



Innovation and Policy in Cancer Pain Management: Systemic Interactions in Tanzania

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INTRODUCTION

There is a well-documented, and devastating, gap between the need for palliation of severe physical pain, from cancer and other conditions such as sickle cell disease, and the availability of medication, in particular morphine and other opioids to treat such pain in African countries

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(Knaul et al., 2018). Interviews in Tanzania in 2019 with cancer patients and health professionals, and a workshop discussing early results of the research with local stakeholders, identified the undertreatment of pain as a major concern in the provision of cancer care in Tanzania. Opioid medication was identified as the key medication for the treatment of severe pain. Shortages were recorded of opioid medication when needed, just as in India (Chapter 11). However, in contrast to India, a lack of local production has led to complete reliance on imports of morphine and other opioids.

Subsequent discussions with policymakers and manufacturers seeking to explain the morphine shortage further made visible the complex multiple interacting health system and industrial supply factors currently contributing to the undertreatment of severe pain in Tanzania. These factors included pricing, accessibility challenges, supply chains difficulties, clinicians' perceptions of opioid medication, and skills and training challenges facing health professionals, regulators and policymakers. Globally, "pain is experienced by 55% of patients undergoing anti-cancer treatment and by 66% of patients who have advanced, metastatic, or terminal disease" (WHO, 2018d, p. 9). One objective of palliative care is to help reduce suffering by preventing or relieving pain. In the case of cancer patients, this could be pain relief or pain management for survivors and also for terminal cancer patients.

Pain management for cancer patients is one of the foremost targets in the treatment process (WHO, 2018d). In a majority of cancer cases, severe pain relief and management can be achieved by inexpensive oral morphine or other opioids (Chapter 11). However, the Tanzanian evidence presented in this chapter shows a widespread lack of access to oral morphine. The associated barriers explored here are mirrored in many low- and middle-income countries (LMICs), including reported gaps in policies and regulatory frameworks, weaknesses in the health systems,

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deficiencies in palliative care, and inadequate pain management services (WHO, 2020).

This chapter and the next pick up from the central argument of Chapter 11: that improving access to effective pain medication requires tackling institutional gaps between clinical, regulatory and industrial domains. This chapter presents a Tanzanian case study of the systemic nature of the gap between need and availability of medication for severe pain, and the serious effects of that gap for late-stage cancer patients. It documents the extent of the gap between need and availability of medication for severe pain and creates one illustrative estimate of the size of the gap. The chapter also explores the potential for local manufacturing of morphine as a possible contributor to closing the identified gaps.

The chapter then sets out to identify why some of the policy efforts to date have had limited impact on the undertreatment of pain with morphine. It does so by tracing critical causal feedback relationships between procurement, prescription, palliative care, import licensing and industrial manufacturing. Analysis of these cross-sectoral relationships with causal loop diagrams (Wolstenholme, 2003), in collaboration with local stakeholders, revealed a fundamental pinch point of two opposing interactions between the processes that should drive increased demand for palliation medicine and the processes sustaining a high inertia, low level of accessibility of morphine.

This need-demand gap model was then used as a focal point for discussion with key industrial, health, regulatory and clinical stakeholders in Tanzania, both to validate the framework that identified the systemic challenges, as well as identify gaps in understanding of local palliation practices. This chapter uses evidence from secondary data, interviews and stakeholder discussions to identify ways forward, including a discussion of the local manufacturing of morphine as one potential contribution to closing the need-demand gap and tackling the deficits in cancer pain management.

FRAMING THE UNDERTREATMENT OF PAIN IN CANCER CARE

Chapter 1 briefly documented Africa's "cancer explosion" and noted the "abyss" of pain management failure this has brought with it (Knaul et al., 2018). The barriers to cancer pain management are diverse world-wide, ranging from patients' acceptance and endurance of pain and patients'

knowledge, to the neglect of pain management by health care providers and negative attitudes towards the effectiveness of analgesics, which include fear of addiction (Orujlu et al., 2022). A Kenyan study of barriers to cancer pain management among oncology nurses revealed a high level of undertreatment of severe pain. Up to 80% of cancer patients in Kenya were reported to suffer from untreated moderate to severe pain, with barriers resulting from factors such as lack of access to medication, restrictions resulting from dispensing guidelines, and fears related to opioid addiction (Onsongo, 2020).

Morphine and other opioids remain the mainstay for severe pain management world-wide. However, unavailability of morphine continues to pose major challenges to patients, especially in LMICs (Sung et al., 2021; WHO, 2020) (see also Chapter 11). Even in cases where morphine is available, access to these essential drugs often confronts significant barriers to cancer pain treatment and management in Africa. Many countries in Sub-Saharan Africa (SSA) are unable to address the enormous unmet need for cancer pain treatment, with evidence indicating that the situation has not been improving over the years. Access to pharmaceutical opioids in LMICs remains “a tiny fraction of the availability in high-income countries” (HRW, 2011; UNODC, 2021).

It is estimated that about 57% of all new cancer cases, globally, occur in LMICs, with the situation exacerbated by a lack of awareness, less attention to preventive strategies, and improvements in quality of life that are reflected in increased life expectancies. With respect to SSA, despite the mounting evidence on the rising incidence and mortality rates resulting from cancer, the disease has so far not received the desired level of attention in both research fields and health care services (Hamdi et al., 2021) as well as in policy and government circles, sometimes due to gaps in evidence to inform appropriate policies and policymaking (Nonvignon, 2021). Cancer pain management—prevention and alleviation of suffering and pain resulting from cancer—in SSA requires early identification and careful assessment of pain and other problems that manifest themselves in physical, psycho-social and spiritual forms (van der Plas et al., 2020) (see also Chapter 3).

In East Africa, there is increasing awareness of the huge need for better palliative care among many stakeholder groups including citizens, government ministries, healthcare leaders, and politicians (Fraser et al., 2018; Hartwig et al., 2014; Kamonyo, 2018). This is vital because as Kamonyo (2018) argues, access to pain relief medicines, a central part of palliative

care, remains “a dream in most African countries” (p. 1). Greater awareness will help improve understanding of challenges related to establishing a robust palliative care agenda in countries within the region and support progress in cancer pain management. Although progress has been slow in the policy environment, within the region Kenya and Uganda are particularly recognised to have made progress in making palliative care and pain relief more accessible to their citizens (Kamonyo, 2018). The Ugandan case is discussed further below.

This chapter draws on interviews, workshops and focus groups in Tanzania in 2019 with cancer patients, health professionals, and many other stakeholders in cancer care (see Chapter 1). Early results from the research and engagement with stakeholders in Tanzania identified the undertreatment of pain as a major concern within cancer care. Although the interviews identified opioid medication as a key resource for the treatment of severe pain, the lack of local production of opioid medications implies reliance on imports. The evidence also made visible the complexity of interacting health system and industrial supply factors that could hinder or contribute to more effective pain management. These factors included the price of morphine, challenges related to access to cancer care, supply chains and regulatory difficulties, perceptions of opioid medication, and capability challenges related to the skills and training gaps facing health professionals and policymakers.

In this chapter we frame cancer pain management as a policy topic specifically in need of evidence-based contributions that can identify key innovations and institutional changes that can be considered by policymakers. Chapter 13 then builds on some of the evidence and ideas in this chapter and uses them to show how scenario building can be used as a policy tool to map critical interactions—both those that contribute to generating undertreatment and those that arise from innovations—and to identify areas where further information is required to complete the scenarios in a form that can be used by policymakers.

Specific to this chapter, we focus on the dimensions and scale of the undertreatment problem in Tanzania. In doing so, we demonstrate the importance of diagnosis of the underlying need-demand gap in line with the dimensions of cancer care and pain management. Pain management is a cross-sectoral, multi-level challenge, cutting across industrial, health care, societal and policy systems. We build on and develop the WHO domains for palliative care development. The WHO identifies three domains—health policy (also described as ‘integration into national health

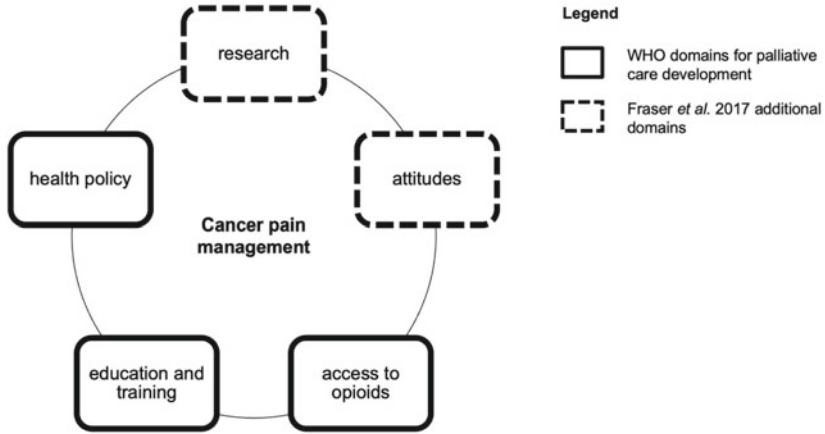


Fig. 12.1 Dimensions of cancer care and pain management (*Source* Authors)

systems’), education and training (of healthcare workers), and drug availability (often described with specific reference to opioids)—as critical to the development of palliative care (HRW, 2011, p. 1). Fraser et al. (2018) have expanded on these three domains to include cultural aspects (public and professional ‘attitudes’) and knowledge (‘research’). Combined, these domains help to demonstrate that palliative care more broadly, like cancer pain management, is multi-dimensional, and requires coordination of actions across policy, industry, community, hospital management and other critical service sectors (Fig. 12.1).

UNDERTREATMENT OF CANCER PAIN IN TANZANIA

The evidence on the undertreatment of cancer pain in Tanzania draws on the experiences of 62 cancer patients; interviews with 22 health professionals in three regions including Dar es Salaam, and focus groups of health professionals, held in the Dar es Salaam specialist cancer hospital, Ocean Road Cancer Institute, and in two regional hospitals (Makene et al., 2022) (see also Chapter 1). A workshop in Dar es Salaam, followed by focus groups with a wide range of stakeholders including regulators, manufacturers, policymakers, clinicians and civil society actors including survivors’ groups, provided further evidence and perspectives.

These stakeholders reaffirmed and deepened our understanding of pain management as an important challenge for cancer care in Tanzania.

Experiences of Pain

A majority of the Tanzanian patients interviewed (53 out of 62) described pain as a central feature of their symptoms. They described pain spreading through parts of their body, and escalating from just “pain” to “severe”, “very severe” and over time “extreme” or “unbearable” pain. Back pain was described as spreading to the chest; vaginal pain to the abdomen; pelvic pain spreading through the back and abdomen and becoming “severe”; lower back pain spreading to the stomach and becoming “unstoppable”; stomach pain becoming “extreme” or “very severe” over time, and leg pain “unbearable”. Pain was central to most interviewees’ experience of cancer.

The interviews showed that people were struggling with high levels of pain, with several patients stating they felt better at the moment when the pain stopped. In the absence of morphine or other forms of opioids, many patients had resorted to repeated use of over-the-counter “pain killers”: basic pain medication that is largely inadequate and ineffective at dealing with moderate to severe pain. Patients reported that rising levels of pain were not effectively managed by hospitals, resulting in low expectations of pain control by patients. Given the levels of pain described, it seems likely that pain as a potential symptom of cancer is often not picked up early, reflecting the evidence that in Tanzania, late diagnosis of cancer is widespread (Chapter 5).

Palliative Care Provision

Tanzanian research participants working at various levels of the health system—national, regional and district—identified the provision of palliation as central to cancer care, including pain relief and management, as well as mitigating side-effects of radiotherapy and blood transfusion. Approaches adopted by health professionals included cooperation with spiritual leaders (Chapter 3). The importance in palliative care among Tanzanian patients and healthcare professionals of strong personal faith, as a way of dealing with exceedingly difficult conditions, has also been documented in other studies (for example, Esmaili et al., 2018). Furthermore, participants stressed the value of other actions to mitigate social and

physical pain including attempts to help patients in financial distress (see also Buhl, 2019; Hartwig et al., 2014). The views of health care professionals interviewed that are echoed elsewhere in the literature included the need for more dedicated palliative care teams to help manage high patient load (see also (Buhl, 2019; Esmaili et al., 2018), and the need to address patients' difficulties in accessing pain relief due to staff shortages (Kohi et al., 2019).

Access to Pain Medication

In Tanzania, the first line of pain relief was the purchase of over-the-counter painkillers, often repeatedly. Only two patients specifically mentioned being given morphine: one at a zonal Lutheran-supported hospital and one at Ocean Road Cancer Institute (ORCI) (the national cancer hospital). One patient mentioned that ORCI provided repeated pain relief as needed. However, many patients may have been unaware of which pain medication they were provided with. Most of the "pain killers", presumed to be non-opioids, mentioned in interviews were dispensed by drug shops, pharmacies, dispensaries, health centres and district hospitals.

Pain medicines mentioned by name were paracetamol and diclofenac, including mentions of their use for late-stage cancer. Provision of paracetamol for cancer pain was mentioned by several participants working at lower tiers of the health system. These health professionals did not have access to more appropriate pain relief and their patients were located at a great distance from ORCI. Reported interviews with staff treating paediatric cancer at Bugando Medical Centre (Esmaili et al., 2018) similarly indicated challenges in accessing morphine which meant that most staff reported the use of paracetamol or diclofenac for pain relief in terminal patients. At the time our research was conducted, morphine was almost entirely unavailable below the zonal hospital level in Tanzania. At the regional hospitals included in the study, morphine was either not available, or was irregularly available. Hospitals below the zonal were therefore not only unlikely to have opioids, but importantly also unlikely to expect to have them. An important implication of these expectations is that these hospitals may well not order opioids for future use: the implication of cumulative under-ordering in the health system is discussed further below.

THE NEED-DEMAND GAP FOR SEVERE PAIN RELIEF

How has such a serious gap arisen between the need for morphine, a vital treatment for pain and pain management for cancer patients, on the one hand, and the supply of morphine and other opioids by the relevant authorities, on the other hand? A key element in the explanation is the gap between the extent of need, as expressed and acknowledged by patients and health professionals, and the national demand for opioid medication as expressed in ordering levels and licensing requests to the International Narcotics Control Board (INCB) for annual morphine imports.

The need for morphine and other opiate-based medication is defined here by the levels of severe physical pain that can be alleviated through medication. Since the import of opioid medication requires licensing, and distribution of controlled medication must be managed nationally, the national demand for the controlled medication is measured in practice by the requested levels of licensed imports. Those licensing levels, procurement based on the annual licence, and the distribution of opioid medication to hospitals, determine the availability of the medication across the country. When the availability of imported medication falls so far below need, a need-demand gap opens up, resulting in high levels of untreated severe pain.

Figure 12.2 illustrates this relationship visually: the demand for the imported medication, at national level, plus the decisions on its distribution within the health system, drive availability at hospital level. This availability, it is accepted, currently falls substantially below need, leaving many patients including those with late-stage cancer in high levels of pain.

MORPHINE ORDERING AND DISTRIBUTION

Imports of controlled opioid medication require licencing from the INCB. INCB reports state that many LMICs, including African countries, consistently request an annual licence for morphine imports that is substantially lower than what is needed (International Narcotics Control Board, 2019) (see also Chapter 11). How is this low level of licensing request determined in Tanzania? Why is it so far below the requirements for meeting need?

Health professional staff interviewed at national and zonal hospital level explained that the Tanzanian public wholesaler, Medical Stores Department (MSD), is the sole institution licensed to import morphine

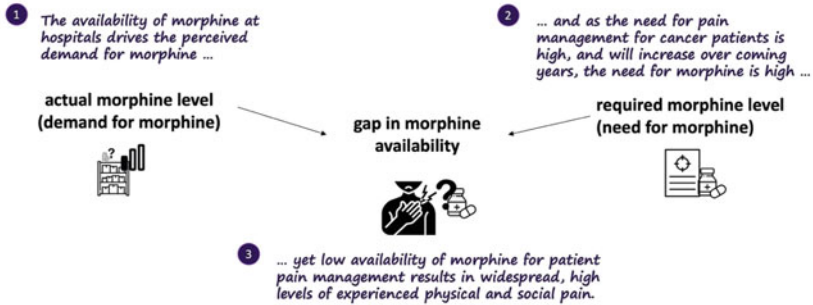


Fig. 12.2 Understanding the need-demand gap in morphine for cancer pain management (*Source* Authors)

and other opiate-based medication for Tanzania.¹ ORCI and the zonal hospitals order morphine through MSD. Regional hospitals could also acquire opioid medication directly from ORCI. The process of obtaining morphine was however described as “very difficult” by one regional hospital pharmacist, who also noted challenges with storing the drug, and the complex requirements that must be met before it could be prescribed to a patient.

A focus group discussion among staff at a regional hospital explored the problem from their perspective. Supplies of morphine at the hospital had run out at that time, and the hospital did not then have a permit in place to order more from ORCI. Cancer patients from the hospital were therefore sometimes referred from the regional level to ORCI to access morphine for severe pain. They or a relative would need to travel to Dar es Salaam to acquire it; otherwise, according to one senior clinician, patients might be treated with tramadol, pethidine or paracetamol if available.

According to Tanzania’s palliative care operating procedures, patients or their relatives who have come from a long distance can be given morphine and/or other medicine for two weeks to one month, depending on how far they have travelled.² Hospitals in Tanzania use pethidine, another controlled medication, for pain control after surgery. Pethidine is much more widely available than morphine in the health system, for surgical use.

This low level of availability of morphine at regional hospital level and below feeds back into ordering and procurement at national level. Hospitals which are accustomed to low levels of availability may not push to

order more. At regional level there are concerns to avoid diversion for illicit sale, which may constrain facilities from requesting supplies. One Regional Medical Officer interviewed commented on the need for close surveillance of morphine prescribing at lower levels of the health system:

Morphine is a narcotic medicine. Therefore, it can't just be left for anyone to prescribe because it might be used for another purpose.

Given these tight constraints and fears of illicit use, lower-level health facilities will not translate their observed need for severe pain management into orders for morphine. Overstretched palliative care teams, and lack of training in severe pain management using morphine may also constrain efforts to increase the amounts of morphine ordered. Participants in a focus group at ORCI highlighted a lack of training in palliative care as an issue.

Procurement decisions at national level are generated from aggregation of stated requirements within the health system. The amounts requested may also be strongly influenced by amounts ordered in the previous year, since additional requests will need to be justified in a context of fears of illicit diversion. The national procurement totals for morphine may therefore suffer from institutional “stickiness” or inertia: they will be similar to previous years’ procurement decisions unless health system stakeholders intervene to argue for a major change. Low procurement levels will then feed back into reinforcing low availability and a large and even increasing need-demand gap (Fig. 12.3).

IS FISCAL CONSTRAINT THE PROBLEM?

Public debate has suggested that the very sharp financial constraints faced by the Tanzanian health sector are at the root of recurrent shortages and prevalent under-ordering (Magubira, 2019). So is the cost of morphine a major constraint on MSD’s demand for imports? A number of sources suggest not. Currently, pain medication appears to represent a very small portion of overall budgets for cancer treatment. An oncologist interviewed stated that the cancer medicines budget for ORCI, of approximately TZS 10 billion (USD 4.4 million), was largely (“95%”) expended on chemotherapy, while pain medication was not currently a large cost. A regional hospital focus group reported that morphine costs

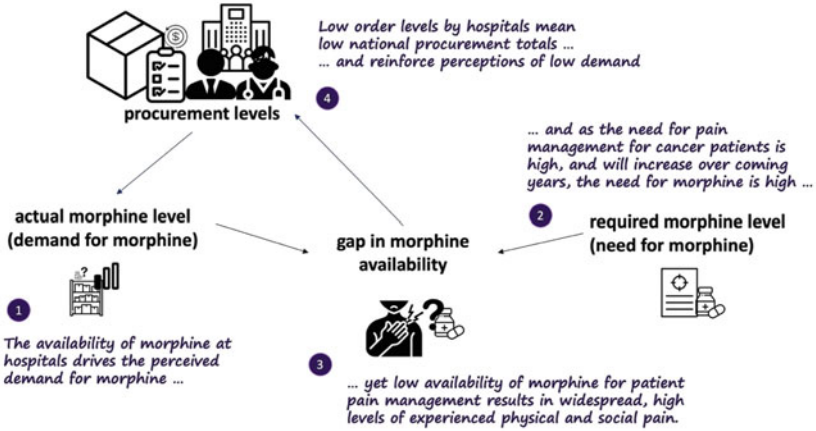


Fig. 12.3 Morphine: relationship between procurement and availability levels (Source Authors)

were not a significant barrier to access by patients: the problem was one of the availability of the medication.

There are however some contradictory accounts from the patients’ and health professionals’ perspectives. Esmaili et al. (2018) identify the cost of morphine, alongside other medicine and costs associated with hospitalisation, as a major impediment to paediatric cancer patients at Bugando Medical Centre (a faith-based zonal hospital) continuing to receive palliative treatment at the end of life. They also found that post-mortem fees that would be incurred should a patient die while in hospital were another significant reason why terminal patients were withdrawn from care including pain management. In 2018, one Tanzanian palliative care specialist argued that the omission of palliation from insurance packages meant that many patients could not afford morphine and were thus suffering severe pain (Qorro, 2019).

Up-to-date trade prices for morphine powder—the form in which morphine is imported—were not easy to obtain. The Lancet Palliative Care Commission (Knaul et al., 2018) used a figure of USD 0.01849 per milligram for sustained release morphine tablets or capsules, the import price cited by Rwanda for 2014.³ The lowest international price found by the Commission would have reduced that in 2014 by 60%. No price was given for wholesale morphine powder import. The Lancet Commission

costed the morphine in their essential package for palliative care at USD 20 per patient at Rwandan prices for 2014, and USD 8 per patient at the lowest international prices then available.

Trends in prices for medical opioids bought by LMICs are also not easy to track after 2015, when the International Medical Products Price Guide ceased annual publication. Before that date, the Guide (MSH, 2015 and previous years) registered prices for morphine in tablet form and other medical opioids including pethidine and tramadol. Figure 12.4 shows that median registered buyer prices in LMICs for morphine sulphate tablets varied but were on an apparently falling trend from 2010–2015, while median prices for morphine sulphate injectable ampoules were rising.

Median buyer prices for pethidine tablets meanwhile had been rising, while prices for pethidine and tramadol injectables were recorded in the MSH data as stable over the same period. In general, there was considerable variation around these median prices, with a number of LMICs paying substantially more than the lowest international prices registered in the Guide. We did not find data for buyer or seller prices for bulk morphine powder.

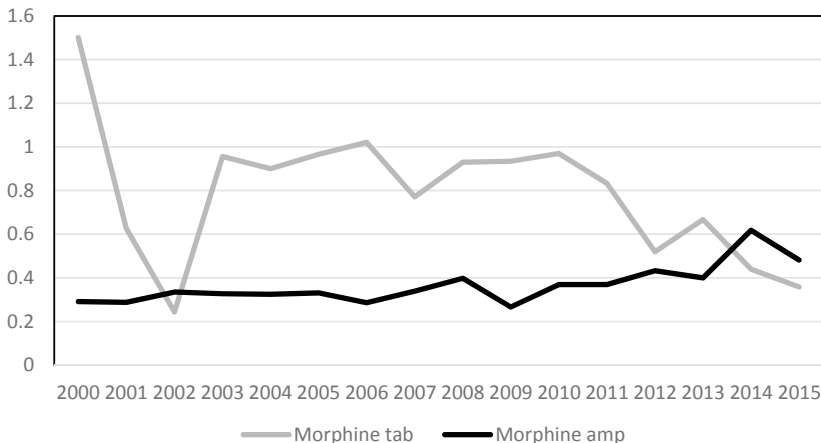


Fig. 12.4 Median buyers' prices: 2000–2015, morphine sulphate 30 mg tablet and morphine sulphate 15 mg/ml ampoule (USD) (*Source* Drawn by authors from MSH (2015) and previous years (online))

Relevant prices include wholesale import prices, and also prices for local distribution. The MSD catalogue at the time of the research (MSD, 2020) gave a sale price of TZS 12,300.00 for 10 ampoules of 10 mg/ml morphine injectable, the only morphine listed (USD 0.53 per ampoule). Pethidine 50mg/ml injectable was priced at TZS 9100.00 for 10 ampoules (USD 0.4 per ampoule). A news report in 2019 reported ORCI prices to hospitals for liquid morphine of 6000 TZS (USD 2.6) per litre and prices at outlying hospitals of 8–10,000 TZS including the markup for staff time and cost of travelling to obtain the medication in Dar es Salaam. That report stated the government was planning to subsidise the price (Magubira, 2019). For comparison, Hill et al. (2016) by contrast gave Indian retail prices (from the Indian maximum permitted price list for controlled prices) for a 30mg morphine tablet as USD 0.08, very considerably lower than the international prices shown in Fig. 12.4. The patchy recent data do therefore imply that Tanzanian prices along the supply chain to patients at the time of the research were substantially higher than those experienced in India.

MEASURING THE NEED-DEMAND GAP FOR MORPHINE: A COMPARISON WITH UGANDA

How large is the need-demand gap for opioid medication in Tanzania? In the absence of comprehensive prevalence and associated data for required medication for pain management, it is hard to estimate need. In order to develop some kind of quantitative estimate, we compare in this section the usage of pain medication in Tanzania with the use in Uganda. Uganda is a country facing comparable challenges, but with a history of successful development of low-cost access to morphine (Amandua et al., 2019; Fraser et al., 2018; Kamonyo, 2018). Uganda is also the highest-ranked African country among low-income countries in the 2015 Quality of Death index, and the second highest ranked in the group of African and Middle Eastern Countries.

Nevertheless, coverage of need is still patchy in Uganda. A statement published by civil society organisations in 2020⁴ noted that the Ugandan government's Health Sector Development Plan 2015/16–2019/20 (MoH, 2015) showed that palliative care services were being offered in only 4.8% of the public hospitals in the country. Since 2015, the coverage seems to have expanded: Kamonyo (2018) stated that there were inpatient and home care programs in 90 of 112 health districts

with at least one accredited health facility. Coverage of palliative care in Uganda depends heavily on non-governmental organisations providing hospice and outreach care at the community level. Morphine for palliative pain control is provided to patients free of charge in Uganda, and is included, as in Tanzania, in the national essential medicines list. Procurement of morphine powder and its constitution into liquid morphine was centralised in Uganda in a collaboration between the Ministry of Health and the NGO Hospice Africa Uganda (Fraser et al., 2018).

Amandua et al. (2019) showed that the “standalone” (NGO) providers of palliative care in Uganda were supported by two sources: 93% of financial running costs had come from donations over five recent years, while the government was providing in kind support in the form of medicines, training and payment (presumably waiver) of taxes. In recent years there has been no budget line for palliative care in the government health budget⁵; the most recent year for which this budget line was given was 2016/17, at Ugandan shillings 155 million (approximately USD 46,000). In general, the Ugandan health budget is very donor-dependent and also relies heavily on charging. Only around 13% of the total health budget is government-funded and the absolute total has been falling, as have payments by the government to non-profit private health providers in Uganda (Ssenyonjo et al., 2018).

Given the greater success in Uganda in extending access to severe pain medication, one illustrative estimate of the need-demand gap in Tanzania can be constructed by comparing imports into the two countries in relation to cancer incidence and population size. Table 12.1 shows the different levels of imports between the two countries, and estimates what would be involved in bringing Tanzanian imports up to Ugandan levels, given the different estimated cancer incidences.

To make this estimate, Table 12.1 compares data on morphine imports licence requests to the INCB for Uganda and Tanzania, taken from International Narcotics Control Board (2019). The prevalence and population data are the 2020 numbers from the WHO’s Globocan global registry of cancer data. Table 12.1 shows that the morphine request for Tanzania for 2020 per estimated cancer case was much lower (at 0.14 grams) than it was for Uganda (0.8 grams).⁶ To request morphine imports equivalent to the Ugandan order in terms of availability/case would have required Tanzania to order 58.6 kg. as compared to the 2020 order of 10.02 kg. Tanzania would therefore have needed to order an extra 48.6 kg or nearly 6 times its 2020 order to match Uganda’s availability per case, according

Table 12.1 Estimates of the Tanzanian morphine ordering gap 2020, using a Uganda comparison

1	Estimated cancer prevalence Tanzania (cases, 2020)	73,303
2	Tanzania population	59,734,213
3	Case to population estimate Tanzania (1/2)	0.00123
4	Morphine requirements to purchase 2020 Tanzania (grams)	10,020
5	Morphine order per case estimate Tanzania (grams) (4/1)	0.14
6	Estimated cancer prevalence Uganda (cases, 2020)	62,548
7	Uganda population	45,741,000
8	Case to population estimate Uganda (6/7)	0.00137
9	Morphine requirements to purchase 2020 Uganda (grams)	50,000
10	Morphine order per case estimate Uganda (grams) (9/6)	0.80
11	Morphine required in Tanzania at Ugandan order/case (grams) (9*(1/6))	58,597
12	Tanzania ordering gap estimate 2020 (grams) (11–4)	48,577

Sources Lines 1, 2, 3: WHO/Globocan <https://gco.iarc.fr/today/data/factsheets/populations/834-tanzania-united-republic-of-fact-sheets.pdf>; Lines 6, 7, 8: WHO/Globocan <https://gco.iarc.fr/today/data/factsheets/populations/800-uganda-fact-sheets.pdf>; Lines 4, 9: INCB https://www.incb.org/documents/Narcotic-Drugs/Technical-Publications/2019/Narcotic_Drugs_Technical_Publication_2019_web.pdf

to INCB published data. We do not have import prices for morphine powder to allow a calculation of the total additional cost of those imports.

Tanzania's population is higher than Uganda's. However, Uganda's estimated cancer case/population ratio is higher than Tanzania's (Table 12.1). Cancer cases furthermore may be underestimated, given the many difficulties patients face in accessing diagnosis (Chapters 4 and 5). At Uganda's higher prevalence rate (line 8), Tanzania's larger population would imply an estimated 81,836 cases (lines 2*8) and a larger ordering gap of 55.5 kgs. This exercise provides just one indicative method of estimating the need-demand gap by volume for morphine in Tanzania, showing the scale of the gap based on higher Ugandan availability/case. Yet, as noted above, the Lancet Palliative Care Commission (Knaul et al., 2018) calculated that Uganda was itself far from achieving use adequate for need. In addition, there is necessarily a large training cost associated with widening access to morphine. In 2004 Uganda legalised the prescribing of oral morphine by clinical officers and nurses who had undertaken nine months palliative care training. This was a key step in widening access, allowing home and local use for palliative care. That training programme was based at Makerere University and run

jointly with the NGO Hospice Africa Uganda. Uganda has undertaken quite widespread integration of palliative care into medical and nursing curricula, including a national palliative care training manual developed by the Ugandan Ministry of Health for health care providers at all levels of service delivery (Fraser et al., 2018). No costing of this training programme appears to be publicly available.

ADDRESSING THE CANCER PAIN MANAGEMENT DEFICIT: MUTUALLY SUPPORTIVE INNOVATIONS

The research presented so far has identified a chain of interconnected factors operating in a systemic way across health care, training, procurement and supply chains to influence the pain management outcomes. Figure 12.5 adds more critical components of cancer pain management to Fig. 12.1, based on this evidence. Innovations in these areas can be linked up systematically to help to tackle the pain management challenges. This section draws on Tanzanian focus group discussions and workshops to outline how this might be done, to help to tackle the persistent gap in severe pain management in Tanzania. It includes the scope for local manufacturing of opiate pain medication to contribute to solutions.

Chapter 7 introduced the concept of an innovation eco-system: a network of local multi-sectoral institutions that reinforce learning, innovation and competence building. This framework can be applied to

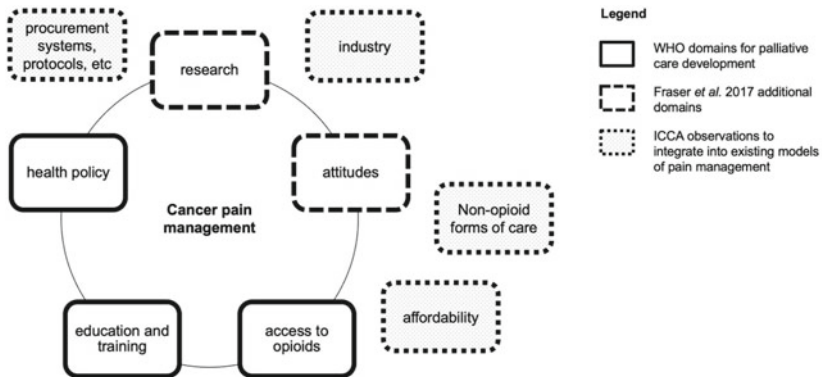


Fig. 12.5 Critical components of cancer pain management (Source Authors)

identifying routes to more effective and inclusive management of severe pain. The innovations required—in terms of product, process, social, organisational and marketing innovations, and innovations in policies and policymaking—necessarily involve highly varied actors and stakeholders such as government Ministries of Industry, Finance, Trade and Health; health professionals and manufacturers; researchers in the public and private sectors; and civil society organisations. Externally they include private overseas investors, development funders, and external institutions including the INCB.

THE SCOPE FOR LOCAL MANUFACTURING

At present, Tanzania imports all its opioid medication.⁷ Discussion with local manufacturers confirmed that they have the technical capability to manufacture oral morphine and other opioid tablets. The main technical barriers identified were in the production of injectable morphine, since Tanzania at the time of the focus group discussions in 2021 did not have a manufacturing plant capable of producing sterile injectables. However, as Chapter 7 documented, the first sterile manufacturing plant in Tanzania began production in 2022. Tanzania is thus developing these upgraded industrial capabilities; in the wider region, Kenya, which already had injectables manufacturing capability, is also seeing further investment (Chapter 7).

The chief barriers to local morphine manufacturing identified were market access and information, and security. As for oncology drug production (Chapter 8), manufacturers identified a lack of market information for pain medication and questioned whether the size of the market was sufficient for a return on investment. The low level of morphine imports—so far below need—reinforced this perception of a small market. As for oncology medication, a policymaker also emphasised the need for a regional approach, and for pooled procurement, to support the viability of local production.

The problem of security in opioid manufacturing multiplies many of these challenges for manufacturers. First, it raises direct production costs. One manufacturer reported that they currently produced a single item, a cough medicine, with a controlled ingredient. The storage and logistics costs for this ingredient were high: USD 4000 per month for secure storage, and each secure transport from storage into the plant cost over USD 500 for a single trip. The security required, because of the danger

of illicit diversion, therefore pushes up the price of any opioid medication, since the API has to be imported, stored and handled securely. However, the huge price gap noted above between Indian and African prices for morphine tablets suggests that despite the security costs there may nevertheless be scope for local manufacturing to be viable and still to lower prices to the health system.

Second, all the regulatory challenges facing exporters (Chapter 7) are multiplied for controlled medication, raising manufacturers' risk. One manufacturer explained that producing a controlled drug means that:

It makes the matter even [more] complicated. ...it will require so many controls which means you will add more risk. There is a risk of handling the material, that the materials are not distributed on the illicit pathway, and should you import, if the market is small, there is a risk of the material expiring before it is even used. (Focus group participant, 2021)

Given these risks, government support for manufacturers to find patient finance might be needed to start investment in local production.

The dangers of illicit use, in a context where there is already a problem of addiction, have to be taken very seriously. One participant argued that the government should explore the scope for local API production—while recognising the dangers of illicit diversion. It was noted that to make the regulatory challenge manageable for manufacturers, while sustaining stringent controls, necessarily requires collaboration among a number of authorities including the Tanzania Medicine and Medical Devices Authority (TMDA), the Drug Control Enforcement Authority (DCEA), the Medical Stores Department (MSD) for procurement, Ministry officials responsible for health, industrial, legal, regulatory and trade issues, the Pharmacy and Poisons Board (PPB) and still others. Regulatory stakeholders however strongly supported the need for such collaboration to increase access to much-needed controlled medication. One participant argued for the government to regard this as a strategic area:

The government can intervene by applying for permits so that it can go into local production [of the API] on its own and term it as a strategic project. Another option is to give local production a special preferential status due to current demand. Because of the increasing number of people with cancer ... we cannot continue to rely solely on imports. The next step is for the government to engage in production to cover that [the need-demand] gap (Focus group participant, 2021).

SKILLS, TRAINING AND MANAGEMENT OF MEDICATION BY HEALTH WORKERS

Focus group participants argued that skills, training, prescription and the culture of managing pain needed to change across the health, regulatory and industrial sectors. The documented need for more industrial pharmacists and industrial chemists (Wangwe et al., 2021) applies also in this field.

An oncologist noted that to raise procurement through the INCB, it is essential to first use each existing consignment within the health system fully. To ensure this, and to increase demand, attitudes needed to change, including prescribing behaviour. Doctors needed to be more aware of the benefits of morphine: they can lack confidence in managing the medication or fear prosecution. One clinician described their efforts to increase the use of pethidine, an opiate, for sickle cell pain and how that had benefited patients, arguing that the same effort was required to benefit cancer patients. Enhanced training in morphine use is therefore needed within medical training. The fear of creating addiction, which appears to hold back prescribing, needs to be addressed so that patients requiring the medication, including those with terminal cancer, are not denied it.

The curriculum for nurses and clinical officers would also need to be enhanced, if controlled medication were to be handled at lower levels in the health sector. For example, as one participant noted, a specialist hospital cancer centre may prescribe pain medication, but the patient should be able to access it at a local hospital or through a pharmacy licensed to supply it. The Uganda case shows the scope for a much more active role for trained nurses in managing severe pain. Uganda also demonstrates the important role of civil society organisations in the palliative care field in supporting wider access to morphine according to need. Focus group participants noted that donor support for “training the trainers” could improve skills and awareness of severe pain management across the Tanzanian health system.

Wider use of licit morphine also requires training and organisational changes in managing security at lower levels of the health sector. The changes include processes for handling and reporting use of controlled medication. For methadone, used to support recovery from addiction, donors have supported costs of licensing and control. For licit morphine, local management and control requires collaboration between enforcement agencies, regulators, supply chain actors, clinicians, pharmacists and

health facility management among others. This has been already occurring: the DCEA for example reported that they were providing short training courses, jointly with the TMDA and government chemistry laboratory agencies, teaching different service providers to manage controlled medication, including how to prescribe them and follow them. The training included supportive supervision. Several participants noted high levels of willingness across the system to make this work.

CONCLUSION: A FOCUS ON POLICIES, REGULATIONS, AND LICENSING

Improving pain management is one important element in Tanzania's commitment to make Tanzania "among countries with low cancer burden"(URT, n.d, p. 10). This chapter has identified the need-demand gap in Tanzania for access to severe pain medication and has noted that this is a widespread phenomenon across Sub-Saharan Africa. As an interview at the INCB also established, African countries including Tanzania can increase their imports of opioid medication at their request, so long as they are able to use the increased allocation. So when this chapter talks of "demand" we refer to the amount the country is annually licensed to import. In Tanzania, as across Sub-Saharan Africa, this is greatly below need.

We have traced the roots of this need-demand gap for severe pain management to a set of interlocking factors. We have argued that cost, while always important in low resource systems, is not the core constraint. Oral morphine is not an expensive medicine. Instead, the low demand is rooted in low *use*: a pattern of low prescribing and management of the medication constrained to a few specialist centres. This low use is aggregated nationally into low national demand, reinforcing the "abyss" of poor control of pain which is increasingly of international concern.

Stakeholder workshops and a brief comparison with Uganda's approach, have identified a series of interlocking areas where innovation could "unstick" the low demand, responding better to patients' needs, raising expressed requirements, growing aggregated demand, and generating a better supply of care for severe pain. They include training and regulatory changes, and potentially also local manufacturing of essential opioid medication. The comparison with India (Chapter 11), which already produces this medication, shows that although local manufacturing in itself does not ensure better access, it is vital to improving the

situation and addressing the need-demand gap in SSA. Indeed, the Indian example also shows that, where demand increases and use becomes more confident and widespread, the capability of local manufacturers to respond is a major policy resource. In the case of SSA, innovation and policy can help steer progress in the right direction.

The next chapter builds on these insights to propose a policy tool—scenario building—that can help identify the key linkages and innovations needed within the health-industrial system.

NOTES

1. A clinician in a major private hospital noted that the hospital sometimes also faced difficulties in ensuring access to morphine.
2. <https://www.orci.or.tz/wp-content/uploads/2020/04/zz.pdf> accessed 7/5/2022.
3. Source: online data appendix, *Lancet* Palliative Care Commission report https://www.mia.as.miami.edu/_assets/pdf/data-appendix-lcgapcpc-oct122017_xk-4-22-201.pdf accessed 4/5/22.
4. Statement by Civil Society Organizations in Uganda on Budget Allocation for Palliative Care Services for the Financial Year 2019/2020 submitted to The Deputy Speaker of Parliament / The Chairperson Committee on Health, written by Organisations working on Palliative Care, Human Rights and Budget Advocacy, Kampala December 2020 <https://pcauganda.org/wp-content/uploads/2020/12/Civil-Society-Statment-on-National-Budget-Allocation-of-Palliative-Care-April-2019-1.pdf> accessed 5 May 2022.
5. According to the Civil Societies' Organisations' statement, see previous note.
6. Tanzania also requested 30 kilos of codeine and 77 kilos of pethidine; these were also substantially lower than Uganda's request for 100 and 150 kilos respectively, despite a lower population (International Narcotics Control Board, 2019).
7. This is also the case in Kenya; one Kenyan manufacturer that previously produced opiate medication had ceased to do so.

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