



Is opioid over-regulation hurting cancer patients?

“While opioids are not the only medication used for the treatment of cancer pain, they are an essential medicine in the armamentarium of those treating people living with a cancer diagnosis.”

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Few dispute the role of opioids in the treatment of pain in patients with advanced cancer. However, while there has been much energy devoted to improving cancer pain management, most of the world's population still lack access to appropriate medications for cancer pain relief. In 2006, 17% of the world's population, primarily those in some industrialized countries, consumed 80% of the world's opioids [1]. The WHO's Access to Controlled Medicines Program documented that 5.5 billion people (83% of the world's population) live in countries with low to nonexistent access to opioids. The regional differences in opioid consumption throughout the world are shown in [Figure 1](#). In 2010, opioid consumption was calculated by the International Narcotics Control Board (INCB) to be 'inadequate' in 50 countries, and 'very inadequate' in more than 100 countries [2]. The Global Task Force for Cancer Control [3] identified the discrepancy in opioid usage between the highest ten consuming countries to be 50,000-times greater than that used by the ten lowest consuming countries. This opioid use discrepancy and, therefore discrepancy in pain and physical suffering, was associated with all cancers, including those for which neither effective cancer treatment nor prevention was possible. The 50,000-times difference was compared with the 4–20-fold differences seen in cancer screening and pediatric cancer control interventions between the highest and lowest ranking countries.

Cancer pain relief should be a critical part of National Cancer Control plans [4]. These plans recognize the value of: prevention; early detection and treatment; and palliative care.

Pain is a significant factor in the experience of cancer and may be a symptom at presentation, a result of both diagnostic tests and therapy and/or as a result of metastatic disease. While many of those surviving with a cancer diagnosis live with residual pain, it is estimated that that 75–80% of patients with metastatic disease have significant pain [5]. This is a particularly significant issue in low- and middle-income countries (LMICs) where many patients present with advanced disease. Already most of the world's cancer patients live in LMICs and by 2050 is estimated that 61% of new cancers will be diagnosed each year in those regions [6], the very countries that lack access to opioids for pain relief.

While the acceptability of opioids in medicine waxed and waned in the 19th and early 20th centuries, the second half of the 20th century saw an increasing focus on opioids in the treatment of cancer pain. The WHO recognized the importance of palliative care in 1986 when it introduced the document 'Cancer Pain Relief' together with the WHO Analgesic Ladder [7]. In the ladder, the WHO laid out the pivotal role of opioids in cancer pain management. In fact, morphine and codeine are defined 'essential drugs' by the WHO Committee on Essential Drugs (i.e., "...they satisfy the health care needs of the majority of the population; they should therefore be available at all times in adequate amounts and in the appropriate dosage forms..." [8]. Furthermore, importantly, a WHO report stated, "A palliative care program cannot exist unless it is based on a rational national drug policy," and this includes "regulations that allow ready access of suffering patients to opioids" [9].



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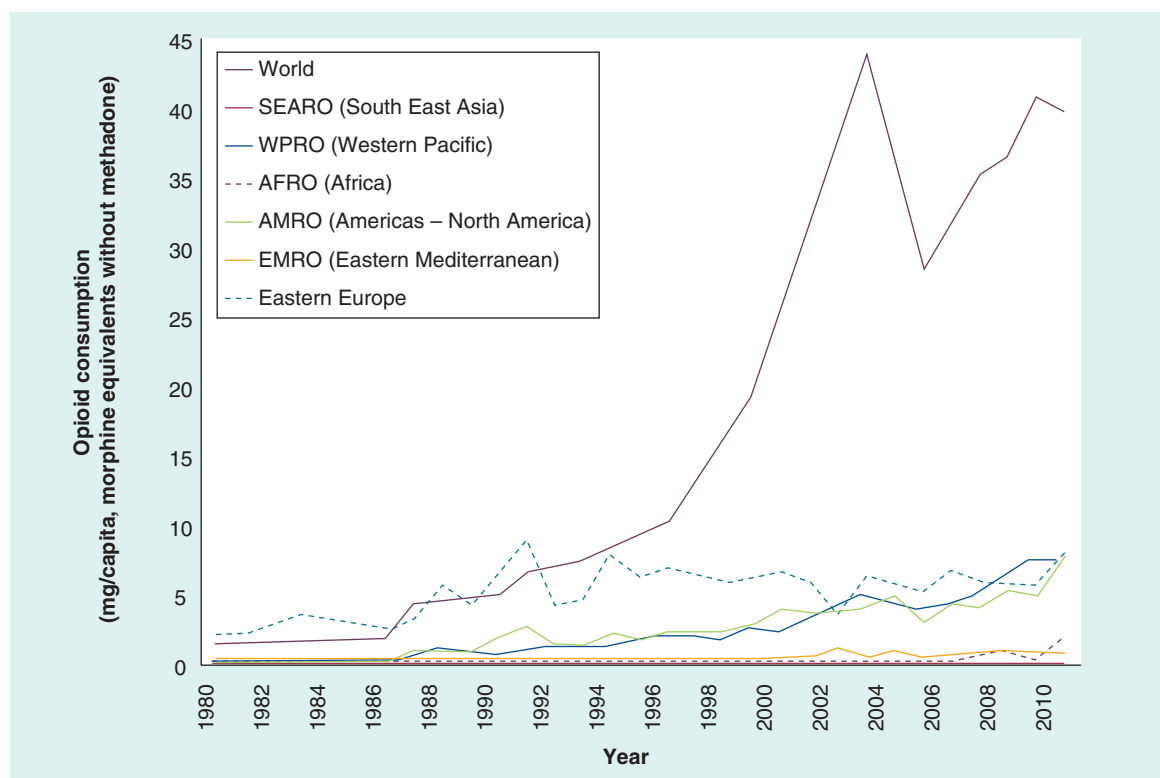


Figure 1. Annual mean opioid consumption (morphine, oxycodone, pethidine, fentanyl and hydromorphone) for selected global regions.

National Drug Policies fall under the purview of the United Nations' Single Convention of Narcotic Drugs of 1961 (amended in 1971 to include psychotropic substances) [10]. The primary aim of the Single Convention is to limit the production of narcotics and psychotropic substances to appropriate medical and scientific use, while preventing misuse and abuse. The aim is not to restrict their appropriate medical use; in fact, the Single Convention has a stated co-aim of "ensuring access for medical and scientific purposes". However, as with the applied controls, there has been considerable push back from the use of these substances for the treatment of cancer pain. The control of opioids (and other narcotic and psychotropic drugs) resides with the INCB, an independent, quasi-judicial organization charged since 1968 with implementing the Single Convention. The INCB's role is to prevent the illicit (illegal) production of, trafficking in, and use of narcotic drugs and to ensure their availability for medical and scientific needs. All countries (even non-signatories) making opioids available for medical use are required by the Single Convention to estimate its national opioid needs and report annually on imports, exports and distribution to the retail level.

Given all these factors favoring opioid use for medical purposes, why is opioid use so low? Despite clear language in the Single Convention that efforts

to restrict the illicit use of opioids should not interfere with the medical and scientific use of opioids, the INCB together with the WHO have discovered that this is not the case. A 1989 survey identified multiple causes blocking opioid use including fear of addiction, poor estimates, lack of resources and poor professional education [11]. These were confirmed by a further INCB survey of 65 countries in 1995 that showed multiple excessively restrictive laws and regulations and fear of legal consequences as additional barriers in most countries [12], results again confirmed in later surveys by both the INCB [13] and the World Palliative Care Alliance [14]. The 1995 INCB report stated, "...an efficient national drug control regimen must involve not only a program to prevent illicit trafficking and diversion, but also a program to ensure the adequate availability of narcotic drugs for medical and scientific purposes." The INCB in multiple reports has called for countries with low consumption to address these barriers and increase their estimates for medical indications [11–13].

It was in this context that the WHO, together with the Pain and Policy Studies Group, home of the WHO Collaborating Center for Pain Policy in Palliative Care, released the expert report 'Achieving Balance in National Opioid Control Policy: Guidelines for Assessment' [15]. In this document, the central Principle of 'balance' was defined, a principle that

was confirmed in the 2011 document ‘WHO Policy Guidelines; Ensuring Balance in National Policies on Controlled Substances, Guidance for Availability and Accessibility for Controlled Medicines’ [16]. The principle has evolved with the current definition taken from the Commission of Narcotic Drugs resolution 53/4 [17]: “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.”

Despite ‘Achieving Balance’ and ongoing efforts to improve opioid consumption, there has still been little increase in opioid consumption in LMICs. The UN Economic and Social Council [18] in a 2005 resolution stated that the medical use of narcotic drugs was indispensable for the relief of pain and suffering, that morphine should be available at all times in adequate amounts and appropriate dosage forms for the relief

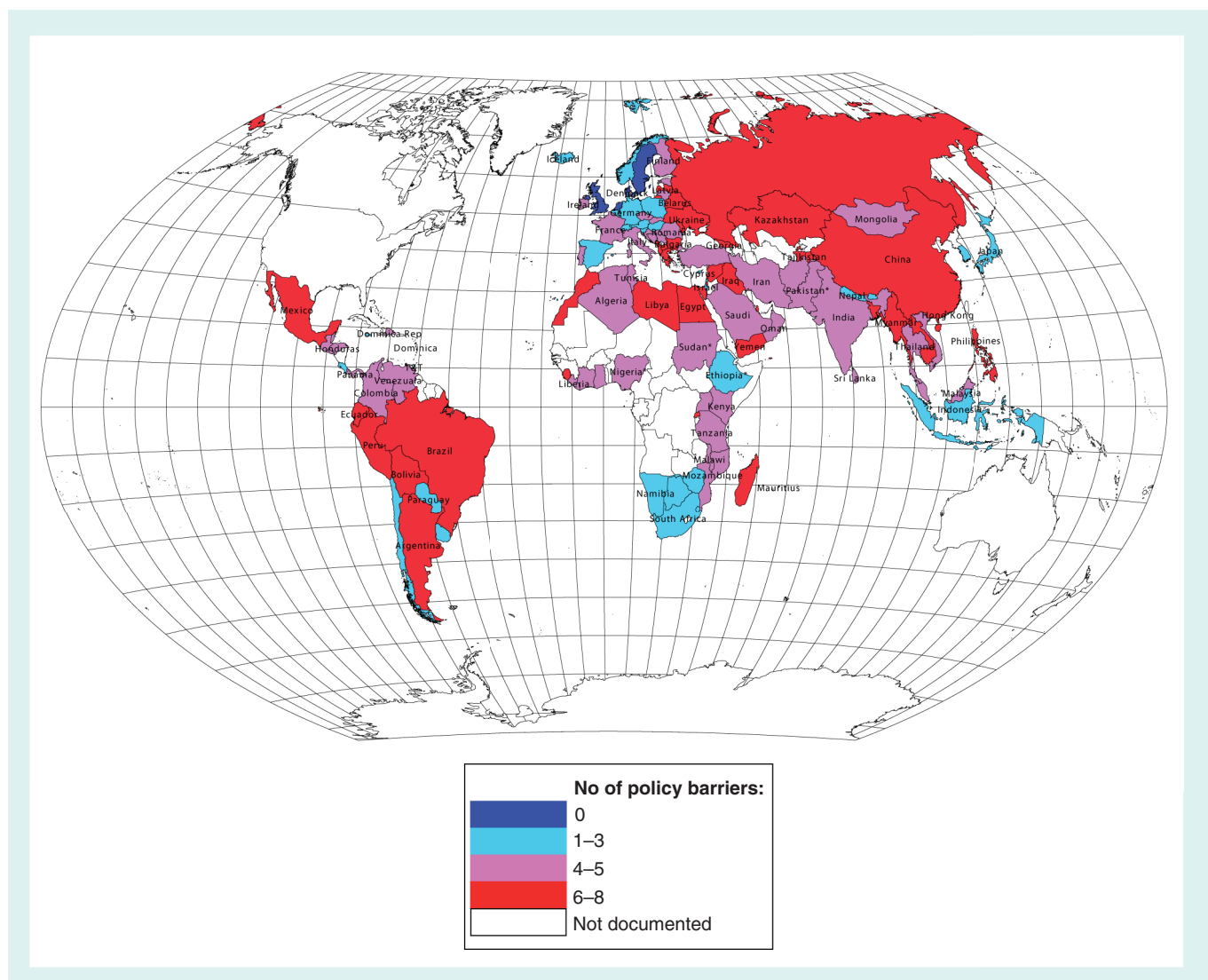


Figure 2. Number of barriers to opioid policy for Europe (18), Africa (19), Asia (20), Middle East (21), Latin America and the Caribbean (22) and India (23).

For color images please see online at www.futuremedicine.com/doi/full/10.2217/cpr.14.6

of severe pain and that the low national consumption of opioids was a matter of great concern. Ongoing INCB reports urged all Governments to take steps to improve the availability of those narcotic drugs for medical purposes [2,13].

The recent Global Opioid Policy Initiative reports, released by a consortium led by Nathan Cherny and the European Society of Medicine Oncology for Europe [19], Africa [20], Asia [21], Middle East [22], Latin American and the Caribbean [23], and for India [24], outline the ongoing impact of regulations on low opioid access (Figure 2). Regulations are not the only reason; lack of medicine availability and lack of clinician education regarding pain management are also significant factors. The extent to which these regulations impact opioid availability have to be looked at a country by country basis. Examples include Georgia, where morphine was dispensed from a pharmacy in a police station; the Ukraine, where regulations only allowed injectable morphine and no more than 50 mg/day; and India, where federal laws have placed such severe penalties on mistakes in prescribing that despite being a major legal opium producer, very little morphine is used for 17% of the world's population. Of note, the Ukraine has recently approved oral morphine and in February 2014, the Indian Parliament approved amendments to the Indian National Drug and Psychotropic Substances Act.

So what does this mean to patients who are enduring cancer-related pain. Clearly in those countries with no opioids, over-regulation is impacting access to opioids. Even in high-income countries, many patients continue

to complain of inadequately treated cancer pain and lack of access to opioids. While efforts in the USA have worked to reduce the barriers to opioids for legitimate clinical purposes, illegal and illegitimate use and its associated problems have and may result in regulations that make it harder for cancer patients to access opioids for medical purposes. One example of this is the state of Kentucky; a reasonable legislative effort in 2012 to shut down illegal 'pill mills', required amendment in 2013 to remove many regulatory barriers to legitimate medical use that had been created by the original resolution [25]. While the CDC continues to draw attention to the many deaths associated with prescription drugs, including opioids, a better understanding and interpretation of the statistics behind this 'epidemic' are needed [26].

While opioids are not the only medication used for the treatment of cancer pain, they are an essential medicine in the armamentarium of those treating people living with a cancer diagnosis. The global community needs to ensure that regulations against these essential drugs are not a cause of increased suffering for cancer patients around the world.

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