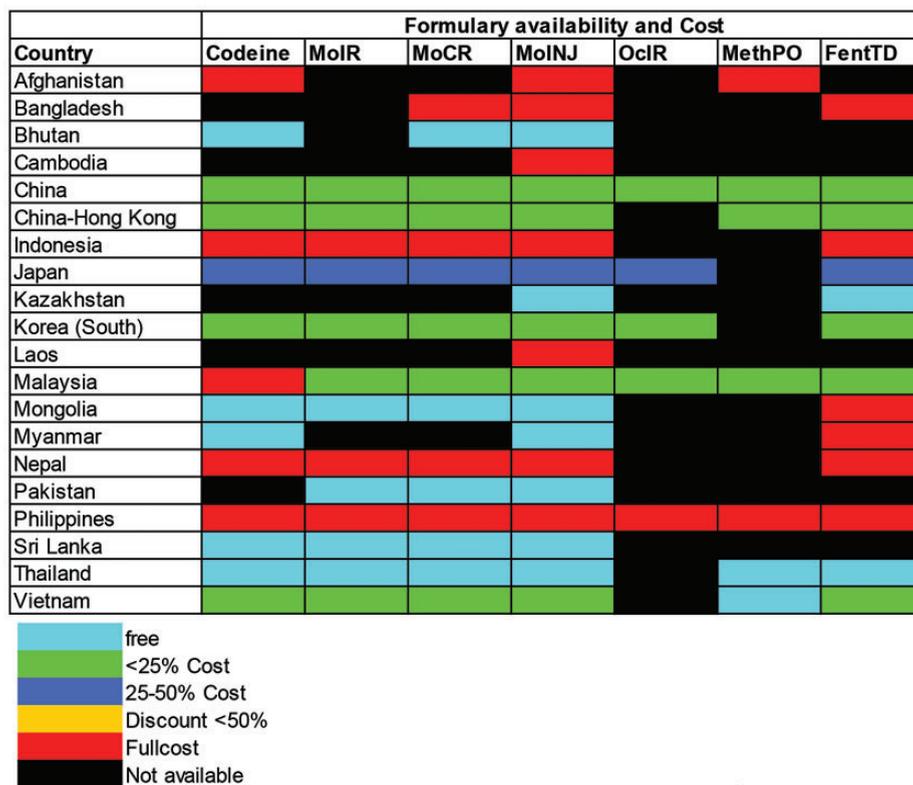
## results

Data are reported on the availability and accessibility of opioids for the management of cancer pain in 20 of 28 countries. No data were submitted from Brunei, Maldives, Mongolia, Singapore, Taiwan, Tajikistan, Turkmenistan and Uzbekistan. The countries in the report represent 2515 million of the region's 2612 million people (96%). Afghanistan is also presented with the Middle East [6], and India is included in a separate paper [4].

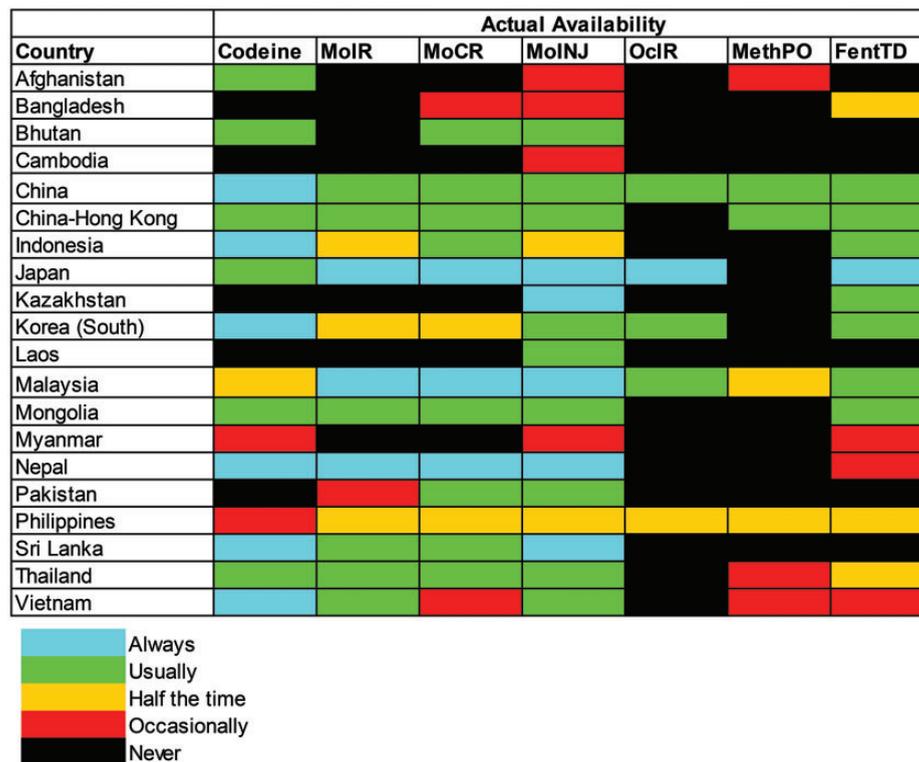
## formulary availability and cost of opioids for cancer pain

The availability of opioids and their cost to consumers are summarized in Figure 3 and show great variability throughout the region. Codeine and Morphine were the mostly commonly available formulations. China, Malaysia and the Philippines had all seven medicine formulations available, while five other countries (China-Hong Kong, Japan, South Korea, Thailand and Vietnam) had six of the seven formulations. Cambodia and Laos only had access to injectable morphine, while Kazakhstan had access to only injectable morphine and transdermal (TD) fentanyl. Seven countries (Afghanistan, Bangladesh, Bhutan, Cambodia, Kazakhstan and Laos) did not have oral immediate release (IR) morphine available. Five countries only had access to three formulations (Afghanistan, Bangladesh, Bhutan, Myanmar and Pakistan). Oxycodone IR was available in five countries, and methadone was available in seven countries. Fourteen of 20 countries had access to TD fentanyl.

In approximately half of the countries (11 of 20), the medicines were provided to patients at no cost or <25% of the



**Figure 3.** Formulary availability and cost to patients of the seven essential opioid formulations of the International Association for Hospice and Palliative Care (IAHPC) in Asian 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.



**Figure 4.** Actual availability of the seven essential opioid formulations of the IAHPC in Asian 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.

cost. Patients paid full cost of all medications in Bangladesh, Cambodia, Indonesia, Laos, Nepal and the Philippines.

Most formulations were reported available 'always' and 'usually' (Figure 4). However, Pakistan reported only occasional IR morphine, while Afghanistan, Bangladesh, Cambodia and Myanmar reported only occasional access for those opioid formulations on formulary.

Country	Eligibility Restriction		
	Outpatients	Inpatients	Hospice
Afghanistan	Always	Always	Always
Bangladesh	Always	Always	Always
Bhutan	Always	Always	Always
Cambodia	Always	Always	Always
China	Always	Always	Always
China-Hong Kong	Always	Always	Always
Indonesia	Always	Always	Always
Japan	Always	Always	Always
Kazakhstan	Always	Always	Always
Korea (South)	Always	Always	Always
Laos	Always	Always	Never
Malaysia	Always	Always	Always
Mongolia	Always	Always	Always
Myanmar	Always	Always	Always
Nepal	Always	Always	Always
Pakistan	Always	Always	Always
Philippines	Always	Always	Always
Sri Lanka	Always	Always	Always
Thailand	Always	Always	Always
Vietnam	Always	Always	Never

Always  
 Only with special authorization  
 Never

Figure 5. Eligibility restrictions for cancer patients in Asian countries.

**regulatory restrictions to accessibility**

Countries used a range of regulatory restrictions to limit accessibility of opioids. Most countries had considerable restriction and these are detailed below and summarised in Table 12.

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

Nine of the twenty countries have no patient restrictions. Six countries (Afghanistan, Bangladesh, Kazakhstan, Myanmar, Pakistan and the Philippines) required registration for all three patient categories (i.e., outpatients, inpatients and hospice patients). In China and Vietnam special authority or registration was required only for outpatients, Mongolia required registration for both outpatients and hospice patients (Figure 5).

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

All physicians are permitted to prescribe opioids in Afghanistan, Bhutan, Cambodia, China-Hong Kong, Indonesia, Japan, Korea, Malaysia, Nepal, Sri Lanka and Thailand. The remaining countries require special authorization for at least one physician group. Bangladesh only allows family doctors to write prescriptions in an emergency situation, while the same applies for surgeons in Mongolia. China does not allow family doctors to prescribe opioids. Nurses are allowed to prescribe with special authority in Bhutan and the Philippines, and in

Country	Prescriber privileges				
	Oncologist	Family Doc	Surgeon	Nurse	Pharmacist
Afghanistan	Always	Always	Always	Always	Always
Bangladesh	Always	Only in emergency	Always	Always	Always
Bhutan	Always	Always	Always	Only with special permit or authorization	Always
Cambodia	Always	Always	Always	Always	Always
China	Always	Never	Only with special permit or authorization	Always	Always
China-Hong Kong	Always	Always	Always	Always	Always
Indonesia	Always	Always	Always	Always	Always
Japan	Always	Always	Always	Always	Always
Kazakhstan	Always	Always	Always	Always	Always
Korea (South)	Always	Always	Always	Always	Always
Laos	Always	Always	Always	Always	Always
Malaysia	Always	Always	Always	Always	Always
Mongolia	Always	Always	Only in emergency	Always	Always
Myanmar	Always	Always	Always	Always	Always
Nepal	Always	Always	Always	Always	Always
Pakistan	Always	Always	Always	Only with special permit or authorization	Always
Philippines	Always	Always	Always	Only with special permit or authorization	Always
Sri Lanka	Always	Always	Always	Always	Always
Thailand	Always	Always	Always	Always	Always
Vietnam	Always	Always	Always	Always	Always

Always  
 Only with special permit or authorization  
 Only in emergency  
 Never

Figure 6. Opioid prescriber privileges for cancer patients in Asian countries.

Country	Prescription forms			
	Duplicate or Triplicate	Special Prescr Forms	ready access to forms	Pay for forms
Afghanistan	restrictive	restrictive	restrictive	restrictive
Bangladesh	restrictive	restrictive	restrictive	restrictive
Bhutan	restrictive	restrictive	restrictive	restrictive
Cambodia	restrictive	restrictive	restrictive	restrictive
China	restrictive	restrictive	restrictive	restrictive
China-Hong Kong	restrictive	restrictive	restrictive	restrictive
Indonesia	restrictive	restrictive	restrictive	restrictive
Japan	restrictive	restrictive	restrictive	restrictive
Kazakhstan	restrictive	restrictive	restrictive	restrictive
Korea (South)	restrictive	restrictive	restrictive	restrictive
Laos	restrictive	restrictive	restrictive	restrictive
Malaysia	restrictive	restrictive	restrictive	restrictive
Mongolia	restrictive	restrictive	restrictive	restrictive
Myanmar	restrictive	restrictive	restrictive	restrictive
Nepal	restrictive	restrictive	restrictive	restrictive
Pakistan	restrictive	restrictive	restrictive	restrictive
Philippines	restrictive	restrictive	restrictive	restrictive
Sri Lanka	restrictive	restrictive	restrictive	restrictive
Thailand	restrictive	restrictive	restrictive	restrictive
Vietnam	restrictive	restrictive	restrictive	restrictive

restrictive  
 not restrictive  
 Not relevant

Figure 7. Prescription restrictions in Asian countries.

emergency situations in the Afghanistan. In Pakistan those who have a special authority are allowed to prescribe and in Afghanistan they are allowed to prescribe in emergency situations (Figure 6).

### requirement for duplicate prescriptions and special prescription forms

Approximately half of the surveyed countries had restrictions on prescription forms. Cambodia, China, Laos, Mongolia, Myanmar, Pakistan, the Philippines and Thailand had restrictive access to these forms, while Cambodia, Mongolia, Pakistan and the Philippines required payment for these prescriptions (Figure 7).

### prescription limits

Half of the countries had limits of  $\leq 2$  weeks of opioids. Afghanistan had a 5-day limit, while Cambodia and Laos, China, Mongolia and Myanmar had a 7-day limit. Bangladesh, Kazakhstan, Pakistan and Vietnam had 10–14 day limits. Malaysia allows a maximum supply of up to 60 days, while South Korea and China-Hong Kong have no limits (Figure 8).

### limitations on dispensing privileges

Most countries reported that opioids were only available in hospital pharmacies. Five countries (Bangladesh, Cambodia, China, Myanmar and Sri Lanka) reported that accessibility to dispensing was very limited (Figure 9).

Country	Max Days Opioids Supplied
Afghanistan	5
Bangladesh	14
Bhutan	30
Cambodia	7
China	7
China-Hong Kong	Physician discretion
Indonesia	
Japan	28
Kazakhstan	10
Korea (South)	Physician discretion
Laos	7
Malaysia	60
Mongolia	7
Myanmar	7
Nepal	
Pakistan	14
Philippines	30
Sri Lanka	28
Thailand	30
Vietnam	10

28+ days  
 15-28 days  
 1-2 weeks  
 < 1 week  
 No submitted data

Figure 8. Maximum number of days opioid supplied on single prescription.

### provision for opioid prescribing in emergency situations

An emergency situation is defined as one when there is an immediate need for relieving 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. Only in Afghanistan were pharmacists allowed to prescribe in emergency situations. Only five states allowed emergency prescribing by fax or phone, namely Bhutan, Indonesia, Laos, Malaysia and Pakistan (Figure 10).

### pharmacist privilege to correct technical errors on a prescription

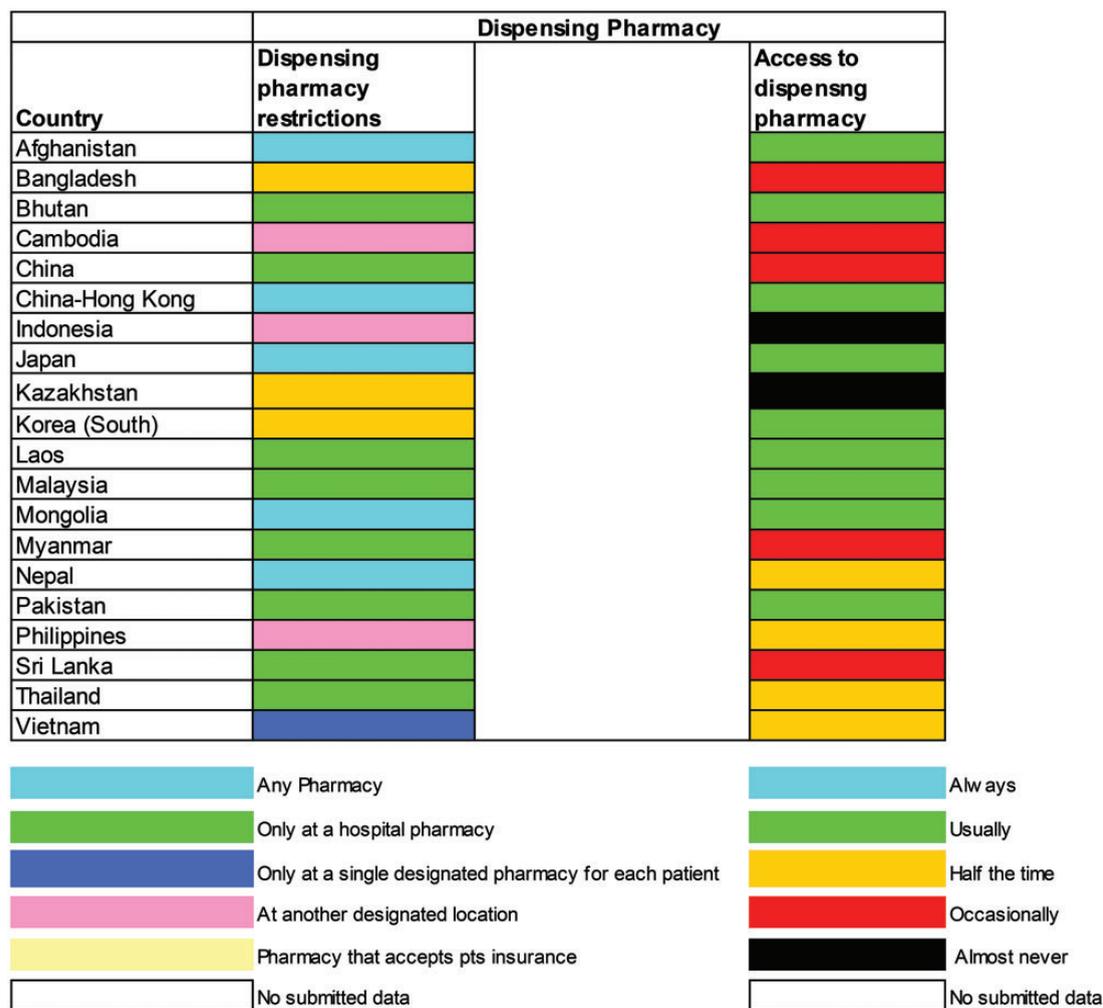
In the situation of a patient presenting with a prescription that contains a technical error (no address, mis-spelling, missing value, etc.), only Bhutan, Japan, South Korea, Laos and Pakistan allowed pharmacists to correct technical errors (Figure 10, last column).

### use of stigmatizing terminology for opioid analgesics in regulations

Over half the country reporters identified negative language existing in drug laws and half had laws forbidding driving while on opioids (Figure 11).

### discussion

Cancer continues to be an increasing problem throughout the world with an increase in cancer incidence in low- and middle-



**Figure 9.** Dispensing pharmacy sites and their accessibility for Asian countries.

income countries. Overall the prevalence of cancer in Asia is high and most cancer patients present with advanced disease, commonly associated with moderate or severe pain.

Opioid consumption has been documented in various formats for Asian countries [7–9]. While many countries have shown an increase in consumption since 2000, most countries have ‘concerning’ consumption as defined by the International Narcotics Control Board (INCB) with a DDD (defined daily doses S-DDD) consumed per million inhabitants per day of <200 mg oral morphine equivalents [9]. The exceptions to this were China-Hong Kong, Japan and South Korea. All surveyed countries in Asia, except South Korea and Japan, have <10% of the anticipated Adequacy of Consumption Measure (ACM) for opioids (Table 1). ACM was not available for China-Hong Kong.

The approach to improving opioid consumption is guided by the WHO policy guidelines, *Ensuring Balance in National Policies on Controlled Substances, Guidance for availability and accessibility of controlled medicines* [10]. 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.

### medication availability

Approximately half the countries surveyed had limited access to the essential opioids as outlined by the IAHPIC [11]. A number of countries have very limited access, particularly access to immediate release oral morphine. It is striking that even in countries with very limited opioid formularies, transdermal fentanyl was often among those formulations available with 14 of the 20 countries having that formulation available. It is widely recognized that pharmaceutical companies and importers are reluctant to invest in the registration and promotion of products, such as immediate release oral 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.

Oral immediate release morphine has generally been available as tablets throughout the region with less reliance on morphine

Country	Pharmacist restrictions	
	Pharmacists accept amergency telephone/fax prescriptions	Pharmacists may correct tech errors
Afghanistan	Yes	Yes
Bangladesh	Yes	Yes
Bhutan	No	No
Cambodia	Yes	Yes
China	Yes	Yes
China-Hong Kong	Yes	Yes
Indonesia	No	No
Japan	Yes	No
Kazakhstan	Yes	Yes
Korea (South)	Yes	No
Laos	No	No
Malaysia	No	Yes
Mongolia	Yes	Yes
Myanmar	Yes	Yes
Nepal	Yes	Yes
Pakistan	No	No
Philippines	Yes	Yes
Sri Lanka	Yes	Yes
Thailand	Yes	Yes
Vietnam	Yes	No

Yes
No
No submitted data

Figure 10. Pharmacy restrictions for Asian countries.

syrup in Asia compared with other regions (e.g. Africa). Low-income countries usually rely on importing medications, while high-income countries often manufacture the various formulations within country. Due to import impediments, Nepal, a low-income country, has commenced production of its own immediate and controlled-release morphine [12].

**education**

Much work needs to be done in educating both patients and clinicians in the region on the role of opioids in cancer pain. Many countries have commenced palliative care training in the region. In Japan, palliative care has developed significantly in the last 15 years as part of its comprehensive cancer control plan [13], including the recent release of new cancer pain guidelines [14]. But in many other counties in Asia, the palliative care knowledge among clinicians has not advanced as effectively. Of 219 Thai physicians, 62.1% had inadequate knowledge and 33.8% had negative attitudes towards opioids for cancer pain relief. The physicians identified both the lack of training opportunities and the periodic shortages of opioids as the greatest barriers to opioid availability [15]. There are Asian data to suggest that even when physicians have appropriate knowledge there are still barriers to implementation. This was illustrated by a survey of 200 clinicians in the Philippines. In this survey the responding physicians demonstrated a high level of awareness of the WHO analgesic ladder (72%) and the availability of opioids in their areas of practice (89.57%) but only 60% had applied for a license

Country	Laws	
	Negative language in drug laws	Driving forbidden
Afghanistan	Yes	Yes
Bangladesh	No	Yes
Bhutan	No	No
Cambodia	Yes	No
China	No	No
China-Hong Kong	No	Yes
Indonesia	No	Yes
Japan	Yes	Yes
Kazakhstan	Yes	Yes
Korea (South)	Yes	No
Laos	Yes	Yes
Malaysia	Yes	Yes
Mongolia	No	No
Myanmar	Yes	Yes
Nepal	No	No
Pakistan	No	Yes
Philippines	Yes	Yes
Sri Lanka	Yes	No
Thailand	Yes	No
Vietnam	No	No

No
Yes
No submitted data

Figure 11. Negative laws regarding opioids in Asian countries.

to prescribe opioids. Furthermore, there was a perceived resistance to prescribe strong pure opioid agonists and a preference to use step 2 combination formulations [16].

Patient concerns regarding the use of opioids for the management of cancer pain have been evaluated in Japan [17]. This study demonstrates the continuing presence of patient barriers and fears regarding the use of opioids to relieve pain.

**government policies and regulations**

Overall, this study found widespread evidence of over-regulation of opioid prescribing for the management of cancer pain. With the exception of Bhutan, Japan, Indonesia Nepal and South Korea, the majority of responding countries in the region reported four or more restrictive regulations that impaired access to opioids for pain relief (Figure 12). Indeed, there is an urgent need for regulatory review and the repeal of unnecessarily burdensome barriers to accessibility. The role of policy makers and regulators is critical in opioid availability. A Thai survey of physicians included a survey of 58 policy makers and regulators [15]. Three quarters of the policy makers and regulators had inadequate knowledge regarding the use of opioids in the management of cancer pain and two-thirds had negative attitudes regarding opioid analgesics.

Combined workshops with clinicians and regulators have taken place in the Philippines, Indonesia and Thailand. However, these alone have not resulted in significant increases in opioid consumption within individual countries. Increases in opioid consumption have been seen in two Asian countries that have engaged in the International Pain Policy Fellowship

Program [18], namely Nepal and Vietnam [19]. India, Bangladesh and Sri Lanka are now participating in the International Pain Policy Fellowship Programs in collaboration with their respective governments. Other recent efforts have been made with the APHN with the support of the Lien

Foundation ‘Train the Trainers’ programs have been carried out in Bangladesh, Myanmar, Laos and Cambodia.

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 [20].

**Table 1.** Comparison of S-DDD and %ACM [7–9] for selected Asian countries

	S-DDD 1997–1999 <sup>a</sup>	%ACM 2006	S-DDD 2007–2009	%ACM 2010
Afghanistan	ND	ND	ND	0.01
Bangladesh	1	0.68	7	0.35
Bhutan	<1	ND	21	7.76
Cambodia	10	ND	6	0.10
China	30	1.10	68	1.18
China-Hong Kong	180	ND	208	ND
Indonesia	10	0.18	20	0.16
Japan	280	13.66	1023	15.54
Kazakhstan	50	ND	70	0.25
Korea (South)	210	7.2	1342	46.99
Laos	5	0.15	3	0.09
Malaysia	40	1.2	116	3.22
Mongolia	15	0.26	56	0.64
Myanmar	<1	0.03	<1	0.01
Nepal	2	0.17	9	0.39
Pakistan	<5	0.05	5	ND
Philippines	10	0.35	11	0.43
Sri Lanka	17	1.09	26	0.77
Thailand	60	1.33	67	1.65
Vietnam	10	0.49	29	0.65

<sup>a</sup>Calculated from International Narcotics Control Board (INCB) graphs. S-DDD, defined daily doses consumed per million inhabitants per day; ACM, adequacy of consumption measure.

## conclusion

With the exception of Japan and South Korea, opioid availability continues to be low throughout most of Asia. Formulary deficiencies are severe in several countries, in particular Bangladesh, Myanmar, Afghanistan, Kazakhstan and Laos. Even when opioids are on formulary they are often unavailable, particularly in the same countries. Access is significantly impaired by widespread over regulation that continues to be pervasive across the region.

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

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Country	Eligibility Restriction	Physician Prescriber Restrictions	No emergency prescriptions by Fx/Phone or non medical prescribing	Limited prescription duration	No pharmacist authority to correct prescription	Increase bureaucratic burden of prescriptions	Restricted dispensing sites	Negative language in laws	Number of restrictive domains (N/8)
Bhutan						Yes	Yes		2
Japan						Yes		Yes	2
Korea (South)			Yes					Yes	2
Indonesia					Yes	Yes	Yes		3
Nepal			Yes		Yes	Yes			3
China-Hong Kong			Yes		Yes	Yes	Yes		4
Malaysia					Yes	Yes	Yes	Yes	4
Pakistan	Yes	Yes				Yes	Yes		4
Vietnam	Yes	Yes	Yes				Yes		4
Mongolia	Yes	Yes	Yes	Yes		Yes			5
Sri Lanka	yes		Yes		Yes		Yes	Yes	5
Thailand			Yes			Yes	Yes	Yes	5
Afghanistan	Yes			Yes		Yes	Yes	Yes	5
Bangladesh	Yes	Yes	Yes		Yes	Yes	Yes		6
Cambodia			Yes	Yes	Yes	Yes	Yes	Yes	6
Philippines	Yes	Yes			Yes	Yes	Yes	Yes	6
Laos	Yes	Yes		Yes		Yes	Yes	Yes	6
China	Yes	Yes	Yes	Yes	Yes	Yes	Yes		7
Kazakhstan	Yes	Yes	Yes		Yes	Yes	Yes	Yes	7
Myanmar	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8

**Figure 12.** Summary for Asian countries of regulatory barriers to opioid access for cancer pain relief.

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

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India is the world's largest democracy with control of opioids divided between the national and state governments. While the global consumption of opioids has increased, the consumption has not increased at the same rate. This is the first comprehensive study of opioid availability and accessibility for cancer patients in India. Data are reported on the availability and accessibility of opioids for the management of cancer pain in 24 of the states that make up India and the Administrative area around Delhi. About 1061 million of the nation's 1189 million people (89%) are covered by this survey. Without exception, opioid availability continues to be low throughout all of India. Even when opioids are on formulary, they are often unavailable. Access is significantly impaired by widespread over-regulation that continues to be pervasive across the nation.

### introduction

India is the most populous democracy in the world. It was highlighted for a separate report by virtue of its vast population and political structure that grants individual states the authority to determine regional regulations for opioid prescribing and dispensing. The population of India is young. In 2010, more than 550 000 deaths caused by cancer (this is probably a major underestimate) were reported, mainly in persons 30–69 years of age. (including cancers of the lip, pharynx and tongue), which can produce severe cancer pain syndromes, and accounts for almost a quarter of all cancers in India [1].

India grows opium in the three Northern states of Uttar Pradesh, Madhya Pradesh, and Rajasthan, and it exports the raw materials used to manufacture opioid analgesics around the world. Paradoxically, very little is produced for local medical use, and India has had very low opioid consumption [2]. While the global opioid consumption of opioids has increased throughout the last 30 years, there has been little increase in opioid consumption in India including morphine consumption (Figure 1), despite increasing economic and health care development throughout the country. When compared with other countries in the region, India's total opioid consumption is lower than most of its neighbors (Figure 2).

The availability of opioids for the management of cancer pain has been severely curtailed by issues related to supply and

distribution that arose as a consequence of the 1985 Narcotic Drugs and Psychotropic Substances Act, (NDPS). Under this law, the cultivation of poppy, collection of opium, and manufacture of morphine are controlled by the central government; the state governments control the sale and distribution of morphine. The law was passed in order to stop trafficking and abuse of drugs. As a consequence, it severely reduced the medical supply of morphine. Despite the discretionary authority of the states to liberalize rules regarding sale and distribution of morphine, up until 2008 only about 13 states in India and 1 union territory have simplified regulations. (India has 28 states and 7 union territories). Thirteen states had modified the rules to improve patient access to morphine; however, in most states, morphine consumption did not improve [2]. The state of Kerala led the way easing regulatory restrictions and by making palliative care available in every part of the state. Consequently, the state of Kerala hosts more than 75% of India's palliative care centers.

The impact of the NDPS is illustrated in a survey of 100 cancer patients treated in a tertiary hospital in the state of Uttarakhand [3]. Ninety-five percent of patients reported substantial pain, 66% received inadequate analgesics and only 6.32% received strong opioids. Impaired access to opioids has a major impact on the quality of life of patients. This is despite a 1990 study in Bangalore that showed in 223 patients that 'intractable cancer pain' could be successfully reduced in all of 17 patients with an average oral morphine dose of 196 mg/day [4].

The catastrophic human consequences of the general unavailability of morphine or other strong pain medication for cancer patients has been highlighted in a detailed report by

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Human Rights Watch entitled *Unbearable Pain: India's Obligation to Ensure Palliative Care* [5].

Hitherto there has been no detailed mapping of the different regulatory barriers encountered across the range of Indian states.

## methodology

See Cherny et al. [6].

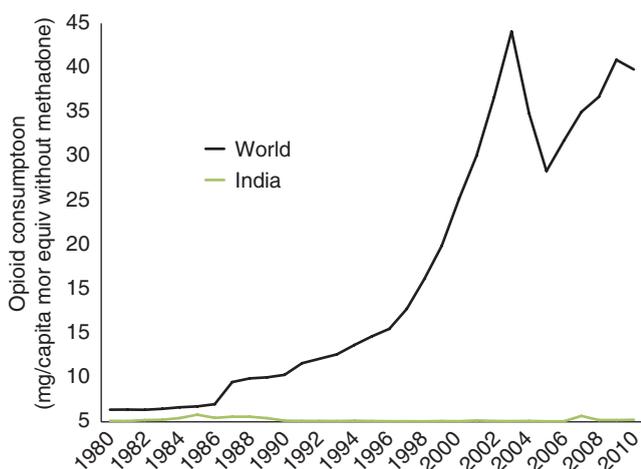
## results

Data are reported on the availability and accessibility of opioids for the management of cancer pain in 24 of the states that make up India and the Administrative area around Delhi. These data are relevant to 1061 million of the region's 1189 million people (89%). The Northeast states refer collectively to the seven states in the North East of India.

## formulary availability and cost of opioids for cancer pain

The availability of opioids and their cost to consumers are summarized in Figure 3 and show many similarities throughout the country. Immediate release oral morphine is available throughout all states of India covered by this survey. Codeine, controlled release morphine and injectable morphine are available in most states. Transdermal (TD) fentanyl is available in all but two states. Oxycodone is only available in Kerala and West Bengal. Goa, Bihar and Odisha have only three of the seven essential medicines available. Greater than 50% of the cost of most medications is borne by patients. For injectable morphine, oxycodone and TD fentanyl, full cost are borne by the patient.

While reporters state that these medications were on formulary, only codeine is always or usually available. All other opioids, including oral morphine, are available occasionally, with one state Jharkhand, never having availability (Figure 4).



**Figure 1.** Comparison of morphine consumption (Morphine equivalence without methadone, mg/capita) between the World and India from 1980 to 2010.

## regulatory restrictions to accessibility

These are detailed below and summarised in Table 12. The Indian States overall have significant regulatory restrictions that limit accessibility of opioids.

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

In general, eligibility within a state was the same for outpatients, inpatients and hospice patients in almost all jurisdictions.

Approximately half the states require special authorizations across all settings. Jharkhand required special authorizations for outpatients but not for inpatients and hospices (Figure 5).

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

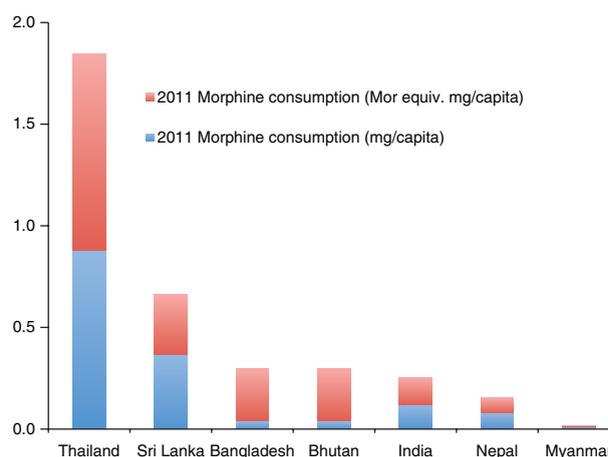
Across all states, there was little restriction on prescribing of opioids by oncologists or surgeons (Figure 6). In most states, primary care physicians require a special authorization to prescribe opioids, and in four states (Bihar, Haryana, Punjab and Tamil Nadu), they could only prescribe opioids in emergency situations. Only the Delhi region allowed prescription by nurses or pharmacists in emergency situations.

### requirement for duplicate prescriptions and special prescription forms

Fifteen of the 25 states and regions require duplicate or triplicate prescriptions (Figure 7). When special forms were required, they were generally available except in Jharkhand and Kerala. In Kerala, physicians need to purchase the prescription forms.

### prescription limits

Generally the maximum number of allowed days for the supply of opioids was 30 days (Figure 8). The maximum

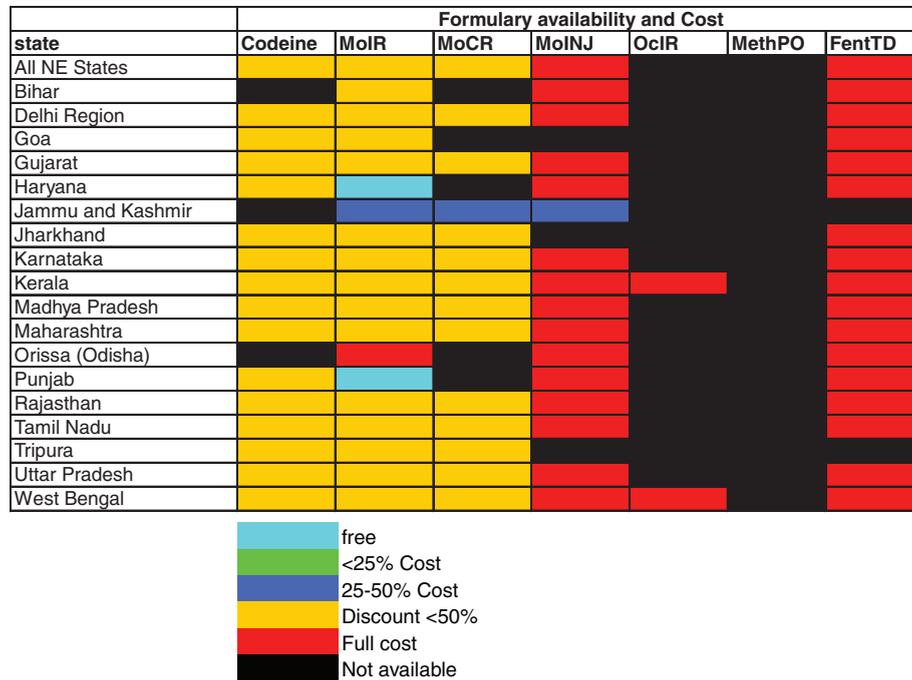


**Figure 2.** Rank Order of Opioid consumption (Morphine Equivalence without methadone, mg/capita) for neighboring Regional Countries.

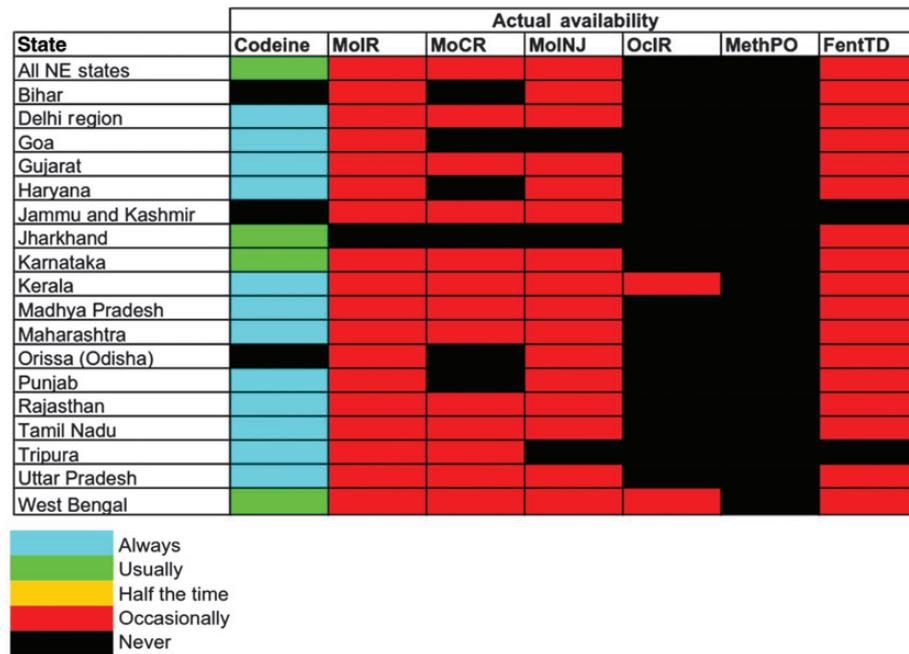
limit in West Bengal was 21 days; in Jammu and Kashmir, 15 days; Tipura, 6 days and the Northeastern States, 3 days.

**limitations on dispensing privileges**

In most states opioids are dispensed only in hospital pharmacies (Figure 9). Hospital pharmacies were the usual place except in



**Figure 3.** Formulary availability and cost to patients of the seven essential opioid formulations of the International Association for Hospice and Palliative Care (IAHPC) in Indian States (Mo, Morphine; Oc, Oxycodone; Meth, Methadone; Fent, Fentanyl; IR, immediate release; CR, Controlled Release; PO, oral; TD, Transdermal). MoIR, immediate release oral morphine; MoCR, Controlled release oral morphine; MoINJ, injectable morphine; OcIR, oral immediate release oxycodone; FentTD, transdermal fentanyl; MethPO, oral methadone.



**Figure 4.** Actual availability of the seven essential opioid formulations of the IAHPC in Indian States. MoIR, immediate release oral morphine; MoCR, controlled release oral morphine; MoINJ, injectable morphine; OcIR, oral immediate release oxycodone; FentTD, transdermal fentanyl; MethPO, oral methadone.

State	Eligibility restriction		
	Outpatients	Inpatients	Hospice
All NE states	Always	Always	Always
Bihar	Only with special authorization	Only with special authorization	Only with special authorization
Delhi region	Only with special authorization	Only with special authorization	Only with special authorization
Goa	Always	Always	Always
Gujarat	Only with special authorization	Only with special authorization	Only with special authorization
Haryana	Only with special authorization	Only with special authorization	Only with special authorization
Jammu and Kashmir	Only with special authorization	Only with special authorization	Only with special authorization
Jharkhand	Only with special authorization	Only with special authorization	Only with special authorization
Karnataka	Only with special authorization	Only with special authorization	Only with special authorization
Kerala	Always	Always	Always
Madhya Pradesh	Only with special authorization	Only with special authorization	Only with special authorization
Maharashtra	Only with special authorization	Only with special authorization	Only with special authorization
Orissa (Odisha)	Only with special authorization	Only with special authorization	Only with special authorization
Punjab	Only with special authorization	Only with special authorization	Only with special authorization
Rajasthan	Only with special authorization	Only with special authorization	Only with special authorization
Tamil Nadu	Only with special authorization	Only with special authorization	Only with special authorization
Tripura	Only with special authorization	Only with special authorization	Only with special authorization
Uttar Pradesh	Only with special authorization	Only with special authorization	Only with special authorization
West Bengal	Always	Always	Always

■ Always  
■ Only with special authorization  
■ Never

Figure 5. Patient eligibility restrictions for cancer patients in Indian states.

three states (Goa, Kerala and West Bengal) where any pharmacy was allowed to dispense opioids. In many states, patient accessibility to the sites of opioid dispensing are reported to be very limited. Pharmacists were not able to accept emergency scripts by fax or telephone and only in four states they were authorized to correct technical errors.

**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. With the single exception of Gujarat, pharmacists were not able to accept emergency scripts by fax or telephone (Figure 10). The Delhi Region permitted non-medical prescribing by a pharmacist or nurse in an emergency situation (Figure 6).

**pharmacist privileges to correct a technical error on a prescription**

In the situation of a patient presenting with a prescription that contains a technical error (no address, misspelling, missing value etc), a pharmacist was allowed to correct this in only 4 of 25 regions (Delhi, Haryana, Punjab and Tripura) (Fig 10 last column).

**use of stigmatizing terminology for opioid analgesics in regulations**

Indian law does not use stigmatizing negative language regarding opioids and restrictions on driving are made on a case-by-case basis in all states (Figure 11) except Kerala where it is prohibited by patients taking opioids, irrespective of the cognitive or attentive function.

**discussion**

Cancer continues to be an increasing problem throughout the world with an increase in cancer incidence in low- and middle-income countries. Many adult patients in India present with advanced disease [1] as do many children with cancer who present late in the course of their disease [7].

India's opioid consumption is among the lowest in the region (Figure 2) and has been documented in various formats [8–10]. While many countries have shown an increase in consumption

State	Prescriber privileges				
	Oncologist	Family Doc	Surgeon	Nurse	Pharmacist
All NE states	Always	Only with special permit or authorization	Always	Always	Never
Bihar	Always	Only with special permit or authorization	Always	Always	Never
Delhi region	Always	Only with special permit or authorization	Always	Only in emergency	Only in emergency
Goa	Always	Always	Always	Always	Never
Gujarat	Always	Only with special permit or authorization	Always	Always	Never
Haryana	Always	Only with special permit or authorization	Always	Always	Never
Jammu and Kashmir	Always	Only with special permit or authorization	Always	Always	Never
Jharkhand	Always	Only with special permit or authorization	Always	Always	Never
Karnataka	Always	Only with special permit or authorization	Always	Always	Never
Kerala	Always	Only with special permit or authorization	Always	Only with special permit or authorization	Never
Madhya Pradesh	Always	Only with special permit or authorization	Always	Always	Never
Maharashtra	Always	Only with special permit or authorization	Always	Always	Never
Orissa (Odisha)	Always	Only with special permit or authorization	Always	Always	Never
Punjab	Always	Only with special permit or authorization	Always	Always	Never
Rajasthan	Always	Only with special permit or authorization	Always	Always	Never
Tamil Nadu	Always	Only with special permit or authorization	Always	Always	Never
Tripura	Always	Only with special permit or authorization	Always	Always	Only in emergency
Uttar Pradesh	Always	Only with special permit or authorization	Always	Always	Never
West Bengal	Always	Only with special permit or authorization	Always	Always	Never

■ Always  
■ Only with special permit or authorization  
■ Only in emergency  
■ Never

Figure 6. Opioid prescriber privileges for Cancer Patients in Indian states.

state	Prescription forms			
	Duplicate or Triplicate	Special Prescr Forms	ready access to forms	Pay for forms
All NE States				
Bihar				
Delhi Region				
Goa				
Gujarat				
Haryana				
Jammu and Kashmir				
Jharkhand				
Karnataka				
Kerala				
Madhya Pradesh				
Maharashtra				
Orissa (Odisha)				
Punjab				
Rajasthan				
Tamil Nadu				
Tripura				
Uttar Pradesh				
West Bengal				

restrictive  
 not restrictive  
 Not relevant

**Figure 7.** Prescription restrictions in Indian states.

since 2000, India has very low and ‘concerning’ consumption as defined by the INCB with a S-defined daily dose (DDD) of <200 mg/day/100 000 people [8]. Indian data including S-DDD per capita and Adequacy of Consumption Measure (ACM) for opioids is compared with neighboring countries in Table 1.

The approach to improving opioid consumption is guided by the WHO policy guidelines *Ensuring Balance in National Policies on Controlled Substances, Guidance for availability and accessibility of controlled medicines* [11]. 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.

### medication availability

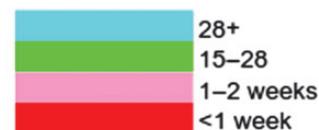
The access to opioids in India is limited to codeine and morphine. Only a few states had accessibility to oxycodone, methadone and fentanyl, but the quantities of morphine consumed continue to be very small. In 2008, India used an amount of morphine that was sufficient to adequately treat only about 40 000 of the estimated 1 million patients suffering from moderate to severe pain due to advanced cancer, about 4% of those needing it [5].

The very low cost of immediate release morphine is itself a barrier to its accessibility. Because of its low cost, profit margins on morphine for both pharmaceutical companies and pharmacies are small, giving the latter little incentive to stock the medication—particularly, considering the extremely complex procedures for procuring it through Indian Licensing rules between states and the Federal Government [5].

### education

Much work needs to be done in educating clinicians in India on the role of opioids in cancer pain. After decades of strict regulation, the medical professionals developed a fear of morphine; many doctors are reluctant to use it and students

State	Max days opioids supplied
All NE states	3
Bihar	30
Delhi region	30
Goa	Physician discretion
Gujarat	30
Haryana	30
Jammu and Kashmir	15
Jharkhand	60
Karnataka	30
Kerala	30
Madhya Pradesh	30
Maharashtra	Physician discretion
Orissa (Odisha)	30
Punjab	30
Rajasthan	30
Tamil Nadu	30
Tripura	6
Uttar Pradesh	30
West Bengal	21



**Figure 8.** Maximum number of days opioid supplied on single prescription.

have been taught to avoid it. Additionally, the general public, including government officials, associates morphine with inevitable dependency and are reluctant to accept its use for medical needs [2].

The Medical Council of India has approved a postgraduate course in palliative care, but the lack of teaching at the undergraduate level has seen few physicians develop careers in palliative care [5]. Only a very small number of medical colleges in India have incorporated instruction on palliative care in the course materials for community health and on pain management for anesthesiology trainees. Some states still have no trained providers in palliative care.

Consumer education is critically important since many people commonly associate morphine with dependency disorder and substance abuse, and/or, with use to relieve pain in the imminently dying [2].

### government policies and regulations

Until the early 1980s, the increase in morphine consumption in India was consistent with increases observed in the rest of the world. However, the enactment of the Narcotic Drugs and Psychotropic Substances (NDPS) Act saw a sudden and significant reduction in opioid consumption. This very complex set of procurement regulations discourages pharmacies and hospitals from stocking it, and health care workers from prescribing it. Consequently, over the next decade, consumption



Figure 9. Dispensing sites for India and accessibility of those sites.

State	Pharmacist restrictions	
	Pharmacists accept emergency telephone/fax prescriptions	Pharmacists may correct tech errors
All NE states	No	No
Bihar	No	No
Delhi region	No	Yes
Goa	No	No
Gujarat	Yes	No
Haryana	No	Yes
Jammu and Kashmir	No	No
Jharkhand	No	No
Karnataka	No	No
Kerala	No	No
Madhya Pradesh	No	No
Maharashtra	No	No
Orissa (Odisha)	No	No
Punjab	No	Yes
Rajasthan	No	No
Tamil Nadu	No	No
Tripura	No	Yes
Uttar Pradesh	No	No
West Bengal	No	No

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Figure 10. Pharmacy restrictions for Indian states.

State	Laws	
	Negative language in drug laws	Driving forbidden
All NE states	No	No
Bihar	No	No
Delhi region	No	No
Goa	No	No
Gujarat	No	No
Haryana	No	No
Jammu and Kashmir	No	No
Jharkhand	No	No
Karnataka	No	No
Kerala	No	Yes
Madhya Pradesh	No	No
Maharashtra	No	No
Orissa (Odisha)	No	No
Punjab	No	No
Rajasthan	No	No
Tamil Nadu	No	No
Tripura	No	No
Uttar Pradesh	No	No
West Bengal	No	No

<span style="display:inline-block; width:15px; height:10px; background-color:lightblue; border:1px solid black;"></span> No
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Figure 11. Negative laws regarding opioids.

State	Eligibility restriction	Physician prescriber restrictions	No emergency prescriptions by Fx/Phone or non medical prescribing	Limited prescription duration	No pharmacist authority to correct prescription	Increase bureaucratic burden of prescriptions	Restricted dispensing sites	Negative language in laws	Number of restrictive domains (N/8)
Delhi region	Yes					Yes	Yes		3
Goa			Yes		Yes	Yes			3
Uttar Pradesh	Yes		Yes		Yes		Yes		4
Punjab		Yes	Yes			Yes	Yes		4
Tripura			Yes	Yes		Yes	Yes		4
West Bengal			Yes		Yes	Yes	Yes		4
Gujarat	Yes	Yes			Yes	Yes	Yes		5
Jammu and Kashmir	Yes	Yes	Yes		Yes	Yes			5
Jharkhand	Yes		Yes		Yes	Yes	Yes		5
Kerala	Yes	Yes	Yes		Yes	Yes			5
Madhya Pradesh		Yes	Yes		Yes	Yes	Yes		5
Nagesh	Yes		Yes		Yes	Yes	Yes		5
Rajasthan		Yes	Yes		Yes	Yes	Yes		5
Tamil Nadu		Yes	Yes		Yes	Yes	Yes		5
Maharashtra	Yes	Yes	Yes		Yes	Yes	Yes		6
Bihar	Yes	Yes	Yes		Yes	Yes	Yes		6
Karnataka	Yes	Yes	Yes		Yes	Yes	Yes		6
Orissa (Odisha)	Yes	Yes	Yes		Yes	Yes	Yes		6
All NE States	Yes	Yes	Yes	Yes	Yes	Yes	Yes		7

**Figure 12.** Summary of regulatory barriers to opioid access for cancer pain relief in India.

**Table 1.** Comparison of S-DDD and %ACM for India and some regional countries (8–10)

	S-DDD 1997–1999	%ACM 2006	S-DDD 2007–2009	%ACM 2010
Bangladesh	1	0.68	7	0.35
India	1	0.08	17	0.22
Myanmar	<1	0.03	<1	0.01
Nepal	2	0.17	8	0.39
Sri Lanka	17	1.09	26	0.77
Thailand	80	1.33	67	1.65

%ACM, percentage of Adequacy of Consumption Measure. S-DDD, Statistical Defined daily Dose per million persons per days.

of morphine dropped by 97% and reached a low of just 18 kg in 1997. As Joranson, Rajagopal and Gilson have pointed out, in that same period, global consumption of morphine increased by 437% [12].

Two major policy factors contributed to this lack of balance: first, there was a 10-year mandatory minimum prison term for violations involving narcotic drugs in the 1985 Act. This led to pharmacies all over the country dropping morphine from their stock, rather than risk penalties. The states adopted complex narcotic drug rules following the 1985 Act [12], requiring ‘import, export and transport licenses to ship any amount of morphine between any two states, as if they were countries.’ This resulted in cumbersome processes in making morphine available around the country.

The Federal government brought about changes in 1998 introducing the ‘model rule’ which permitted states to simplify their opioid regulations. It simplified the licensing and authorized the state Drugs Controller to ‘recognize’ medical institutions and allow them to possess morphine and to designate at least one qualified medical practitioner to prescribe morphine, ensure adequate stock, future needs, and maintain

records and security. Despite this initiative many states still operate under outdated rules that severely impede availability of morphine. This is true for most states apart from Kerala which consumes 30% of the country’s opioids while only having 2.5% of its population [5].

A ‘public interest litigation’ was filed by the Indian Association of Palliative Care in 2007, pleading for access for morphine to patients in pain in the country. As a consequence of that application, the Indian Supreme Court ruled that all states must provide morphine at no cost to its residents. Failure to comply with the ruling requires that the state will have to send its Chief Secretary to appear before the Supreme Court.

In 2013, efforts are underway to bring about Federal control of opioid laws. These efforts are ongoing through a major revision of the NDPS Act, which is currently being addressed. The bill incorporates major changes that include the following:

- 1) Ensuring that a patient using narcotic drugs or psychotropic substances as medicine is not considered a substance abuser.
- 2) Enabling the Central government to ensure proactively the availability of narcotic drugs and psychotropic substances for medical and scientific use.
- 3) Transfer to the Federal from the State government the power to permit and regulate the possession, transport, interstate import, sale, purchase, consumption or use of medicinal opium and opioid medications.
- 4) Simplifying the process of licensing for import, export and transport of opioids.

## conclusion

Opioid availability continues to be critically low throughout most of India. There is urgent need for the progress to be made in the slow process of regulatory reform to bring about improved access to opioids, essential medicines for the relief of suffering.

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**disclosure**

The authors have declared no conflicts of interest.

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# 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

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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,

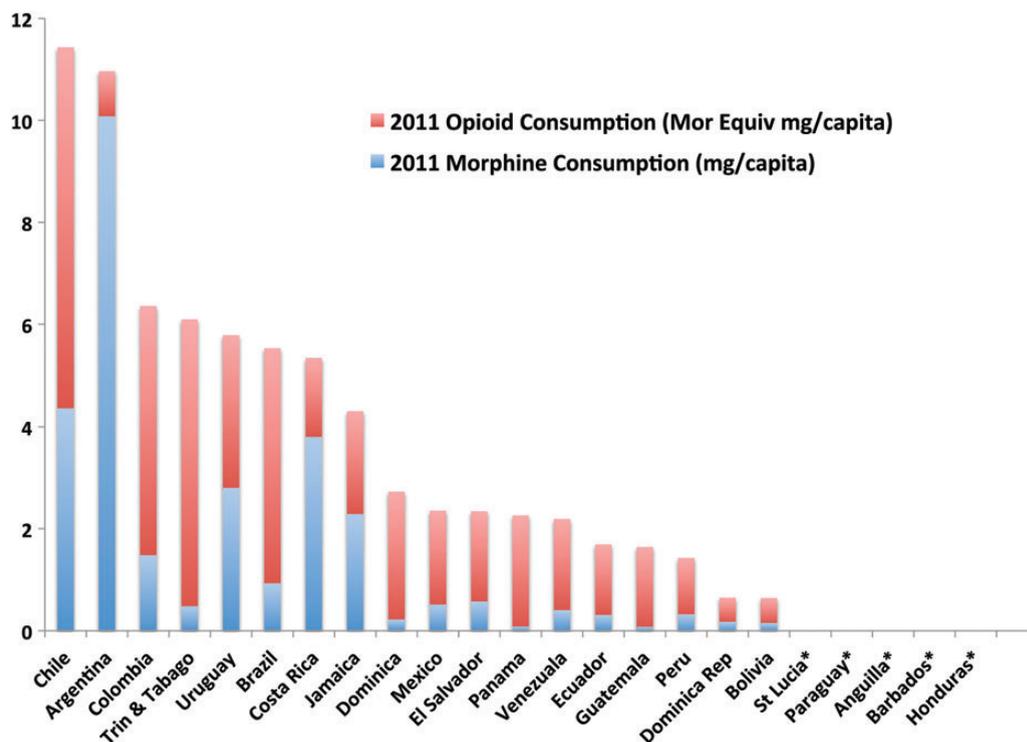


Figure 1. Rank order of opioid consumption (mg/capita in morphine equivalence without methadone) for surveyed Latin American and Caribbean countries.

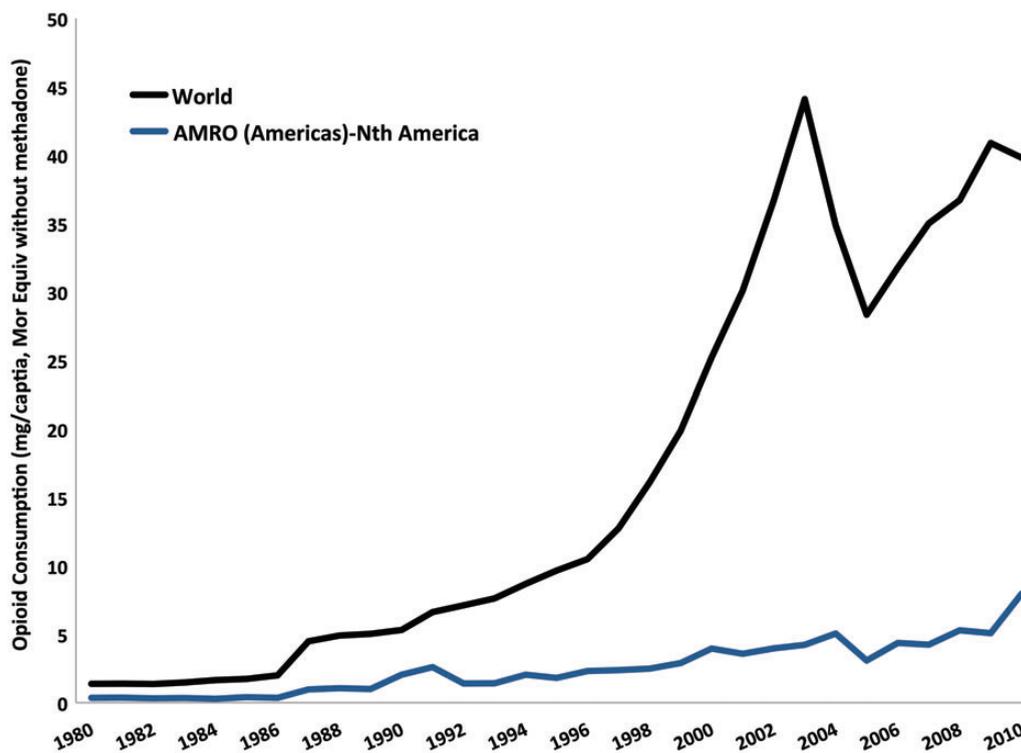


Figure 2. Comparison of opioid consumption (mg/capita in morphine equivalence without methadone) the World, the WHO Regional Offices for the Americas (AMRO), without North America from 1980 to 2010.

Country	Formulary availability and Cost						
	Codeine	MoIR	MoCR	MoINJ	OciR	MethPO	FentTD
Anguilla	free	<25% Cost	<25% Cost	Not available	<25% Cost	<25% Cost	Not available
Argentina	25-50% Cost	free	free	free	free	free	25-50% Cost
Barbados	free	free	free	free	Not available	free	Full cost
Belize	free	free	free	free	Not available	free	Full cost
Bolivia	Full cost	Full cost	Not available	Full cost	Not available	Full cost	Not available
Brazil	Full cost	Full cost	Full cost	Full cost	Not available	Full cost	Full cost
Chile	free	free	Full cost	free	Not available	free	Full cost
Colombia	free	free	Not available	free	Not available	free	Not available
Costa Rica	free	free	free	free	Not available	free	free
Dominica	Not available	Not available	Not available	Not available	Not available	Not available	Not available
Dominican Republic	<25% Cost	<25% Cost	<25% Cost	<25% Cost	<25% Cost	<25% Cost	<25% Cost
Ecuador	Full cost	Not available	Full cost	Full cost	Not available	Not available	Not available
El Salvador	free	Not available	free	free	Not available	Not available	free
Guatemala	Full cost	Full cost	Full cost	Full cost	Full cost	Full cost	Full cost
Honduras	Full cost	Not available	Not available	Full cost	Not available	Not available	Full cost
Jamaica	free	free	free	free	Not available	Not available	free
Mexico	Not available	Full cost	Not available	Full cost	Not available	Full cost	Full cost
Panama	free	free	free	free	Not available	free	free
Paraguay	Not available	Not available	Not available	free	Not available	Not available	Full cost
Peru	Full cost	Full cost	Full cost	Full cost	Full cost	Not available	Full cost
St. Lucia	Full cost	Full cost	Full cost	Full cost	Full cost	Not available	Not available
Trinidad & Tobago	free	Not available	free	free	Not available	free	Not available
Uruguay	<25% Cost	<25% Cost	<25% Cost	<25% Cost	Not available	<25% Cost	<25% Cost
Venezuela	Full cost	free	free	free	free	Full cost	free

■ free  
■ <25% Cost  
■ 25-50% Cost  
■ Discount <50%  
■ Full cost  
■ Not available

**Figure 3.** Formulary availability and cost to patients 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.

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

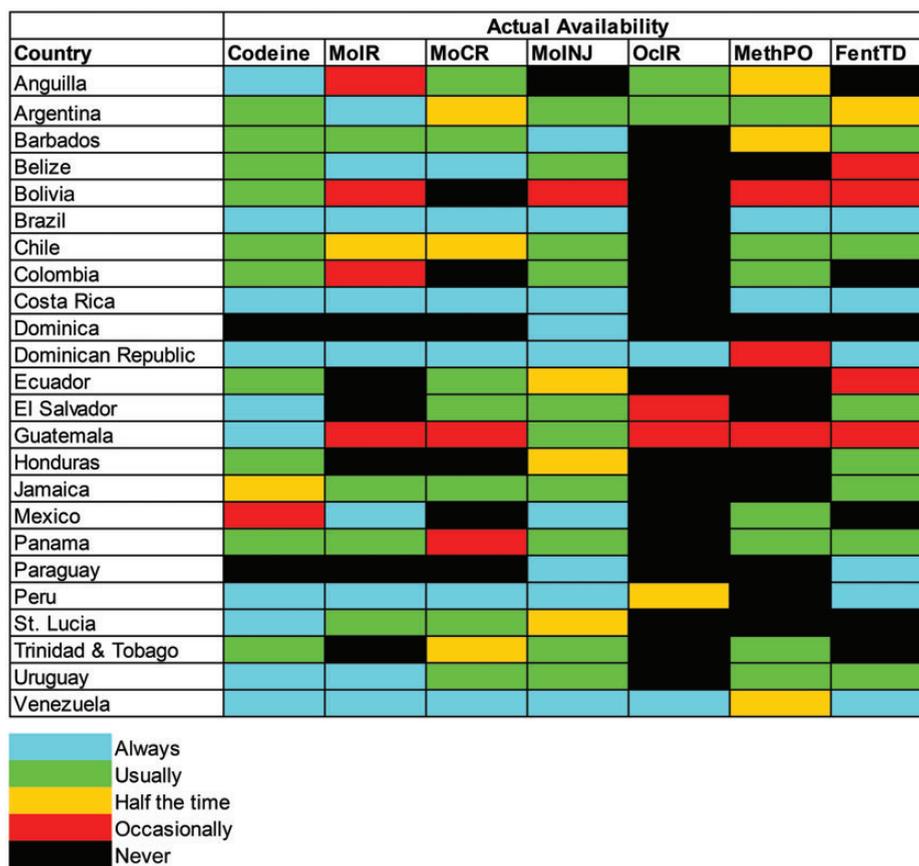
Data for Latin America and the Caribbean are reported on the availability and accessibility of opioids for the management of cancer pain in 24 of 33 countries. The reported data is relevant to 560 million of the region's 595 million people (94%). Surveys were received from Anguilla, Argentina, Barbados, 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



**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.

occasionally (Anguilla, Bolivia, Colombia and Guatemala) (Figure 4).

**regulatory restrictions to accessibility**

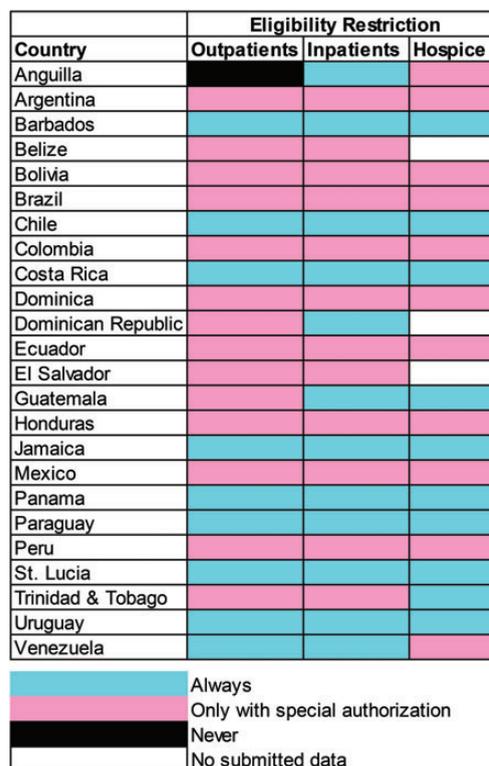
Regulatory restrictions limiting accessibility to opioids were widely reported. They are detailed below and summarized in Table 12.

**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 5.** Eligibility restrictions for cancer patients in Latin American and Caribbean countries.

Country	Prescriber privileges				
	Oncologist	FamilyDoc	Surgeon	Nurse	Pharmacist
Anguilla	Always	Always	Only in emergency	Only with special permit or authorization	Only with special permit or authorization
Argentina	Only with special permit or authorization	Only with special permit or authorization	Only with special permit or authorization	Never	Only with special permit or authorization
Barbados	Always	Always	Always	Never	Never
Belize	Always	Only with special permit or authorization	Always	Never	Never
Bolivia	Only with special permit or authorization	Only with special permit or authorization	Only with special permit or authorization	Never	Never
Brazil	Only with special permit or authorization	Only with special permit or authorization	Only with special permit or authorization	Never	Never
Chile	Always	Always	Always	Never	Never
Colombia	Always	Always	Always	Never	Never
Costa Rica	Always	Always	Always	No submitted data	No submitted data
Dominica	Always	Always	Always	Never	Never
Dominican Republic	Always	Always	Always	Never	Never
Ecuador	Only with special permit or authorization	Only with special permit or authorization	Only with special permit or authorization	Never	Never
El Salvador	Always	Always	No submitted data	No submitted data	No submitted data
Guatemala	Always	Always	Always	Never	Never
Honduras	Only with special permit or authorization	Only with special permit or authorization	Only with special permit or authorization	Never	Never
Jamaica	Always	Always	Always	Only with special permit or authorization	Never
Mexico	Only with special permit or authorization	Only with special permit or authorization	Only with special permit or authorization	Never	Never
Panama	Always	Always	No submitted data	No submitted data	No submitted data
Paraguay	Always	Always	Always	Never	Never
Peru	Always	Always	Always	Never	Never
St. Lucia	Always	Always	Always	Only with special permit or authorization	Never
Trinidad & Tobago	Always	Always	Always	Never	Never
Uruguay	Always	Always	Always	Only in emergency	Never
Venezuela	Always	Always	Always	Never	Never

Always
Only with special permit or authorization
Only in emergency
Never
No submitted data

**Figure 6.** Opioid prescriber privileges 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.

Country	Prescription forms			
	Duplicate or Triplicate	Special Prescr Forms	Ready access to forms	Pay for forms
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 & Tobago				
Uruguay				
Venezuela				

restrictive  
 not restrictive  
 Not relevant

Figure 7. Prescription restrictions in Latin American and Caribbean countries.

### 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

Country	Max Days Opioids Supplied
Anguilla	36
Argentina	10
Barbados	30
Belize	Physician discretion
Bolivia	limited by dose
Brazil	
Chile	30
Colombia	30
Costa Rica	10
Dominica	30
Dominican Republic	14
Ecuador	3
El Salvador	30
Guatemala	30
Honduras	30
Jamaica	14
Mexico	30
Panama	30
Paraguay	Physician discretion
Peru	15
St. Lucia	Physician discretion
Trinidad & Tobago	
Uruguay	Physician discretion
Venezuela	30

	28+ days
	15-28 days
	1-2 weeks
	< 1 week
	No submitted data

Figure 8. Maximum number of days opioids supplied on single prescription.

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 within 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.

Country	Dispensing Pharmacy		Access to dispensing pharmacy
	Dispensing pharmacy restrictions		
Anguilla	Green		Yellow
Argentina	Yellow		Yellow
Barbados	Light Blue		Green
Belize	Light Blue		Green
Bolivia	Pink		Red
Brazil	Light Blue		Light Blue
Chile	Light Blue		
Colombia	Dark Blue		Red
Costa Rica	Light Blue		Green
Dominica	Pink		Light Blue
Dominican Republic	Green		Yellow
Ecuador	Green		Red
El Salvador	Pink		Red
Guatemala	Pink		Red
Honduras	Light Blue		Red
Jamaica	Green		Yellow
Mexico	Pink		Yellow
Panama	Dark Blue		Red
Paraguay	Light Blue		Red
Peru	Pink		Red
St. Lucia	Green		Yellow
Trinidad & Tobago	Light Blue		Yellow
Uruguay	Light Blue		Green
Venezuela	Green		Red

	Any Pharmacy		Always
	Only at a hospital pharmacy		Usually
	Only at a single designated pharmacy for each patient		Half the time
	At another designated location		Occasionally
	No submitted data		No submitted data

**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

Country	Pharmacist restrictions	
	Pharmacists accept emergency telephone/fax prescriptions	Pharmacists may correct tech errors
Anguilla	Yes	No
Argentina	Yes	No
Barbados	Yes	No
Belize	Yes	No
Bolivia	Yes	No
Brazil	Yes	No
Chile	Yes	No
Colombia	Yes	No
Costa Rica	No	No
Dominica	Yes	No
Dominican Republic	Yes	No
Ecuador	Yes	No
El Salvador	No	No
Guatemala	Yes	No
Honduras	Yes	No
Jamaica	No	No
Mexico	Yes	No
Panama	Yes	No
Paraguay	Yes	No
Peru	Yes	No
St. Lucia	No	No
Trinidad & Tobago	No	No
Uruguay	Yes	No
Venezuela	Yes	No

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

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

Country	Laws	
	Negative language in drug laws	Driving forbidden
Anguilla	No	No
Argentina	Yes	No
Barbados	Yes	No
Belize	Yes	No
Bolivia	Yes	No
Brazil	Yes	No
Chile	No	No
Colombia	No	No
Costa Rica	No	No
Dominica	No	No
Dominican Republic	No	No
Ecuador	Yes	No
El Salvador	No	No
Guatemala	No	No
Honduras	Yes	No
Jamaica	Yes	No
Mexico	Yes	No
Panama	Yes	No
Paraguay	No	No
Peru	Yes	No
St. Lucia	No	No
Trinidad & Tobago	Yes	No
Uruguay	Yes	No
Venezuela	Yes	No

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

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, Peru, 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.

**Table 1.** Comparison of S-DDD and % Adequacy of Consumption Measure (ACM) [6–8]

	S-DDD 1997–1999	%ACM 2006	S-DDD 2007–2009	%ACM 2010
Anguilla	–	–	–	–
Argentina	220	1.22	433	6.30
Barbados	575	ND	260	ND
Belize	ND	ND	ND	ND
Bolivia	<5	ND	3	0.12
Brazil	110	5.94	218	6.81
Chile	160	3.67	388	5.14
Colombia	130	1.93	295	3.32
Costa Rica	100	2.67	120	2.96
Dominica	15	3.05	46	3.41
Dominican Republic	10	0.42	24	0.53
Ecuador	30	0.73	62	0.74
El Salvador	NR	1.85	90	2.42
Guatemala	10	0.71	48	0.95
Honduras	ND	ND	ND	0.26
Jamaica	100	2.8	86	3.20
Mexico	NR	0.67	85	4.51
Panama	60	1.85	119	1.99
Paraguay	80	0.19	38	1.04
Peru	20	ND	5	1.07
St Lucia	60	5.01	91	5.42
Trinidad and Tobago	NR	ND	140	5.52
Uruguay	160	ND	164	2.01
Venezuela	20	0.71	71	1.98

<sup>a</sup>Calculated from INCB graphs.

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

## 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].

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## disclosure

The authors declared no conflicts of interest.

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Country	Eligibility Restriction	Physician Prescriber Restrictions	No emergency prescriptions by Fx/Phone or non medical prescribing	Limited prescription duration	No pharmacist authority to correct prescription	Increase bureaucratic burden of prescriptions	Restricted dispensing sites	Negative language in laws	Number of restrictive domains (N/8)
St. Lucia							Yes		1
Trinidad & Tobago	Yes							Yes	2
Uruguay					Yes	Yes			2
Chile			Yes		Yes	Yes			3
Costa Rica				Yes	Yes	Yes			3
Jamaica				Yes			Yes	Yes	3
Paraguay			Yes		Yes	Yes			3
Anguilla	Yes	Yes				Yes	Yes		4
Barbados			Yes		Yes	Yes		Yes	4
El Salvador	Yes				Yes	Yes	Yes		4
Panama			Yes		Yes	Yes	Yes	Yes	4
Colombia	Yes		Yes		Yes	Yes	Yes		5
Dominica	Yes		Yes		Yes		Yes		5
Dominican Republic	Yes		Yes	Yes		Yes	Yes		5
Guatemala	Yes		Yes		Yes	Yes	Yes		5
Venezuela			Yes		Yes	Yes	Yes	Yes	5
Argentina	Yes	Yes		Yes	Yes	Yes		Yes	6
Belize	Yes	Yes	Yes		Yes	Yes		Yes	6
Brazil	Yes	Yes	Yes		Yes	Yes		Yes	6
Honduras	Yes	Yes	Yes		Yes	Yes		Yes	6
Peru	Yes		Yes		Yes	Yes	Yes	Yes	6
Bolivia	Yes	Yes	Yes		Yes	Yes	Yes	Yes	7
Mexico	Yes	Yes	Yes		Yes	Yes	Yes	Yes	7
Ecuador	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8

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

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

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The Middle East is a heterogeneous region with substantial variability in social development, wealth and palliative care development. The region has few democracies, strong but diverse religious affiliations, and many of the region's counties are involved in political upheavals or regional conflicts. While the global consumption of opioids has increased throughout the last 30 years, there has been little increase in opioid consumption in the Middle East. This is the first comprehensive study of opioid availability and accessibility of opioids in the Middle East. Data are reported on the availability and accessibility of opioids for the management of cancer pain in 16 of 24 countries. The data are relevant to 329 million of the region's 403 million people (82%). The survey found that with the exception of Israel, opioid availability continues to be low throughout most of the Middle East. Formulary deficiencies are severe in several countries in particular Afghanistan, Iraq, Lebanon, Libya, Palestine and Tunisia. Even when opioids are on formulary, they are often unavailable, particularly in these same countries. Access is also significantly impaired by widespread over-regulation that is pervasive across the region.

## introduction

The Middle East is a heterogeneous region with substantial variability in social development, wealth and palliative care development. The region has few democracies, strong but diverse religious affiliations, and many of the region's counties are involved in political upheavals or regional conflicts. Few countries in the region have palliative care policies and in many parts of the region pain management has been surrounded by myth, irrationality and cultural bias [1].

Most countries in the Middle East lack government policies concerning cancer control and palliative care. The majority of patients with cancer are diagnosed with advanced-stage disease and, often, the only realistic treatment options are pain relief and palliative care. Registry data from the region indicate that the regional burden of cancer continues to increase largely because of an aging and growing local population coupled with an increasing adoption of cancer-causing behaviors, particularly smoking [2].

With few exceptions, palliative care services are overall not well developed. However, some progress has been made in some

countries including Jordan, and several of the Gulf states (Saudi Arabia, Oman and Qatar) [3].

Many countries in the Middle East still have low opioid consumption [4, 5] (Figure 1). While the global consumption of opioids has increased throughout the last 30 years, there has been little increase in opioid consumption in the Middle East (Figure 2), despite increasing economic and health care development in some countries of the region.

Supported by the USA's National Cancer Institute (NCI), the Middle East Cancer Consortium (MECC) has invested substantial efforts in promoting palliative care and palliative care education for health care professionals across the Middle East [6]. The goal of these educational activities is to create a Middle Eastern nucleus of clinical leaders who will facilitate continuing educational activities throughout the region. Indeed, such programs have been undertaken in Israel, Turkey, Jordan, Palestine, Egypt, Cyprus and Oman.

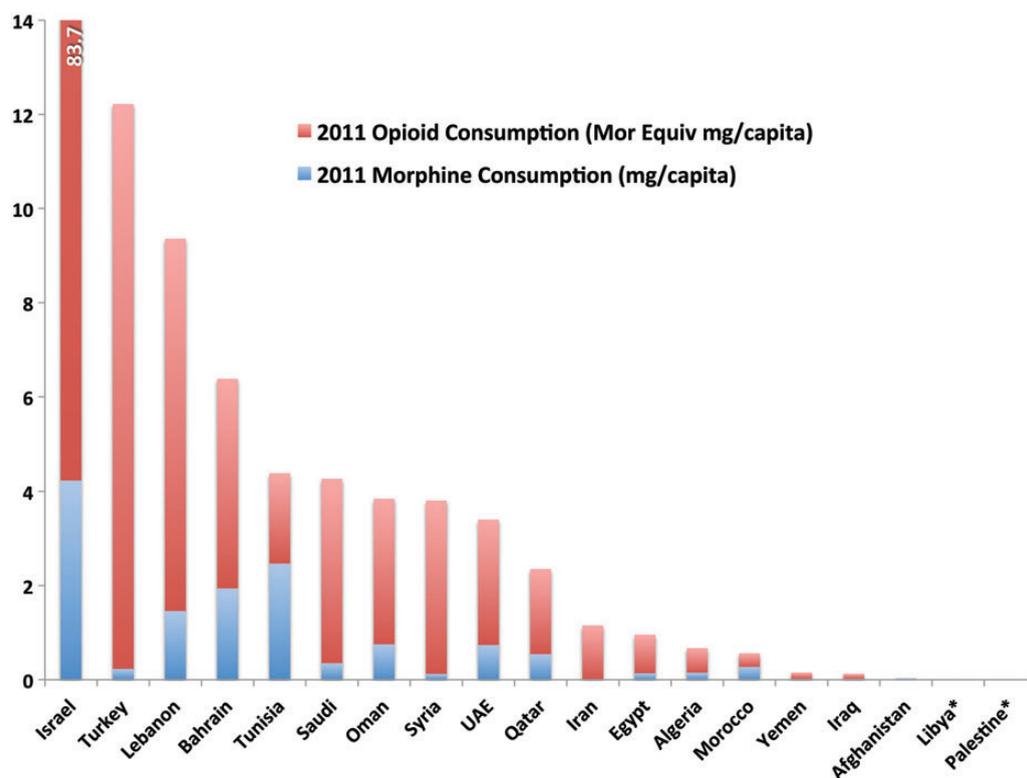
This is the first comprehensive study of opioid availability and accessibility of opioids in the Middle East.

## methodology

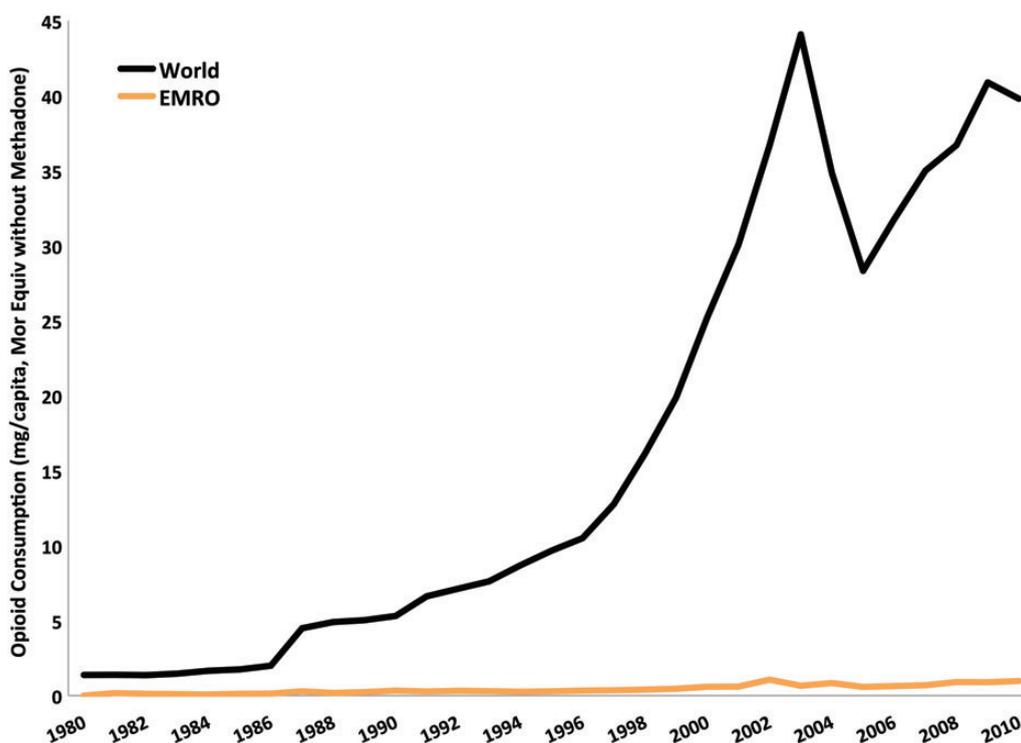
See Cherny and Cleary [7]. The Middle East is defined for the purpose of this study as countries within North Africa, the Eastern Mediterranean and Gulf States and Afghanistan.

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**Figure 1.** Rank order of opioid consumption<sup>1</sup> (morphine equivalence, mg/capita) for surveyed Middle East countries. Opioids included: fentanyl, hydromorphone, morphine, oxycodone, pethidine. \*Not reported.



**Figure 2.** Comparison of opioid consumption (mg/capita of morphine equivalence without methadone) for the World versus the Middle East Regional Organization (EMRO) countries from 1980 to 2010.

Representatives from 21 countries were invited to submit reports.

## results

Data are reported on the availability and accessibility of opioids for the management of cancer pain in 16 of 21 countries. No data were submitted from Azerbaijan, Bahrain, Jordan, Kuwait and United Arab Emirates. The data are relevant to 329 million of the region's 403 million people (82%). Algeria, Egypt, Libya, Morocco and Tunisia are also presented in the African report [8]. Afghanistan is also presented in the Asian report [9].

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

The availability of opioids and their cost to consumers are summarized in Figure 3 and show great variability throughout the region. Israel, Qatar and Saudi Arabia had all seven essential opioid formulations available, while Algeria, Iran, Morocco and Syria had available six of the seven formulations. While six countries (Afghanistan, Iraq, Lebanon, Libya, the OPT and Tunisia) reported no immediate release (IR) morphine and four countries had no sustained release morphine (Afghanistan, Iran, Iraq and Libya), all but two countries (Afghanistan and Iraq) had transdermal (TD) fentanyl available. Oxycodone IR was available in six countries and methadone was available in six countries. Iraq had the most limited formulary with only codeine and injectable morphine available. Libya had codeine, injectable morphine and fentanyl TD available.

In the majority of countries (11 of 16), the cost of these medications was free, or <25% of the drug cost was charged to the patient. The opioid analgesics were always or usually available. The cost of medications was fully borne by patients in Afghanistan, Lebanon, Morocco and Syria. Afghanistan, Iraq, Lebanon, Libya. Palestine had interrupted supplies of controlled release and injectable morphine. With the exception of Israel, oxycodone, methadone and fentanyl, when on formulary, were not regularly available in most countries (Figure 4).

### regulatory restrictions to accessibility

Countries used a range of regulatory restrictions to limit accessibility of opioids. With the exception of Israel, most countries had considerable restrictions on the accessibility of opioid analgesics as described below and summarized in Figure 12.

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

Israel, Morocco and Turkey had no restrictions on the eligibility of a patient to receive prescriptions for opioid analgesics, while Lebanon, Libya and Syria had no restrictions on inpatients (Figure 5). In all other countries, patients required a permit or needed to be registered to receive opioids even in an inpatient

setting. Opioids for outpatients were never allowed in Iran and Iraq.

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

In Afghanistan, Israel and Morocco, all physicians were permitted to prescribe opioids (Figure 6). Special authorization was required in most countries for both surgeons and family doctors. Surgeons could only prescribe in emergencies in Algeria and Libya and not at all in Palestine. Major restrictions were in place for family doctors to prescribe opioids in most countries (Iran, Iraq, Libya, Oman, Palestine, Qatar, Syria and Yemen). Nurses and pharmacists were allowed to prescribe opioids in an emergency only in Afghanistan.

### requirement for duplicate prescriptions and special prescription forms

Special prescription forms were required, and in most of these countries access to these forms is restricted (Figure 7). Libya, Morocco and Tunisia charged physicians for these prescription forms. Israel had the least restrictive availability of prescription forms.

### prescription limits

Eight countries allow physicians to prescribe an amount of opioid analgesics to a patient for more than 2 weeks (Figure 8). Afghanistan, Libya, Morocco and Palestine had a limit of 7 days or less; Qatar and Turkey 10 days and Egypt 14 days. Supply in Iran depended on the opioid type.

### limitations on dispensing privileges

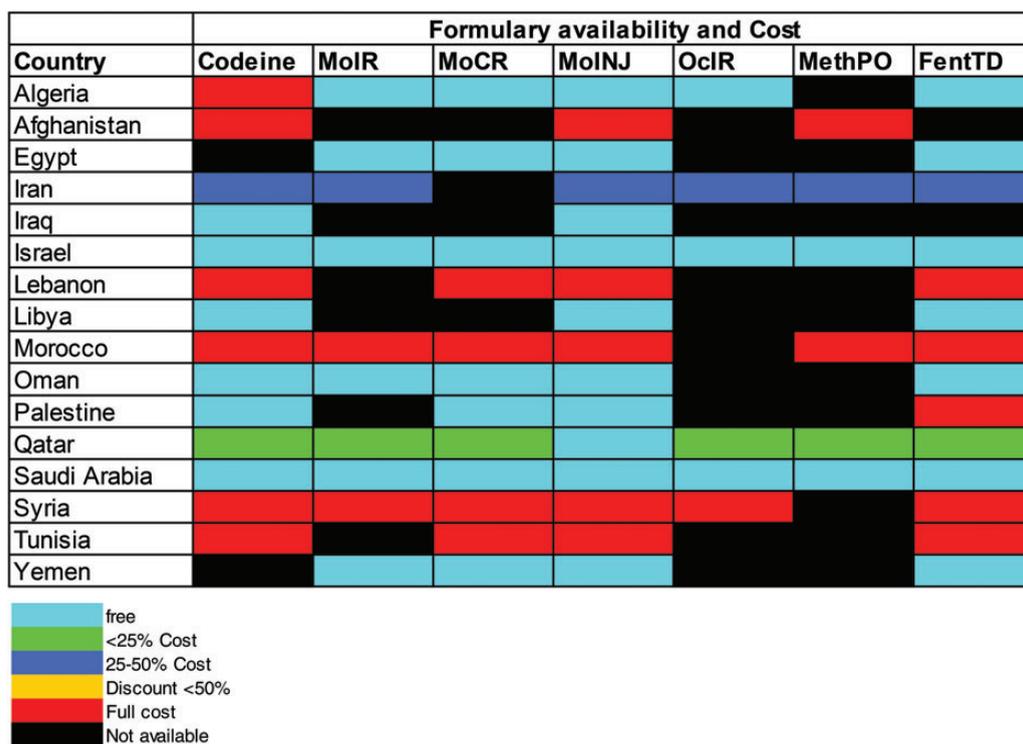
Afghanistan and Morocco report opioids as being available from any pharmacy and that they were usually available (Figure 9). Most other countries reported that opioids were only available in hospital pharmacies. Six countries reported access to the dispensing pharmacies was limited at least half the time and in Iraq they were almost never accessible.

### provision for opioid prescribing in emergency situations

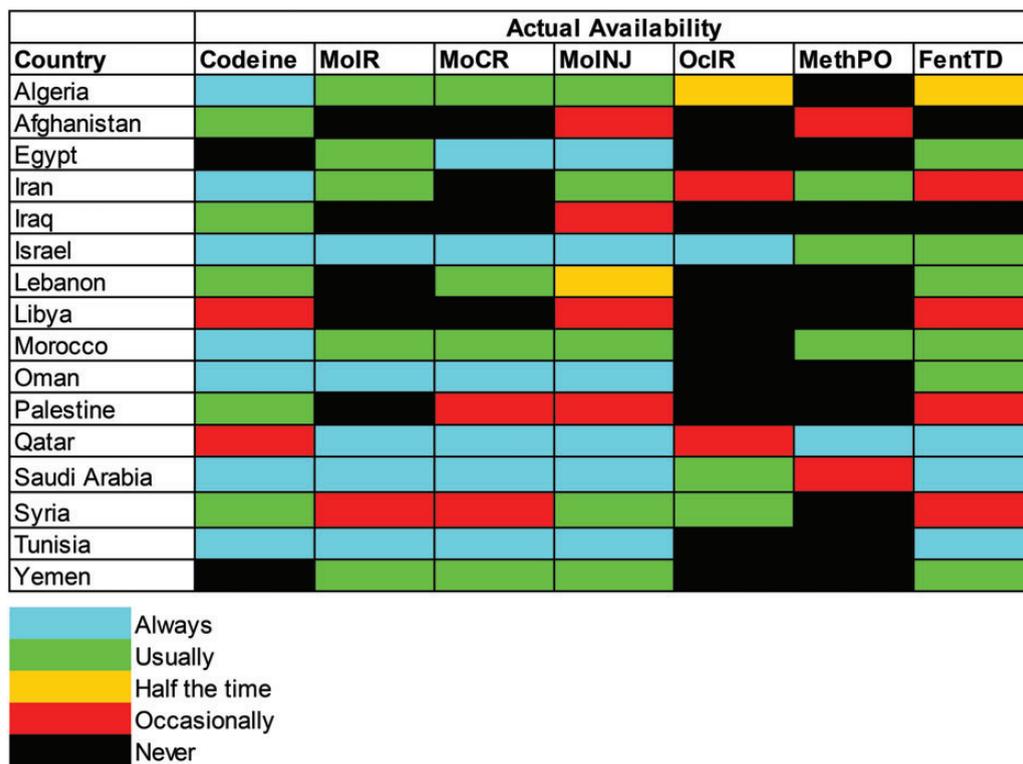
An emergency situation is defined as one when there is an immediate need to relieve strong cancer pain but the physician is not able to physically provide a prescription. Examples include a pain crisis at night, on a public holiday or in a remote region. Only in Afghanistan were pharmacists allowed to prescribe in emergency situations. Few countries allowed for telephone or faxed prescriptions or nurse-generated prescriptions.

### pharmacist privilege 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.), Afghanistan, Algeria, Iran, Libya, Oman and Saudi



**Figure 3.** Formulary availability and cost to patients of the seven essential opioid formulations of the International Association for Hospice and Palliative Care (IAHPC) in Middle East 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.



**Figure 4.** Actual availability of the seven essential opioid formulations of the IAHPC in Middle East 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.

Country	Eligibility Restriction		
	Outpatients	Inpatients	Hospice
Algeria	Always	Always	Always
Afghanistan	Only with special authorization	Only with special authorization	Only with special authorization
Egypt	Only with special authorization	Only with special authorization	Only with special authorization
Iran	Never	Only with special authorization	Only with special authorization
Iraq	Never	Only with special authorization	Only with special authorization
Israel	Always	Always	Always
Lebanon	Only with special authorization	Always	Only with special authorization
Libya	Only with special authorization	Always	Only with special authorization
Morocco	Always	Always	Always
Oman	Only with special authorization	Only with special authorization	Only with special authorization
Palestine	Only with special authorization	Only with special authorization	Only with special authorization
Qatar	Only with special authorization	Only with special authorization	Only with special authorization
Saudi Arabia	Only with special authorization	Always	Only with special authorization
Syria	Only with special authorization	Only with special authorization	Only with special authorization
Tunisia	Only with special authorization	Only with special authorization	Only with special authorization
Yemen	Only with special authorization	Only with special authorization	Only with special authorization

Always  
 Only with special authorization  
 Never  
 No submitted data

Figure 5. Patient eligibility restrictions for cancer patients in Middle East countries.

Country	Prescriber privileges				
	Oncologist	Family Doc	Surgeon	Nurse	Pharmacist
Algeria	Always	Always	Always	Always	Always
Afghanistan	Only with special permit or authorization				
Egypt	Only with special permit or authorization				
Iran	Only with special permit or authorization				
Iraq	Only with special permit or authorization				
Israel	Always	Always	Always	Always	Always
Lebanon	Only with special permit or authorization				
Libya	Always	Always	Always	Always	Always
Morocco	Always	Always	Always	Always	Always
Oman	Always	Always	Always	Always	Always
Palestine	Only with special permit or authorization				
Qatar	Only with special permit or authorization				
Saudi Arabia	Always	Only with special permit or authorization	Always	Always	Always
Syria	Always	Always	Always	Always	Always
Tunisia	Always	Always	Always	Always	Always
Yemen	Always	Always	Always	Always	Always

Always  
 Only with special permit or authorization  
 Only in emergency  
 Never

Figure 6. Opioid prescriber privileges for cancer patients in Middle East countries.

Arabia allowed pharmacists to correct technical errors (Figure 10, last column).

### use of stigmatizing terminology for opioid analgesics in regulations

Eight countries had negative language in drug laws: Afghanistan, Iraq, Israel, Lebanon, Morocco, Palestine, Syria

Country	Prescription forms			
	Duplicate or Triplicate	Special Prescr Forms	ready access to forms	Pay for forms
Algeria	restrictive	restrictive	restrictive	restrictive
Afghanistan	not restrictive	restrictive	restrictive	restrictive
Egypt	restrictive	restrictive	restrictive	restrictive
Iran	restrictive	restrictive	restrictive	restrictive
Iraq	not restrictive	restrictive	restrictive	restrictive
Israel	not restrictive	restrictive	restrictive	restrictive
Lebanon	restrictive	restrictive	restrictive	restrictive
Libya	restrictive	restrictive	restrictive	restrictive
Morocco	restrictive	restrictive	restrictive	restrictive
Oman	restrictive	restrictive	not restrictive	restrictive
Palestine	restrictive	restrictive	restrictive	restrictive
Qatar	restrictive	restrictive	restrictive	restrictive
Saudi Arabia	restrictive	restrictive	not restrictive	restrictive
Syria	restrictive	restrictive	restrictive	restrictive
Tunisia	restrictive	restrictive	not restrictive	restrictive
Yemen	restrictive	restrictive	restrictive	restrictive

restrictive  
 not restrictive  
 Not relevant

Figure 7. Prescription restrictions in Middle East countries.

Country	Max Days Opioids Supplied
Algeria	30
Afghanistan	5
Egypt	14
Iran	depends on opioid type
Iraq	No submitted data
Israel	30
Lebanon	15
Libya	7
Morocco	7
Oman	30
Palestine	7
Qatar	10
Saudi Arabia	30
Syria	30
Tunisia	28
Yemen	15

28+ days  
 15-28 days  
 1-2 weeks  
 < 1 week  
 No submitted data

Figure 8. Maximum number of days opioid supplied on single prescription.

and Turkey (Figure 11). Driving was forbidden for patients taking opioid medication in eight countries.

**discussion**

Cancer continues to be an increasing problem throughout the world with an increase in cancer incidence in low- and middle-income countries. Many adult patients and children in these Middle East countries present with advanced disease [10, 11].

Opioid consumption has been documented in various formats for Middle East countries [3, 12–14]. While many countries have shown an increase in consumption since 2000, all countries but Israel have ‘inadequate’ consumption as defined by the International Narcotics Control Board (INCB) with a defined daily dose for statistical purposes per day per million people (S-DDD) of <200 mg oral morphine equivalents [14]. All surveyed countries in the Middle East, except Israel, have <10% of the anticipated Adequacy of Consumption Measure (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* [15]. 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.

**medication availability**

The majority of 16 countries surveyed here had limited access to the essential opioids as outlined by the IAHPC. It is striking that even in countries with very limited opioid formularies, TD fentanyl was usually among those medicines available. It is widely recognized that pharmaceutical companies and importers are reluctant to invest in the registration and promotion of products that do not generate significant profit, such as IR oral morphine or oxycodone. In contrast, where there is scope for profit from the promotion and marketing of proprietary products, such as TD fentanyl, there is greater commercial motivation. It is interesting to note that Jordan (not a respondent in this survey), which is among the countries with a relatively low GDP in the region, initiated their own manufacturing process for IR morphine [16].

**education**

Much work needs to be done in educating both patients and clinicians in the region on the role of opioids in cancer pain. In a survey of final year medical students in Saudi Arabia [17], disturbingly half of the respondents considered cancer pain as untreatable, 40% considered it a minor problem, and almost 60% consider the risk of substance dependency syndrome to be high with legitimate opioid prescription. In a survey of 122



**Figure 9.** Dispensing sites for Middle East countries and accessibility of those sites.

Country	Pharmacist restrictions	
	Pharmacists accept emergency telephone/fax prescriptions	Pharmacists may correct tech errors
Algeria	Yes	No
Afghanistan	No	No
Egypt	No	No
Iran	No	No
Iraq	No	No
Israel	No	No
Lebanon	No	No
Libya	No	No
Morocco	No	No
Oman	No	No
Palestine	No	No
Qatar	No	No
Saudi Arabia	No	No
Syria	No	No
Tunisia	No	No
Yemen	No	No



**Figure 10.** Pharmacy restrictions for Middle East countries.

physicians in six university hospitals in Tehran, inadequate education and training in this aspect of care was highlighted as a significant barrier to pain management [18]. This lack of knowledge was higher in non-oncology specialists. Almost 70% of oncologists at the National Center for Cancer and Research in Qatar reported awareness of guidelines for pain relief but only 60% indicated that they applied them in their practice [19]. Among nurses in the same hospital, just over half were aware of the WHO Three-step Ladder on Cancer Pain Relief [20] and the authors called for an increase in formal palliative care education. Many countries have commenced palliative care training in the region [21, 22].

Patient concerns regarding the use of opioids for the management of cancer pain have been evaluated in Jordan [23], Morocco [24] and Oman [25]. All of these studies demonstrate high levels of patient reluctance and fears regarding the use of opioids to relieve pain.

### government policies and regulations

With the exception of Israel, every responding country in the region reported very high levels of restrictive regulations that impaired access to opioids for pain relief (Figure 12). Indeed, there is urgent need for regulatory review and the repeal of unnecessarily burdensome barriers to accessibility.

Efforts to improve the situation have been initiated, especially through the Middle East Cancer Consortium [26]. While there has been progress in some countries for the development of palliative care in the Middle East [3, 27], overall there has not been any substantial increase in opioid consumption since 2006.

Country	Laws	
	Negative language in drug laws	Driving forbidden
Algeria	Yes	No
Afghanistan	Yes	No
Egypt	Yes	No
Iran	Yes	No
Iraq	Yes	No
Israel	Yes	No
Lebanon	Yes	No
Libya	Yes	No
Morocco	Yes	No
Oman	Yes	No
Palestine	Yes	No
Qatar	Yes	No
Saudi Arabia	Yes	No
Syria	Yes	No
Tunisia	Yes	No
Yemen	Yes	No



**Figure 11.** Negative laws regarding opioids.

As part of a WHO demonstration project, a model for pain relief and palliative care for the Middle East has been established in Jordan. A major educational and program initiative was undertaken at the King Hussein Cancer Centre (KHCC) in

**Table 1.** Comparison of DDD and %ACM [12–14]

	S-DDD 1997–1999	%ACM 2006	S-DDD 2007–2009	%ACM 2010
Afghanistan	ND	ND	ND	0.01
Algeria	60	0.3	160	0.63
Bahrain <sup>a</sup>	100	5.8	225	6.55
Egypt	45	0.76	50	1.29
Iran	20	1.46	40	1.70
Iraq	5	ND	10	0.21
Israel	1300	38	3500	42.31
Jordan <sup>a</sup>	50	5.81	80	5.24
Kuwait <sup>a</sup>	70	5.12	185	13.16
Lebanon	80	0.476	180	3.55
Libya	10	4.85	75	2.43
Morocco	20	0.54	30	0.82
Oman	40	3.15	60	2.99
Palestine	–	–	–	–
Qatar	110	7.1	160	4.24
Saudi	50	4.0	190	5.76
Syria	20	3.81	80	5.16
Tunisia	60	3.46	120	2.64
Turkey	120	5.74	580	7.28
UAE <sup>a</sup>	40	1.84	180	4.68
Yemen	0	0.12	10	0.24

<sup>a</sup>Countries that did not respond to GOPI survey.

%ACM, percentage of Adequacy of Consumption Measure; S-DDD, defined daily dose per million persons per day.

Country	Eligibility Restriction	Physician Prescriber Restrictions	No emergency prescriptions by Fx/Phone or non medical prescribing	Limited prescription duration	No pharmacist authority to correct prescription	Increase bureaucratic burden of prescriptions	Restricted dispensing sites	Negative language in laws	Number of restrictive domains (N/8)
Israel			Yes		Yes			Yes	3
Tunisia	Yes		Yes		Yes	Yes			4
Algeria	Yes	Yes	Yes			Yes	Yes		5
Afghanistan	Yes			Yes		Yes	Yes	Yes	5
Iran	Yes	Yes	Yes			Yes	Yes		5
Oman	Yes	Yes	Yes			Yes	Yes		5
Saudi Arabia	Yes	Yes	Yes			Yes	Yes		5
Libya	Yes	Yes	Yes	Yes		Yes	Yes		6
Morocco			Yes	Yes	Yes	Yes	Yes	Yes	6
Yemen	Yes	Yes	Yes		Yes	Yes	Yes		6
Egypt	Yes	Yes	Yes	Yes	Yes	Yes	Yes		7
Iraq	Yes	Yes	Yes		Yes	Yes	Yes	Yes	7
Lebanon	Yes	Yes	Yes		Yes	Yes	Yes	Yes	7
Qatar	Yes	Yes	Yes	Yes	Yes	Yes	Yes		7
Syria	Yes	Yes	Yes		Yes	Yes	Yes		7
Palestine	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8

Figure 12. Summary of regulatory barriers to opioid access for cancer pain relief in Middle East countries.

Amman. This program included the development of palliative care services for inpatients, outpatients and patients at home. Regulations governing opioid prescribing have been changed to facilitate effective pain management. The national opioid quota has been increased. Cost-effective, generic, immediate-release morphine tablets are now being produced in Jordan. These initiatives have led to a substantial increase in palliative care service utilization. The achieved changes and the unusually rapid and effective institutionalization of palliative care serve as a model for other countries in the Middle East [16].

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 [28].

**conclusion**

With the exception of Israel, opioid availability continues to be low throughout most of the Middle East. Formulary deficiencies are severe in several countries, in particular Afghanistan, Iraq, Lebanon, Libya, Palestine and Tunisia. Even when opioids are on formulary they are often unavailable, particularly in these same countries. Access is also significantly impaired by widespread over-regulation that is pervasive across the region.

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

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**disclosure**

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## Next steps in access and availability of opioids for the treatment of cancer pain: reaching the tipping point?

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The reports of the Global Opioid Policy Initiative (GOPI) project to evaluate the availability and accessibility of opioids for the management of cancer pain in Africa, Asia, Latin America and the Caribbean, and the Middle East, together with the previous 2010 European Society for Medical Oncology (ESMO)/European Association for Palliative Care (EAPC) report from Europe, have provided critical data in demonstrating the deficiencies in many countries throughout the world. Formulary deficiencies and over-regulation are pandemic and must be addressed. This process is challenging and will require concerted and sustained efforts by clinical leaders and advocacy groups partnering with international and regional organizations and, of course, with national governments and their competent authorities. There is a growing international expertise and infrastructure to coordinate advocacy and strategic planning based on the World Health Organization (WHO) Model of Education, Policy Reform and Medication Availability.

### introduction

‘The use of controlled substance should be limited to medical and scientific purposes while preventing their abuse misuse and diversion.’—The Single Convention of Narcotic Drugs (1961) (ref).

The Single Convention, the world’s guiding document on the use of controlled substances, goes on to state that opioids are essential for the relief of pain. Critically, the Convention does not state that the use of controlled substances should be limited for medical and scientific purposes, only limited to their medically defined use. However, the limitation of the use of opioids for medical and scientific purposes has been much of the reality of the Single Convention’s implementation for over 50 years.

An increase in opioid consumption has been seen throughout the world in the last 30 years, but little of this increase has occurred in low- and middle-income countries (LMICs) (Figure 1). Many have highlighted the extent of this global discrepancy [1–4]. Cherny et al. (2010) described many of the formulary and regulatory reasons for the difference in opioid consumption for cancer pain management between Eastern and Western Europe [5]. This 2013 volume now contains documentation of the formulary and regulatory reasons for low opioid consumption for Africa [6], Asia [7], India [8] Latin America and the Caribbean [9], and the Middle East [10]. The combined data for all these regions are illustrated graphically for formulary availability (Figure 2) and regulatory barriers

(Figure 3). Most of the world’s population lacks the necessary access to opioids for cancer pain management and palliative care, as well as acute, post-operative, obstetric and chronic non-cancer pain.

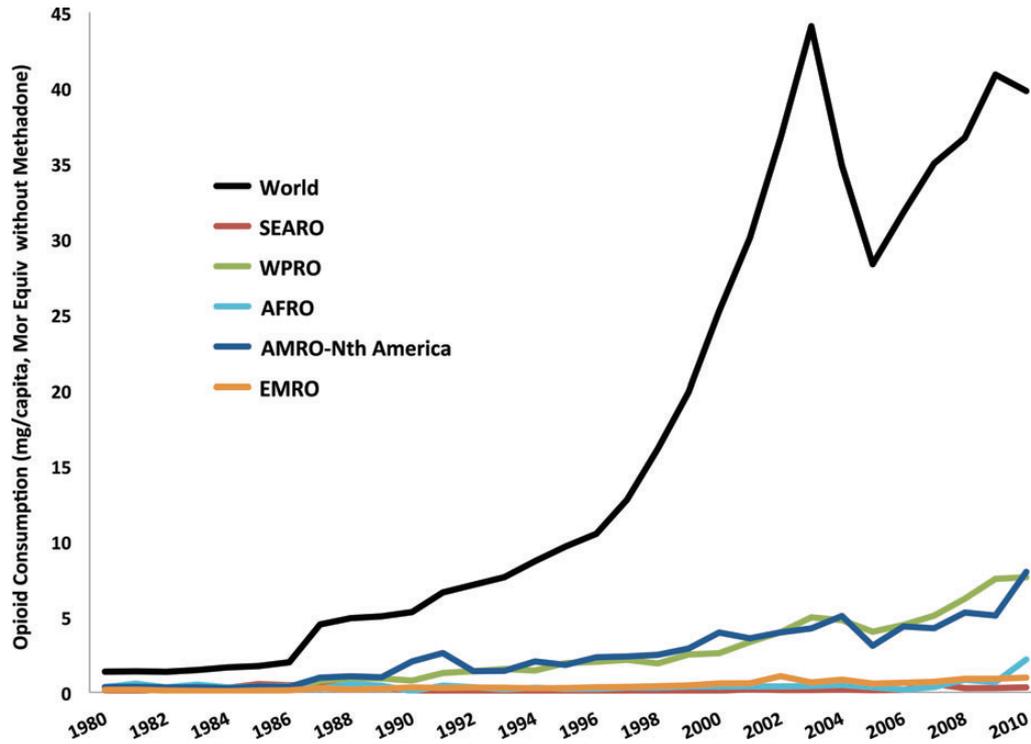
One could draw a pessimistic view that little progress has been made in LMICs. But progress has been and continues to be made in many countries as documented by the International Narcotic Control Board (INCB, 2010) and from Duthey and Scholten, 2013 [4]. Sixty-seven countries showed a >10% increase in opioid consumption between 2006 and 2010 as measured by %ACM (percentage of Adequacy of Consumption Measure). While a smaller number had a decrease in %ACM and other nations still fail to report their consumption to the INCB, the global community may be approaching a ‘tipping point’ in terms of improving access to opioids for medical and scientific purposes. What evidence do we have for this?

### the commission on narcotic drugs

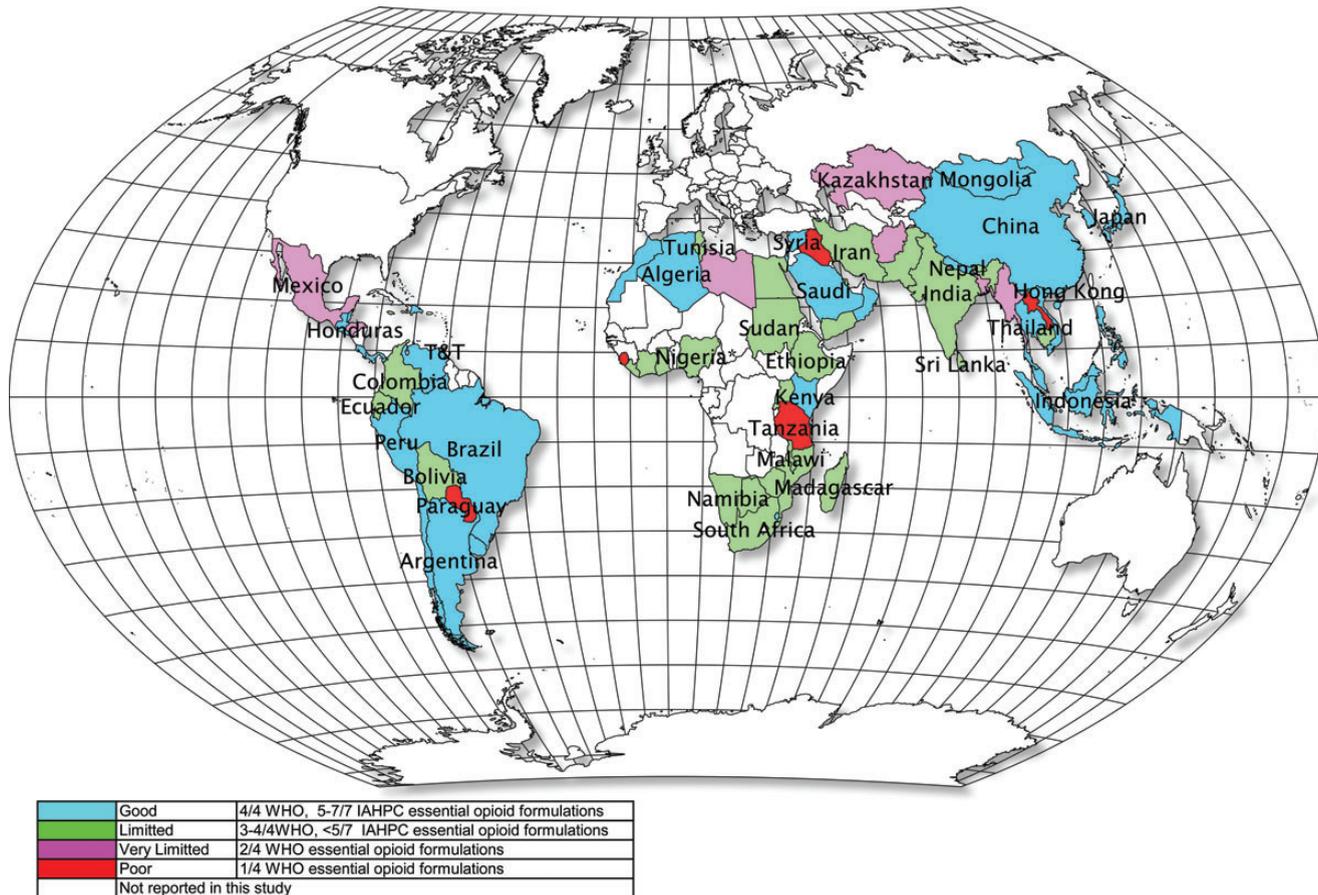
The Commission on Narcotic Drugs (CNDs) is a United Nations body established in 1946 to assist in supervising the application of the international drug control treaties. In 1991, the United Nations General Assembly (UNGA) further expanded the mandates of the CND to enable it to function as the governing body of the United Nations Office on Drugs and Crime (UNODC).

In recent years, the CND has passed resolutions addressing the lack of access to opioids for the relief of pain. Resolutions express concern about the low level of the use of opioids for medical purposes and call on nations to identify means of improving this (<http://daccess-dds-ny.un.org/doc/UNDOC/LTD/V11/815/54/PDF/V1181554.pdf?OpenElement>).

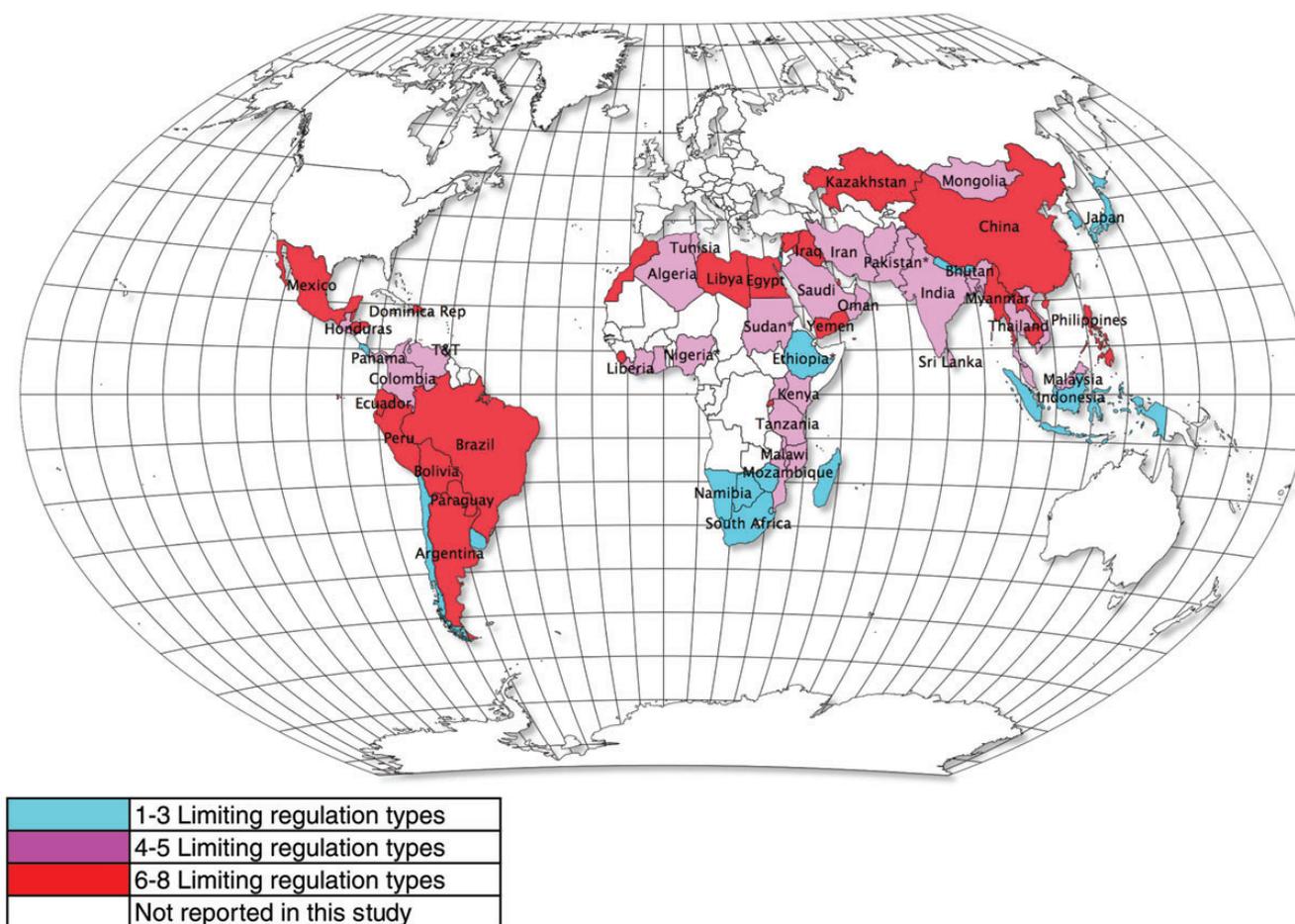
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**Figure 1.** Comparison of opioid consumption (mg/capita) in morphine equivalence without methadone. SEARO = South East Asia, WPRO = Western Pacific, AFRO = Africa, AMORO-North America = Latin America and Caribbean (America not including North America), EMRO = Middle East (Eastern Mediterranean).



**Figure 2.** Summary map for formulary availability (not actual availability) of the seven essential opioid formulations of the International Association for Hospice and Palliative Care (IAHPC).



**Figure 3.** Summary map for the number of regulatory barriers types for all regions covered in the report.

Furthermore, the UNGA in its special session on Non-Communicable Disease’s (NCDs) in New York, in 2011, included palliative care as an important health system issue that needs to be addressed in dealing with NCDs.

**the world health organization**

The World Health Organization (WHO) has been charged with implementing a Global Monitoring Framework for NCDs and has determined a surrogate indicator to measure the progress in palliative care. This NCD indicator will be opioid consumption measured as morphine equivalents of opioids (excluding methadone) consumed per cancer death. Using data collected by the INCB, this process adds to ongoing work within the WHO to promote palliative care as a means to reduce suffering caused by NCDs. Although the targets and indicators of the Global Action Plan on the Prevention and Control of NCDs 2013–2020 are voluntary, and therefore not binding on any nation, the inclusion marks a significant global acknowledgement of the need to improve access to palliative care.

While recognizing that this indicator is a surrogate and neither a perfect nor a direct measure, it is an objective and measurable indicator that reflects progress in palliative care interventions, without the need for initiating a new large scale

and potentially costly data collection. The data included in these reports are opioid consumption measured as morphine equivalents of opioids consumed per person, a measure used by the Pain and Policy Studies Group (PPSG). The WHO has proposed this metric as a Universal Health Care Indicator for Palliative Care.

World Health Organization. WHO Model List of Essential Medicines 18th ed. Geneva: World Medical Association 2013. ([http://www.who.int/medicines/publications/essentialmedicines/18th\\_EML\\_Final\\_web\\_8Jul13.pdf](http://www.who.int/medicines/publications/essentialmedicines/18th_EML_Final_web_8Jul13.pdf)). The WHO also continues to address palliative care with seven collaborating centers that specifically address palliative care in their terms of reference. Furthermore, in 2014, the WHO Secretariat has been requested by Member States to bring to the World Health Assembly a resolution that lays out the importance of palliative care and appropriate access to opioids in public health. A dedicated resolution has the promise to set out a road map for the international community to improve availability and access to palliative care services.

**the role of regional organizations**

While each nation will have responsibility for improving palliative care services for its residents, there is increasing potential for the influence of regional government

**Table 1.** International and Regional Civil Society Organizations with a focus on palliative care

International
UICC's Global Access to Pain Relief Initiative (GAPRI)
International Association for Hospice and Palliative Care (IAHPC)
Pain and Policy Studies Group, University of Wisconsin Carbon Cancer Center (PPSG)
Worldwide Palliative Care Alliance (WPCA)
International Association for the Study of Pain
International Childrens' Palliative Care Network
International Palliative Care Initiative (IPCI) of the Open Society Foundation (OSF)
Multinational Association of Supportive Care in Cancer (MASCC)
International Network for Cancer Treatment and Research (INCTR)
Human Rights Watch
Regional
European Association for Palliative Care (EAPC)
European Society for Medical Oncology (ESMO)
African Palliative Care Association (APCA)
African Organization for Research and Training in Cancer (AORTIC)
Asian Pacific Hospice and Palliative Care Network (APHN)
Middle East Cancer Consortium (MECC)
Latin American Palliative Care Association (ALCP)
Latin American and Caribbean Society for Medical Oncology (SLACOM)
SAARC Federation of Oncology (SFO)

organizations. Ministers of Health and other ministry representatives of 15 African counties recently met in South Africa and strongly supported improving the availability of palliative care throughout their region. This meeting, that also addressed issues of opioid availability, preceded the combined meeting of the African Palliative Care Association (APCA) and the Hospice and Palliative Care of Association of South Africa. The engagement with international and regional organizations within Civil Society (Table 1) can provide powerful support for advocacy with national regulatory authorities.

### the role of individual governments

The information provided in this supplement advances the previous work of Cherny et al. [5] for Europe. The reports of this volume for the States of India and the regions of Africa, Asia, the Middle East, Latin America and the Caribbean provide critical substrate data for the evaluation of regulatory policies that may be undermining opioid availability for the management of cancer pain. While the call has come out for improvement in opioid availability from global and regional organizations, the responsibility for this improvement ultimately lies with each nation's government.

It is incumbent upon responsible individual governments to evaluate their regulatory structures for over-regulation and to undertake the necessary legislative and regulatory reforms to ensure accessibility to essential pain relieving medications.

This approach is illustrated in the case study of the Ukraine which was highlighted in the European report [5] for its limited opioid formulary (only injectable morphine) and which can now be commended as a nation making progress. Concerted efforts supported by the Open Society Institute, reports from

Human Rights Watch [11], together with the investment in local clinical champions through programs such as the PPSG's International Pain Policy Fellowship (IPPF) Program [12], have led to the government approving the manufacture and distribution of immediate-release oral morphine in the Ukraine with concurrent changes in policy. No longer should Ukrainians like Vlad, a young man with an inoperable brain tumor, or Artur, a former KGB colonel with metastatic prostate cancer, whose stories were so shockingly displayed in reports [11] and documentaries [12], have to endure the severe pain caused by their cancers. The national data derived from the European Society for Medical Oncology (ESMO); and the European Association for Palliative Care (EAPC) survey provided for Eastern Europe was not the only tool used to bring about change in the Ukraine, but it proved to be an important tool to drive much education and advocacy throughout Europe to improve opioid availability.

### the cornerstone trinity: medication availability, education, and policy reform

Once a nation's government has determined that it can and is ready to make necessary changes, the global community is ready and willing to support these efforts. But the efforts for change have to span the cornerstone trinity and be directed at medication availability, education, and policy reform. The checklist provided in the WHO policy guidelines, *Ensuring Balance in National Policies on Controlled Substances, Guidance for availability and accessibility of controlled medicines*, is a useful initial tool [13]. Furthermore, review of legislation and comparison with model laws that have just been updated by the UNODC, together with a parallel review of regulations, are an important part of the process.

India's Narcotic Drugs and Psychotropic Substances (NDPS) Act is a prime example of this. The amendment that is currently before the Federal Parliament was crafted through the collaboration of the India Government's Departments of Revenue and Health and Family Services with many organizations, including the Indian Association of Palliative Care, the two WHO Collaborating Centers in India addressing palliative care, and the PPSG with three IPPF awardees supported by the Livestrong Foundation. The Human Rights Watch report on the lack of availability of opioids provided significant stimulus for action, as did coverage in both mainstream and social media [14]. The global palliative care community is watching the winter session of the Indian Parliament for the successful passing of this amendment.

Many of the impactful solutions do not require major changes in law. IPPF awardees in Jamaica collaborated with the 'Competent Authority', specifically the Office of Dangerous Drugs in the Ministry of Health. Simple dialog with advocates was sufficient to inform and activate the needed change in the tone and focus of regulatory activity. The Ministry of Health issued a press release highlighting this refocus: 'Pain management and palliative care must address patient and family discomfort and restore persons to their productivity level. It is important that we understand new methods of pain management and prevent misuse. Opioids are important and

effective and we have to examine the policies and legal framework surrounding their use, as we may need to adjust them to allow us greater flexibility and protect the health worker.’

### the collaborative approach

Champions within a country should not be concerned about disclosure of civil society collaborators for fear of losing financial support. While it can be argued strongly that there is never enough philanthropic support for these efforts, it continues to be a priority for a number of funders. The new global and political awareness described above will hopefully encourage engagement from new global philanthropic organizations and bilateral donors to provide the funds to scale up successful models in more countries.

In the past, it has often been easier for individual associations, NGO's, and philanthropic organizations to work independently within a country. A coordinated approach, harnessing the expertise and synergies of leaders across the fields of public health, palliative care, pain management, education, regulation, and law is necessary to create a united voice and achieve the ‘tipping point’ for a real change and sustained impact. The Union for International Cancer Control, through the ‘Global Access to Pain Relief Initiative—GAPRI’ ([www.uicc.org/programmes/gapri](http://www.uicc.org/programmes/gapri)), aims to take on this convening role. Similarly, the International Association for Hospice and Palliative Care, in collaboration with the European Association for Palliative Care and other partners, have initiated the Prague Charter, urging governments to ensure access to palliative care and essential pain relief medicines for all patients in need [15].

There should be great optimism that, through collaboration and united efforts of the leading palliative care and oncology organizations who participated in this report, many of the formulary and regulatory issues related to the difference in opioid consumption at regional and national levels can be overcome. It may be that with the recognition of this problem by the World's governing bodies, we reach our ideal goal in ensuring adequate access to affordable and effective pain medications for all cancer patients.

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