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# Journal Pre-proof

## Availability of Internationally Controlled Essential Medicines in the COVID-19 Pandemic

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Availability of Internationally Controlled Essential Medicines in the COVID-19 Pandemic

**JPSM Fast Track Submission**

**Title:** Availability of Internationally Controlled Essential Medicines in the COVID-19 Pandemic

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**Abstract**

Section 2 of the 2019 World Health Organization (WHO) Model List of Essential Medicines includes opioid analgesics formulations commonly used for the control of pain and respiratory distress, as well as sedative and anxiolytic substances such as midazolam and diazepam. These medicines, essential to palliative care, are regulated under the international drug control conventions overseen by United Nations (UN) specialized agencies and treaty bodies and under national drug control laws. Those national laws and regulations directly affect bedside availability of Internationally Controlled Essential Medicines (ICEMs). The complex interaction between national regulatory systems and global supply chains (now impacted by COVID-19 pandemic) directly affects bedside availability of ICEMs and patient care. Despite decades of global civil society advocacy in the UN system, ICEMs have remained chronically unavailable, inaccessible and unaffordable in Lower-and-Middle Income Countries, and there are recent reports of shortages in High Income Countries as well. The most prevalent symptoms in COVID-19 are breathlessness, cough, drowsiness, anxiety, agitation and delirium. Frequently used medicines include opioids such as morphine or fentanyl and midazolam, all of them listed as ICEMs.

This paper describes the issues related to the lack of availability and limited access to ICEMs during the COVID-19 pandemic in both intensive and palliative care patients in countries of all income levels and makes recommendations for improving access.

**Key Message**

Global shortages and stockouts of internationally controlled essential medicines for palliative and critical care in the context of the COVID-19 pandemic call for coordinated strategic interventions to improve access and relieve preventable suffering.

**Key Words**

Essential medicines, palliative care, morphine, COVID-19, breathlessness

## Introduction

Section Two of the 2019 World Health Organization (WHO) Model List of Essential Medicines includes opioid analgesics formulations commonly used for the control of pain and respiratory distress, as well as sedative and anxiolytic substances such as midazolam and diazepam (1). As these essential palliative care medicines are regulated under the international drug control conventions overseen by United Nations (UN) specialized agencies and treaty bodies (2) and under national drug control laws, we refer to them as Internationally Controlled Essential Medicines (ICEMs).

The complex interaction between regulatory systems and global supply chains, as well as limited training, affect availability of ICEMs and patient care. The Lancet Commission on Pain and Palliative Care reported that of the total number of tons of morphine-equivalent opioids distributed in the world per year, only 0.1 metric tons is distributed to low-income countries (LICs), reflecting a huge abyss in access to relief and resulting in massive, avoidable suffering (3). While several authors, multilateral agencies and academia have used other different methods to estimate the actual need vs the reported consumption, these all demonstrate similar inequities in availability and access (4, 5). All these methods have been used for statistical purposes only and not as measures of therapeutic appropriateness.

Despite decades of global civil society advocacy in the UN system, ICEMs have remained chronically unavailable, inaccessible and unaffordable in Low-and-Middle Income Countries (LMICs). This in spite of the fact that the WHO and other UN treaty bodies recognize palliative care and pain relief as elements of the right to health (6). Shortages in High Income Countries have recently been reported as well, due to the increase in demand as a result of the COVID-19 pandemic (7).

The authors, along with representative of other palliative care organizations and academia, have long advocated for the principle of “balance,” which represents the 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 their non-medical use, diversion and trafficking, two primary goals of the international control system. (8)

This paper describes the issues related to the lack of availability and limited access to ICEMs in during the COVID-19 pandemic in both intensive and palliative care patients in countries of all income levels and makes recommendations for improving access.

### **Systems level availability issues**

Palliative care providers in LMICs facing the pandemic with already low stocks and fragile importation, production and supply chains, as well as unduly restrictive regulations controlling access, have contacted the authors with concerns about projected increases in demand for morphine and other ICEMs (Z. Ali, personal communication, April 15, 2020; S.Rana, personal communication, April 24, 2020).

The International Narcotics Control Board (INCB) is the UN Organization charged with monitoring the implementation of the drug control conventions, including global trade in ICEMs. For several years, even before the COVID-19 pandemic, the INCB has reported that the availability of these medicines is low to inadequate, (9) and in response to the pandemic, recently published a press release calling on governments to take the necessary steps to ensure continued access to controlled medicines for pain relief and palliative care and for mental health and neurological conditions by fast tracking shipments of controlled medicines to health systems and supporting appropriate training of healthcare providers (10).

The European Union (EU) Executive Steering Group on Shortages of Medicines Caused by Major Events, which provides strategic leadership for urgent and coordinated action on shortages within the EU in this pandemic, has set up with the pharmaceutical industry a system to fast-track interaction on shortages between industry and the EU Executive Steering Group (11).

### **Provider level availability issues**

The most prevalent symptoms in COVID-19 are breathlessness, cough, drowsiness, anxiety, agitation and delirium. Frequently used medicines to treat some of these symptoms include opioids such as morphine, fentanyl and midazolam. Recent reported data indicate that the median-maximum dose/24h for patients with confirmed COVID-19 referred to hospital palliative care are morphine, 10-30mg; fentanyl, 100-200mcg; alfentanil 500-1000 mcg and for midazolam, 10-20mg. (12) Symptom control for rising cohorts of COVID-19 and other palliative

care patients in countries with low or no access to ICEMs will be seriously compromised. Major hospitals in the US and nine university hospitals in Europe have recently reported dangerous shortages of ICEMs and have requested governments to increase procurement. (13, 14) Several US medical associations sent an urgent letter to the Drug Enforcement Administration (DEA) reporting that the increase in the number of patients requiring ventilation has resulted in an increase in the demand for several opioids, some of which were already in shortage prior to the COVID-19 outbreak. (15) They request that supply be rapidly increased to ensure that hospitals can access the medications they need to treat COVID-19 patients. In addition, public health experts and physicians recently asked the governors of US states that still practice the death penalty to release their stockpiled drugs in order to prioritize the needs and lives of patients (14). And in the UK, the National Health Service is reportedly working to increase stocks while at the same time facing many challenges. (17)

## Recommendations

1. As palliative care practitioners and global advocates with experience and knowledge about countries with low and inadequate access to ICEMs, we urge representatives of palliative care associations in all countries currently coping with, or preparing for this or for future pandemics, to contact their health ministries and national Competent Authorities to ensure that they are aware of the INCB recommendations mentioned in its press release cited above. These include ensuring the maintenance of sufficient buffer stocks and using simplified control procedures for the export, transportation and provision of ICEMs. .
2. We urge palliative care associations to consider recommending their national competent authorities to utilize pooled procurement mechanisms such as the Pan American Health Organization Strategic Fund, the Pharmaceutical Procurement Service in the Organization of Eastern Caribbean States, the Gulf Corporation Council, and UNICEF and to resupply and build buffer stocks, as the markets will take advantage of increased demand to raise prices.

3. The Lancet Commission on Pain and Palliative Care developed and costed an Essential Package that is the minimum a health system, however resource-constrained, should make universally accessible. The Essential Package includes medications for safe and effective palliative care and pain relief for both adults and children largely based on the WHO Model List. Its medicines and equipment, including morphine and diazepam, can all be safely prescribed or administered in a primary care setting where health professionals have received basic training in palliative care.
4. As many frontline health workers will be unfamiliar with the use of opioids and benzodiazepines in the context of the pandemic, we recommend accelerated clinician training, including online, for COVID-19 related symptom control. Training specialist nurses to prescribe and deliver opioids to palliative care patients in all home care settings (as in Uganda and Rwanda) aligns with WHO calls to invest in nurses in this International Year of the Nurse and Midwife.

## Conclusion

The Human Rights Council, the World Health Assembly, and some regional treaty bodies recognize palliative care and pain relief as elements of the right to health. (11) Governments have a minimum core obligation to protect this right with immediate effect, even in the face of a disastrous humanitarian emergency such as the COVID-19 pandemic. Global health experts describe lack of access to essential palliative care medicines as a critical public health issues, and opioids, in particular morphine, as essential for the relief of severe health-related suffering. The additional COVID-19 burden of health-related suffering only underscores the government obligation to take a balanced approach to the regulation of internationally controlled substances, and to make strategic interventions, in partnership with clinical associations, to ensure the availability, accessibility, and affordability of essential medicines for primary, intensive, and palliative care.

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