

The appropriate citation for this article is:

Bosnjak S, Maurer MA, Ryan KM, Leon MX, Madiye G (2011) Improving the availability of opioids for the treatment of pain: The International Pain Policy Fellowship. *Journal of Supportive Care in Cancer*. 19(8):1239-1247, DOI: 10.1007/s00520-011-1200-2

Special Article

Improving the availability and accessibility of opioids for the treatment of pain: The International Pain Policy Fellowship

Snezana Bosnjak,¹ Martha A. Maurer,² Karen M. Ryan,² Marta X. Leon,³ & Gabriel Madiye⁴

1. Institute for Oncology and Radiology of Serbia, Belgrade, Serbia; 2. Pain & Policy Studies Group, World Health Organization Collaborating Center for Pain Policy and Palliative Care, University of Wisconsin School of Medicine and Public Health, Carbone Cancer Center, Madison, Wisconsin, USA; 3. University de La Sabana, Bogota, Colombia; 4. Shepherd's Hospice, Freetown, Sierra Leone

Abstract

Opioid analgesics are simultaneously indispensable medicines for the treatment of moderate to severe pain and harmful when abused. The challenge for governments is to balance the obligation to prevent diversion, trafficking and abuse of opioids with the *equally important* obligation to ensure their availability and accessibility for the relief of pain and suffering. Over the last 30 years, significant progress has been made toward improving access to opioids as measured by increasing global medical opioid consumption. However, this progress is marked by ongoing large disparities among countries, with most increases in medical opioid consumption attributed to high-income countries, not low- and middle-income countries (LMICs). The International Pain Policy Fellowship (IPPF) was developed by the Pain & Policy Studies Group, with the central goal of developing national leaders from LMICs and empowering them to improve availability and accessibility of opioids for the treatment of pain. To date, two classes of fellows have been selected, representing 17 fellows from 15 countries. Progress achieved by the leadership of 3 fellows from Sierra Leone, Colombia, and Serbia is highlighted in this paper. The fellows from each country were successful at initiating collaboration with relevant governmental bodies, national authorities and professional societies, which resulted in a new supply of oral opioids in Sierra Leone and Serbia, and improvements in the distribution of already available opioids in Colombia. All fellows were instrumental in facilitating evaluation of national policy. The IPPF program empowers fellows with the necessary knowledge, skills and guidance to improve the availability and accessibility of opioids for the treatment of pain.

Introduction

Opioid analgesics (opioids) are indispensable medicines for the treatment of moderate to severe pain. The use of chronic opioid therapy to treat cancer pain is well-established [1-3] and it is also considered appropriate for treating chronic non-cancer pain in carefully selected patients [4] and pain in AIDS [5]. The availability of opioids is a critical part of effective supportive and palliative care [6]. At the same time, opioids have the potential to be abused and are legally classified as *controlled substances* (“narcotics”) by the Single Convention on Narcotic Drugs, 1961 (Single Convention) [7], the international treaty governing opioids, as well as by corresponding national drug control laws. The Single Convention stipulates a dual obligation that governments must control narcotic drugs to prevent their diversion and abuse while ensuring their adequate availability for medical and scientific purposes. This is known as the “Principle of Balance,” the prevailing international standard in formulating opioid control policy [8]. The challenge for governments is therefore to balance the obligation to prevent diversion, trafficking and abuse of opioids as controlled substances with the *equally important* obligation to ensure their availability and accessibility for the relief of pain and suffering. This public health challenge has grown in prominence over the past 15 years in some high-income countries as there has been an increase in the abuse and diversion of strong opioids that has correlated with their increased availability for medical and scientific purposes. The dual nature of opioids, that they are simultaneously essential in medical practice and harmful when abused, underlies and contributes to the problem of opioid accessibility. Opioid control measures tend to focus on the harmful aspect of opioids and are often inappropriately restrictive, rendering opioids inaccessible for patients who need them for medical purposes. It is estimated that in over 80% of the world population, pain is inadequately treated because people lack

access to opioids, causing needless suffering of patients and their families [9].

Global progress toward improving access to opioids

Historically, the World Health Organization (WHO) has considered a country’s annual consumption of morphine to be an indicator of access to opioids for the treatment of pain [10]. WHO has regarded morphine as a gold standard for the relief of moderate to severe pain associated with cancer [2, 3] and has included morphine in its *Model Essential Medicines List* since 1977 [11]. However, over the past two decades the number of alternative strong opioids and the range of their formulations marketed for the treatment of pain have increased. Therefore, a more complete picture of a country’s ability to treat moderate to severe pain would consider the consumption of other opioids, in addition to morphine. In response to this need, a morphine equivalence metric has been developed, which first involves calculation of the equianalgesic amounts of individual strong opioids consumed in a country, then summation into a single value (called total opioid consumption). The morphine equivalence metric allows for a more valid comparison of opioid consumption across countries as an indicator of access to opioids (see Table 1).

Figure 1 presents the long-term trends in the global medical consumption of 6 opioids (fentanyl, hydromorphone, methadone, morphine, oxycodone and pethidine) in morphine equivalence, as well as their total consumption. These consumption data are reported annually by governments to the International Narcotics Control Board (INCB), the highest international drug regulatory authority, and represent the amounts of opioids distributed to the retail level, such as hospitals, clinics, hospice or palliative care programs to be used for medical care (i.e., treatment of pain or opioid dependence) [12]. Global opioid

consumption trends clearly illustrate the progress toward improving access to opioids over the last 30 years. Morphine consumption began to notably increase beginning in 1986 following the release of the WHO recommendations for cancer pain management, often referred to as the *WHO 3-step analgesic ladder* [2], reflecting improved awareness, education and better access to pain control. In the 1990s, global consumption of fentanyl, methadone, and oxycodone increased as new formulations (i.e., transdermal fentanyl and extended-release oxycodone) and new indications (i.e., methadone for the treatment of opioid dependence) were introduced. Throughout the time period, pethidine consumption has continuously decreased, likely replaced by other opioids and as a result of the realization that it is inappropriate for the treatment of chronic pain due to the accumulation of a toxic metabolite [1].

Differences between countries in access to and availability of opioids

Despite the impressive increase in global medical consumption of opioids in the last 30 years, there have been large disparities among countries in their access to opioids as measured by their medical consumption. Figure 2 displays the 2008 per capita consumption of opioids [12] for moderate to severe pain in morphine equivalence for 163 countries. While a small number of countries (34) are above the global mean of 53.6 mg per capita, the vast majority of countries (129) are below the mean. The global median value in 2008 was 3 mg per capita. Comparing total medical consumption of opioids [12] trend between high and low- and middle-income countries (LMIC) (Figure 3), it is clear that much of the global progress to improve access to opioids has been in high-income countries, not LMICs. Indeed, in 2008, LMICs, comprising 83% of the population, accounted for only 9% of the global consumption of morphine [12]. In contrast, high-income countries, comprising 17% of the population, accounted for almost all (91%) global consumption of morphine. Low consumption of morphine and other opioids in LMICs likely reflects inadequate pain and symptom management in these countries.

Table 1 Morphine Equivalence Metric

The Pain & Policy Studies Group developed a morphine equivalence (ME) metric for 6 opioids used to treat moderate to severe pain:

fentanyl,
hydromorphone,
methadone,
morphine,
oxycodone
pethidine

The ME metric is:

- Based on annual opioid consumption data reported by Governments to the International Narcotics Control Board
 - Developed by applying conversion factors from the WHO Collaborating Center for Drugs Statistics Methodology,
 - Allows for equianalgesic comparisons between countries of the total consumption of these 6 opioids.
-

Barriers to opioid availability and accessibility

In the last two decades, a number of surveys have been conducted to identify barriers to adequate availability and accessibility of opioids for the relief of pain. In 1995 [13] and 2007 [14], INCB surveys of government drug control authorities found many barriers to the medical use of opioids, such as concern about addiction to opioids and restrictive laws and regulations (see Table 2). A 2006 survey of hospice and palliative care providers from Asia, Africa, and Latin America found similar barriers to accessing oral morphine including, 1) excessively strict national laws and regulations, 2) fear of addiction, tolerance, and side effects,

3) poorly developed health care systems and supply, and 4) lack of knowledge on the part of health care professionals, the public, and policy makers [15]. A recent survey of barriers to adequate opioid availability and accessibility in 21 Eastern European countries and 20 Western European countries found there were many regulatory barriers to opioid availability that have the potential to interfere with appropriate pain management in many of these countries [16]. Finally, the cost of opioids has also been identified as a barrier to opioid availability [17, 18].

Table 2 Barriers to availability of opioid analgesics as identified by 1995 and 2007 International Narcotic Control Board Surveys of Governments

| |
|---|
| Fear of addiction to opioids |
| Lack of training of health care professionals about the use of opioids |
| Laws or regulations that restrict the manufacture, distribution, prescribing or dispensing of opioids |
| Reluctance to prescribe or stock opioids stemming from fear of legal consequences |
| Overly burdensome administrative requirements related to opioids |
| Insufficient amount of opioids imported or manufactured in the country |
| Fear of diversion |
| Cost of opioids |
| Inadequate health care resources, such as facilities and health care professionals |
| Lack of national policy or guidelines related to opioids |

The main barriers that were identified in the above-mentioned surveys were regulatory barriers and the fear of addiction. Regulatory barriers are often present in excessively restrictive national drug control laws or regulations and reflect drug regulators' primary focus on control efforts and the prevention of

diversion and abuse of opioids. However, such attitudes and policies are based on outdated principles which were formulated before the value of using chronic opioid therapy for managing pain, in particular cancer pain, was recognized. The exaggerated fear of addiction is another frequently identified barrier to opioid availability rooted in the historical scientific understanding of addiction, which has since evolved. For example, many health care practitioners, patients, their families, drug regulators and members of the general public believe that a patient will become dependent ("addicted") once they use an opioid analgesic. However, the WHO has clearly set the criteria for a diagnosis of dependence syndrome (formerly referred to as addiction) [19]. According to WHO criteria, the mere presence of physical dependence or tolerance in a patient receiving opioids for pain control is not sufficient for diagnosis. Rather, physical dependence and tolerance are considered normal *physiological* consequences of chronic treatment with opioids that can be medically managed (i.e., by tapering down the dosage slowly to avoid withdrawal or by increasing the dose in the case of tolerance). It is the additional *psychological* symptoms of compulsive behavior despite continued harm that are needed for a diagnosis of drug dependence syndrome, and these symptoms are the root of longer term dysfunction for the patient and society. Misperceptions about addiction and negative attitudes towards the use of opioids have created a strong stigma against these medicines. Fundamental changes in attitude and knowledge as well as in policy and administrative systems are critical for sustainable availability and accessibility of opioids for patient care.

International imperative to remove barriers to patient care

For nearly three decades there has been clear guidance from United Nations (UN) health and regulatory agencies regarding the need for

governments to address opioid availability and accessibility. These high-level bodies have repeatedly called on governments to identify and remove barriers that block patient access to opioid -based medicines. At a recent meeting of the UN Commission on Narcotic Drugs in March 2010, there was a resolution adopted called “Promoting adequate availability of internationally controlled licit drugs for medical and scientific purposes while preventing their diversion and abuse” [20]. This resolution noted the concern of the INCB that some governments need to take specific measures to ensure adequate access to opioid-based medicines in line with the international drug control conventions. Additionally, non-governmental professional and advocacy groups have made numerous declarations over the years calling on healthcare professionals and governments to improve pain and palliative care, by addressing barriers to the availability of opioids to manage pain. Two notable examples of such efforts from the mid-1990s are the Declaration of Florianopolis [21, 22] and the Report of Santo Domingo [23] which were recommendations resulting from meetings of palliative care experts, drug regulators and leaders from the WHO for improving opioid availability.

Initiatives to Improve Opioid Availability and Accessibility

The global pain and palliative care field has been actively working with countries to improve the availability and accessibility of opioids for the treatment of pain. Examples of recent initiatives include the WHO Access to Controlled Medicines Program [9], the Global Access to Pain Relief Initiative [24], Human Rights Watch reports focused on pain relief and palliative care [25-27], and the Drug Control and Access to Medicines Consortium [28]. Under the leadership and guidance of the Pain & Policy Studies Group (PPSG), important progress to improve opioid availability has been made in India [29], Italy [30] and Romania [31]. This

work evolved into a multi-country initiative aimed at increasing the rate of improvements to opioid availability in countries.

International Pain Policy Fellowship

The International Pain Policy Fellowship (IPPF) was developed by the PPSG, a WHO Collaborating Center at the University of Wisconsin, and is funded by the Open Society Foundations and LIVESTRONG. The central goal of the IPPF initiative is to develop national leaders from LMICs to improve availability of, and access to, opioid analgesics in their countries for the treatment of pain related to cancer and AIDS. The 2-year Fellowship is intended for mid-career health professionals, health care administrators, policy experts, or lawyers. The application process is competitive and fellows are selected based upon demonstrated national leadership to develop pain management and/or supportive or palliative care, the strength of commitment to improving opioid availability in their country, and their potential ability to develop a working relationship with government officials [6].

The Fellowship consists of 1) education regarding the role of international drug control treaties, governments, and healthcare professionals in making opioid analgesics available and accessible for the treatment of pain, while also preventing their abuse and diversion; 2) a one-week training session at the University of Wisconsin and 3) follow up technical assistance to the fellows for the duration of the 2-year Fellowship. The curriculum for the training session was based on WHO guidelines for achieving balance in national opioids control policies [8], which are a tool that can be used to evaluate national policies and systems according to the “Principle of Balance.” These authoritative guidelines were recently revised by WHO with an expanded focus on all controlled medicines [32]. The guidelines provide the most current WHO definition of dependence syndrome and related terminology and provide recommendations on how to adequately

address the risk of diversion and abuse of opioids. To more directly address these issues, PPSG has developed a module on *Abuse, Addiction and Diversion*, which provides the fellows information about the most current medical and scientific understanding of addiction and clarifies confusion about addiction-related terminology which is often found in national drug control policies. The module also includes guidance for how the fellows can prevent diversion of opioids in their countries without impeding pain management and according to the needs and constraints of their country.

During the training session, the fellows used the first edition of the WHO Guidelines to identify barriers and prepare detailed national Action Plans describing their activities to improve patient access to opioid analgesics for the next two years [33]. These Action Plans are ambitious, each addressing unique national environments, and must be flexible to respond to the dynamic landscape, including political changes and other unforeseen factors that impact national healthcare priorities. In cooperation with international experts, the IPPF training empowers fellows with knowledge and skills necessary to cooperate with the Government on the implementation of the action plan. The ultimate goal is to identify and remove existing barriers and improve the availability and accessibility of opioid analgesics for patients in need. To date, two classes of fellows have been selected, one in 2006 and the second in 2008, representing 17 fellows from 15 countries. Progress achieved by the leadership of 3 of the fellows from Sierra Leone, Colombia, and Serbia, who were selected as grantees in 2006, is highlighted.

Sierra Leone

In 2006, when the fellow from Sierra Leone began his work, there was no oral morphine available to the 6 million people in Sierra Leone. Oral morphine was not a registered product at

the time, partially because the registration process for morphine was expensive and time intensive [34]. In response to this need, the fellow initiated a collaborative effort with the Pharmacy Board of Sierra Leone and the Ministry of Health and Sanitation (MoHS) to approve and implement the importation of morphine sulphate powder that could be reconstituted into an oral morphine solution to treat moderate to severe pain due to cancer and HIV/AIDS.

In October 2008, Shepherd's Hospice, the only hospice in the country, received the first shipment of 500 grams of low-cost morphine sulphate powder. This happened after nearly 2 years of the fellow's efforts, working with the Pharmacy Board, to advocate for the importation of morphine powder, identify a supplier, and establish the import amount. The fellow then established a morphine solution production laboratory, oversaw the training of hospice staff regarding how to reconstitute the powder and the hospice first began treating patients with oral morphine in February 2009.

When morphine became available, the challenge was to ensure that appropriate measures were taken to prevent its diversion or abuse. Procedures were written describing the safe-handling practices to ensure the powder and solution were safely available for patients and not diverted or abused. In addition, the fellow developed a record-keeping database to track the use of the new supply of morphine and demonstrate to the Pharmacy Board that there has been no diversion of the morphine powder, as all of it can be accounted for in the spreadsheet. Considering that there were no cases of diversion, the Government of Sierra Leone has agreed to allow for the importation of double the amount of morphine sulphate powder for the coming year, which is an increase from 500 grams to 1 kilogram. The fellow continues to be involved in discussions with the MoHS to introduce palliative care, and the use of oral morphine, into the public hospital system, in an effort to expand the

number of patients able to access morphine for the treatment of pain.

Colombia

While some countries, such as Sierra Leone, are facing the challenge of a complete absence of oral opioids in their country, other countries, such as Colombia, with a population of 45 million, are struggling to ensure that opioids already available are adequately accessible to patients in need. When the fellow from Colombia began her work in 2006, morphine was very poorly distributed throughout the country. Within the capital city region, Bogota, morphine was inconsistently available. In addition, there was poor distribution of the morphine supply from the warehouses in Bogota to pharmacies in the 32 states [35] because regional drug control authorities, as well as pharmacies and hospitals in the states were not requesting morphine from the National Drug Control Authority at the Ministry of Health.

As an initial step, the fellow conducted a survey to identify barriers to opioid availability in Colombia, and found that regional drug control authorities considered a lack of human resources and administrative difficulties to be the central barriers to opioid availability, while the physicians were reluctant to prescribe opioids because they knew that, in many cases, the prescriptions would not be filled. This was because insurance companies did not pay for them, and many patients could not pay for them out of pocket. Poor accessibility of opioids in hospitals and pharmacies because of limited hours for dispensing opioids was another identified factor [35]. A second activity to address the distribution and demand issue was a national opioid availability workshop held in 2007 to jointly review with health care providers and regulators the barriers and identify possible solutions and the steps needed to overcome those barriers. The workshop resulted in a Ministry of Health resolution

ordering regional offices to ensure availability of opioids 24 hours a day, seven days a week (24/7) in at least one institution per state, for example a hospital or a pharmacy. At the beginning of 2009, only 4 states made opioid analgesics available 24 hours a day/7 days a week. At present, 31 states have at least one pharmacy location with 24/7 access to hydromorphone, methadone, morphine and pethidine. In August 2010 a virtual conference for health care providers around the country was held to inform them of the procedures and locations of each pharmacy dispensing opioids in each state. In addition, the national drug control authority now has a no-cost phone number, accessible throughout the country, for patients to report difficulties they are experiencing related to adequate access to opioids. The fellow is now working with the Regulatory Commission of Health, the entity in charge of inclusion of medications in the National Obligatory Health Plan, on the inclusion of additional opioid formulations, in Colombia's National Obligatory Health Plan.

Serbia

The inadequate and inconsistent availability of oral opioids for managing chronic pain due to cancer has been reported as a significant barrier to palliative care development in Serbia [36-39], with a population of around 7.5 million people. At the beginning of the IPPF in 2006, Serbia faced an acute shortage of oral morphine. There was a termination in the supply of modified -release (MR) morphine due to an interruption in the process of importing the drug, and immediate-release (IR) morphine had never been available. To overcome this situation the fellow developed an action plan with the goals of a) re-establishing the availability of oral opioids for the treatment of moderate to severe cancer pain (first focusing on IR morphine), b) initiating education at all levels about the key role of opioids for the management of cancer pain and their fundamental safety in medical practice, and c) initiating the evaluation and updating of

relevant legislation to acknowledge both the prevention of abuse and dependence and the need for opioids in medical practice.

As a result of successful collaboration with the Ministry of Health, relevant Governmental bodies, professional societies, non-governmental organizations, and with international experts, IR oral morphine was registered for the first time in the country's history in 2008. While it has not been possible yet to re-initiate the registration of MR morphine, MR hydromorphone was successfully registered as an alternative strong opioid for oral use in 2008. The fellow also made significant progress in improving education about the use of opioids for cancer pain management. In collaboration with the Academy of Medical Science of the Serbian Medical Society, the textbook *Pharmacotherapy of Cancer Pain* was published in Serbian, providing a valuable educational resource about the key role of opioids in cancer pain management [40]. In addition, the fellow and her colleagues developed two educational brochures on opiophobia intended for health care providers, drug regulators and patients and their families with the support of an educational grant from International Association for the Study of Pain [41, 42]. The brochures addressed common concerns and misunderstandings about abuse, addiction, tolerance and adverse effects of opioids. A campaign to increase community awareness and education was started by engaging with the media: radio, TV, and newspaper [43, 44].

In 2008, the Serbian Ministry of Health established a National Commission for Palliative Care (Commission) and the fellow was initially appointed as Vice-president of the Commission, and later as President. The Commission formulated a palliative care strategy which was officially adopted and approved by the MoH in March 2009 [45]. The strategy recognized: 1) that opioids are essential for pain relief/palliative care, 2) the need for drug control policy that balanced the obligation to

prevent abuse with the obligation to ensure availability of opioids for medical purposes, and 3) the need and willingness of Serbian Government to examine drug control policies for potential barriers and update them in accordance with the principle of balance. In late 2009 the Government of Serbia began the process of revising its national drug control policy and formulated the first draft Law of Psychoactive Controlled Substances [45]. In response to the first draft, the Commission, in collaboration with PPSG and the team leader from the WHO Access to Controlled Medicines Program, undertook an analysis to assess whether the draft Law was balanced and provided suggestions to the MoH about how to amend the draft in accordance with WHO recommendations [8], international drug control conventions [7, 46] and relevant international resolutions [47-49]. Lastly, a national opioid availability workshop was held in April 2010, co-organized by the MoH and WHO country office. With 250 participants, this was a clear manifestation of Governmental willingness to address barriers for the use of opioids for pain and palliative care as well as to establish a dialogue between drug control authorities and healthcare professionals in order to improve availability of and access to opioids in Serbia. With this positive experience, Serbia now also has the opportunity to contribute to the Access to Opioid Medication in Europe (ATOME) project funded by the European Commission under the 7th framework programme [50].

Discussion

The results of the fellows from Sierra Leone, Colombia and Serbia are representative examples of progress achieved through the IPPF towards access to opioids. All three of the fellows showed success in identifying barriers to opioid availability and access as well as in collaborating with government representatives to remove barriers and succeed with their planned objectives. The fellows in Sierra Leone and Serbia were successful at initiating

collaboration with relevant governmental bodies, national authorities and professional societies, which resulted in a new supply of oral opioids in their countries, the necessary first step towards better patient care. In Colombia the fellow was able to improve demand for opioids, their distribution, and patient access to already available opioids by engaging with government officials and partnering with experts. All fellows were instrumental in facilitating the policy change process.

The fellows' initiatives to increase access to and availability of opioids to treat moderate to severe pain related to cancer and HIV/AIDS were guided by the "Principle of Balance" and therefore continually recognized the equally important obligation of preventing abuse and diversion of opioids. In Serbia, the fellow developed educational materials clarifying addiction-related terminology and worked with drug regulators to ensure that the national law on controlled substances was balanced. In Sierra Leone, the fellow carefully documented the use of the new supply of oral morphine and developed written procedures to provide guidance for maintaining adequate control, while ensuring that patients would have access to morphine. A similar effort was implemented in India in the late 1990s and demonstrated that the introduction of a new supply of morphine to be used in patients' homes did not result in any cases of abuse or diversion [51]. In the pain and palliative care field, increased attention is being focused on providing tools for how to prevent diversion and abuse in throughout the system for distributing opioids [52, 53].

As evidenced by the 3 fellows highlighted in this paper, there is not a singular solution that is appropriate for all countries, but rather plans to address barriers must be tailored to the specific needs of that country. Furthermore the complexity of the systemic barriers in each country requires an in-depth, time intensive, analysis by the fellow and international expert

mentors to fully understand the most effective approach for addressing the issues.

Conclusion

Opioid analgesics are simultaneously indispensable medicines for the treatment of moderate to severe pain and effective supportive and palliative care and yet harmful when abused. This dual nature of opioids underlies and contributes to barriers impeding their availability and accessibility. Such barriers play a role in striking disparities in access to opioids between high-income and low and middle-income countries. For nearly three decades, and as recently as a 2010 Commission on Narcotic Drugs Resolution, there has been clear guidance from United Nations health and regulatory agencies regarding the need for governments to continually balance their obligation to control opioids against their equally important responsibility to ensure their availability and accessibility for patients in need. The IPPF program has been successful in developing national leaders from LMICs who have engaged with government to identify and remove barriers that block patient access to opioid analgesics. The fellows in Sierra Leone, Colombia and Serbia, for example, were empowered with the necessary knowledge, skills and guidance to implement their action plans and improve the availability and accessibility of opioids for the treatment of cancer and AIDS related pain in their countries, while also making efforts to prevent abuse and diversion. Fortunately there is hope for further progress as efforts to address opioid availability and accessibility in LMICs are continuing to expand globally and the IPPF is planning for a third class of fellows.

Acknowledgments

The authors are grateful to the Open Society Foundations International Palliative Care

Initiative and LIVESTRONG for the generous support of the International Pain Policy Fellowship. Additionally, the authors would like to thank the government representatives, professional organizations, non-governmental organizations, colleagues and numerous international experts who have been instrumental in the successes in Serbia, Colombia, and Sierra Leone.

References

1. Fallon M, Cherny NI, Hanks G (2010) Opioid analgesic therapy. In: Hanks G, Cherny NI, Christakis NA, Fallon M, Kaasa S, Portenoy RK (eds) Oxford Textbook of Palliative Medicine, 4th edn. Oxford University Press, New York, pp. 661-698
2. World Health Organization (1986) Cancer pain relief. World Health Organization, Geneva
3. World Health Organization (1996) Cancer pain relief: with a guide to opioid availability. World Health Organization, Geneva.
4. Chou R, Fanciullo GJ, Fine PG, Adler JA, Ballantyne JC, Davies P, Donovan MI, Fishbain DA, Foley KM, Fudin J, Gilson AM, Kelter A, Mauskop A, O'Connor PG, Passik SD, Pasternak GW, Portenoy RK, Rich BA, Roberts RG, Todd KH, Miaskowski C (2009) Clinical guidelines for the use of chronic opioid therapy for chronic noncancer pain. *The Journal of Pain* 10:113-130
5. Woodruff R, Cameron D (2010) HIV/AIDS in Adults. In: Hanks G, Cherny NI, Christakis NA, Fallon M, Kaasa S, Portenoy RK (eds) Oxford Textbook of Palliative Medicine, 4th edn. Oxford University Press, New York, pp. 1195-1230
6. Joranson DE, Ryan KM, Maurer MA (2010) Opioid policy, availability and access in developing and nonindustrialized countries. In: Fishman SM, Ballantyne JC, Rathmell JP (eds) *Bonica's Management of Pain*, 4th edn. Lippincott Williams & Wilkins, Baltimore, pp. 194-208
7. United Nations (1973) Single Convention on Narcotic Drugs, 1961 (as amended by the 1972 protocol amending the Single Convention on Narcotic Drugs, 1961). United Nations, Geneva
8. World Health Organization (2000) Achieving balance in national opioids control policy: Guidelines for assessment. World Health Organization, Geneva
9. World Health Organization (2007) Briefing Note: Access to controlled medications programme. January 9, 2007, World Health Organization, Geneva
10. Foley KM, Wagner JL, Joranson DE, Gelband H (2006) Pain control for people with cancer and AIDS. In: Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, Jha P, Mills A, Musgrove P (eds) *Disease Control Priorities in Developing Countries*. Oxford University Press, New York, pp. 981-993
11. World Health Organization (2011) World Health Organization Essential Medicines Library, Morphine, <http://apps.who.int/emlib/MedicineDisplay.aspx?Language=EN&MedIDName=217%40morphine>. Accessed 11 January 2011
12. International Narcotics Control Board (2010) Narcotic drugs: Estimated world requirements for 2010 - Statistics for 2008. United Nations, New York
13. International Narcotics Control Board (1996) Report of the International Narcotics Control Board for 1995: Availability of opiates for medical needs. United Nations, New York
14. International Narcotics Control Board (2009) Report of the International Narcotics Control Board on Follow-up to the Twentieth Special Session of the General Assembly, 2008. United Nations, New York
15. Adams V (2007) Access to pain relief - an essential human right. Help the Hospices for the Worldwide Palliative Care Alliance, London
16. Cherny NI, Baselga J, De Conno F, Radbruch L (2010) Formulary availability and regulatory barriers to accessibility of opioids for cancer pain in Europe: A report from the ESMO/EAPC Opioid Policy Initiative. *Annals of Oncology* 21:615-26
17. De Lima L, Sweeney C, Palmer JL, Bruera E (2004) Potent analgesics are more expensive for patients in developing countries: A comparative study. *J Pain Palliat Care Pharmacother* 18:59-70
18. Bruera E, De Lima L (2005) Opioid cost: A global problem. *Palliat Med* 19:504
19. World Health Organization (2006) The ICD-10 classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines. World Health Organization, Geneva
20. United Nations Economic and Social Council (2010) Promoting adequate availability of internationally controlled licit drugs for medical and scientific purposes while preventing their diversion and abuse; Resolution 53/4. Report on the fifty-third session of the Commission on Narcotic Drugs; 8-12 March 2010; Agenda item 9; Implementation of the international drug control treaties.

21. Stjernswärd J, Bruera E, Joranson DE, Allende S, Montejo G, Quesada-Tristan L, Castillo G, Schoeller T, Rico Pazos MA, Wenk R, Pruvost M, De Lima L, Mendez E, Nunez Olarte J, Olalla JF, Vanegas G (1995) Opioid availability in Latin America: The declaration of Florianopolis. *J Pain Symptom Manage* 10:233-6.
22. Stjernswärd J, Joranson DE (1995) Opioid availability and cancer pain - an unnecessary tragedy. *Support Care Cancer (Europe)* 3:157-158.
23. De Lima L, Bruera E, Joranson DE, Vanegas G, Cepeda S, Quesada L, Wenk R, Pavajeau MC, Derio L, Montejo G, Castillo G, Ruiz F, Pupo AR, Carles B, Paredes E, Schoeller T (1997) Opioid availability in Latin America: the Santo Domingo Report - progress since the Declaration of Florianopolis. *J Pain Symptom Manage* 13: 213-9.
24. Anderson T (2010) Cancer doctors pledge to widen access to pain relief in developing countries. *Br Med J. doi: 10.1136/bmj.c4645*
25. Human Rights Watch (2009) "Please, do not make us suffer any more...": Access to pain treatment as a human right. Human Rights Watch, New York
26. Human Rights Watch (2009) Unbearable pain: India's obligation to ensure palliative care. Human Rights Watch, New York
27. Human Rights Watch (2010) Needless pain: Government failure to provide palliative care for children in Kenya. Human Rights Watch, New York
28. Drug Control and Access to Medicine Consortium (2011) Drug Control and Access to Medicines Consortium web site. <http://www.dcamconsortium.net/>. Accessed 11 January 2011
29. Joranson DE, Rajagopal MR, Gilson AM (2002) Improving access to opioid analgesics for palliative care in India. *J Pain Symptom Manage* 24:152-159
30. Blengini C, Joranson DE, Ryan KM (2003) Italy reforms national policy for cancer pain relief and opioids. *Eur J Cancer Care* 12:28-34
31. Mosoiu D, Ryan KM, Joranson DE, Garthwaite JP (2006) Reforming drug control policy for palliative care in Romania. *Lancet* 367:2110-2117
32. World Health Organization (2011) Ensuring balance in national policies on controlled substances: Guidance for availability and accessibility of controlled medicines. World Health Organization, Geneva.
33. Pain & Policy Studies Group (2008) Increasing Patient Access to Pain Medicines around the World: A Framework to Improve National Policies that Govern Drug Distribution. Madison, Wisconsin, USA: University of Wisconsin Paul P. Carbone Comprehensive Cancer Center. http://www.painpolicy.wisc.edu/online_course/welcome.htm
34. McNeil DG (September 9, 2007) Drugs banned, world's poor suffer in pain. *The New York Times*, New York, NY: Vol. CLVI p. A1, A12
35. Leon MX, De LL, Florez S, Torres M, Daza M, Mendoza L, Agudelo N, Guerra L, Ryan K (2009) Improving availability of and access to opioids in Colombia: description and preliminary results of an action plan for the country. *J Pain Symptom Manage* 38:758-766
36. Bosnjak S, Milicevic N, Lakicevic J (2006) Palliative care in Serbia and Montenegro: Where are we now? *Archive of Oncology* 14:8-10
37. Lynch T, Clark D, Centeno C, Rocafort J, Flores LA, Greenwood A, Prail D, Brasch S, Giordano A, De Lima L, Wright M (2009) Barriers to the development of palliative care in the countries of Central and Eastern Europe and the Commonwealth of Independent States. *J Pain Symptom Manage* 37:305-315
38. Bosnjak S, Milicevic N, Lakicevic J (2007) Serbia and Montenegro. In: Centeno C, Clark D, Lynch T, Rocafort J, Flores LA, Greenwood A, Brasch S, Prail D, Giordano A, De Lima L (eds) *EAPC atlas of palliative care in Europe*. IAHP Press, Milan, pp. 250-257
39. Clark D, Wright M (2002) Transitions in end of life care: Hospice and related developments in Eastern Europe and Central Asia. Open University Press, Buckingham
40. Bosnjak S, Beleslin DB, Vuckovic-Dekic LJ (2007) Farmakoterapija kancerskog bola (Pharmacotherapy of Cancer Pain). Monografije naučnih skupova AMN SLD, serija B 1, Belgrade
41. Bosnjak S, Bakic N, Dragicevic M, Dimitrijevic J (2009) Šta Plaši Bolesnika I Porodicu? (Educational brochure on opioiphobia for patients). (<http://www.uitbs.org.rs/>) Accessed 11 January 2011
42. Bosnjak S, Susnjak S, Dimitrijevic J (2009) Šta plaši zdravstvene radnike (Educational brochure on opioiphobia for health professionals). (<http://www.uitbs.org.rs/>) Accessed 11 January 2011
43. Vreme Zdravlja (2009) Opiofobija ne leci bol, Intervju: Dr. Snezana Bosnjak. pp. 32-33. <http://www.vreme.com/download.php/system/storage/pdf/980zdrav3.pdf> Accessed 11 January 2011
44. Bosnjak S (2010) Palijativno zbrinjavanje pacijenata. Belgrade, Serbia: B92. <http://www.b92.net/info/vesti/index.php?yyyy=2010&m>

[m=03&dd=07&nav_category=12&nav_id=416125](http://www.zdravlje.gov.rs/index.php)

Accessed 11 January 2011

45. Republic of Serbia (2011) Ministry of Health website, <http://www.zdravlje.gov.rs/index.php> Accessed 11 January 2011

46. United Nations (1971) Convention on Psychotropic Substances, 1971. United Nations, Geneva

47. Council of Europe (2003) Recommendation 2003, 24 of the Committee of Ministers to member states on the organization of palliative care. Adopted by the Committee of Ministers at the 860th meeting of the Ministers' Deputies; 12 November 2003.

48. United Nations Economic and Social Council (2005) Demand for and supply of opiates used to meet medical and scientific needs; Resolution 2005-26. Report on the forty-eighth session of the Commission on Narcotic Drugs E/2005/28; 19 March 2004 and 7-11 March 2005; issued 22 July 2005.

49. United Nations Economic and Social Council (2005) Treatment of pain using opioid analgesics; Resolution 2005-25. Report on the forty-eighth session of the Commission on Narcotic Drugs E/2005/28; 19 March 2004 and 7-11 March 2005; issued 22 July 2005.

50. Access to Opioid Medication in Europe (2011) Access to Opioid Medication in Europe (ATOME) <http://www.atome-project.eu/> Accessed 11 January 2011

51. Rajagopal MR, Joranson DE, Gilson AM (2001) Medical use, misuse, and diversion of opioids in India. *Lancet* 358:139-143.

52. African Palliative Care Association (2010) Guidelines for Ensuring Patient Access to, and Safe Management of, Controlled Medicines. Africa Palliative Care Association, Kampala

53. Jamaica Ministry of Health (2010) Policy for Patient Access and Safe Management of Controlled Drugs. Jamaica Ministry of Health, Kingston

Fig. 1 Global trend (1980 – 2008) for medical consumption (mg/capita) of fentanyl, hydromorphone, methadone, morphine, oxycodone, and pethidine compared with the total consumption of all 6 opioids displayed in morphine equivalence

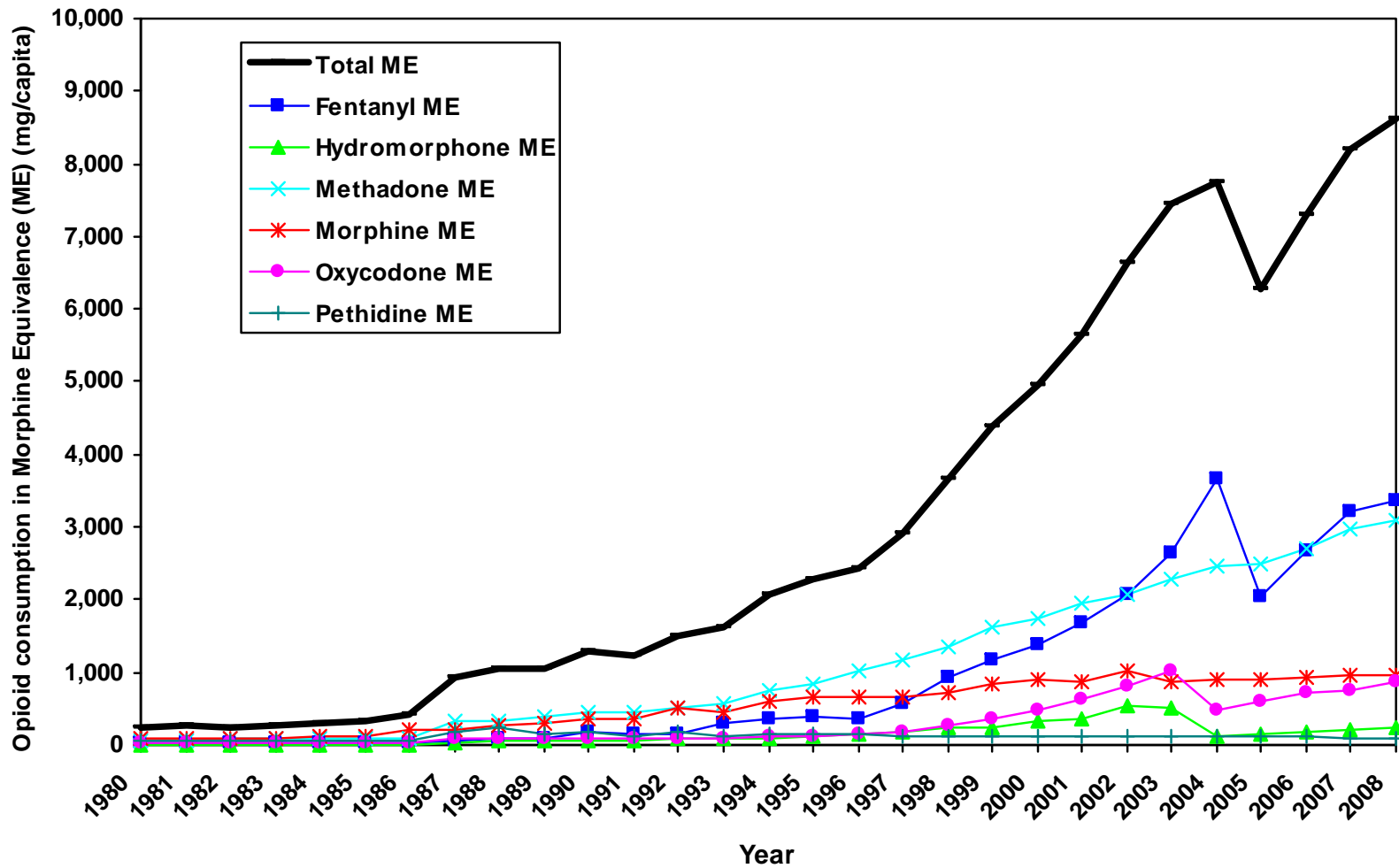


Fig. 3 Global trend (1980 – 2008) for total medical consumption (mg/capita) of 6 opioids (fentanyl, hydromorphone, methadone, morphine, oxycodone, and pethidine) compared with the total medical consumption of all 6 opioids in high vs low and middle-income countries, displayed in morphine equivalence

