Pain and Policy Studies Group: Two Decades of Working to Address Regulatory Barriers to Improve Opioid Availability and Accessibility Around the World

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Abstract

For two decades, the Pain & Policy Studies Group (PPSG), a global research program at the University of Wisconsin Carbone Cancer Center, has worked passionately to fulfill its mission of improving pain relief by achieving balanced access to opioids worldwide. PPSG's early work highlighted the conceptual framework of balance leading to the development of the seminal guidelines and criteria for evaluating opioid policy. It has collaborated at the global level with United Nations agencies to promote access to opioids and has developed a unique model of technical assistance to help national governments assess regulatory barriers to essential medicines for pain relief and amend existing or develop new legislation that facilitates appropriate and adequate opioid prescribing according to international standards. This model was initially applied in regional workshops and individual country projects and then adapted for PPSG's International Pain Policy Fellowship, which provides long-term mentoring and support for several countries simultaneously. The PPSG disseminates its work online in several ways, including an extensive Web site, news alerts, and through several social media outlets. PPSG has become the focal point for expertise on policy governing drug control and medicine and pharmacy practice related to opioid availability and pain relief. J Pain Symptom Manage 2018;55:S121–S134. © *2017 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.*

Key Words

Opioid analgesics, cancer pain, policy, laws, regulations

Introduction

The global burden of unrelieved pain is a critical public health issue. The World Health Organization (WHO) estimates that worldwide 5.5 million terminal cancer patients and one million end-stage HIV/AIDS patients are suffering without adequate treatment for moderate-to-severe pain.[1] Relief of such pain, a critical component of palliative care, cannot be accomplished without improving the availability and accessibility of opioid analgesics. While there are many pharmacological and nonpharmacological modalities to treat pain, experts have long recommended strong opioid analgesics in the class of morphine for the treatment of moderate-to-severe pain, such as that experienced by cancer patients.[2,3] In fact, for over 30 years, morphine has been recognized by WHO as an essential medicine,[4] recommending its use in relieving pain due to cancer and AIDS.[5]

Furthermore, the United Nations (UN) Single Convention on Narcotic Drugs, 1961, as amended by the 1972 Protocol, the primary international treaty governing the use of controlled medicines, strongly supports the use of opioids for pain relief stating that "the medical use of narcotic drugs continues to be indispensable for the relief of pain and suffering, and adequate provision must be made to ensure the availability of narcotic drugs for such purposes."[6] UN bodies and other international drug regulatory bodies, such as the International Narcotics Control

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Board (INCB), have acknowledged that their emphasis historically has been only on restricting opioid misuse and abuse, rather than also on ensuring availability of medicinal opioids.[7] However, beginning in the late 1980s, these organizations published numerous reports encouraging governments to meet their obligation about maintaining medication availability for pain relief and palliative care.[7–12] Importantly, in the last several years, the INCB, the United Nations Economic and Social Council, and the United Nations Office on Drugs and Crime (UNODC) have made unprecedented high-level statements and have developed initiatives directed at improving the availability of opioids for pain relief.[13–16]

Despite the medical and scientific evidence supporting the use of opioids for cancer pain[17–19] and the high-level UN recommendations to ensure their adequate availability, recent studies found that 75% of the world's population lacks adequate access to opioid analgesics for medical purposes.[20–22] In 2014, high-income countries (representing 21% of the world's population) consumed 92% of total global morphine consumption, whereas low- and middle-income countries (LMICs) (representing 79% of the world's population) consumed a mere 8% of the total global morphine (see Fig. 1).[23] The lack of sufficient medication availability is often due to unduly strict national drug control policies and systems, which are increasingly acknowledged to be among the most significant barriers to the availability of opioid medications for palliative care, especially in developing countries.[7,9,10,13] These policies and systems originated when much of the global disease burden was characterized by acute and often infectious conditions. Resulting policies were overly restrictive and frequently allowed only short-term use of opioid medications in inpatient settings. Such policies have become outdated as chronic diseases have become more prevalent and the science of pain has evolved.

Recognizing the dire need to improve the availability of opioids globally to relieve pain, especially when pain is severe, the Pain & Policy Studies Group (PPSG), a global research program at the University of Wisconsin Carbone Cancer Center, School of Medicine and Public Health, established a mission to improve global pain relief by achieving balanced access to opioids worldwide. "Balance" in the policy context refers to international, national, and state policies that strive to ensure both the adequate availability of pain medication for patient care and the avoidance of their diversion and abuse. PPSG's work, guided by a public health approach, aims to address governmental and regulatory environments governing professional health care practice relating to pain management, including barriers to legitimate access of prescription opioid analgesics that are essential for severe pain relief and palliative care. Such efforts are achieved through effective public policy, communications, and outreach efforts. PPSG's activities have focused historically on researching and disseminating information about global undertreatment of pain, disparities in global opioid consumption, methods to identify and address policy barriers at the national level, and providing ongoing technical assistance to colleagues to help them improve availability and access to opioids in their countries. At the same time, PPSG's work is guided by the principle of balance acknowledging that the strength of a country's drug control system needs to be maintained or enhanced so that increased availability does not contribute to societal harms, which is also a government's obligation under the Single Convention.[6]

The PPSG is globally recognized for its work and leadership to improve availability of opioid pain

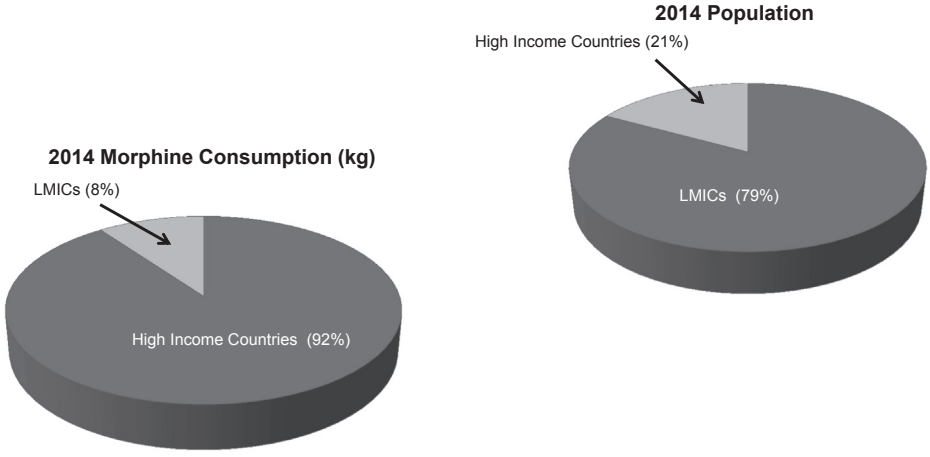

Fig. 1. Disparity of 2014 morphine consumption (kg): high-income vs. low- and middle-income countries (LMICs).

medicines,[24] having been at the forefront of this effort since its creation in 1996. PPSG's work has benefitted greatly from our designation as a World Health Organization Collaborating Center (WHOCC). Currently, it is the WHOCC for Pain Policy and Palliative Care.

Global Outreach

Drug Control

PPSG has a long history of working collaboratively with the highest global drug control authorities including the INCB, the Commission on Narcotic Drugs (CND), and the UNODC. For example, PPSG assisted the INCB secretariat with their 1995 survey of national governments about the impediments to opioid availability and helped to draft the resulting seminal Special Supplemental Report, "Availability of Opiates for Medical Needs."[9] More recently, PPSG participated in a multiagency expert working group that drafted the 2012 INCB/WHO joint publication "Guide on Estimating Requirements for Substances under International Control."[25] The guide was designed to assist countries with low medical consumption of controlled substances in improving their methods for calculating their national estimated requirements for controlled medicines. PPSG's role as an academic and research organization and a WHOCC has made these unique relationships possible. PPSG has been successful at maintaining a dialog about country-level efforts to address systemic barriers to opioids for pain management, as well as engaging with countries struggling to meet their treaty obligations and consuming extremely low amounts of opioids for medical purposes.

As a part of PPSG's work with INCB and UNODC, PPSG provides information about the status of opioid availability at the country level. Such information is typically obtained from in-country colleagues and then written up by PPSG staff to emphasize the aspects most relevant for INCB and UNODC. For example, for the past decade, PPSG has provided information to INCB to include their annual reports about countries' national legislative and regulatory barriers to adequate availability and their progress in addressing such barriers.

In the late 2000s with support from the U.K. Department for International Development (DfID), PPSG collaborated with colleagues in the harm reduction field to explore approaches for combining advocacy efforts to promote the inclusion of access to controlled medicines in the larger global drug policy discussions. To complement this work, Open Society Foundations (OSF) International Palliative Care Initiative (IPCI) and the OSF Global Drug Policy Program supported PPSG in the hiring of a staff person with a legal background who focused half of her time on access to medicines in the context of harm reduction. A key part of the DfID-supported project involved the initial, pioneering efforts in 2009 to advocate for including access to opioids as an important agenda item at the CND in Vienna. Subsequently, each year incremental progress has been made and other pain and palliative care colleagues have become involved. Advocacy work with the CND has continued, partially supported by OSF/IPCI, and for the seventh consecutive year, availability of controlled medicines for medical and scientific purposes was on the CND agenda, signifying that it continues to be recognized as important as drug control by international drug control authorities responsible for implementing the Single Convention. Furthermore, two United Nations Economic and Social Council resolutions were passed in 2010[14] and 2011[15] as a result of these joint advocacy activities. These efforts are particularly relevant now to ensure that access to controlled medicines is recognized as a pillar of global drug policy. Notable progress was achieved by pain and palliative care advocates at the 2016 United Nations General Assembly Special Session (UNGASS) on the World Drug Problem, which resulted in an outcome document that included access to controlled medicines as a stand-alone priority for the next UNGASS in 2019.

Health

As a WHOCC, PPSG has a long track record of working with global health authorities. PPSG has collaborated with the WHO Cancer Control, Non-Communicable Diseases, Essential Medicines, and HIV/AIDS Programs to develop methods to achieve more balanced national drug regulatory policies and has accrued experience in implementation and evaluation. For example, in 1996, PPSG drafted a section on opioid availability in the second edition of WHO's seminal cancer pain guidelines.[26] In 1999, PPSG led the creation of the Guidelines "Achieving Balance in National Opioids Control Policy," issued by the WHO.[27] Formally endorsed by the INCB, this important policy evaluation tool, and now its successor document, "Ensuring Balance in National Policies on Controlled Substances,"[7] which included PPSG participation, provides the background and rationale for national policy and systems evaluation and revision to improve availability and patient access to controlled medicines, including opioid analgesics.[28]

PPSG continues to engage with global health authorities to promote access to opioids as a critical part of palliative care. In 2011, a UNGASS was held to address the growing threat of noncommunicable diseases (NCDs) on the future of the world. Through considerable advocacy of the global palliative care community, including PPSG, palliative care was

included in the resulting Global Monitoring Framework,[29] which was developed by WHO and the World Health Assembly (WHA) following the 2011 UNGASS meeting. Importantly, the NCD Global Monitoring Framework establishes nine outcomes and 25 indicators, including a palliative care indicator. Given the lack of new resources allocated to these indicators, the palliative care indicator chosen was opioid consumption per cancer death. The data that will be used for this indicator are national opioid consumption data reported by governments to the INCB and provided to PPSG as a WHOCC. PPSG is working with collaborators, including the INCB and WHO, to calculate this indicator and disseminate it widely.

PPSG collaborated with global palliative care colleagues to advocate for the WHA to adopt a palliative care resolution, urging member states to integrate palliative care into health care systems, to improve training for health care workers, and to ensure that essential medicines, including strong pain medicines, are available to patients. During the WHA meeting in May 2014, health ministers from around the world adopted, for the first time in its history, a palliative care resolution.[30] The resolution calls on the WHO to increase its technical assistance to member countries on the development of palliative care services. Working with colleagues, PPSG is currently using the opportunities created by the WHA resolution to advocate for improved availability of palliative care and provide technical assistance to countries to integrate palliative care and opioid availability into their health systems. PPSG continues to be actively involved in a WHO Technical Advisory Group on Palliative Care established to guide the implementation of the 2014 WHA Resolution.

Addressing Opioid Availability at the Country Level

PPSG has a long-standing, established, track record of working directly within countries to identify and address their systemic barriers to opioid availability for pain relief and palliative care. It has developed a unique model of technical assistance[31] to help national governments, upon invitation, assess regulatory requirements to essential medicines for pain relief and amend existing or develop new legislation that facilitates appropriate and adequate opioid prescribing according to international standards (see Table 1). PPSG's early national projects included India,[32] Italy,[33] and Romania.[34]

PPSG Regional Workshop Model

In the late 1990s, PPSG developed a model approach for conducting regional opioid availability workshops.[35] Since the early 2000s, PPSG has cooperatively organized or participated in several workshops[5,36–40] with the WHO, national and/or regional nongovernment organizations, of which, many have been supported and co-organized by OSF/IPCI. These multiday workshops brought together carefully selected teams of pain and palliative care regional and national leaders and health care and regulatory professionals, including representatives of the national drug control authority, from five or six countries in a geographic region. Drawing together participants from the same region, who often share common experiences related to opioid availability and face similar challenges, facilitates finding solutions to the common challenges and increases the likelihood of sustainable partnerships and a sense of ownership of the accomplishments. These workshops are centered around a strategic planning process to develop specific action plans designed to be implemented by the country teams following the workshop. Leadership, availability of resources, and technical cooperation has been critically important to successful follow-up implementation of action plans. Over the years, other organizations in the global pain and palliative care field have implemented similar workshops and meetings building on this model.[38,41,42]

Regional Workshop and Romania Country Project

A noteworthy example of a regional workshop leading to a country project was the collaborative effort between palliative care experts and the PPSG to improve opioid availability in Romania. In 2002, the WHO European Regional Office and OSF/IPCI sponsored a six-country regional workshop on opioid availability for palliative care in Budapest, Hungary, with the intention of selecting one country to receive follow-up support to implement their action plan.[36] Romania was identified as the country with the most potential for making policy changes because 1) it had many regulatory barriers that restricted patient access to opioids; 2) it had palliative care leaders who were highly motivated to work on making changes; and 3) the Ministry of Health (MoH), including national drug regulators, announced its decision to appoint a special MoH Commission to explore what regulatory changes were necessary and provide recommendations for change to improve patient access to opioids.

In 2003, with funding from the OSF/IPCI and the United States Cancer Pain Relief Committee, the PPSG began a three-year project that included Romanian health care practitioners, the MoH and its commission, and the WHO. Following an invitation from the MoH Commission, the PPSG assisted with the review and analysis of national policy and regulations to develop a set of policy change recommendations that were presented to the Minister of Health in July

Table 1
PPSG Model of Addressing Regulatory Barriers to Opioid Availability

Step	Description
1. Assessing the country opioid availability situation	• Collect and review available information about a country's pain and palliative care situation, for example: ○ amount of opioid medication currently being used ○ whether there are activities underway to improve opioid availability • Assess the level of government support, which is absolutely necessary to have at the onset of the process to improve the regulatory policies and environment for opioid availability in a country
2. Identification of barriers to opioid availability	• Identify the regulatory barriers to adequate opioid availability by using the WHO guidelines[7,28] which have become central resources, offering frameworks for understanding, and specific criteria for assessing regulatory barriers ○ The current guidelines contain a Country Assessment Checklist that can be used to guide an assessment activity within a group of interested stakeholders • Use additional methods of identifying barriers such as interviews with key informants or focus groups with those who are familiar with patient care, unmet needs, and the national regulatory framework.
3. Develop an action plan	• Use the PPSG process and tools to guide country stakeholders through the creation of an action plan • Identify three to five of the most important opioid availability problems in a country which, if successfully addressed, would contribute to significant immediate and sustained improvements in patient access to pain medications. • Detail the objectives, activities, and resources necessary for eliminating each barrier in the action plan
4. Implementing the action plan and technical assistance	• Throughout the process of implementing the Action Plan, seek guidance from international expert mentors, such as PPSG staff. • To facilitate this mentorship and with support from OSF/IPCI, PPSG established an International Expert Committee (IEC), comprised of pain and palliative care experts who have experience in working with government and wish to expand this work, in consultation with the PPSG. ○ PPSG provides IEC members with background and resource information on opioid availability and IEC members share their experiences working with governments and serve as mentors to in-country advocates implementing an action plan to improve opioid availability.

PPSG = Pain & Policy Studies Group; WHO = World Health Organization.

2003. During the next two years, the MoH drafted a revised narcotics control law, which was adopted by the Romanian Parliament in November 2005. A team from the MoH, including drug regulators, and members of the Commission were invited to the PPSG offices in 2004 to draft a regulation to implement the new law. The regulations, which were a vast simplification of the old administrative process required for patients to obtain opioids for pain relief, were approved in 2006 and became effective in 2007.[34]

With support from OSF/IPCI, PPSG continued to support Romania throughout the initial process of implementing the new law and regulation, including the development of a national program to educate health care professionals about how to prescribe opioid analgesics under the new regulations. A critical national meeting was held in Bucharest in 2006 including representatives of palliative care, cancer, HIV/AIDS, the national drug regulatory body, medical education, and the antidrug law enforcement agency to discuss how the new laws and regulations would be successfully implemented. The meeting provided an opportunity to educate all stakeholders about opioids for treating pain under the new laws and regulations, address questions, and achieve a consensus. PPSG continued its engagement with the Romanian project by participating in a newly formed Curriculum Planning Committee, which included experts in palliative care and pharmacy from the University of Wisconsin, to develop a training of trainers program to reach physicians and pharmacists throughout the country.[43]

The International Pain Policy Fellowship

In order to expand leadership for improving opioid availability in more countries and increase the rate of positive changes, in the mid-2000s the PPSG developed the International Pain Policy Fellowship (IPPF).[44] The program was inaugurated in 2006 with support from the OSF/IPCI, and subsequently sustained by IPCI, Livestrong, the United States Cancer Pain Relief Committee, and the National Cancer Institute. The goal of the IPPF is to empower motivated health professionals and policy makers from LMICs with the knowledge and skills necessary to identify and overcome barriers to the use of opioids for pain control and palliative care in their country, without sacrificing the security of the existing drug control system.

The IPPF is intended for health professionals (e.g., physicians and pharmacists), health care administrators, policy experts, social workers, or lawyers from LMICs who have an interest in improving availability of opioid medicines for pain relief and palliative care. Fellows are chosen through a rigorous application process that includes a review of their curriculum vitae, experience in research, potential for successful change in the country, and support from their employer. Beginning with the second cohort, fellows were encouraged to identify a government representative from the MoH (or its equivalent) who recognized the importance of the program and committed to support the IPPF activities and attend the initial training workshop. Fellows are provided a modest stipend to

commit a portion of their professional time to IPPF activities. To date, there have been four cohorts of fellows, comprising 30 individuals from 25 countries, which represents about one-third of the world's population (see Table 2).

The IPPF program has four components that build on PPSG's model of addressing opioid availability at the country level:

1. Training program: At the beginning of the fellowship program, PPSG conducts an intensive training workshop to provide fellows foundational information about the roles and function of the international drug control system and how to become a strategic change agent for opioid availability in their country. PPSG staff and expert mentors assist the fellows in identifying barriers in their country's policies and systems governing the use of controlled medicines. Fellows then develop an Action Plan to define three to five barriers to opioid availability in their countries and detail the objectives, activities, and resources necessary for eliminating each barrier. These Action Plans are ambitious, each addressing unique and dynamic national environments characterized by political changes (such as national elections) and other unforeseen factors that impact national health care priorities.
2. In-Country Project using the Action Plan: Each fellow is responsible for implementing the Action Plan during the remainder of the IPPF.
3. Mentorship: Throughout the IPPF, PPSG staff and international expert mentors (see Table 3) are in frequent contact via e-mail and telephone with each fellow to provide technical assistance related to their in-country project to ensure progress in meeting the Action Plan objectives. Examples of technical assistance include:
   - expert review and comments on new or amended policies,
   - analysis of opioid supply chain systems,
   - writing strategic letters of support to key government officials or decision makers to further their support of the fellows' work,
   - when invited, assisting in the organization and presentation at national workshops or high-level meetings with MoH officials to provide international expert opinion or to facilitate government action regarding opioid availability,
   - acting as a liaison between the fellow and the WHO (headquarters and regional offices) or the INCB, in an effort to encourage government officials to support the fellow's activities or to introduce the fellow to these international organizations to encourage support for their in-country work,
   - upon request, traveling to fellow's country to attend a national workshop or meet with government officials, such as the office of the MoH to raise awareness of the opioid availability challenges,
   - problem-solving and strategizing when road blocks arise, and
   - facilitating communication and sharing of strategies and resources between fellows and other experts in various fields (pharmacy, nursing, education, and so forth).
4. Update and Review Meeting: At the midpoint of the IPPF program, an Update and Review meeting is held to provide fellows an opportunity to network and develop strategies to overcome outstanding challenges as well as to share approaches that have led to success. This type of meeting can capitalize on the inevitable changes in national landscape that typically occur during the fellowship period by providing a real-time forum to review and respond to both their achievements and challenges, and to utilize the collective experiences of the entire group that may allow fellows to share methods for handling a particular obstacle that may be common among them.

Table 2
International Pain Policy Fellows

2006 Cohort
Jorge Eisenchlas (Argentina)
Marta Leon (Colombia)
Daisy Amanor-Boadu (Nigeria)
Rosa Buitrago (Panama)
Snezana Bosnjak (Serbia)
Gabriel Madiye (Sierra Leone)
Henry Ddungu (Uganda)
Nyguyen Thi Phuong Cham (Vietnam)
2008 Cohort
Hrant Karapetyan (Armenia)
Irina Kazaryan (Armenia)
Pati Dzotsenidze (Georgia)
Eva Rossina Duarte (Guatemala)
Margaret Dingle Spence (Jamaica)
Verna Walker-Edwards (Jamaica)
Zipporah Ali (Kenya)
Bishnu Paudel (Nepal)
2012 Cohort
Kristo Huta (Albania)
Rumana Dowla (Bangladesh)
Farzana Khan (Bangladesh)
Priyadarshini Kulkarni (India)
Shalini Vallabhan (India)
Nandini Vallath (India)
Taalaigul Sabyrbekova (Kyrgyzstan)
Nadarajah Jeyakumaran (Sri Lanka)
Suraj Perera (Sri Lanka)
Nataliia Datsiuk (Ukraine)
2014 Cohort
Abraham Mengistu (Ethipoia)
Mawuli Gyakobo (Ghana)
Christian Ntizimira (Rwanda)
Nahla Gafer (Sudan)
Lewis Banda (Zambia)

Table 3
Pain & Policy Studies Group International Expert Committee

Professor Snezana Bosnjak, MD, PhD (2012)
Institute for Oncology & Radiology of Serbia
Belgrade, Serbia
Professor Rosa Buitrago, BS, MCPh (2011)
Universidad de Panama
Panama City, Panama
Ms. Mary Callaway (2006)
Open Society Foundations, International Palliative Care Initiative
New York, New York, USA
Dr. Stephen Connor, PhD (2010)
Worldwide Hospice and Palliative Care Alliance
Alexandria, Virginia, USA
Dr. Henry Ddungu, MD (2011)
Fred Hutchinson Cancer Research Center
Kampala, Uganda
Ms. Liliana De Lima, MHA (2006)
International Association for Hospice and Palliative Care
Houston, Texas, USA
Dr. John Ely, MD (2006)
Midwest Palliative and Hospice Care Center
Minneapolis, Minnesota, USA
Dr. Frank Ferris, MD (2006)
Palliative Medicine at Ohio Health
Columbus, Ohio, USA
Dr. Eric L. Krakauer, MD, PhD (2006)
Harvard Medical School Center for Palliative Care
Boston, Massachusetts, USA
Dr. Virginia Le Baron, APRN, PhD (2014)
University of Virginia School of Nursing
Charlottesville, Virginia, USA
Dr. Thomas Lynch, PhD (2012),
The Johns Hopkins School of Medicine
Baltimore, Maryland, USA
Dr. Bishnu D. Paudel, MD (2012)
National Academy of Medical Sciences
Kathmandu, Nepal
Dr. MR Rajagopal, MD (2006)
Pallium India
Thiruvananthapuram, India
Additional expert mentors from the African Pain Policy Fellowship
Dr. Jack G.M. Jagwe, FRCP, FRCP (Edin)
Hospice Africa Uganda
Kampala, Uganda
Dr. Zipporah Ali, MD, MPH, DipPallCare, HonDUniv
Kenya Hospices and Palliative Care Association
Nairobi, Kenya
Dr. Fred Sebisubi, MD
Ministry of Health
Kampala, Uganda
Dr. Olaitan Soyannwo, MBBS
University of Ibadan
Ibadan, Nigeria

The progress fellows made and outcomes achieved with assistance and direction from PPSG staff and expert mentors are measured by assessing the extent to which barriers were overcome by the end of the fellowship program and subsequent increases in opioid consumption. Numerous examples of positive outcomes resulting from the fellows, working with government representatives, experts, and PPSG staff and colleagues both within and outside their countries, are summarized in Table 4. Additionally, several articles have been published describing fellow's in-country efforts to improve opioid availability and accessibility.[45–50]

These positive country-level outcomes, facilitated by the IPPF program, have likely contributed to increases in the medical consumption of opioids from the very small amounts consumed prior to the IPPF. For example, in Kenya, the fellow reports that morphine consumption has more than doubled in recent years, particularly in hospitals in Nairobi (Z. Ali personal communication). In Serbia, the national data indicate that between 2006 and 2012, total consumption of strong opioids increased more than twofold. Between 2009 and 2014, the amount of immediate-release oral morphine sold to hospitals in Serbia more than tripled and the institutional data from the National Cancer Hospital reveal that there was an increasing trend in the amount of strong opioids used per hospitalized patient at that institution.[49] Furthermore, a recent study found that Serbia's adequacy of opioid consumption increased by nearly 83% between 2006 and 2010.[21] Likewise, between 2003 and 2010, morphine consumption in Vietnam increased each year.[48] Despite these increases, there is a considerable way to go to achieve adequate consumption in these countries.

After completing the IPPF, several fellows have become members of the PPSG International Expert Committee, a select group of professionals with expertise in opioid availability. In that capacity, they have served as mentors to subsequent fellows. Within their home countries, many of the fellows developed a reputation as champions for access to opioid medicines have published articles about their work, attended international meetings on forming policy, and successfully advocated for positive changes in the laws and regulations in their countries. PPSG conducted semi-structured interviews with a sample of fellows to gather feedback about their experiences with the IPPF. Qualitative analyses of the interviews found that fellows described the knowledge and experience gained through the IPPF as career-changing and many have continued to pursue their work to address barriers to opioid availability, long after their formal program involvement has ended.

In early 2016, PPSG announced updates to its Web site highlighting the IPPF. The updates include a revamped introductory page[44] which describes the IPPF and features a new informational booklet about the IPPF. The purpose of the booklet is to provide a brief overview about the program, introduce the fellows that have participated in the program since its inception in 2006, and highlight fellowship successes. PPSG has also produced individual one-page web profiles on each fellow that summarize their background, fellowship successes, ongoing progress, and challenges/future needs.

Table 4
Examples of IPPF Successes

Opioid prescribing
- Georgia: New prescription form now allows two opioids to be prescribed on the same form, while requiring only one additional signature for monitoring purposes but not for treatment approval (Ministry of Labour, Health and Social Affairs)
- Panama: Prescription validity increased from 48 hours to five days (executive decree)
- Vietnam: After an opioid regulation change, there is no longer a maximum dose of opioids per day, patients in addition to cancer and AIDS patients may receive an opioid prescription for up to seven days per prescription (Ministry of Health Regulation).

Opioid availability
- Ukraine: Registered oral morphine tablets for the first time ever and a local company agreed to produce oral morphine tablets (immediate and sustained release) (Ministry of Health).
- Guatemala: Began manufacture of immediate-release oral morphine, making it available at the national cancer hospital (by government license to local pharmaceutical company)
- Sierra Leone: First-ever shipment of morphine powder received by the only hospice, resulting in the development of record-keeping databases and written procedures on safe-handling; subsequent larger shipments arrived based on positive outcomes (National Pharmacy Board)

National policy/strategy
- India: Developed national strategy for palliative care, with an objective to "Refine the legal and regulatory systems and support implementation to ensure access and availability of opioids for medical and scientific use while maintaining measure for preventing diversion and non-medical use" (Ministry of Health and Family Welfare)
- Nepal: Created National Association for Palliative Care to develop national palliative care policy, clinical tools to improve pain management, and sponsor trainings for healthcare workers on palliative care (palliative care providers)
- Serbia: Approved National Palliative Care Strategy that recognized: opioids as essential for pain relief and palliative care, and the need to examine national drug control laws and conform them to international drug control conventions (Ministry of Health)

Opioid distribution system
- Colombia: Ordered regional controlled medication offices to ensure continuous availability of morphine (i.e., 24 hours a day and 7 days a week) in at least one pharmacy per region (Ministry of Health Resolution)
- Jamaica: Initiated a transport permit for transferring opioids from distributors to health care facilities, as well as among health care institutions, facilitating the safe, government-managed distribution of opioids to all pharmacies (National Drug Regulatory Office)

Accessibility of opioid medicines
- Albania: Added immediate- and sustained-release morphine to list of reimbursable medicines (Ministry of Health)
- Colombia: Added methadone, hydromorphone, and injectable morphine to the list of medicines to be dispensed free of charge to patients with a prescription (Ministry of Health, National Obligatory Health Plan)
- Kenya: Eliminated a tax on oral morphine powder, making it more affordable for hospices and palliative care programs (Ministry of Finance)

Education/training
- Sudan: Established the first "Palliative Care in Oncology" course and a training program, "Pain Management for 100 Health Professionals," which involved practitioners from 22 different hospitals (Ministry of Higher Education)
- Serbia: Developed educational brochures for health care professionals and drug regulators about the modern use of opioids to manage cancer pain (Ministry of Health)
- Bangladesh: Organized a series of workshops throughout the country to inform drug regulators and law enforcement officials about the importance of opioids for pain and palliative care and to discuss their roles (Palliative Care experts and national Department of Narcotics Control)

IPPF = International Pain Policy Fellowship.

Policy

For over two decades, PPSG and its predecessor organization, the Pain Research Group, have developed and continually refined the conceptual framework and tools to evaluate laws and other relevant policies governing drug control and medicine/pharmacy practice related to opioid availability and pain relief. The initial work focused on synthesizing the principle of balance and developing a framework and criteria to evaluate the extent to which policies were balanced in relation to medication availability and was pilot tested by applying it to national laws and regulations in a number of countries in Latin America.[35] This culminated in the development and publication of the WHO guidelines "Achieving balance in national opioids control policy: Guidelines for assessment" in 2000,[27] PPSG was also involved in the revision and publication of the second edition of the WHO guidelines.[7]

Global Policy Evaluation

In 2013, PPSG developed a set of policy evaluation criteria corresponding to the obligations from the UN Single Convention on Narcotic Drugs and to factors related to the internationally based conceptual framework of balance. The resulting criteria were informed both by the WHO Ensuring Balance Guidelines[7] and the PPSG criteria developed for the U.S. policy work.[51] In a pilot phase, these criteria were used to evaluate laws and other relevant policies governing drug control and medicine and pharmacy practice in four Latin American countries. The results are detailed in a report available on the PPSG Web site.[52] Policy language was identified that has the potential to either enhance or impede pain management. The purpose is to inform policy makers, pain and palliative care advocates, and other stakeholders about the potential policy barriers and to provide them with the precise negative policy language that is problematic

or positive language that could strengthen the policies. PPSG also conducted a systematic policy analysis for the five African countries in the fourth cohort of fellows, applying the same criteria that were developed for the pilot project. The results identify current policy issues that may directly inform the fellow's continuing strategic efforts to address these issues. PPSG plans to further refine and improve these criteria for broader future application in other countries.

Access to Opioid Medications in Europe

PPSG provided consultation and technical expertise for the Access to Opioid Medication in Europe (ATOME) project, an initiative of the WHO that was launched in 2009 as a collaborative project for better access to opioid medicines, focusing on 12 European countries (Bulgaria, Cyprus, Estonia, Greece, Hungary, Latvia, Lithuania, Poland, Serbia, Slovenia, Slovakia, and Turkey).[41] The overall goal was to examine the reasons why opioid medicines for moderate-to-severe pain and for the treatment of opioid dependence were not being used adequately, to elaborate tailor-made recommendations for improving the accessibility, availability, and affordability of controlled medicines, and to disseminate them to governments, health care professionals, other key decision-making bodies as well as to the general public. In February 2011, two PPSG staff members presented PPSG's policy work at an ATOME workshop to train lawyers and national counterparts from all 12 countries on how to review national controlled substance legislation according to the principle of balance. PPSG staff members also presented and facilitated at two workshops that same year, each involving six of the 12 countries. In May 2011, PPSG staff met with the lawyers from the Utrecht University who were leading the policy evaluation portion of the project, to share its evaluation methods and experience with the project leaders. Finally, PPSG participated in an ATOME policy meeting involving nine countries in January 2013.

Global Opioid Policy Initiative

PPSG was involved in the Global Opioid Policy Initiative, with the European Society for Medical Oncology, the European Association for Palliative Care, and partner organizations. The purpose of the initiative was to design, collect, analyze, and disseminate an international survey: "Availability and accessibility of opioids for cancer pain in Asia, Africa, Middle East, and Latin America: A survey of National Representatives." Data were collected and analyzed and initial results from the survey were presented at the 2012 European Society for Medical Oncology meeting in Vienna. Together with the leadership of this project, the PPSG Director co-authored several publications describing the results in a 2013 special supplemental issue of the *Annals of Oncology*.[53–59]

Model Law Development

Another area of work related to policy has been PPSG's efforts to ensure that a valuable balanced UN Model Law related to controlled medicines is available for governments to utilize when they are revising their national legislation. Historically, the UNODC offered UN Member States model legislation and regulations related to controlled substances for UN Member States to consult while creating their own laws and regulations, in order to assist with the implementation and adherence to international treaties.[60] PPSG identified and evaluated the UN model laws related to controlled medicines that had been published finding that they focused largely on drug abuse and not on ensuring adequate medication availability.[61,62] In a recent study examining a sample of laws governing controlled substance use in 15 countries, PPSG found that most countries' laws did not contain the accessibility provisions of the Single Convention.[62]

In 2009, with support from the U.K. DfID, PPSG continued its efforts to encourage the development of a UN Model drug control law, in collaboration with the UNODC. PPSG was instrumental in facilitating the organization of an informal technical consultation on "access to opioid-based medicines for the treatment of pain" organized by the Prevention, Treatment and Rehabilitation Section of the UNODC, which took place in January 2011 in Vienna, Austria. The purpose of this technical consultation was to discuss further actions to be taken on the already established scientific basis for a necessary response to acute and unnecessary suffering caused by the unavailability of opioid-based medications and to develop a discussion article on the progress of activities to be submitted to the CND in March 2011 for further discussion. The following year, the CND passed a second resolution regarding availability of controlled drugs for medical purposes, calling on the UNODC to review and revise their model laws to be more balanced and to issue a technical guide for countries that would offer guidance for implementing the new model laws.[15]

UNODC initiated a process to update and reissue a revised model laws and over the years, incremental progress was made by the UNODC regarding the revision of their model laws. At the CND annual meeting in 2013, a representative of the UNODC addressed the plenary session to describe the work accomplished to date; a well-attended side event also was held to discuss the model law revision process. In April 2016, UNODC announced that new model laws were close to being released in 2016.

PPSG Web site and Communications

With support from OSF/IPCI and the US Cancer Pain Relief Committee, the PPSG disseminates its work through online communications, including an extensive Web site, news alerts, and through several social media outlets. Key components of the Web site include PPSG publications, global, regional and country opioid consumption trends, information about the IPPF program, and an online course.

PPSG Web Site

Opioid Consumption Data. Over the years, PPSG has become a recognized resource in the international pain and palliative care field for global opioid consumption statistics. Since the late 1990s, PPSG has annually received from the INCB consumption data for six principle opioids used to treat moderate-to-severe pain: fentanyl, hydromorphone, methadone, morphine, oxycodone, and pethidine. PPSG has developed an in-house global database of opioid consumption data and also provides these data on its Web site.[63]

There are several useful applications for these data, including identifying the extent that a country has available opioids that can relieve moderate-to-severe pain, to determine any notable changes in medication availability over time and as an outcome measure of efforts to improve opioid availability. As a result, these statistics can be valuable resources for policy makers, practitioners, advocates, or anyone interested in improving opioid availability. PPSG has published several peer-reviewed articles describing the opioid consumption data.[64–66]

Morphine Equivalence. Historically, the WHO has considered a country's annual consumption of morphine to be the primary indicator of the extent that opioids are used to treat severe cancer pain and an index to evaluate improvements in pain management.[67] However, additional opioid analgesic medications and formulations such as fentanyl, hydromorphone, and oxycodone have been introduced in global and national markets over the past 20 years and should be taken into consideration when studying opioid consumption in a country, region, and globally. Therefore, with support from OSF/IPCI, PPSG developed a morphine equivalence (ME) metric for each principle opioid used to treat moderate-to-severe pain that is expressed in terms of ME and adjusted for population.[31,65] The ME allows an equianalgesic comparison of the consumption of morphine with other opioid medications at the national, regional, and global levels. A total ME statistic combines consumption of several principle opioid analgesics into one metric, using conversion formulas established by the WHO Collaborating Centre for Drug Statistics Methodology in Oslo, Norway. ME is now an integral part of the PPSG's Web site.

Global, Regional, and Country Opioid Consumption Trends. Each year PPSG updates the extensive opioid consumption data on its Web site with the most recently available data from the INCB.

Country Profiles. In addition to the opioid consumption data, PPSG annually assembles key information from INCB reports and UN publications for each country and provides this information on individual country profiles pages.[68]

Web site Tools to Explore Opioid Consumption Data. Since 2010, the PPSG has incorporated three new interactive web features[69] for exploring opioid consumption data and generating hypotheses about patterns of opioid consumption:

1. Interactive global map allows users to select the drug and year (1964 to most recent) to display, providing an immediate visual image of the variation in consumption of opioids throughout the world,
2. Interactive graphs for exploring opioid consumption trends for a particular country, which allow users to explore relationships over time between opioid consumption and other country characteristics such as the Human Development Index,
3. User-created custom graphs: Most recently in 2016, PPSG launched another tool for exploring these data which allows users to create custom graphs and download them for use in presentations or publications.

Online Course. Another resource available on the PPSG Web site is an online course, which provides ready access to fundamental information about opioid availability and policy and real-world examples to a global audience. PPSG launched the online course, "Increasing Patient Access to Pain Medicines around the World: A Framework to Improve National Policies that Govern Drug Distribution,"[70] in 2008 with support from the National Hospice and Palliative Care Organization's Foundation for Hospices in sub-Saharan Africa. This course is about the relationship between government policies that affect the medical availability of opioid analgesics and patients who experience moderate-to-severe pain. With seven lessons, the course was designed to provide a synthesis of the critical background material and current methods that have been developed to improve national policies governing medical availability of essential pain medicines for cancer and HIV/AIDS patients. It is intended

for an international audience of health care professionals, local and national policy makers, pain and palliative care advocates, government drug regulatory personnel, national health policy advisors, and health policy scholars with an interest in pain management or palliative care.

It is a self-paced course that can be taken at the convenience of the learner. The course does not provide credit toward a degree program or continuing professional education credits; however, users wishing to earn a certificate of completion have the opportunity to do so. The course is a prominent feature on the PPSG Web site and is also accessible through the International Association for Hospice and Palliative Care Web site. Since its launch, over 600 individuals have registered for the course, and roughly 20% of those who registered have successfully completed the entire course and have been issued certificates of completion from PPSG.

In addition to being a web resource, the online course has served as the foundation for PPSG's IPPF training curriculum, providing new fellows with critical background information as they begin to address opioid availability in their own countries.

Social Media

In addition to the Web site, PPSG has established the use of social networking tools, including Facebook, Twitter, YouTube, Pinterest, LinkedIn, and blogging to continue the high visibility of its global activities. These tools are available on the PPSG Web site home page (www.painpolicy.wisc.edu) and are important for transmitting brief updates about PPSG activities and its staff, effectively drawing people to our Web site for further information. Sending messages via Twitter can be an especially effective method of communicating with people in less-developed countries who may not have dependable access to the Internet, but who do have a mobile phone to receive Tweets. Over time, the PPSG has advanced its use and scope of social networking tools and plans to continue to increase the number of messages sent out about our work using these tools.

Conclusion

In 2016, as PPSG celebrated the 20th anniversary of its founding, we reflected back on the numerous opportunities to lead and contribute to the global progress made to improve the availability of opioids to relieve pain relief for patients around the world. PPSG is a part of a global pain and palliative care field comprised of many organizations with complementary knowledge and skill sets that in combination have been a powerful force in promoting increased access to opioids and palliative care. PPSG has become a focal point for expertise on laws and other relevant policies governing drug control and medicine and pharmacy practice related to opioid availability and pain relief. PPSG has contributed to the promotion of the principle of balance and the development of our unique model of technical assistance to help national governments assess regulatory barriers to essential medicines for pain relief and amend existing or develop new legislation that facilitates appropriate and adequate opioid prescribing according to international standards. However, we realize that the majority of the world's population continues to lack sufficient access to opioid medicines and that sustained efforts are needed to continue to make policy and regulatory improvements to ultimately relive patient suffering. As the field is facing challenges, including reduced funding opportunities, lack of coordination, and the increasing prevalence of NCDs in LMICs, support and action on the part of UN agencies, governments and numerous palliative care NGOs are needed to address these challenges.

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References

1. World Health Organization. Access to Controlled Medications Programme: Improving access to medications controlled under international drug conventions. Geneva: World Health Organization, 2012.

2. World Health Organization. Cancer pain relief. Geneva: World Health Organization, 1986.

3. Jacox A, Carr DB, Payne R, et al. Management of cancer pain. Clinical practice guideline number 9, AHCPR No. 94–0592. Rockville, MD: Agency for Health Care Policy and Research, U.S. Dept of Health and Human Services, Public Health Service, 1994.

4. World Health Organization. WHO model list of essential medicines, 1st ed. Geneva: World Health Organization, 1977. Available from http://www.who.int/selection_medicines/committees/en/. Accessed August 8, 2016.

5. World Health Organization. A community health approach to palliative care for HIV/AIDS and cancer patients in sub-Saharan Africa. Geneva: World Health Organization, 2004.

6. United Nations. Single convention on narcotic drugs, 1961, as amended by the 1972 protocol amending the single convention on narcotic drugs, 1961. New York, NY: United Nations, 1972.

7. World Health Organization. Ensuring balance in national policies on controlled substances: Guidance for availability and accessibility of controlled medicines. 2nd and rev ed. Geneva: World Health Organization, 2011.

8. International Narcotics Control Board. Report of the International Narcotics Control Board for 1989: Demand for and supply of opiates for medical and scientific needs. Vienna: United Nations, 1989.

9. International Narcotics Control Board. Report of the International Narcotics Control Board for 1995: Availability of opiates for medical needs. New York, NY: United Nations, 1996.

10. International Narcotics Control Board. Report of the International Narcotics Control Board for 1999. New York, NY: United Nations, 2000.

11. United Nations Economic and Social Council. Demand for and supply of opiates used to meet medical and scientific needs; Resolution 2005-26. New York, NY: United Nations, 2005.

12. International Narcotics Control Board. Report of the International Narcotics Control Board on the availability of internationally controlled drugs: Ensuring adequate access for medical and scientific purposes. New York, NY: United Nations, 2011.

13. International Narcotics Control Board. Availability of internationally controlled drugs: Ensuring adequate access for medical and scientific purposes: Indispensable, adequately available and not unduly restricted. New York, NY: United Nations, 2016.

14. United Nations Economic and Social Council. Promoting adequate availability of internationally controlled licit drugs for medical and scientific purposes while preventing their diversion and abuse; Resolution 53/4. New York, NY: United Nations, 2010.

15. United Nations Economic and Social Council. Promoting adequate availability of internationally controlled narcotic drugs and psychotropic substances for medical and scientific purposes while preventing their diversion and abuse; Resolution, 54/6. New York, NY: United Nations, 2011.

16. United Nations General Assembly. Our joint commitment to effectively addressing and countering the world drug problem; Resolution S-30/1. New York, NY: United Nations, 2016.

17. Caraceni A, Hanks G, Kaasa S, et al. Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC. Lancet Oncol 2012;13: e58–e68.

18. Portenoy RK, Ahmed E. Principles of opioid use in cancer pain. J Clin Oncol 2014;32:1662–1670.

19. Wiffen PJ, Wee B, Moore RA. Oral morphine for cancer pain. Cochrane Database Syst Rev 2016:CD003868.

20. Seya MJ, Gelders SFAM, Achara OU, Milani B, Scholten WK. A first comparison between the consumption of and the need for opioid analgesics at country, regional and global level. J Pain Palliat Care Pharmacother 2011;25: 6–18.

21. Duthey B, Scholten W. Adequacy of opioid analgesic consumption at country, global, and regional levels in 2010, its relationship with development level, and changes compared with 2006. J Pain Symptom Manage 2014;47: 283–297.

22. Berterame S, Erthal J, Thomas J, et al. Utilisation and barriers to accessing opioid analgesics: a country, regional and global study. Lancet 2016;387:1644–1656.

23. International Narcotics Control Board. Narcotic drugs: Estimated world requirements for 2016-Statistics for 2014. New York, NY: United Nations, 2016.

24. Stjernswärd J, Clark D. Palliative medicine - a global perspective. In: Doyle D, Hanks GWC, Cherny N, Calman K, eds. Oxford Textbook of Palliative Medicine, 3rd ed New York: Oxford University Press, 2004:1199–1224.

25. International Narcotics Control Board. World Health Organization. Guide on estimating requirements for substances under international control. Vienna: United Nations, 2012.

26. World Health Organization. Cancer pain relief: With a guide to opioid availability, 2ng ed. Geneva: World Health Organization, 1996.

27. World Health Organization. Achieving balance in national opioids control policy: Guidelines for assessment. Geneva: World Health Organization, 2000.

28. Gilson AM, Maurer MA, Ryan KM, Skemp-Brown M, Husain A, Cleary JF. Ensuring patient access to essential medicines while minimizing harmful use: a revised WHO tool to improve national drug control policy. J Pain Palliat Care Pharmacother 2011;25:246–251.

29. World Health Organization. NCD Global monitoring framework 2016. Available from http://www.who.int/nmh/global_monitoring_framework/en/. Accessed August 8, 2016.

30. World Health Assembly. Strengthening of palliative care as a component of comprehensive care throughout the life course. WHA67.19. Geneva: World Health Organization, 2014.

31. Joranson DE, Ryan KM, Maurer MA. Opioid policy, availability and access in developing and nonindustrialized countries. In: Fishman SM, Ballantyne JC, Rathmell JP, eds. Bonica's Management of Pain, 4th ed. Baltimore, MD: Lippincott Williams & Wilkins, 2010:194–208.

32. Joranson DE, Rajagopal MR, Gilson AM. Improving access to opioid analgesics for palliative care in India. J Pain Symptom Manage 2002;24:152–159.

33. Blengini C, Joranson DE, Ryan KM. Italy reforms national policy for cancer pain relief and opioids. Eur J Cancer Care 2003;12:28–34.

34. Mosoiu D, Ryan KM, Joranson DE, Garthwaite JP. Reforming drug control policy for palliative care in Romania. Lancet 2006;367:2110–2117.

35. Joranson DE. Improving availability of opioid pain medications: Testing the principle of balance in Latin America. Innovations in End-of-Life Care 2003;5. Available from http://www.painpolicy.wisc.edu/sites/www.painpolicy.wisc.edu/files/balance_Joranson03.pdf. Accessed September 1, 2017.

36. World Health Organization Regional Office for Europe. Assuring availability of opioid analgesics for palliative care. Meeting report of opioid availability workshop held in Budapest, Hungary. Copenhagen: World Health Organization Regional Office for Europe, 2002.

37. African Palliative Care Association. Advocacy workshop for palliative care in Africa: A forcus on essential pain medication accessibility. Kampala: African Palliative Care Association, 2007.

38. African Palliative Care Association. Advocacy workshop for palliative care in Africa: A forcus on essential pain medication accessibility in Southern Africa. Kampala: African Palliative Care Association, 2008.

39. Pain & Policy Studies Group. Availability of opioid analgesics in the world and Asia with a special focus on: Indonesia, Philippines, Thailand. In: Workshop on Assuring Availability and Accessibility of Opioid Analgesics for Pain and Palliative Care. Boracay Island, Philippines. Madison: Pain & Policy Studies Group, 2008.

40. Pain & Policy Studies Group. Availability of opioid analgesics in the world and Europe, with a special focus on: Armenia, Republic of Moldova, Ukraine. In: Workshop on Assuring Availability and Accessibility of Opioid Analgesics for Pain and Palliative Care. Chisinău, Republic of Moldova. Madison: Pain & Policy Studies Group, 2008.

41. Junger S, Larjow E, Linge-Dahl L, et al. Access to opioid medication in Europe: Final report and recommendations to the Ministries of Health. Bonn: Pallia Med Verlag, 2014.

42. De Lima L, Pastrana T. Evaluation of the effectiveness of workshops on the availability and rational use of opioids in Latin America. J Palliat Med 2016;19:964–971.

43. Mosoiu D, Mungiu OC, Gigore B, Landon A. Romania: changing the regulatory environment. J Pain Symptom Manage 2007;33:610–614.

44. Pain & Policy Studies Group. International Pain Policy Fellowship 2016. Available from http://www.painpolicy.wisc.edu/international-pain-policy-fellowship. Accessed August 8, 2016.

45. Leon MX, De Lima L, Florez S, et al. Improving availability of and access to opioids in Colombia: description and preliminary results of an action plan for the country. J Pain Symptom Manage 2009;38:758–766.

46. Bosnjak S, Maurer MA, Ryan KM, Leon MX, Madiye G. Improving the availability and accessibility of opioids for the treatment of pain: the International Pain Policy Fellowship. J Support Care Cancer 2011;19:1239–1247.

47. Leon MX, Florez S, De Lima L, Ryan K. Integrating palliative care in public health: the Colombian experience following an International Pain Policy Fellowship. Palliat Med 2011;25:365–369.

48. Krakauer EL, Cham NTP, Husain SA, et al. Toward safe accessibility of opioid pain medicines in Vietnam and other developing countries: a balanced policy method. J Pain Symptom Manage 2015;49:916–922.

49. Bosnjak S, Maurer MA, Ryan KM, et al. A multifaceted approach to improve the availability and accessibility of opioids for the treatment of cancer pain in Serbia: results from the International Pain Policy Fellowship (2006-2012) and recommendations for action. J Pain Symptom Manage 2016;52:272–283.

50. Paudel BD, Ryan KM, Skemp-Brown M, et al. Opioid availability and palliative care in Nepal: Influence of an international pain policy Fellowship. J Pain Symptom Manage 2015;49:110–116.

51. Pain & Policy Studies Group. Achieving balance in federal and state pain policy: A guide to evaluation (CY 2013). Madison, WI: Pain & Policy Studies Group, 2014. Available from http://www.painpolicy.wisc.edu/sites/www.painpolicy.wisc.edu/files/Evalguide_CY2013.pdf. Accessed August 8, 2016.

52. Pain & Policy Studies Group. Improving global opioid availability for pain & palliative care: A guide to a pilot evaluation of national policy. Madison, WI: University of Wisconsin Carbone Cancer Center, 2013. Available from http://www.painpolicy.wisc.edu/sites/www.painpolicy.wisc.edu/files/Global%20evaluation%202013.pdf. Accessed August 8, 2016.

53. Cherny NI, Cleary J, Scholten W, Radbruch L, Torode J. 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. Ann Oncol 2013;24(Suppl 11):xi7–xi13.

54. Cleary J, Powell RA, Munene G, et al. Formulary availability and regulatory barriers to accessibility of opioids for cancer pain in Africa: a report from the Global Opioid Policy Initiative (GOPI). Ann Oncol 2013;24(Suppl 11):xi14–xi23.

55. Cleary J, Radbruch L, Torode J, Cherny NI. Formulary availability and regulatory barriers to accessibility of opioids for cancer pain in Asia: a report from the Global Opioid Policy Initiative (GOPI). Ann Oncol 2013;24(Suppl 11):xi24–xi32.

56. Cleary J, Simha N, Panieri A, et al. Formulary availability and regulatory barriers to accessibility of opioids for cancer pain in India: a report from the Global Opioid Policy Initiative (GOPI). Ann Oncol 2013;24(Suppl 11):xi32–xi40.

57. Cleary J, De Lima L, Eisenchlas J, Radbruch L, Torode J, Cherny NI. 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). Ann Oncol 2013;24(Suppl 11):xi41–xi50.

58. Cleary J, Silbermann M, Scholten W, Radbruch L, Torode J, Cherny NI. 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). Ann Oncol 2013;24(Suppl 11):xi51–xi59.

59. Cleary J, Radbruch L, Torode J, Cherny NI. Next steps in access and availability of opioids for the treatment of cancer pain: Reaching the tipping point? Ann Oncol 2013; 24(Suppl 11):xi60–xi64.

60. United Nations Office on Drugs and Crime. Model Laws 2016. Available from https://www.unodc.org/unodc/en/legal-tools/model-treaties-and-laws.html. Accessed August 8, 2016.

61. Pain & Policy Studies Group. Do international model drug control laws provide for drug availability? J Pain Palliat Care Pharmacother 2009;23:145–152.

62. Husain SA, Skemp-Brown M, Maurer MA. How do UNODC model laws compare to a single convention obligations to ensure drug availability? Bull World Health Organ 2014; 92:108–116.

63. Pain & Policy Studies Group. Opioid Consumption 2016. Available from http://www.painpolicy.wisc.edu/opioid-consumption-data. Accessed August 8, 2016.

64. Gilson AM, Maurer MA, LeBaron VT, Ryan KM, Cleary JF. Multivariate analysis of a countries' government and health-care system influences on opioid availability for cancer pain relief and palliative care: more than a function of human development. Palliat Med 2013;27:105–114.

65. Gilson AM, Maurer MA, Ryan KM, Rathouz PJ, Cleary JF. Using a morphine equivalence metric to Quantify opioid consumption: examining the capacity to provide effective treatment of Debilitating pain at the global, regional, and country levels. J Pain Symptom Manage 2013;45:681–700.

66. Hastie BA, Gilson AM, Maurer MA, Cleary JF. An examination of global and regional consumption trends 1980-2011. J Pain Palliat Care Pharmacother 2014;28: 259–275.

67. Foley KM, Wagner JL, Joranson DE, Gelband H. Pain control for people with cancer and AIDS. In: Jamison DT, Breman JG, Measham AR, et al, eds. Disease Control Priorities in Developing Countries, 2nd ed New York, NY: Oxford University Press, 2006:981–993.

68. Pain & Policy Studies Group. Country Profiles. Available from http://www.painpolicy.wisc.edu/countryprofiles Accessed August 8, 2016.

69. Pain & Policy Studies Group. Interactive tools to explore the opioid consumption data. Available from http://www.painpolicy.wisc.edu/explore-data Accessed August 8, 2016.

70. Pain & Policy Studies Group. Increasing Patient Access to Pain Medicines around the World: A Framework to Improve National Policies that Govern Drug Distribution. Madison: Pain & Policy Studies Group, 2008. Available from https://uwmadison.co1.qualtrics.com/jfe/form/SV_aVicN7U4DTkuaiM. Accessed February 23, 2017.