

Reform of drug control policy for palliative care in Romania

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Unrelieved pain from cancer and HIV/AIDS is a substantial worldwide public-health problem. Inadequate pain relief is partly due to excessively strict national drug-control policies that constrain medical use of essential medicines such as morphine. Romania's drug-control policies are more than 35 years old and impose an antiquated regulatory system that is based on inpatient post-surgical management of acute pain that restricts prescription authority and makes access to opioid treatment difficult for outpatients with severe chronic pain due to cancer or HIV/AIDS. A Ministry of Health palliative-care commission used WHO guidelines to assess and recommend changes to Romania's national drug control law and regulations. The Romanian parliament has adopted a new law that will simplify prescribing requirements and allow modern pain management. Achievement of adequate pain relief is a vital part of worldwide health and will be dependent on reform of anti-drug regulations in many countries.

BACKGROUND

Cancer

According to WHO, there are about 22 million people with cancer in the world. Every year, around 10 million individuals are diagnosed with cancer and more than 6 million die from the disease. Tragically, these numbers are expected to double by 2020. More than 50% of new cases and deaths from cancer occur in developing countries.¹ In central and eastern Europe, cancer mortality continues to rise despite an overall fall in cancer mortality for the entire region since the early 1990s.² In Romania, with a population of 22 million, cancer is estimated to be the second leading cause of death.^{3,4} In 2002, it was estimated that there were over 41,000 deaths and almost 60,000 new cases of cancer in Romania.⁵ In men, lung, stomach, and colorectal cancers caused most deaths, whereas lung, colorectal, and prostate cancers accounted

for most new cases. In women, breast, cervical, and colorectal cancers accounted for most deaths and most new cases.⁵ In Romania, more than two-thirds of cancer patients are diagnosed at the late incurable stage of cancer.³

AIDS

According to a UNAIDS report, in 2005, AIDS resulted in the deaths of 3.1 million people and the total number of people living with HIV reached 40.3 million—the highest ever level. According to the report the epidemic is growing in eastern Europe and central Asia and the number of deaths from AIDS in eastern Europe (62,000) has almost doubled since 2003. Ukraine has the highest rate of HIV in adults (1.4%) in Europe and the Russian Federation, with an estimated 860,000 people living with HIV, has the largest AIDS epidemic in all of Europe.⁶ According to a UNAIDS/WHO publication,⁷ Romania might have the

highest number of HIV infections in the sub-region of central and south eastern Europe. The writers of the report estimated that, in 2003, the number of people with HIV in Romania was between 5500 and 14 000. Many of the infections happened in the late 1980s and early 1990s in Romanian children who contracted HIV through blood transfusions, unscreened blood products, and re-use of contaminated needles. More recently, there has been a steady rise in HIV infection in adults related to sexual activity and injection-drug use.^{6,7}

Pain and national health priorities

For people with cancer or AIDS, uncontrolled pain and other symptoms can be severe. Unrelieved pain has especially serious results for the quality of life of cancer patients when their disease is diagnosed at a late stage, as is most often the case in developing countries. WHO has decreed that adequate pain control is an essential component of cancer control and patient care; there is no other measure that can improve the quality of life of the population as much as palliative care.¹ A large proportion of cancer treatment resources—i.e., surgery, radiotherapy, and chemotherapy—should be dedicated to palliative care in both developed and developing countries.

WHO has also recognized the need to provide palliative care for patients with AIDS.^{8,9} Many workers have reported that patients with AIDS have severe pain, especially as the disease progresses, and have outlined options for treatment of pain in AIDS.¹⁰⁻¹² The Council of Europe has recognized that palliative care should be developed further in European countries, especially with respect to the present

disparity between availability and quality of care.^{13,14}

There are many non-drug treatments, such as radiotherapy, that can relieve pain. However, oral morphine and other opioid analgesics are the mainstay for relieving moderate to severe pain in both cancer and AIDS patients according to several organisations.^{15,16} Indeed, codeine and morphine have been classified as essential medicines by WHO.¹⁷ Essential medicines are those that satisfy the priority health-care needs of the population, and which should be available at all times in adequate amounts, in the appropriate doses, with assured quality and adequate information, and at a price the individual and community can afford.¹⁸ WHO views the consumption of opioids, including morphine, to be an indicator of a country's capability to relieve moderate to severe pain.¹⁹ The organization believes that opioid analgesics are absolutely necessary for pain relief and palliative care, and should be sufficiently available to meet all legitimate medical needs in a country.¹⁹

For more than 40 years, drug-control treaties and recommendations by UN organizations have established governments' responsibility to make opioids available for pain relief. The 1961 Single Convention on Narcotic Drugs states, "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."²⁰ Most governments are party to this convention and therefore are obligated to ensure the adequate availability of opioid

analgesics for the relief of pain and suffering.

Availability of drugs for pain

Unfortunately, patients who need pain relief seldom receive the treatment that WHO recommended in 1986, 20 years ago. Indeed, UN health and drug regulatory organizations have recognized that inadequate availability of opioid drugs is a serious impediment to the ability of many countries' health-care systems to relieve pain and suffering.²¹ Examples of obstacles include burdensome licensing requirements, punitive legal sanctions, complex prescription regulations, and limits on dose and prescription quantity.²¹

In 1989, the International Narcotics Control Board²² issued its first report in cooperation with WHO, stating that the medical need for opiates was not being fully satisfied, and urged governments to critically examine and revise the ways they assess domestic needs for opiates so that their future estimates would meet actual requirements. The report also advised that governments examine the extent to which their health-care systems and laws and regulations allowed the use of opiates for medical needs.

In 2005, the International Narcotics Control Board repeated its request that governments examine the extent to which their health-care systems, laws, and regulations allow the medical use of opioids; identify possible impediments; and develop action plans for long-term strategies for pain management—all with the aim of easing supply and availability of opioid analgesics for all appropriate indications.²³ The board pointed out that in

2003, only six countries together accounted for 79% of worldwide consumption of morphine, and that consumption in developing countries (with almost 80% of the world population) accounted for only 6%.²³ In view of this continuing disparity, the board requested that governments take steps to increase the medical use of opiates in their countries to meet their needs for the treatment of pain.²³ Also in 2005, the 58th World Health Assembly requested that the WHO Director General consider ways to fund palliative-care programmes in developing countries and to collaborate with the International Narcotics Control Board to improve availability of opioid analgesics.²⁴ Other authoritative governmental and scientific bodies, such as the Council of Europe¹³ and the US Institute of Medicine²⁵ continue to call for removal of regulations that impede patient access to pain drugs.

Assessment of national control policies

In 2000, WHO issued guidelines to help government and non-government organizations in any country to work together to assess national policies for opioids control, identify regulatory impediments, and take action to improve availability of opioid analgesics. The guidelines introduced the principle of balance, and defined that to mean that efforts to prevent illicit narcotics use and trafficking should not restrict the availability of opioid analgesics essential for pain relief.²⁶ These guidelines were endorsed by the International Narcotics Control Board,²⁷ and contain a 16-criteria framework for assessment of national policy and administration, including estimation of yearly requirements for opioids, reporting of consumption statistics, and

administration of an effective system for distribution of opioids to institutions that care for patients. A 16-item checklist guides the user through a simple yes or no assessment of a country's policies and to identify potential difficulties. A new user will need to become familiar with the entire 37-page document and national policies and their administration. The guidelines will help to identify policies in need of change, and will provide recommended policy language. The guidelines are available in 14 languages (Bulgarian, English, French, German, Italian, Lithuanian, Mongolian, Polish, Romanian, Russian, Serbian, Spanish, Turkish, and Ukrainian).²⁶ Additional languages, including Arabic, Chinese, and Portuguese, are forthcoming.

Palliative care and opioids in Europe

In Europe, the amount of opioid analgesics used for pain relief varies greatly between countries.^{28,29} In eastern Europe, there is great disparity between palliative-care services, ranging from nascent to advanced programmes with formal palliative care standards and government support.^{3,30-34} The more developed programmes might enable governments to meet expected increases in patients with cancer and AIDS predicted by WHO and UNAIDS.

Eastern Europe is especially at risk of inadequate availability of essential drugs needed by patients with cancer, AIDS, and other illnesses. The consumption of opioid analgesics per head in the ten highest-ranking countries in eastern Europe is less than 30% of that in western Europe,³⁵ and the growth in morphine consumption in western Europe has consistently exceeded that of the rest of Europe over the past 15 years. This persistent disparity, especially in

view of the increasing incidence of HIV/AIDS and cancer in eastern Europe should be addressed if European goals for palliative care are to be met.¹³ Figures 1 and 2 show European regional and worldwide consumption of morphine in 2003³⁶ for the countries that report annual consumption statistics to the International Narcotics Control Board, as required by the Single Convention on Narcotic Drugs, 1961.

Palliative care in Romania

In the late 1980s, efforts were made to develop palliative care services, which were initially directed to the plight of children, especially those with AIDS. The palliative-care movement gained momentum in the late 1990s, with the support of philanthropists from the UK. The first homecare based hospice in Romania, Hospice Casa Sperantei opened in Brasov in 1992 covering an area with a population of 400,000. A pediatric unit was added in 1996, and adult and pediatric inpatient facilities and a day centre were opened in 2002. The inpatient facility was the first independent hospice in Romania.³

In 1997, the Romanian Association for Palliative Care was created and a palliative care resource-training centre was opened in Brasov. The centre is well equipped to host educational conferences and group training in palliative care. In 2000, palliative care was recognized by the Ministry of Health as a medical subspecialty, and 146 doctors have taken courses and graduated in this discipline. In 2002, standards for palliative care were completed in a partnership project between the Romanian Association for Palliative Care and the National Hospice and Palliative Care Organization from the USA. At the end of 2004, Romania had ten

hospital-based inpatient services, nine hospice home-care teams, two day-care services, and the leading palliative care service in Brasov. This service in Brasov combines a palliative care resource-training centre with an inpatient hospice unit, day care centers, outpatient clinics, home-care teams both for children and adults, and an educational facility with the capacity to care for 450–500 patients at a time.

Most opioid analgesics are available in Romania, apart from buprenorphine. Injectable morphine, hydromorphone, pethidine, and methadone tablets are produced in the country. All others (including oral morphine and fentanyl patches) are imported.

Barriers to the use of opioid analgesics in Romania

Poor education and bias against opioids by health-care professionals is an underlying barrier to the use of opioid analgesics, including morphine in Romania. Morphine is not included in the drug list for emergencies in acute hospitals, and as a result, most hospitals do not have morphine available in their pharmacies. Usually pethidine is used instead, even for chronic pain. The outpatient use of opioids is restricted further by Romania's narcotics control policies, which are more than 35 years old, dating to the beginning of Nicolae Ceausescu's regime. They impose a complex, restrictive, and burdensome regulatory system for prescribing opioids, such that it is difficult and sometimes

impossible for outpatients to receive more than a few days' supply of this class of pain medication (panel 1). With this system, not even oncologists or hospice medical directors have independent prescribing authority, and cannot practice modern cancer pain management according to WHO guidelines, including titration and change of drug, dose, or route.

In February, 2002, the Pain and Policy Studies Group (University of Wisconsin Comprehensive Cancer Center/WHO Collaborating Center for Policy and Communications in Cancer Care), WHO European regional office, and the Open Society Institute sponsored a workshop on assuring availability of opioid analgesics for palliative care, in Budapest, Hungary.³⁷ At this workshop, invited stakeholders representing cancer, AIDS, palliative care, and government drug regulation from Bulgaria, Croatia, Hungary, Lithuania, Poland, and Romania made preliminary assessments of their national opioids control policies using WHO guidelines and they completed action plans to address regulatory barriers and patient access to drugs for pain. Subsequently, Romania was selected to be a pilot country for continued follow up work because; (1) regulatory barriers severely restricted access to pain relief, (2) palliative-care leaders were eager to address the problem; and (3) the Ministry of Health of Romania recognized the problem by appointing a palliative-care commission to make recommendations.

Panel 1: Barriers to outpatient access to opioid analgesics in Romania

Short-term prescribing

All physicians may issue prescriptions for maximum of 3-day supply; written on triplicate prescription form with dry stamp

Longer-term prescribing

Special authorization prescriptions are possible under the following restrictions:

- Only oncologists from outpatient departments of state hospitals may issue authorizations. There are one to two such oncologists in a district with a population of 300,000 to 600,000. The authorization is issued in four copies; one each for the pharmacy, the family doctor, the patient, and the oncologist
- In each district, only one to two pharmacies dispense opioid analgesics, and are usually located in the district's major city. These pharmacies must have special authorization from the Ministry of Health to store and dispense strong opioids
- Patient diagnosis limited to: incurable cancer, advanced arthritis at the gangrene stage, cardiopathy with severe dyspnoea
- The family doctor or hospice physician must issue a certificate confirming the patient has severe pain
- The patient's family must take the certificate to the outpatient department of the state hospital (sometimes traveling 100 km) to receive the authorization
- The oncologist decides the type and amount per day of opioid, and nominates a specific pharmacy to dispense
- The patient's family then takes the authorization back to the family doctor who issues the prescription with a dry stamp and a triplicate prescription for 10–15 days.
- The family doctor cannot make any changes to the type or amount of opioid, even if the patient's status changes
- The patient's family then takes the paperwork to the dispensing pharmacy to receive the drug
- If the specified opioid (type or strength) is not in stock in the pharmacy, the process needs to be repeated from the beginning
- The authorization is valid for 3 months. If a change is needed in the type of dose before this, the whole process must be repeated from the beginning
- The dry stamp prescriptions are numbered and can be obtained free of charge from the oncologist who is allowed to issue the opioid authorizations. The oncologist must track and give monthly reports to the local health board of the names of the family doctors who have received dry stamp prescriptions and how many they have received

Other barriers

- Historically, the maximum daily dose of morphine was 60 mg. Although this longstanding restriction has recently been removed, this limitation might have become an ingrained practice for many health-care professionals, and thus might need sustained education to overcome
- A patient can receive only one opioid via one route at a time, so a second drug cannot be prescribed for break-through pain in patients receiving slow-release opioids
- General lack of education on pain management and palliative care in undergraduate and postgraduate medical training
- Fears of the general population toward morphine

ROMANIAN MINISTRY OF HEALTH COMMISSION

In 2003, the Ministry of Health and its commission, the Commission of Specialists in Pain Therapy and Palliative Care, invited the Pain and Policy Studies Group to collaborate in preparation of recommendations for changing the regulatory policy in Romania. The Commission members were unanimous that opioid availability and the regulatory and administrative requirements were the main barriers to achieving pain relief. The first step was to study the Romanian narcotics-control policies and understand their implementation and effect on medical practice and patient care. The Pain and Policy Studies Group did a comprehensive analysis of the existing Romanian law and regulations, which guided the work of the Commission. A Romanian and Pain and Policy Studies Group working party reviewed the policies using the 2000 WHO guidelines and created a report with policy recommendations³⁸ that was consistent with medical and scientific knowledge and with international guidelines for opioids control policy. On July 16, 2003, the recommendations were personally presented to the Minister of Health by a Commission member and the Pain and Policy Studies Group. The report asked the Romanian government and Ministry of Health to address points in the 1969 law and 1970 regulations (panel 2).

New law and regulations for Romania

The Ministry of Health pharmaceutical department began drafting legislation to replace the national narcotics law on the basis of the recommendations of the Commission. The drafting process was intensive, with the Pain and Policy Studies

Group providing review and comment, close line-by-line reading, analysis of drafts and related documents, and several working meetings in Romania. In summer, 2005, the proposed law entered Romanian Parliament, and had passed both the Senate and Chamber of Deputies by Nov 1, 2005. After its publication in the government publication, the Official Monitor, the Ministry of Health has 6 months to complete the accompanying regulations.

To concentrate on drafting the new regulations that would implement the law when adopted, the Pain and Policy Studies Group sponsored a 1-week study visit to Madison, Wisconsin, USA, by a five-member team from Romania to begin drafting the new opioid prescribing regulations. The regulations are important, since they will provide detailed instructions for the conditions under which prescriptions for opioids can be issued for years to come. The team members, each with various credentials, represented the fields of general medicine, oncology, pharmacy, pharmacology, and law, with specializations in pain management and palliative care. They drafted the sections of the new regulations that are particularly relevant to prescribing opioid analgesics, with comments from the Pain and Policy Studies Group. According to the draft law and regulations, special authorization is no longer necessary for opioids to be prescribed for outpatients. Specialists will have independent prescribing authority, the proposed prescription amount is for 30 days with no limit to dose, patient eligibility based on diagnosis has been removed, and non-specialists will be able to prescribe opioid analgesics after receiving certified training. In March 2006, meetings will be

held in Bucharest to plan for the finalization and dissemination of the new regulations, and the design and implementation of certified training aimed at health-care professionals, regulators, police, and the public.

DISCUSSION

Romania might be the first country with a government-sponsored effort to undertake a fundamental guideline-based, comprehensive assessment of drug-control policy to address regulatory barriers and improve access to opioids for pain and palliative care. However, other governments have made incremental changes. In 2001, the Italian Ministry of Health recommended changes that resulted in a new law that simplified opioid prescribing requirements, replacing a complex triplicate prescription form with a simple form that is similar to a standard prescription form, increasing the amount that can be prescribed on one prescription form from an 8-day supply to a 1-month supply, and prescribing two drugs or dose units on the same prescription.³⁹ In 1992, France increased the number of days that oral morphine could be prescribed from 7 to 14 days,⁴⁰ and then to 28 days in 1995.⁴¹ Germany has raised the allowed prescription amount several times.^{42,43}

Improving national drug-control policy requires activities on many different levels, and can be complex and time consuming. The Romania project required the Pain and Policy Studies Group to learn about the country and its government and culture, the status of palliative care, and the key figures. Much attention was paid to establishing communications, working relationships, and trust. The Pain and Policy Studies

Panel 2: Aspects of opioid prescription that the Romanian Commission and Pain and Policy Studies Group have asked the Romanian government and Ministry of Health to address

Government to:

- Add key language from the 1961 UN Single Convention on Narcotic Drugs that affirms the need for opioid analgesics to treat pain and suffering
- Remove several provisions, including outdated definitions, restrictive maximum doses, dose unit limitations, and the lengthy and burdensome authorization process for long-term prescribing
- Allow more than one opioid analgesic to be prescribed on one prescription form
- Allow the physician to change the drug and dose according to patient need.

Ministry of Health to:

- Clarify which opioid analgesics are licensed to be imported and manufactured in the country
- Clarify the record-keeping requirements for opioid analgesic prescriptions
- Clarify which office is responsible for submitting statistics and reports to the International Narcotics Control Board
- Clarify the method used to estimate the amounts of opioids that will be needed in the coming year
- Work with the House of Insurance to ensure that opioid analgesics are fully reimbursed
- Review the National Cancer Control Programme to make sure that pain relief and palliative care are a high priority
- Consider establishing a national AIDS programme that makes pain relief and palliative care a high priority
- Include present legal requirements in the curriculum for the certified training programme
- Work with the Ministry of Education to ensure that pain treatment is included in medical, pharmacy, and nursing textbooks.

Group and commission surveyed the national regulatory environment in meetings and focus groups, and studied the drug-distribution system and identified weaknesses that might inhibit patient access to opioid analgesics. Educational and policy materials (including producing translations when necessary) were adapted for presentations; the team traveled, sometimes on short notice, when opportunities emerged that needed face-to-

face interaction. Additionally, the Pain and Policy Studies Group created and maintained a dedicated portion of our website to Europe, specifically eastern Europe.⁴⁴ This website contains opioid-consumption statistics by country, has links to WHO guidelines in every available language, includes Pain and Policy Studies Group news relating to eastern Europe, and contains several Pain and Policy Studies Group monographs with supplemental information. The page dedicated to Romania has additional documents relevant to the continuing project, including the formal recommendations from the Ministry of Health commission to the Minister of Health.³⁸

Many national drug laws date back to when opioids were mainly used for short-term pain control in hospitals after surgery, before the emergence of chronic diseases and symptoms that need long-term outpatient drug therapy. Further, national narcotics laws and their administration are often focused mainly on fighting drug trafficking and misuse. The International Narcotics Control Board has recommended that national narcotics laws ensure adequate availability of controlled drugs for medical and scientific purposes. To do this, governments will need additional guidance that includes model policies and procedures they can use to achieve more balanced national narcotics control policies that address trafficking and misuse as well as the medical needs of patients with pain.

This project added to our knowledge about achieving a more balanced drug-control policy. We think the progress in Romania is due to several factors. First, Romania has developed a strong foundation in palliative

care so that unmet patient needs for pain medicines are apparent. Second, there is strong leadership from experts in palliative care and related specialties who represented patient needs to the government. Third, the government was willing to consider changing national policy and they appointed commissions and designated staff. Fourth, external guidance and skills from WHO helped provide a strong public health and regulatory framework. Fifth, the use of international criteria-based guidelines helped with assessment of national policy. Last, grant resources enabled dialogue between the partners, study of the issues and the regulatory environment, and drafting of new policy.

The ultimate goal of the Ministry of Health Commission when revising the national opioids control policy was to improve patient access to opioids and pain relief. However, there are many intervening variables in the health-care infrastructure between policy change and improved pain treatment. Policy change is necessary, but not usually sufficient to improve patient care. However, if infrastructure issues are addressed, such as education, training, and reimbursement, then patient care is more likely to improve. One outcome indicator used by WHO to track the effect of a policy intervention is national consumption of strong opioid analgesics in the year before and the year after the policy change, including total yearly consumption in kg, g, and mg per head, in relation to worldwide and regional means. Additionally, individual institutions could track the effect on patient care by examining statistics about the total amount of strong opioids dispensed and prescribed per patient.

The International Narcotics Control Board reported, "In 2004, as in recent years, no cases involving the diversion of narcotic drugs from licit international trade into illicit channels were detected, despite the very large quantities of drugs and the large number of transactions involved."²³ However, in the event of misuse or diversion of opioid analgesics, we recommend that pain and palliative-care experts engage immediately with governments and the media if necessary to emphasize that the response to diversion should be guided by the principle of balance, which states unequivocally that the source of misuse should be swiftly identified and addressed, without alteration of legitimate medical practice and patient care. Although diversion and misuse might occur, we should remember that opioid analgesics are essential to restoring quality of life to people with severe pain, and therefore must remain available.

As the AIDS epidemic continues its scourge, as behaviors such as smoking increase the frequency of cancers, and as the worldwide population ages, delivering good pain management will become increasingly vital to public health. Governments should heed the call of UN regulatory and scientific organizations to integrate pain management and palliative care into their health systems and address regulatory barriers to availability of essential pain medicines. Because efforts to improve opioid availability often mean a country's national policy for control of narcotics has to be

changed, health-care practitioners must be prepared to collaborate with drug regulators.

Romania's regulatory scheme has been in effect for over 35 years; generations of health professionals have been trained in this restrictive regulatory environment. We hope that the Romania project will serve as a positive example of how an outdated and restrictive national antinarcotics law can be reformed into one that embodies the essential principle of balance, retaining essential control over the security and distribution of controlled drugs, while allowing physicians to practice modern pain medicine and care for their patients.

As Romania and other countries prepare for accession to the European Union, updating national narcotics laws in countries with low opioid consumption could make a major contribution to health care by allowing medical practices that are regarded as mainstream in other European nations. Continued leadership with national governments from WHO and the International Narcotics Control Board will be necessary if we are to make a difference in pain and suffering for people with cancer or HIV/AIDS. For the sake of future generations of patients with pain, we invite wide discussion of Romania's efforts to improve the regulatory environment for pain management.

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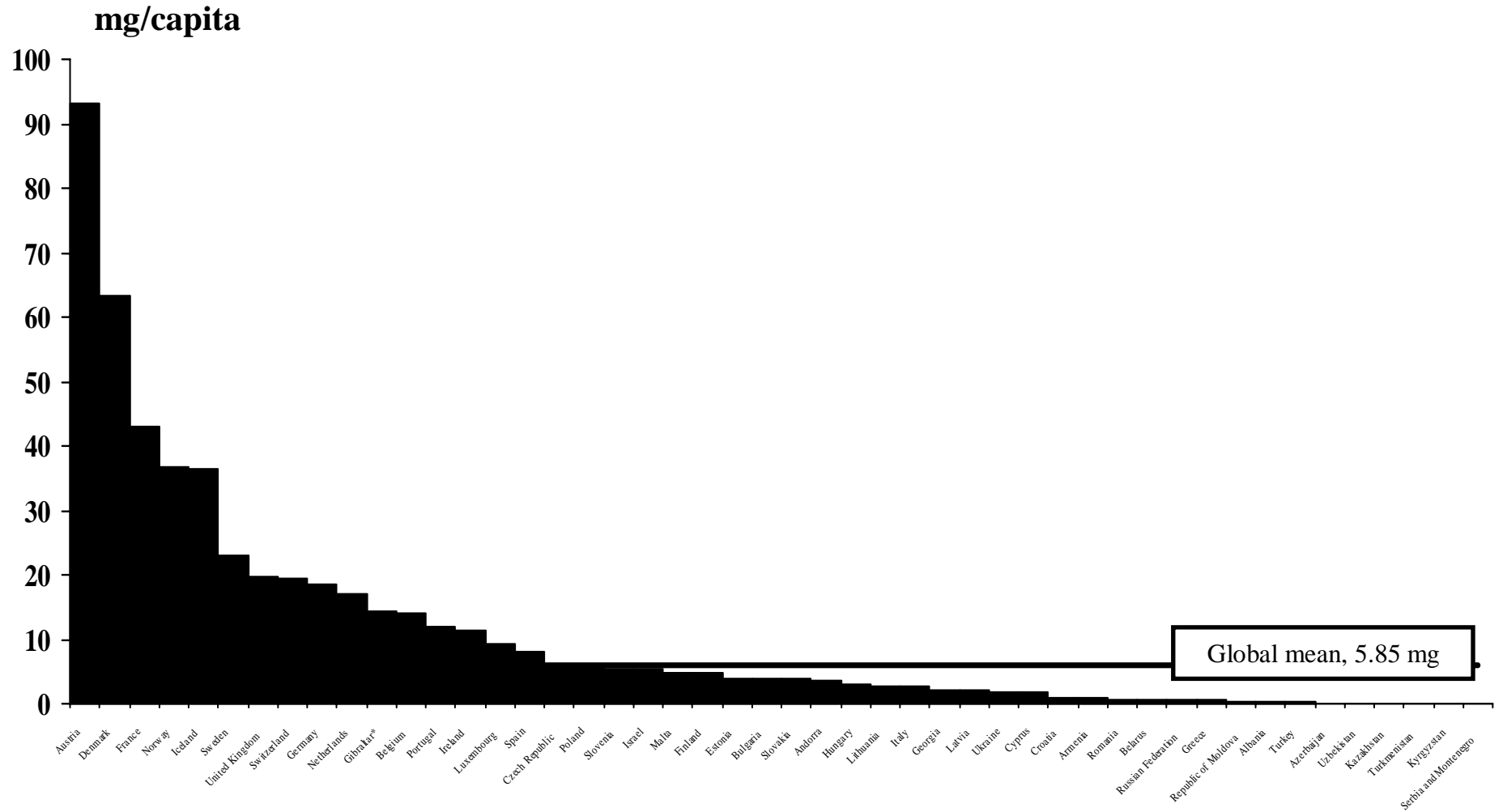
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Figure 1

Consumption of Morphine in Europe mg/capita, 2003

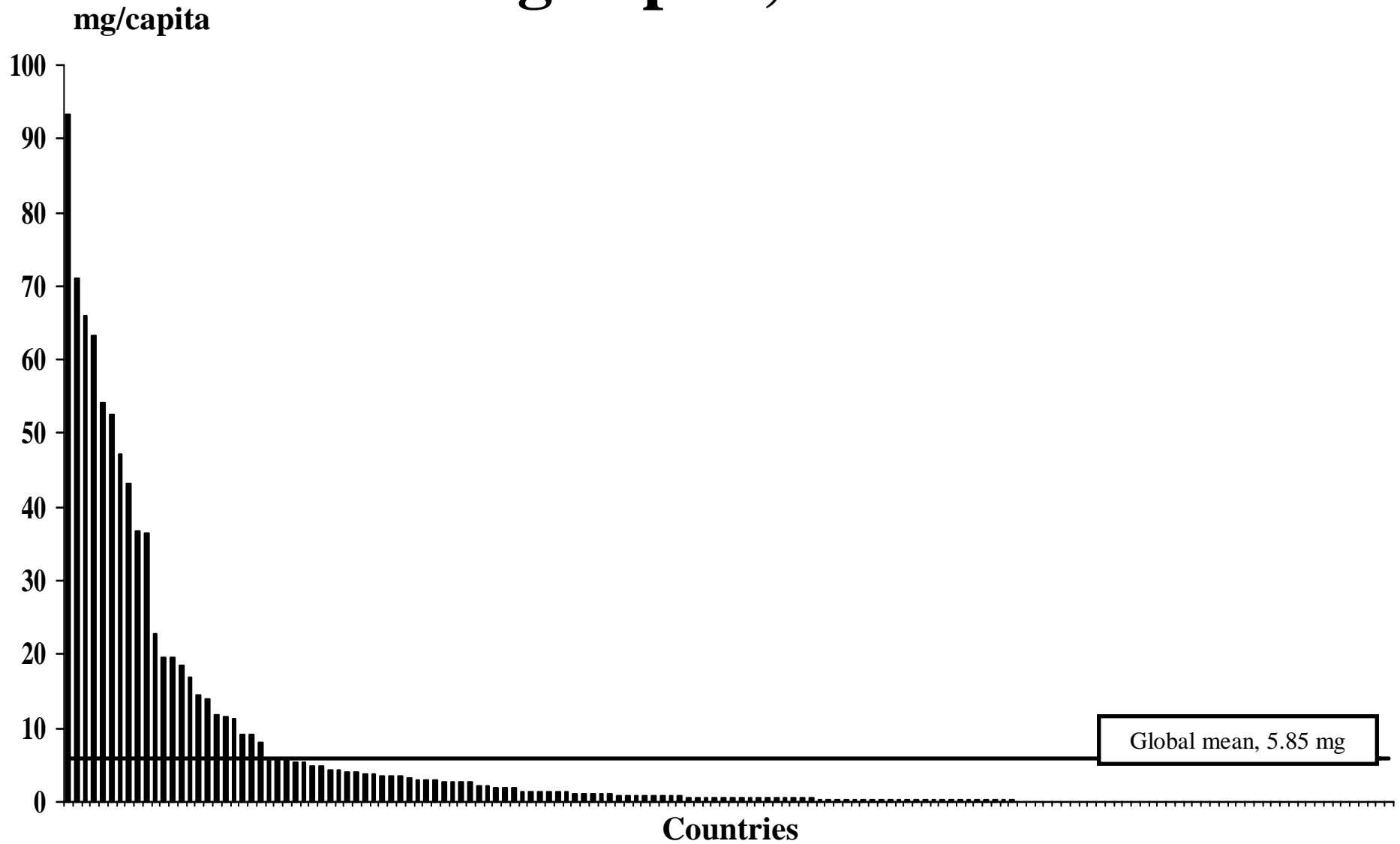


Source: International Narcotics Control Board; United Nations "Demographic Yearbook
By: Pain & Policy Studies Group, University of Wisconsin/WHO Collaborating Center, 2005

The global mean is calculated by adding the individual mg/capita statistics for all countries and then dividing by the number of countries

Figure 2

Global Consumption of Morphine mg/capita, 2003



Source: International Narcotics Control Board; United Nations "Demographic Yearbook
By: Pain & Policy Studies Group, University of Wisconsin/WHO Collaborating Center, 2005

The global mean is calculated by adding the individual mg/capita statistics for all countries and then dividing by the number of countries