



Toward a More Complete Indicator of Opioid Consumption Trends

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Background: Pain management is a critical component of palliative care. The World Health Organization (WHO) has recommended that low- and middle-income countries devote major resources to palliative care since most of their citizens are diagnosed with cancer at the late stage when pain is prevalent and severe.^{1,2} Recently, the United Nations Economic and Social Council,³ the World Health Assembly,⁴ and the WHO⁵ have called on national governments to improve the treatment of pain, especially in developing countries; to ensure the medical availability of opioid analgesics; and to recognize that providing palliative care is an urgent and humanitarian responsibility. Likewise, the International Narcotics Control Board (INCB), the independent and quasi-judicial United Nations body that implements the international drug control conventions, has consistently recognized the importance of narcotic drugs for medical purposes.⁶

The WHO has considered a country's annual consumption of morphine to be an indicator of the extent that opioids are used to treat severe cancer pain and as an index to evaluate improvements in pain management.⁷ The WHO and the INCB have long recognized that pain is inadequately treated globally, as reflected by the low consumption of morphine in most countries, and by the great disparity in morphine consumption between countries.^{8,9} However, other opioid analgesic medications and formulations have emerged in global markets over the past 20 years. This raises questions about the role of morphine and other opioids as measures of a country's ability to provide pain relief.

Project aim: The Pain & Policy Studies Group/WHO Collaborating Center for Policy and Communications in Cancer Care (PPSG/WHOCC) has explored the development of:

- (1) a morphine equivalence (ME) statistic for each principal opioid used to treat severe pain, which allows for a comparison of the consumption of morphine to the equianalgesic consumption of other medications; and
- (2) a **Total ME** statistic that represents in one metric the aggregate consumption of these principal opioid analgesics used for severe pain.

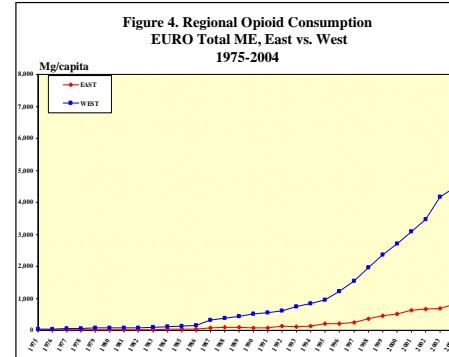
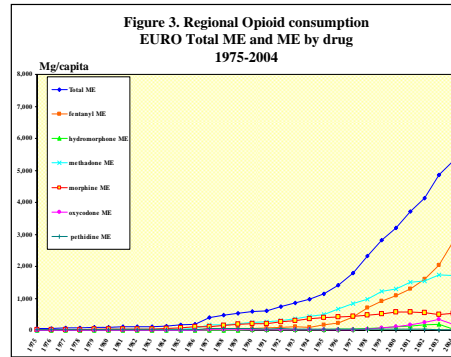
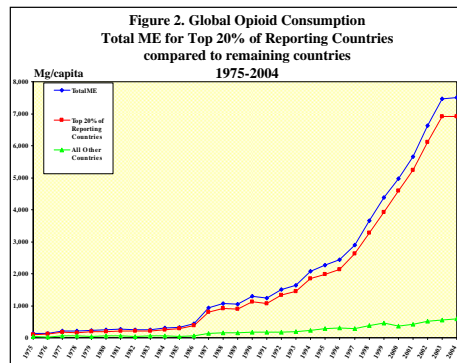
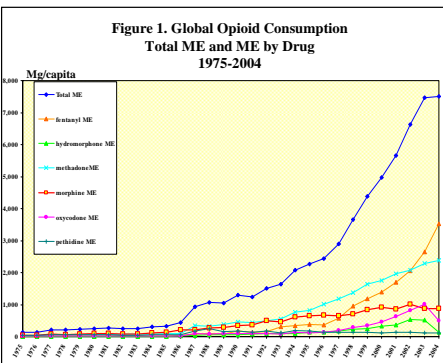
Methods: We selected the following study drugs to calculate the Total ME because they are the opioids that are indicated for severe pain:

- fentanyl
- hydromorphone
- methadone
- morphine
- oxycodone
- pethidine

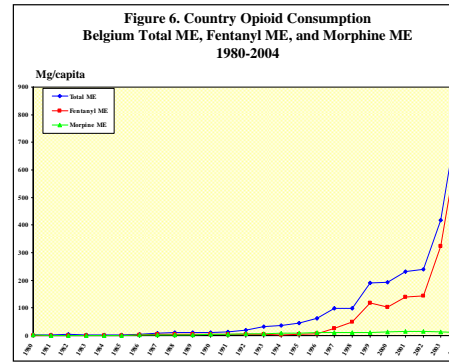
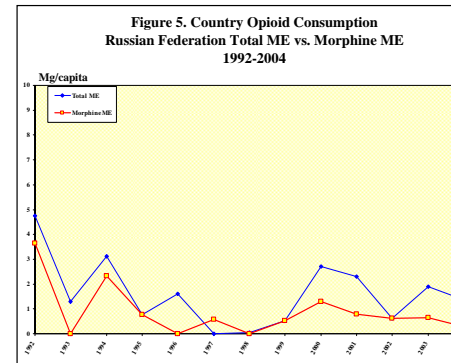
The PPSG/WHOCC receives annual opioid consumption statistics reported to the INCB by national governments. In order to calculate both the ME by drug and Total ME from these statistics, we applied conversion formulas created by the WHO Collaborating Centre for Drug Statistics Methodology in Oslo, Norway.¹⁰

Results: The 30-year trend displayed in **Figure 1** demonstrates that global opioid consumption measured in Total ME was much greater than morphine alone, especially after the mid-1980s. In recent years, fentanyl, methadone, oxycodone, and hydromorphone, respectively, had the greatest impact on the Total ME statistic.

Figure 2 demonstrates that the global increase in Total ME is not spread evenly throughout reporting countries. Rather, the increase is clustered within those countries that report high consumption and are typically high-income countries. For instance, in 2004, the top 20% of reporting countries accounted for 88% of Total global ME, and 88% of these countries (29 of 34) were high-income countries.



Figures 5 and 6 illustrate the disparate roles of morphine consumption as a proportion of Total ME in two EURO countries; the Russian Federation and Belgium. In the Russian Federation (**Figure 5**), morphine has been a relatively accurate and stable indicator of the low level of opioid medications used to treat pain. However, in Belgium (**Figure 6**), morphine has consistently been a very small part of an increasing trend in Total ME consumption while fentanyl has been a more accurate indicator of this increasing trend. There are surely social, cultural, economic, historic, and others reasons that account for such differences.



Limitations: There are inherent limitations to the data that must be considered when interpreting the results. The ME consumption data do not distinguish between different clinical uses. This is relevant for opioids that have clinical indications in addition to analgesia, such as fentanyl (as an anesthetic) and methadone (as a treatment for addiction). Inclusion of uncorrected ME consumption data for these drugs will overstate their influence on the Total ME statistic. Future efforts will be made to quantify the proportion of the ME consumption amount that is used for indications other than analgesia, to create a "corrected" consumption amount for fentanyl and methadone.

Discussion: Prior to 1986, the consumption of morphine alone was a reasonable measure of Total ME. Starting with the WHO's call in the mid 1990s for more attention to relieving cancer pain, and then the emergence in the mid 1990s of new drugs and formulations to treat pain, consumption of morphine alone as an indicator of pain treatment has become less valid, especially in some countries. While global Total ME consumption has increased substantially in the past decades, there is a continuing disparity between low- and high-income countries, both globally and in the EURO region.

A positive trend of these data is the long-term decline in pethidine consumption, both globally and within the EURO region. This is a welcome development in light of the potential toxicity of long-term use of pethidine.

Additional studies using the ME statistic are needed to further examine the role of opioid consumption as an indicator of treating pain over the past 20 years. What other events in the pain management/palliative care field may have influenced the changes in the consumption of strong opioids? What are the countries for which morphine consumption alone was the most and least accurate, and what might this signify? What are the strong opioids that account for most of the global and regional increase in consumption? The ME statistic may be a useful tool to examine these types of questions at the global, regional, and country levels.

Finally, this pilot study identified an important contribution for fentanyl and methadone in the Total ME increase over time. Future studies should correct for these medications' other clinical indications to focus solely on their use for pain relief, especially methadone's use for addiction treatment. This procedure will ultimately provide a much more precise measure of national opioid consumption for pain treatment.

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