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Examining Influences on the Availability of and Access to Opioids for Pain Management and Palliative Care

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Abstract

This Commentary relates to the recently-published essay in *PLOS Medicine*, entitled “Untreated Pain, Narcotics Regulation, and Global Health Ideologies.” The article describes regulatory and other systemic barriers preventing the accessibility of opioid analgesics and contributing to patients not receiving adequate pain relief. Four main points highlighted in the essay are discussed in this commentary: (1) the role of international treaties in medication availability, (2) the role of the International Narcotics Control Board in medication availability, (3) the role of regulatory policy in treating pain, and (4) the role of opioid analgesics in treating pain. Recent authoritative statements and activities suggest a strengthened infrastructure within which governments currently can work to improve the availability of controlled medicines to enhance patient pain and palliative care services.

Keywords: opioid availability, pain, controlled medicine, Single Convention, INCB, WHO

A recent essay by King and Fraser, published in the April 2013 issue of *PLOS Medicine*, highlighted the important global health problem of unrelieved pain and underscored the complexity of regulatory and other systemic barriers that often prevent patients from receiving adequate treatment for their pain.¹ Concerns were expressed about the function of international treaties, as well as the International Narcotics Control Board (INCB) (a quasi-governmental body responsible for implementing the international conventions), in promoting a generally prohibitive regulatory environment regarding medication availability, including opioid analgesics. Although national, state, and other jurisdictional policies governing opioid prescribing undoubtedly pose significant barriers to adequate pain relief, we suggest that the overall influence of international treaties and the INCB on this situation is not as straightforward, and perhaps even less restrictive, than is commonly perceived. In fact, King and Fraser raised a number of points that warrant further consideration when formulating responses to the global unavailability of controlled medicines for pain management, palliative care, and end-of-life care.¹ These points included:

- (1) The role of international treaties in medication availability,
- (2) The role of the INCB in medication availability,
- (3) The role of regulatory policy in treating pain, and
- (4) The role of opioid analgesics in treating pain.

This commentary elaborates on each of these points, in an attempt to offer a broad perspective based on our insights from many years of experience collaborating with international and national authorities and country governments in our efforts to improve the global availability of opioid analgesics for medical and scientific purposes.

Point 1: The role of international treaties in medication availability

The Single Convention on Narcotic Drugs on Narcotic Drugs, 1961, as amended by the 1972 protocol, (Single Convention)² is the primary international treaty governing the use of controlled medicines, which outlines a broad drug control framework for governments. A government's enactment of a closed drug distribution system, as required under the Single Convention, is meant to ensure appropriate availability of controlled medicines such as opioid analgesics for medical purposes and to prevent diversion, illicit trafficking, and abuse. This central aim of the Single Convention has come to be known as the Central Principle of Balance:

“The central principle of “balance” represents a dual obligation of governments to establish a system of control that ensures the adequate availability of controlled substances for medical and scientific purposes, while simultaneously preventing abuse, diversion and trafficking. Many controlled medicines are essential medicines and are absolutely necessary for the relief of pain, treatment of illness and the prevention of premature death. To ensure the rational use of these medicines, governments should both enable and empower healthcare professionals to prescribe, dispense and administer them according to the individual medical needs of patients, ensuring that a sufficient supply is available to

meet those needs. While misuse of controlled substances poses a risk to society, the system of control is not intended to be a barrier to their availability for medical and scientific purposes, nor interfere in their legitimate medical use for patient care.”³

King and Fraser¹ portrayed a seemingly intrinsic conflict between these dual objectives within the Single Convention, suggesting that they are mutually exclusive and cannot coexist. And yet, we would argue that the treaty’s underlying concept of Balance represents complementary goals, both of which are aimed at reducing public harm from detrimental outcomes (i.e., opioid availability can palliate patient suffering, while mitigating diversion can lessen the occurrence of substance abuse); such an interpretation is directly supported by the INCB, which has acknowledged this as the ultimate aim of the Single Convention.⁴

In terms of drug control, the Single Convention has a very limited number of broad compulsory control measures regarding the therapeutic use of relevant medicines, such as:

- Governments must adopt legislative and administrative measures to limit exclusively to medical and scientific purposes all manufacture, distribution and possession within the country, (Article 4)²
- All persons and enterprises involved in import, export, production, manufacture, trade and distribution must be controlled under government license, (Articles 29, 30)²
- Quantities manufactured and exported must be within the quantities of drugs required for medical and scientific purposes, as officially estimated by governments and confirmed by the INCB, (Articles 12, 19, 21)²
- Governments must report the amounts of opioids imported, exported, manufactured and consumed (distributed to the retail level) to allow the INCB to examine governments’ compliance with the Single Convention, (Article 20)²
- Possession of drugs is not permitted except under legal authority; (Article 33) therefore, medical prescriptions from duly authorized persons are required for dispensing to individuals, (e.g., patients), and (Article 30)²
- Records of acquisition and disposal are to be kept by governmental authorities, manufacturers, traders, scientific institutions and hospitals. (Article 34)²

Paradoxically, a common perception is that the Single Convention details complex and specific requirements by which governments must abide. On the contrary, there is great latitude about how a government can design the drug control system to meet these broad treaty mandates. Anderson & Davis⁵ have even detailed the varied approaches that each of three countries took to meet the identical requirements. Governments must move beyond the presumed restrictiveness of the Single Convention regarding opioids for pain relief and take advantage of its inherent flexibility when revising their national policies governing the use of controlled substances.

Point 2: The role of the INCB in medication availability

Similarly, the roles and obligations of the INCB often are misunderstood, and the responsibilities of individual governments deemphasized, with respect to meeting the dual aims of the Single Convention. The INCB's role is to monitor and promote compliance with the Single Convention,⁶ but the ultimate accountability for meeting the dual objectives lies with governments that are signatories (or parties) to the Convention. These roles are delineated in the Single Convention, which states that:

“in co-operation with Governments... [the INCB] shall endeavor to limit the cultivation, production, manufacture and use of drugs to an adequate amount required for medical and scientific purposes, to ensure their availability for such purpose and to prevent illicit cultivation, production, manufacture of, and illicit trafficking in and use of drugs.” (Article 9, paragraph 4)²

The accompanying Commentary on the Single Convention further clarifies that this language should be interpreted to mean that governments or signatory countries have an equal responsibility to meet these dual aims, particularly since the INCB does not have direct administration in those countries.(Article 2, Paragraph 5)⁷ Therefore, while the INCB periodically issues letters to governments noting concerns about compliance with the Single Convention, or includes statements in its annual reports calling for corrective actions, the INCB has no formal jurisdiction or authority to take policy action in a country. Despite this absence of authority, the INCB is committed to working cooperatively with governments and has expressed a willingness to provide technical assistance when needed.⁸ However, any ability of the INCB and other UN bodies to be more proactive in assisting governments with meeting their obligation to ensure availability of controlled medicines ultimately is dependent on receiving adequate resources.

A widespread belief also exists that the INCB directly limits the availability of controlled medicines for medical and scientific purposes. It is indeed true that United Nations bodies and other international drug regulatory bodies, including the INCB, acknowledge that their emphasis historically has been on the control aspect of the Single Convention, rather than on ensuring availability.³ By the late-1980's, however, the INCB and other UN bodies began publishing numerous statements encouraging governments to meet their obligation about maintaining medication availability, such as for pain relief and palliative care.^{3, 4, 9-15} Along with this acknowledgement has come recommendations that governments review their laws and regulations to identify barriers and take actions to amend or repeal those barriers.^{3, 9, 10, 14}

Importantly, in the last several years, the INCB, the Commission on Narcotic Drugs (CND) and the UN Economic and Social Council (ECOSOC) have made unprecedented high-level statements and have developed initiatives directed at improving the availability of opioids for pain relief. In 2005, the ECOSOC passed two Resolutions, one that recognized the importance of the use of controlled medicines for the relief of pain¹⁶ and another calling on member states to remove barriers that may impede the medical use of opioids for pain relief and inviting the World Health

Organization (WHO) and INCB to explore an assistance mechanism to facilitate the adequate treatment of pain with opioids.¹³ In 2010, the CND passed a Resolution, entitled “Promoting adequate availability of internationally controlled licit drugs for medical and scientific purposes while preventing their diversion and abuse,” calling on member states to work with the INCB and United Nations Office on Drugs and Crime (UNODC) to review and update policies and drug control frameworks to achieve patient access to needed medications.¹⁴ Distinct from the INCB, the UNODC has the specific role of offering guidance to member states to assist them in implementing international treaties, including providing support in drafting national drug policies such as those that govern opioids for medical purposes. The Resolution also encouraged INCB to continue its work with the WHO to develop guidelines for calculating estimated requirements. In response to this Resolution, the INCB published a special supplement to their Annual Report highlighting the global problem of inadequate opioid availability, noting progress in some countries and offering several recommendations to promote continued improvements.⁴ The recommendations included: examining methods used for determining drug estimates each year, identifying and working step by step to remove impediments to availability of controlled drugs for medical use, ensuring that national laws contain elements of the Single Convention and that there is a body created to administer these laws, and determining whether the existing laws create undue burdens on availability to controlled drugs for prescribing and/or dispensing for patients with a medical need.⁴

The following year, the CND passed a second resolution regarding availability of controlled drugs for medical purposes.¹⁵ The 2011 Resolution called 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. As a result, progress now is being 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. Importantly, for the fourth consecutive year, availability of controlled medicines for medical and scientific purposes was on the CND agenda, signifying that it continues to be recognized as equally important as drug control by international drug control authorities responsible for implementing the Single Convention.

Taken together, these recent Resolutions represent significant momentum to raise the issue of medication availability with UN bodies and pave the way for concrete actions on the part of UN bodies and member states, and other governments. For example, in 2012, the INCB and WHO jointly published the “Guide on Estimating Requirements for Substances under International Control” (the Guide), to assist governments in improving their methods and process for calculating their national requirements for controlled medicines.¹⁷ The Guide was designed to address the needs of countries with low consumption of controlled substances for medical purposes in an effort to improve their estimates to better reflect actual requirements. This publication, and the multi-agency expert working group that drafted it, represent collaboration among international drug regulatory and health authorities. The INCB continues to offer

support for governments in their use of the Guide.⁸ In addition, the UNODC, the WHO and the Union for International Cancer Control (an international NGO) recently announced an initiative to improve access to controlled medicines for pain relief while preventing their diversion and abuse. This effort will include assistance to improve country level activities such as data collection, regulatory revision and reform, training about estimates and statistics, procurement and distribution and community-based health care.⁸ These notable activities suggest that INCB, the UNODC and the WHO are taking unprecedented actions with limited resources and working within their mandates and expertise to encourage governments to improve opioid availability.

Point 3: The role of regulatory policy in treating pain

Another assertion by King and Fraser¹ is that drug policy reform is necessary, but not sufficient, to address untreated pain, and that more complex and comprehensive solutions are required. We enthusiastically support, and have always maintained, this contention – a successful approach to improving opioid availability needs to be multifaceted and extend beyond policy change, and the WHO has explicitly recognized this for almost two decades. In 1996, in its seminal publication, entitled “Cancer Pain Relief: A Guide to Opioid Availability,” the WHO contributed a framework for developing or improving palliative care and pain relief within a country that comprised three key components:

1. Government policies that ensure the integration of palliative care services into the structure and financing of the national health care system;
2. Educational programs that provide support for the training of health care professionals, volunteers, and the public;
3. Drug availability supported by appropriate drug control policies and their administration to ensure the availability of essential medicines for the management of pain and other symptoms, in particular, opioid analgesics for pain relief. (WHO, 1996, p.43)¹⁸

Such a multi-pronged construct continues to be recognized as important,¹⁹ and represents, to the extent feasible, the conceptual foundation for the Pain and Policy Studies Group’s (PPSG’s) global efforts to improve policy and regulatory barriers to opioid availability. Our International Pain Policy Fellowship (IPPF) program identifies and trains health care professionals and government members (when possible) from low- and middle-income countries (LMICs) to achieve the safe and effective use of pain medicines in their own countries. When drafting action plans for their in-country projects, all Fellows are encouraged to address all three aspects of the WHO framework when appropriate and practicable.

An illustrative example of this comprehensive approach comes from the IPPF activities of the Fellow from Colombia, a Palliative Care physician and professor of medicine.²⁰ Related to government policy, she engaged with colleagues at the University of La Sabana, the National Cancer Institute, the National Association of Palliative Care and the Colombian International Association for the Study of Pain to advise and provide recommendations for two legislators who were working on the

development of a palliative care law. To address the need for increased education about pain management and palliative care, the Fellow worked with colleagues and collaborated with the Ministry of Education to implement a mandatory course in palliative care symptom management for undergraduate medical students at the University of La Sabana. The hope is for the course to eventually be offered in all medical schools throughout the country. The Fellow also was involved in developing an online course in palliative care and a continuing education course for primary care health professionals. Lastly, related to opioid accessibility throughout the country, the Fellow identified the issue of poor distribution of morphine supply from warehouses in Bogota, the capital city, to pharmacies in 32 states. Working with the cooperation of other healthcare professionals, the Fellow organized a national workshop in November 2007 involving the Ministry of Health (MoH), the WHO, the Pan American Health Organization, and the PPSG to determine the relevant barriers to medication distribution. The regional drug control regulatory authorities also participated, providing an opportunity to sensitize them about the importance of an adequate availability of opioids in their regions to achieve a better quality of care for patients. Ultimately, the MoH issued a new Resolution that ordered the regional drug control offices to ensure the availability of morphine 24 hours a day and 7 days a week, in at least one pharmacy per state. By the end of the Fellow's IPPF experience, approximately 4 years after the Resolution passed, there were 32 such pharmacies, one in each state.

Point 4: The role of opioids in treating pain

Finally, King and Fraser¹ make the critical and valid point that pain treatment should be multimodal, extending beyond opioid analgesics to include other pharmacologic and even non-pharmacologic treatments. Guidance from the WHO dating back to 1986, acknowledges the need for a varied approach to pain management and that not all types of pain will respond equally, if at all, to opioids.²¹ With the "Three-step Analgesic Ladder," the WHO recommended, and continues to recommend,³ using various types of analgesics (in combination with adjuvant drugs when needed) depending on the severity of the patient's pain; adjuvant medications, such as anti-emetics, laxatives, corticosteroids, and psychotropic drugs, are indicated for a variety of reasons such as treating adverse effects of analgesics, enhancing pain relief, and treating co-occurring psychological problems such as depression or anxiety. Step 1 of the ladder involves the use of non-opioid analgesics, such as acetylsalicylic acid, paracetamol, ibuprofen, indomethacin, and other nonsteroidal anti-inflammatory drugs to treat mild pain. Step 2 relates to the use of opioids for mild to moderate pain, such as codeine, tramadol, or dextropropoxyphene, alone or in combination with non-opioids and/or adjuvant medications. Step 3 includes opioid analgesics for moderate to severe pain, such as morphine, oxycodone, or fentanyl, again in combination with non-opioids and/or adjuvant medications when needed. As initially conceptualized, the intensity of the patient's pain determines the step of the analgesic ladder upon which to begin treatment. Therefore, when pain is severe, as is often the case in LMICs where the majority of patients are diagnosed with late-stage disease, there is solid evidence that opioids are regarded as the most effective and affordable treatment.^{22;23} Although the concept of a ladder and the necessity of the second step has been debated^{22;24} and

recently removed from recent WHO guidelines,²⁵ the third step involving opioids has been retained for nearly 30 years.^{22;26} Importantly, in the last decade, the integration of non-pharmacologic approaches to treating pain has become recognized as a standard of practice by which to aspire.^{27;28}

Conclusions

This Commentary sought to extend the discussion in King and Fraser's¹ recent essay by elaborating on several key themes, including the extent that international treaties and the INCB can ensure availability of controlled medicines, as well as the function of regulatory policy and opioid analgesics when providing pain care services. When considering these issues, a number of conclusions can be reached. It remains vital for Governments to embrace their role and responsibility to fulfill the dual obligations of the Single Convention and, when revising their national policies governing the use of controlled medicines, they should recognize and take advantage of the flexibility allowed by the Single Convention. Such efforts can benefit from the practical guidance provided by high-level UN Bodies in the form of powerful Resolutions, and emerging unprecedented initiatives such as the UNODC Model Law Revision and a joint INCB/WHO Guide on estimating requirements. In addition, for many years the WHO has been involved in a variety of activities designed to strengthen a government's commitment to improving the provision of palliative care. Notable among these efforts is the WHO's multifaceted framework for developing a country's infrastructure that supports palliative care and pain relief, which promotes efforts to improve regulatory and policy barriers that are coupled with education and training for healthcare practitioners about the modern medical use of opioids and adopting and enacting national policies to help achieve these objectives. Finally, numerous national and international authorities recommend that effective pain treatment should be multimodal, extending beyond opioid analgesics to include other pharmacologic and non-pharmacologic therapies.

We hope it is apparent from the activities described in this commentary that significant advancement has been made in recent years to enhance the global availability of controlled medicines for medical purposes. Of course, further work and continued progress is necessary, especially in certain countries. Fortunately, there currently is a clear conceptual foundation, which is supported by international authorities, for maintaining and strengthening a government's ability to provide effective pain and palliative care services to improve the treatment of patients suffering from cancer and other chronic conditions.

Declaration of interest:

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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