Left behind in pain

Extent and causes of global variations in access to morphine for medical use and actions to improve safe access

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Foreword

The world is facing two crises related to the use of opioids. In the first, inappropriate use and over-prescription combined with the wide availability of illicit unregulated opioids, such as fentanyl, in some countries is causing significant harm and loss of life. In the second, a lack of access to opioids such as morphine in many parts of the world means that millions of people continue to suffer preventable pain.

It is the latter crisis that is highlighted in this report: the persistent lack of access to morphine for medical use, particularly in low- and middle-income countries. This report underscores the fact that morphine is an essential medicine and a gold standard for pain relief that has been included in the WHO Model List of Essential Medicines since 1977. Despite its importance, safe access to morphine is hampered by a range of factors, including a lack of coordination along the supply chain, inadequate physical, financial and skilled human resources, weak governance, and misconceptions about pain and opioids.

This report presents a complementary set of areas for action that aim to improve safe access to morphine, such as providing or extending safe access to more people in need, improving governance and resourcing, developing competencies and skills, and raising awareness about the benefits and potential harm associated with opioid use. The success of the actions proposed will depend on collaboration and cooperation among all stakeholders at national, regional and global levels.

Leaving people in pain when effective medicines are available for pain management, especially in the context of end-of-life care, should be a cause of serious concern for policy-makers. We must therefore urgently advocate for safe and timely access to morphine for those in medical need through balanced policy, everywhere. I believe that this is not only the right thing to do medically and morally, but also that it is wholly achievable, guided by science, our commitments to human rights, universal health coverage and the United Nations *Single Convention on Narcotic Drugs, 1961* and *Convention on Psychotropic Substances, 1971*. Indeed, these two UN conventions stress the "indispensable" need for access to narcotics, including morphine, for medical use.

The title of this report, *Left behind in pain*, is a sobering reality that we must confront and address together. In 2030, as the Sustainable Development Goals draw to an end, I hope we will be able to publish a report entitled "No one left behind in pain". That would be an achievement that we could be proud of. Let's fulfil it together.

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Executive summary

Morphine is an essential medicine for relieving moderate to severe pain. It is also essential for treating severe breathlessness that is refractory to treatment of the underlying cause, especially at the end of life. Its medical uses span multiple clinical settings in today's medical practice, including surgical care, cancer care, palliative care, emergency care, paediatric care, and long-term care. It is the most basic requirement for the provision of palliative care, as noted by the Lancet Commission on Palliative Care and Pain Relief: "[morphine] must be available both as an oral, immediate-release preparation and as an injectable preparation for any patient with moderate or severe pain or with terminal dyspnoea".

Safe and timely access to morphine is important for public health, but access is known to be concerningly inadequate in many countries. This report describes the extent and causes of global variations in access to morphine for medical use. It seeks to understand the enablers for and barriers to safe access to morphine for medical use, and proposes actions through balanced policy to address them.

All available data point to a great disparity in access to morphine for medical use, and strong opioids more broadly. In 2021, over 80% of the morphine available (in weight) was distributed for consumption to countries within the World Health Organization (WHO) Region of the Americas (mostly in North America) and European Region, and to high-income countries.[1] When expressed as defined daily dose (DDD) per million people per day, the median estimated consumption level of morphine was 125.9 DDD per million people per day in high-income countries compared to 24.9, 6.7 and 2.0 DDD per million people per day in upper-middle-, lower-middle- and low-income countries, respectively. However, consumption levels varied considerably across country income tiers and did not correspond to medical need, as indicated by the estimated number of days in pain and with dyspnoea per capita. This disparity in access to morphine (and strong opioids) for medical use was confirmed in a WHO survey of stakeholders (see Web Annexes A and B): 50% of the respondents from low-income countries and 18% of the respondents in lower-middle-income countries reported that at least 8 in 10 people did not receive morphine or other strong opioids despite medical need.

Multiple barriers hinder access to morphine when in medical need; one of them is a lack of availability, particularly in lower-income countries. In the WHO survey, one in four respondents from low-income countries, lower-middle-income countries and upper-middle-income countries reported that morphine in immediate formulation was available less than half of the time when needed for medical use; this contrasts with one in 25 respondents from high-income countries. In countries with weak financial and social protection, patients needing morphine or other opioids could incur impoverishing or catastrophic expenditure because of their need for many other essential medicines or care (such as cancer medicines, palliative care, surgical care) and other associated costs (e.g. travel), thereby compelling them to forgo some of these essential medicines, including morphine.

[1] Country income classification of low, lower-middle, upper-middle and high are determined by the World Bank based on gross national income per capita.

The supply of morphine and other strong opioids for medical use is regulated internationally by the United Nations *Single Convention on Narcotic Drugs, 1961* and *Convention on Psychotropic Substances, 1971* and is subject to the laws of individual countries. As a result, the supply process can be lengthy as it requires strong coordination among multiple parties involved in decision-making and authorizations. Poor process coordination can disrupt supply of morphine and other strong opioids, thereby delaying or obstructing access for people in need.

A suite of inextricably linked underlying factors can also enable or hinder safe and timely access to morphine for medical use for both adults and children. These factors are governance structure, resource availability, capacity-building, legislation and policies, and service provision. For example, respondents to the WHO survey highlighted several barriers, including legislation or policies being overly focused on preventing illicit use and unduly restrictive administrative requirements for prescribing or dispensing morphine. Others noted the importance of having financial resources that are predictable, stable and adequate to meet the demand for morphine and clinical services. Skilled, adequate and enabled workforce is also a key determinant of safe access to morphine and workforce development should remain a priority for many countries. More broadly, engaging the community and people in need of morphine is needed to better understand the basis of their views and identify service providers, via education and broader health promotion activities. This can dispel any misconceived beliefs about pain and opioids, and build trust in the use of morphine for medical purposes.

A list of potential areas for action to improve safe access to morphine has been identified from the literature. Each of these areas for action should encompass a set of supporting policies and activities that are carefully planned, carried out, and regularly monitored and revised according to different national and regional contexts. Notwithstanding, respondents from all six WHO regions identified developing small-scale or state-wide programmes and establishing regional or local manufacturing of morphine products as among the top five priorities to improve access to morphine for medical use. Other top five priorities identified by respondents from different regions include:

- establish and implement a package of essential services and products to facilitate rational use of morphine;
- establish affordable pricing for morphine for medical use;
- establish hub-and-spoke distribution networks;
- expand access for people with health conditions other than cancer and HIV and for children; and
- expand access for long-term care facilities, home-based care and hospice institutes.

Many of these areas for action are complementary to one another. For example, small-scale or state-wide programmes on improving access to morphine for medical use should include a package of essential services and products, formulated according to accepted standards or guidelines, such as the WHO Model Lists of Essential Medicines and the WHO Essential Package of Palliative Care. Such programmes should also establish affordable pricing and ensure access for all people in need of morphine (e.g. non-cancer patients) and in all relevant service contexts (e.g. long-term care). The backbone of these programmes is a skilled clinical workforce. Governments should work with relevant stakeholders to find ways to streamline the process of procurement and supply and address any inefficiency in the supply chain due to legal or unduly restrictive administrative requirements.

The persistent disparity in access to morphine for medical use globally, and the associated suffering, must be a cause for concern. In taking actions to improve safe access to morphine, health and human rights must be at the centre of all policies.

1. Opioids such as morphine are essential medicines – safe and universal access matters

1.1 Medical uses of morphine

Morphine is an essential medicine used for relieving acute or chronic, moderate to severe pain, triggered by causes such as major trauma, surgery, heart attack and cancer. Pain relief is felt almost immediately when an adequate dose of morphine is injected, or within 30 minutes when taken orally. The pain-relief effect of a dose of injected or immediate-release oral morphine typically lasts between 3 and 6 hours. Slow-release oral formulations can provide relief lasting 8 to 12 hours, while a continuous intravenous infusion may provide constant relief. In adults and children with advanced respiratory disease and terminal illness (e.g. end-stage cancer, advanced chronic obstructive pulmonary disease), morphine also can be used for managing chronic moderate or severe breathlessness (dyspnoea) that is refractory to treatment of the underlying cause.

The effect of opium for pain relief has been known for millennia. Morphine was first extracted from opium poppy plants in the early 1800s and its medical uses have since been well recognized. Morphine has been listed in the World Health Organization (WHO) Model List of Essential Medicines (EML) for the management of pain since the first edition of the list was published in 1977 *(1)*, and in the WHO EML for children since its first edition published in 2007 *(2)*. The 2019 *WHO Guidelines for the pharmacological and radiotherapeutic management of cancer pain in adults and adolescents* provides a strong recommendation that "Regularly dosed immediate-release oral morphine, or regularly dosed slow-release morphine, should be used to maintain effective and safe pain relief whenever oral dosing is possible. With either formulation, immediate-release oral morphine should be used as rescue medicine" *(3)*.

In today's medical practice, morphine, together with other strong opioids, are essential in various clinical settings, including surgical care, cancer care, palliative care, emergency care, paediatric care, and long-term care. For instance, as a basic requirement for provision of palliative care, experts have recommended that:

> [Morphine] must be available both as an oral, immediate-release preparation and as an injectable preparation for any patient with moderate or severe pain or with terminal dyspnoea *(4)*.

1.2 Morphine can be used safely for medical purposes

Like other medicines and other opioids, morphine use is associated with side-effects, including constipation, drowsiness, and less often confusion, dry mouth, nausea and vomiting. Clinical guidance in managing these common side-effects is well established.

People receiving morphine (and other strong opioids) in doses high enough to cause sedation may also experience respiratory depression. If severe and left untreated, respiratory depression can be fatal. Nevertheless, when internationally accepted dosing guidelines are followed, evidence suggests that significant respiratory depression is uncommon or rare, and clinically manageable *(5)*. The

risk and severity of sedation and respiratory depression are dependent on various factors. For example, people receiving morphine for the first time, or older people, are particularly at risk, while factors such as excessive dosage, route of administration, the presence of other health conditions (e.g. lung disease or heart failure), and the concurrent use of other medicines that may depress respiration (e.g. some sedatives) could increase the severity.

After longer-term use, people receiving morphine may build tolerance to its pharmacological effects, that is, a decrease in effectiveness with the same dose. When this occurs, people require higher doses to achieve the same level of pain relief, but the higher doses do not significantly increase the risk of developing the serious adverse effects noted above. How frequently tolerance occurs among patients treated with morphine is uncertain. Clinical experience in specific medical contexts, such as palliative care, suggests that occurrence is rare. In fact, patients often require higher doses of morphine or strong opioids for pain relief as their disease worsens.

Like other opioids and other psychoactive substances, illicit use, prolonged use, misuse, and use without medical supervision of morphine can heighten the risk for harmful use, development of opioid use disorder and other health problems *(6)*. People receiving opioids for medical purpose may also use excessive dosages as a coping strategy for emotional distress, known as opioid-related chemical coping. For example, a systematic literature review[2] estimated that the occurrence of opioid dependence, abuse or opioid use disorder *following* medical use of opioids for pain management was 4.7% (95% confidence interval: 2.1% to 10.4%) *(7)*. This review noted substantial heterogeneity in the study estimates ranging from 0.2% to 34.2%, reflecting the variations in study design, methodology and quality *(7)*. Understanding the risk of developing these mental disorders can inform the risk–benefit of using morphine. For example, non-pharmacological and non-opioid medicines should be used to treat chronic non-cancer pain to the extent possible before use of opioids, while access to morphine or other opioids for individuals receiving palliative and hospice care must be established.

1.3 Unequal and inadequate access to morphine hampers efforts to alleviate pain

Pain is a major public health problem globally. Poorly controlled pain is disabling; it causes physical, psychological, social and spiritual suffering. Each year, it is estimated that people across the world live between 6 billion and 21 billion days in physical and psychological serious health-related suffering associated with a need for palliative care and pain relief *(4)*. About one in two deaths every year worldwide is estimated to be associated with serious health-related suffering. Among these deaths 2.5 million are children, 98% of whom live in low- and middle-income countries[3] *(4)*.

Pain management, including the appropriate use of morphine, can alleviate serious health-related suffering by improving quality of life. However, access to morphine and other strong opioids is unequal and inadequate globally. An

[2] Twelve studies involving 310 408 participants who received opioid analgesics for medical purposes for various periods: 3–12 months for six studies, and varied or unknown for six studies.

[3] Country income classification of low, lower-middle, upper-middle and high are determined by the World Bank based on gross national income per capita (*6*).

estimate shows that more than 95% of all the opioids (in morphine equivalent doses) were distributed to high-income countries, with only 0.03% being distributed to low-income countries *(4)*. Moreover, even when morphine is available in these countries, a patient with medical need for opioids may have, *on average*, access to as little as 10 mg morphine-equivalent opioids per year *(4)* – that is, less than half a day of the standard starting dose for adults. Many have no access at all.

1.4 Balancing the benefits and harms of morphine use

Striking a balance between maximizing the medical benefits of opioids, such as morphine, and minimizing the potential harms of use or misuse, has been a long-standing policy goal both at international and national levels.

At the international level, the United Nations (UN) *Single Convention on Narcotic Drugs, 1961* (as amended by the 1972 Protocol) *(9)* and *Convention on Psychotropic Substances, 1971 (10)* are the two main legal instruments for facilitating global cooperation on controlling the production and distribution of narcotic and psychoactive substances, which include morphine and other opioids. While aiming to combat substance misuse and illicit trade, both conventions emphasize the "indispensable" need to maintain access to narcotic and psychoactive substances for medical use, as stated in their preambles:

> *Recognizing that the medical use of narcotic drugs continues to be indispensable for the relief of pain and suffering and that adequate provision must be made to ensure the availability of narcotic drugs for such purposes (9).*

> *Recognizing that the use of psychotropic substances for medical and scientific purposes is indispensable and that their availability for such purposes should not be unduly restricted (10).*

At the national level, some countries have sought to implement balanced policies in line with their obligations to the conventions and according to national contexts. Several national and subnational jurisdictions seem to have achieved a balance where increase in opioid prescriptions did not increase level of opioid-related harm (e.g. Germany) *(11)*. However, stark global disparities exist in access to opioids for medical use globally: many countries have very limited access for medical use while a few high-income countries are experiencing an "opioid overdose epidemic" due to inappropriate use and over-prescription combined with the wide availability of illicit unregulated opioids (e.g. fentanyl) *(12)*. This suggests that achieving a balance must remain a high priority in many countries and globally.

1.5 Background of this report

WHO is committed to improving safe access to essential opioids for medical use, in accord with its mandates conferred by the World Health Assembly through various resolutions, particularly resolution WHA67.19 *Strengthening of palliative care as a component of comprehensive care throughout the life course (13)* and resolution WHA67.22 *Access to essential medicines (14)*. WHO is also bound to promote and protect human rights and to pursue primary care and universal health coverage according to covenants, resolutions, and principles endorsed by the United Nations Human Rights Council and the United Nations General Assembly.

As noted in section 1.1, morphine is considered the most basic essential medicine for managing acute or chronic, moderate to severe pain, particularly in palliative care. It is also less expensive than other derivative and synthetic opioids, such as oxycodone and fentanyl, which have been associated with the "opioid overdose epidemic" in a few high-income countries. For these reasons, this report focuses

on morphine, presents the status regarding access to morphine and other strong opioids for patients in need globally (Chapter 2); main system barriers to, and enablers for safe access to morphine (Chapter 3); and potential priority actions for improving safe access to morphine for medical use through balanced policy (Chapter 4). It contains information gathered from various sources, including a targeted review of published literature, and quantitative analyses of the data published by the International Narcotics Control Board (INCB) and the proprietary data from IQVIA MIDAS.

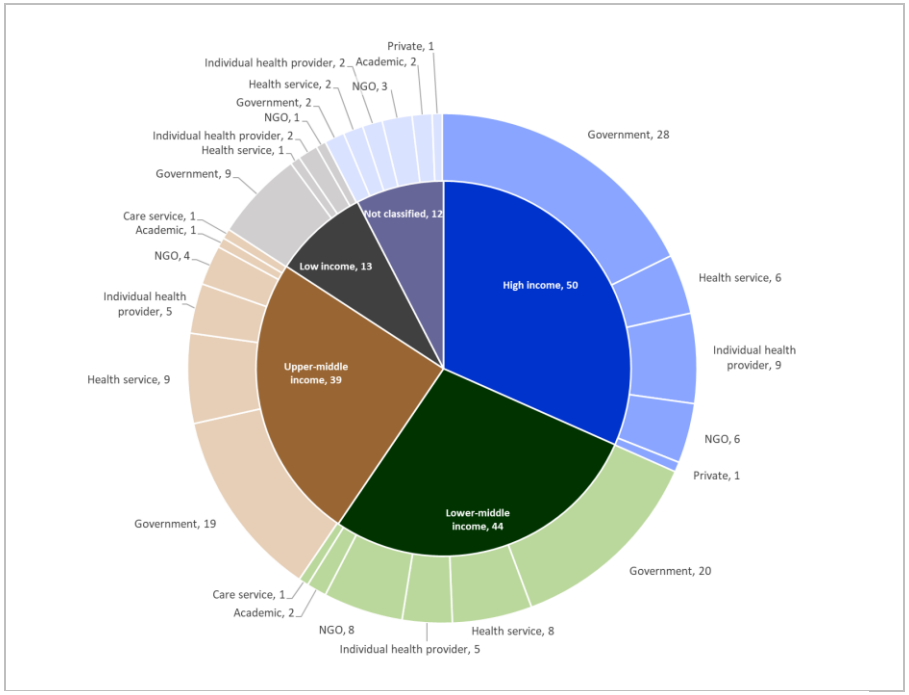
This report also presents findings from the WHO survey *Assessing barriers, enablers and priority actions for improving access to morphine for medical use: a survey of stakeholders* (hereafter referred to as WHO survey). This survey presented a questionnaire made available in all six official languages of the UN (Web Annex A contains the English version). It sought responses from government agencies, civil society, clinicians and clinical services, academic experts and experts from international organizations. These stakeholders were recruited between 6 July and 23 September 2022 through the following methods:

- invitations through circular letters issued by the secretariat to the WHO governing bodies;
- invitations through membership database of professional organizations (e.g. non-State actors in official relations with WHO); and
- direct contacts to partner organizations (e.g. UN agencies and humanitarian agencies).

This survey received a total of 356 valid responses representing stakeholders in 105 WHO Member States and organizations based in multiple locations. The responses covered 159 combinations of country-stakeholder-viewpoint pairs (Fig. 1.1). More detailed methodology and findings of this survey are presented in Web Annex B. The survey was exempted from review by the WHO Research Ethics Review Committee (ERC.0003688).

By presenting the status of and evidence concerning access to morphine for medical use, this report seeks to turn the struggle to achieve balanced policy into a global mission to promote actions that improve safe access to morphine, so that no one will be left behind in pain or exposed to the harms of substance use disorder.

Fig. 1.1. Distribution of survey respondents to the WHO survey, by World Bank country income classification and stakeholder group



NGO: nongovernmental organization.
Source: WHO survey (Web Annex B).

2. Supply, demand and access to morphine for medical use

2.1 Global supply of morphine for pharmaceutical use

Morphine used for pharmaceutical manufacturing is extracted from raw opium and poppy straws rich in morphine. According to data reported to the INCB, in 2021, Türkiye, Australia, France and China were the main cultivators of opium poppy (*Papaver somniferum*) for the production of poppy straws rich in morphine for pharmaceutical production (Fig. 2.1) *(15)*. Extractions from these raw materials combined with the existing stocks from past year's production, 235 000 kg of morphine was available for further pharmaceutical manufacturing in 2021 (Fig. 2.1) *(15)*.

Morphine can be compounded into various pharmaceutical dosage forms (e.g. injections, tablets, capsules, granules, liquid) by commercial companies. Ten pharmaceutical companies[4] contributed to 80% of the global sales of commercially available morphine products (in volume) between 2015 and 2020 *(16)*. The supply market of morphine products remained competitive in 2020, despite a trend of increasing market concentration since 2017 and short supply of certain dosage forms. In particular, the supply of morphine products has been limited in many middle- and low-income countries *(16)*.

Of the available stocks of morphine in 2021, 166 000 kg was converted into substances in Schedule III[5] of the Single Convention on Narcotic Drugs of 1961, or substances not covered by the 1961 Convention (as amended by the 1972 Protocol) *(9)*. Specifically, morphine was commonly converted into codeine, a Schedule III substance, which accounted for more than 90% of all morphine converted (Fig. 2.1).

After accounting for the amount of morphine distributed for consumption (see section 2.2) and losses during the manufacturing process or destruction, about 135 800 kg of morphine was reported as remaining in stock at the end of 2021 (Fig. 2.1).

2.2 Global distribution of morphine for medical use is unequal and not based on need

In 2021, 33 115 kg of morphine was distributed for medical (and scientific) uses globally. The distribution of morphine for medical consumption was highly unequal globally, with over 80% of morphine being distributed for consumption in countries within the WHO Region of the Americas and European Region, and in high-income countries based on World Bank's classification (Fig. 2.1). Within the Region of the Americas, morphine distributed for consumption was concentrated in the United States of America (76.7%) and Canada (12.6%) (Fig. 2.1).

[4] Boehringer Ingelheim, Ethypharm, Gerot Lannach, Hikma, Mallinckrodt Pharmaceuticals, Mundipharma, Pfizer, Dongbei Pharmaceutical Group Co Shenyang No1 Pharmaceutical Factory, Taiji Group Southwest Pharmaceutical Chengdu and Teva.

[5] Preparations containing narcotic drugs that are intended for medical use and are unlikely to be abused (e.g. preparations containing codeine, dihydro-codeine).

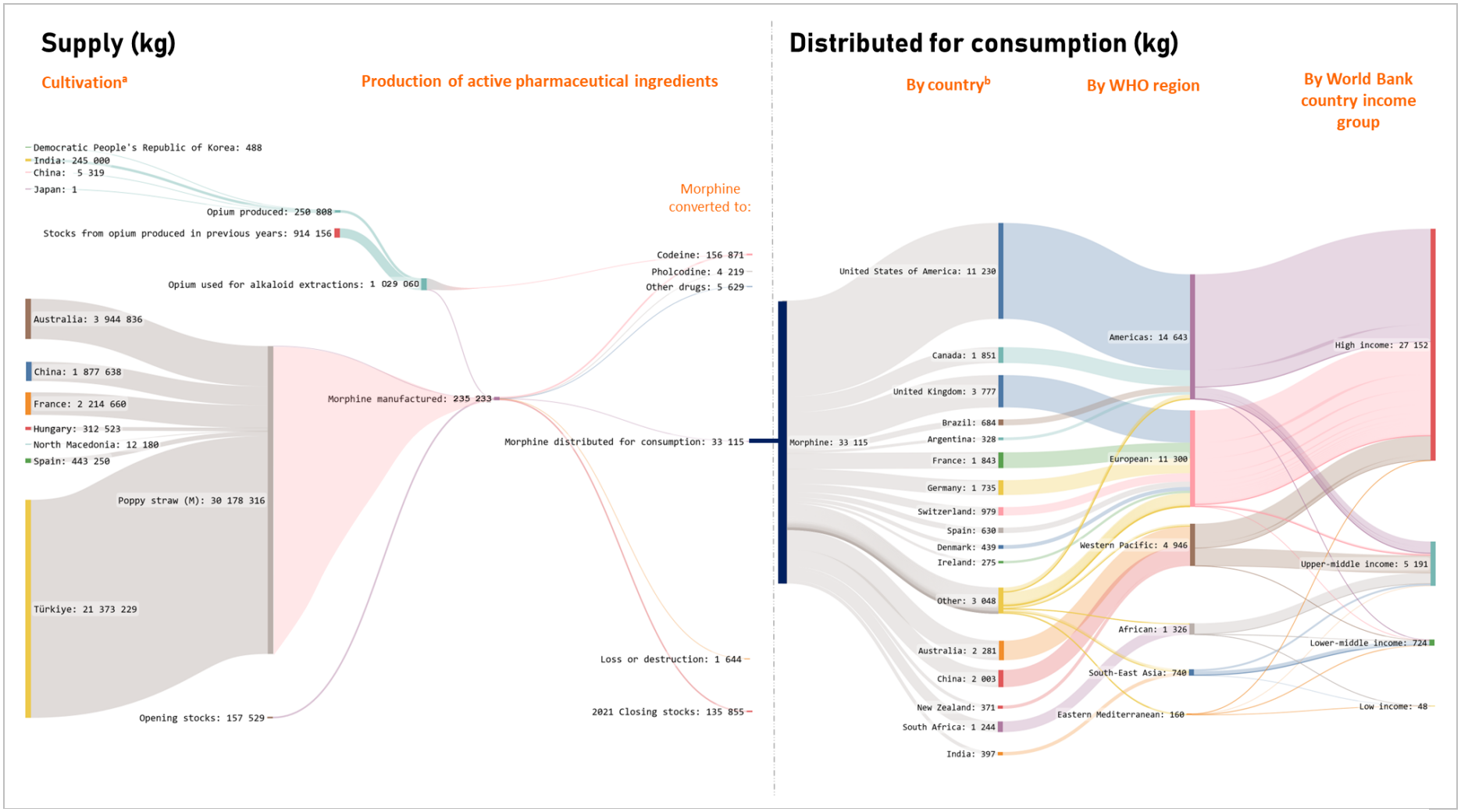
When expressed as defined daily dose (DDD)[6] per million people to facilitate comparison, a higher level of morphine was distributed for consumption in high-income countries than lower-income countries in 2021, as indicated by the median consumption of 125.9 DDD per million people per day in high-income countries compared with 24.9, 6.7 and 2.0 DDD per million people per day in upper-middle-income countries, lower-middle-income countries and low-income countries respectively (Fig. 2.2). The consumption levels varied significantly, with considerable overlaps in consumption levels across country income tiers. Similar trends were observed for the consumption of strong opioids other than morphine (i.e. fentanyl, hydrocodone, hydromorphone, oxycodone and pethidine): in 2021, the collective consumption levels of strong opioids other than morphine were 3028.6, 152.3, 6.7 and 2.4 DDD per million people per day, respectively, in high-income countries, upper-middle-income countries, lower-middle-income countries and low-income countries. This means that there are a range of factors affecting people's access to morphine and other strong opioids for medical use.

No correlation was observed between overall consumption levels of opioids and medical need for opioids, as indicated by the estimated number of days with moderate or severe pain or dyspnoea per capita *(17)* (Fig. 2.3). Although the needs of some low-income countries were comparable to high-income countries, the former reported much lower levels of opioid consumption (Fig. 2.3).

In many lower-income countries morphine consumption was proportionally higher than other opioids (Fig. 2.4). This suggests that lower-income countries are much more dependent on morphine to meet the medical need of their population. For this reason, people in need of pain relief in these countries would be most affected by the unavailability of morphine.

[6] DDD is the assumed average dose of a medicine needed for treating a health condition in an adult. The DDD of morphine is set as 100 mg for oral administration and 30 mg for parenteral route for pain relief. The INCB defined the DDD for morphine as 100 mg to reflect its increased consumption by oral administration. The purpose of such conversion is to facilitate the comparison of morphine, rather than indicating the preferred route of administration.

Fig. 2.1. Global production and distribution of morphine for consumption in 2021



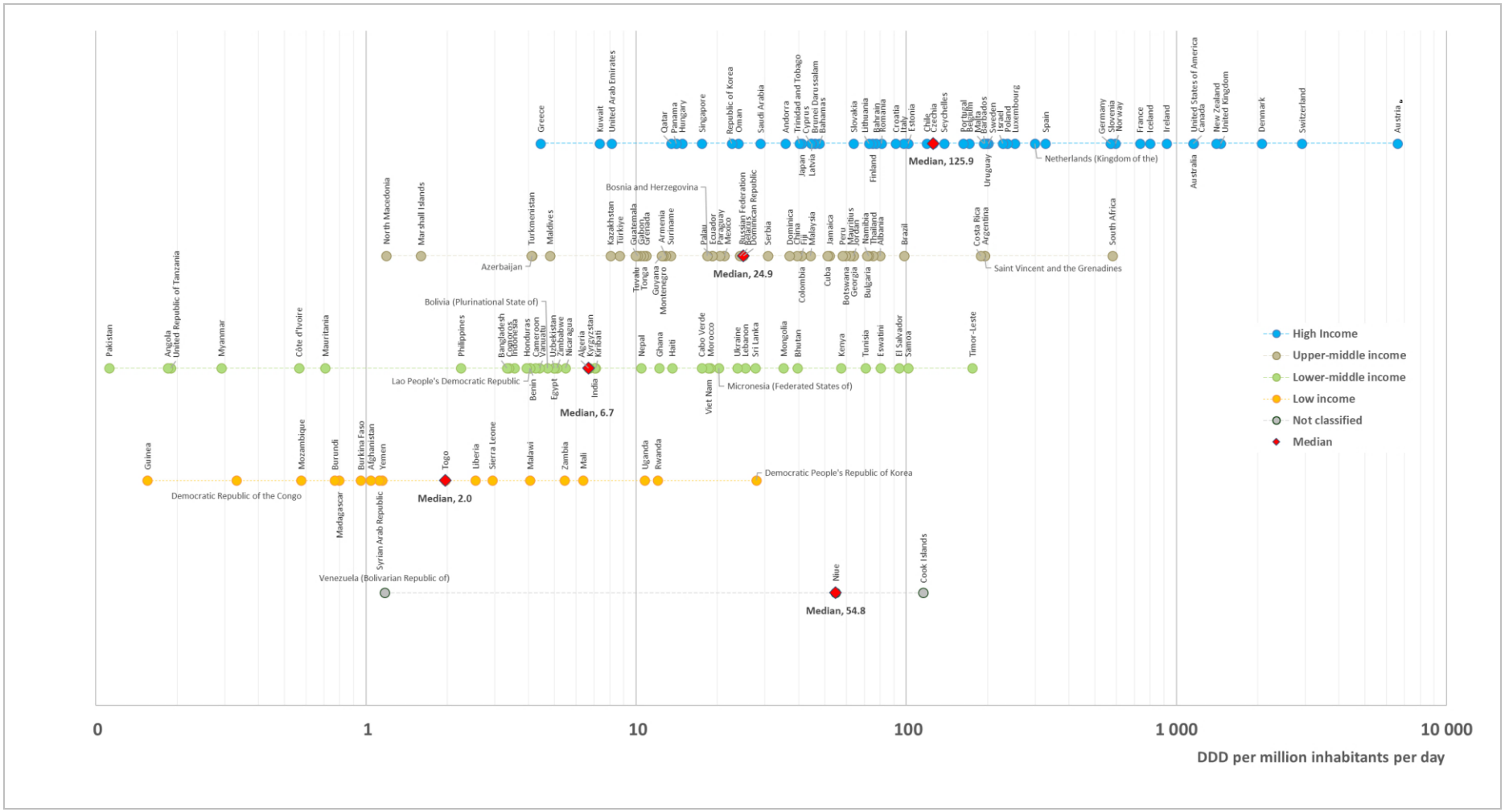
Poppy straw (M): poppy straw rich in morphine;

[a] Total anhydrous morphine alkaloid contained in different varieties of concentrate of poppy straw can vary significantly. Cultivation is to illustrate source countries that have reported data to the INCB only.

[b] All other countries not shown reported consumption data to the INCB.

Source: WHO analysis of data presented in tables I–VI, and XII of INCB report *(15)* and communication with INCB. Please refer to the report for detailed country data and explanations in text or footnotes.

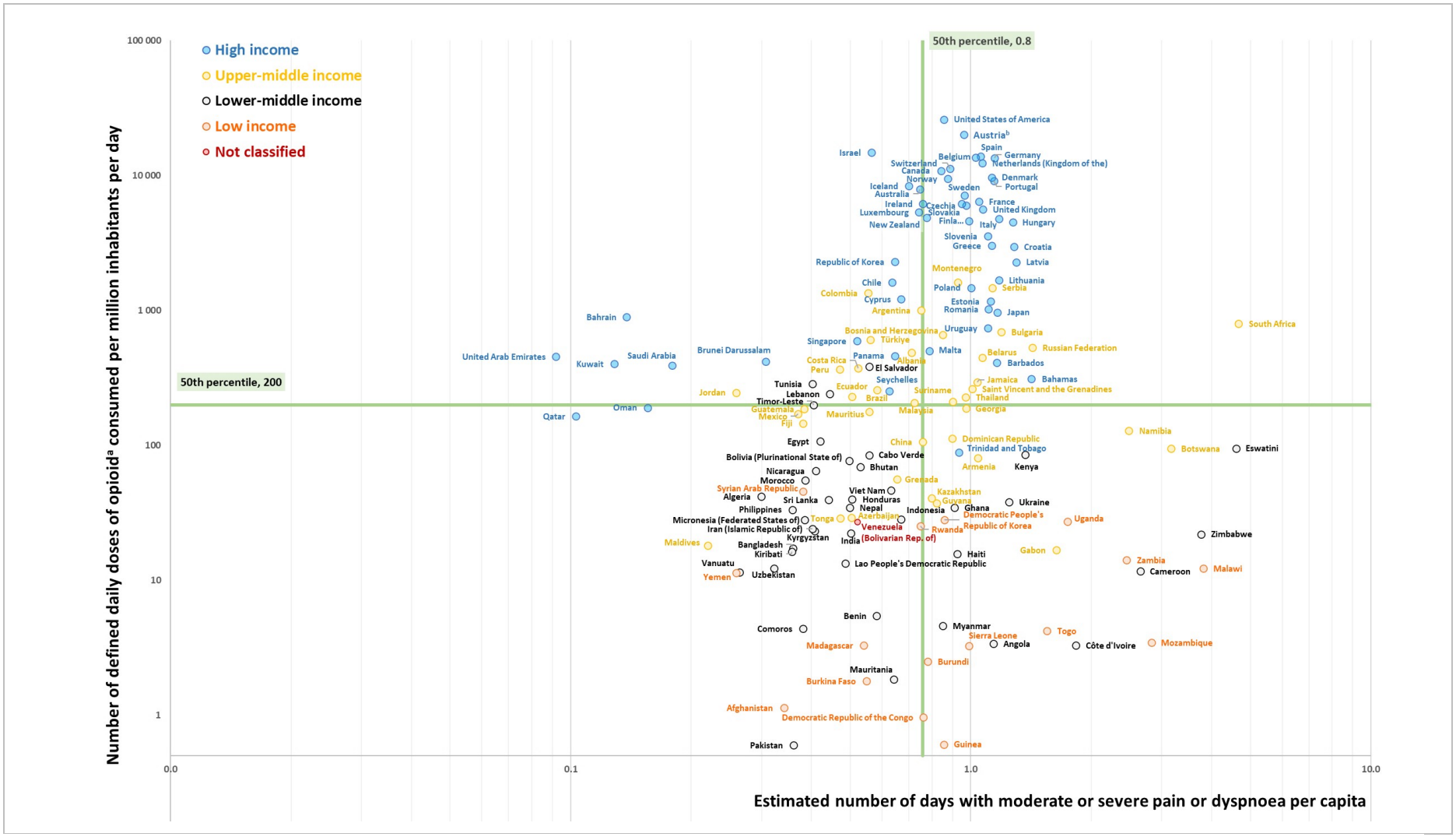
Fig. 2.2. Average consumption of morphine (2019–2021), by World Bank country income classification



[a] The reported estimate for Austria included slow-release morphine used for opioid substitution therapy, which was uncommon in other countries.

Source: WHO analysis of INCB data (Table XVI.1a) *(15)*.

Fig. 2.3. Comparison of consumption of opioids and estimated need for pain relief or dyspnoea

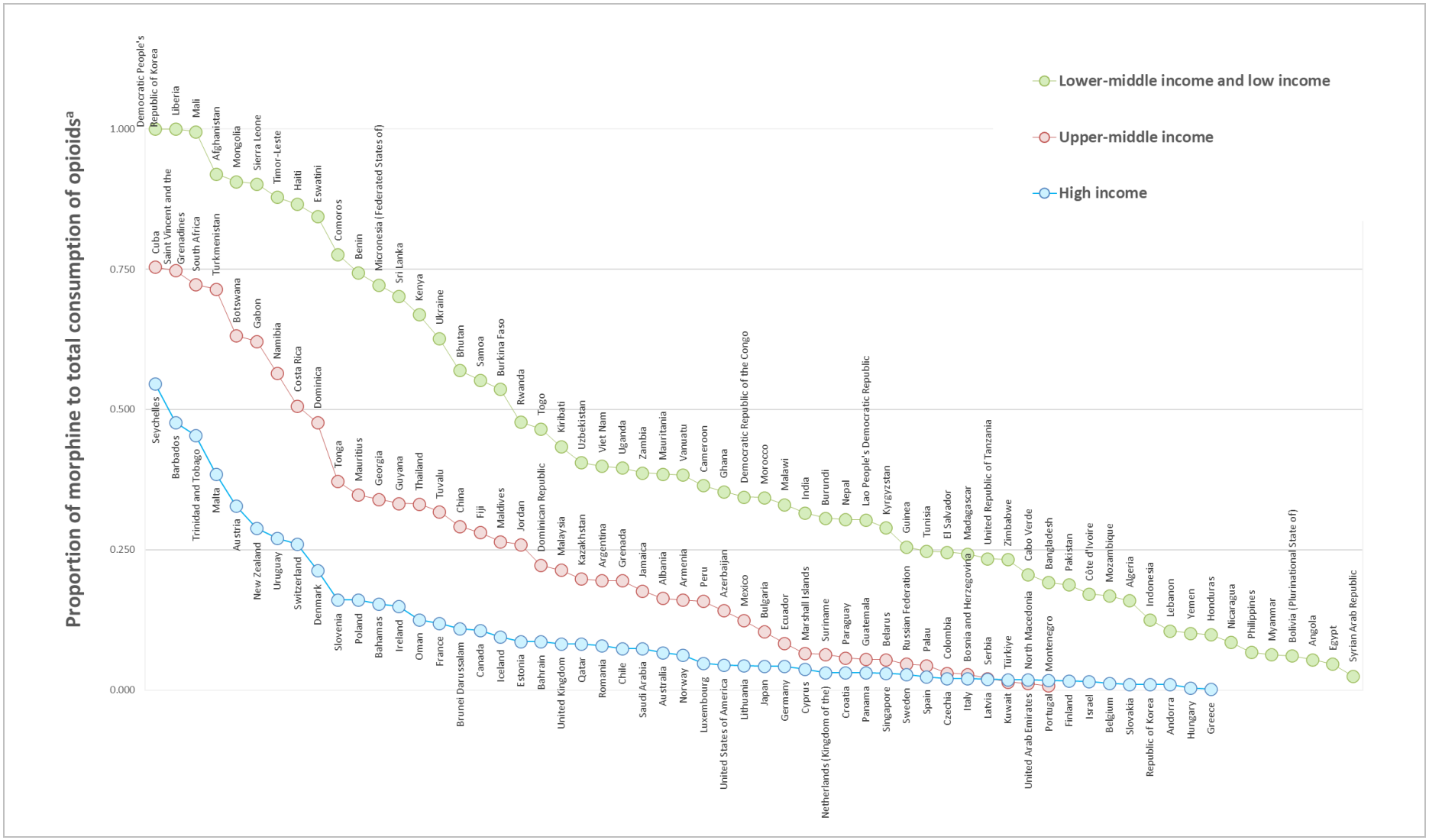


[a] Except buprenorphine, codeine and methadone, which are used mostly for purposes other than management of moderate or severe pain or refractory dyspnoea.

[b] The reported estimate for Austria included slow-release morphine used for opioid substitution therapy, which was uncommon in other countries.

Source: WHO analysis of data reported by INCB (Table XVI.1a) *(15)* and Knaul et al. *(17)*.

Fig. 2.4. Morphine consumption as a proportion of the total consumption of opioids



[a] Except buprenorphine, codeine and methadone, which are used mostly for purposes other than management of moderate or severe pain or refractory dyspnoea.
Source: WHO analysis of INCB data *(15)*.

2.3 Unavailability of morphine products hampers access

Morphine is available as commercial products made by pharmaceutical companies (see footnote 4) and preparations compounded in a pharmacy according to prescription (i.e. extemporaneous preparations) in various dosage forms, including injectable solutions, tablets, capsules, granules, oral liquids, and pen injectors. These dosage forms are formulated to provide options for various needs, such as immediate relief, constant pain control, infrequent dosing, swallowing difficulties or to give to children. As a basic requirement for provision of palliative care, experts have recommended that morphine "must be available both as an oral, immediate-release preparation and as an injectable preparation for any patient with moderate or severe pain or with terminal dyspnoea" *(4)*.

According to the WHO survey, morphine injections were reported to be the first or second most used dosage form globally, except for in low-income countries where morphine in immediate-release tablets was more commonly used. In the WHO South-East Asia Region, Eastern Mediterranean Region and Western Pacific Region, morphine in extended-release tablets was reported as the most used dosage form. Morphine in oral liquid and other dosage forms were much less commonly used, which may have an impact on specific populations (e.g. children). Lack of availability of these less expensive dosage forms may also have an impact on patient affordability, especially in low- and middle-income countries.

Morphine products are not always available for medical use, particularly in lower-income countries. In the WHO survey, about 1 in 4 respondents from low- and middle-income countries reported that immediate-release formulations of morphine were only available less than half of the time when needed for medical use in their contexts; this contrasts with about 1 in 25 respondents from high-income countries. Availability was reported to be even lower across all formulations of morphine and other opioids in low- and middle-income countries, with about 1 in 3 respondents indicating product availability less than half of the time when in need, compared to about 1 in 8 respondents in high-income countries (Web Annex B).

As a result of the inconsistent availability, 50% of respondents in low-income countries and 18% of respondents in lower-middle-income countries reported that at least 8 in 10 people did not receive morphine or other strong opioids despite medical need. Regionally, a higher proportion of survey respondents from the European Region (54%) and Eastern Mediterranean Region (45%) reported all patients received morphine according to accepted clinical guidelines and practice, compared with respondents from the Western Pacific Region (25%), Region of the Americas (23%), South-East Asia Region (17%) and African Region (14%) (Web Annex B). In the absence of strong opioids, patients might have to resort to opioids weaker than morphine (e.g. tramadol, codeine), which would not provide adequate pain relief because their effects are limited by pharmacological "ceiling effect"; and others might have to resort to accessing opioids from improper and illicit sources. Even worse, some patients might have to self-medicate with harmful doses of more accessible pain medicines such as non-steroidal anti-inflammatory drugs, causing serious health complications.

To address the lack of availability of commercial products and to meet certain clinical service needs at an affordable cost, some health systems have initiated programmes to provide oral morphine solution reconstituted from morphine powder, that is, extemporaneous preparations. Examples include programmes in Uganda *(18)*, Kenya *(19)*, Rwanda *(20)*, Eswatini and Nigeria *(21)*.

2.4 Pricing of morphine products

The pricing of morphine products, and their costs and affordability for people in need, is an important consideration when assessing accessibility. The WHO survey found significant variations in the reported prices of morphine products. The variations could be due to a range of factors, such as market conditions of supply and demand, prices reported at different points along the supply and distribution chain and reporting inaccuracies. Notwithstanding, the median reported prices per 10 mg/1 mL ampoule of injectable morphine were generally below US$ 2. The survey observed that immediate-release tablets were priced lower than extended-release tablets, and prices were generally lower than US$ 1 per tablet. This observation is consistent with price data collected in a proprietary database of medicine sales via wholesalers, manufacturers, retailers or imports (i.e. IQVIA MIDAS), and prices reported in public government databases (Table 2.1). However, prices in some lower-income countries could be similar or higher than prices in higher-income countries (e.g. procurement price of morphine 10 mg/1 mL injection in the Philippines was higher than in the United Kingdom of Great Britain and Northern Ireland (United Kingdom). This could be one of the factors contributing to unaffordable access.

A significant proportion of the respondents in the WHO survey, particularly in the Eastern Mediterranean Region (91%) and European Region (90%), indicated that at least 80% of people in need could afford to pay for morphine products because they had financial coverage from public insurance, and to a lesser extent, private insurance; some could afford the cost even when they had no health insurance coverage. However, the reported level of affordability was associated with the country income level, with more respondents indicating financial hardship among patients in lower-income countries (low income 31%; lower-middle income 25%; upper-middle income 11%; high income 10%). This may reflect the lower likelihood of having financial and social protection in lower-income countries, as well as pricing of products not in line with the health system or people's ability to pay. Furthermore, patients needing morphine or other opioids typically also need access to other essential medicines or care (e.g. laxatives, cancer medicines, palliative care, surgical care), increasing the cost. The cumulative health care costs and other associated costs, such as travel, could present a significant barrier to access and risks of incurring impoverishing or catastrophic expenditure.

Table 2.1. List prices of morphine 10 mg/1 mL ampoule for injection

Country or area	Price type	Price (US$) per unit[a]
Brazil	Ex-factory[b]	0.42
Canada (Ontario)	Reimbursement[b]	1.90
Chile	Procurement (public sector)[b]	0.15
China	Reimbursement[c]	0.58
Denmark	Reimbursement[b]	3.16
France	Ex-factory[b] (excluding taxes)	0.83
Ghana	Reimbursement	0.43
India	Retail[b] (excluding local taxes)	0.36
Japan	Reimbursement[a]	2.78
Malaysia	Retail[c]	0.92
Oman	Retail	1.14
The Philippines	Procurement (public sector)[c]	1.42
South Africa	Retail[b]	0.45
Thailand	Reimbursement (public sector)[b]	0.20
United Kingdom	Procurement – hospital	0.31

[a] Prices in local currencies were converted to US dollars based on 2021 official period average exchange rates published by the World Bank. Prices may include taxes and service charges.
[b] Regulated maximum or fixed prices, which could be based on the cheapest product
[c] Suggested prices for consumer reference only.
Source: (22–36).

2.5 Supply chain compliance with legal requirements is one access determinant

Like other substances subject to the control of international conventions (section 1.4), the supply of morphine for medical use is regulated internationally and is subject to the laws of individual countries. Legislative requirements in individual countries could determine the organization of the supply chain for the manufacturing, exportation, importation and distribution of raw materials and morphine products. These requirements could also affect stocking, prescribing and dispensing by health facilities and health professionals. This means that only authorized organizations or individuals are permitted to oversee the production, supply and distribution of morphine and other strong opioids for medical use.

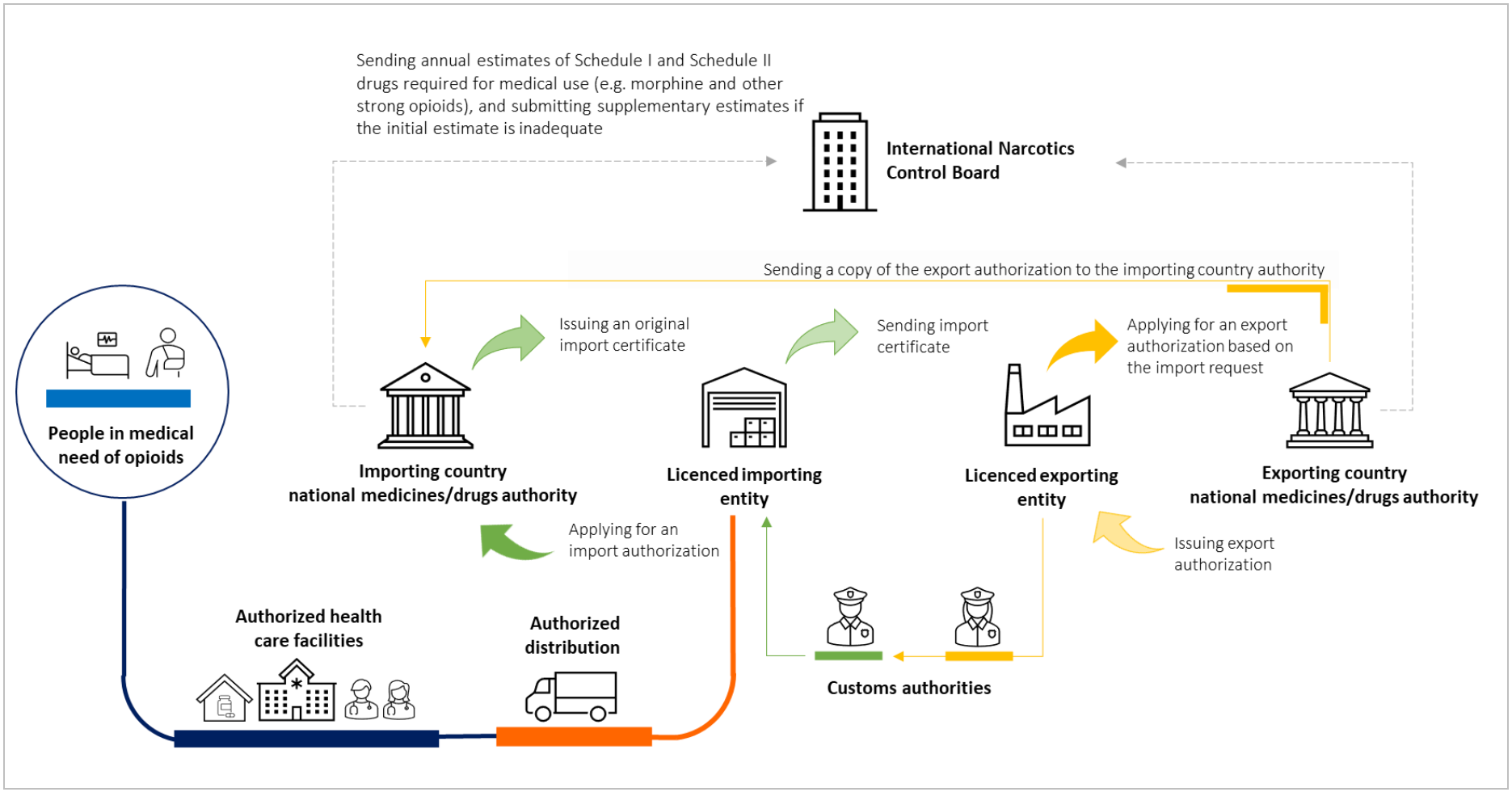
Fig. 2.5 illustrates a general process from the exporting and importing to the distribution and supply of morphine and other strong opioids for medical use. The supply process can be lengthy as it requires coordination among multiple parties involved in decision-making and authorizations *(3)*. Such processes require organizations or individuals who are proficient with the regulations and the processes involved, including supply chain security to prevent diversion. For example, all information on the import licence must perfectly match the information contained on the export licence. The licence would be denied in case of mismatch and would potentially add months to the process.

2.6 Expanded roles of health professionals have supported access

National legislative requirements could also specify the clinical contexts and scope of authority for health professionals to prescribe, dispense or administer morphine for people with medical needs. According to the WHO survey, morphine is provided for medical use in health facilities, in descending order of likelihood, that provide tertiary, secondary, primary and long-term care (e.g. long-term care facilities). Specialty and general medical doctors were reported to have similar roles in prescribing and to a much lesser extent, carrying morphine products or administering morphine to people in need. Nurses were mostly restricted to administering morphine to people in need. In some contexts, specialist nurses are permitted to prescribe morphine for medical use. Pharmacies and pharmacists were primarily responsible for dispensing morphine for medical use, while nurses, community health workers and trained or supervised family members may be permitted to carry morphine to patients while performing their duty without the risk of being charged with possession of a controlled substance.

The population with chronic conditions managed outside of tertiary and secondary health care settings continues to grow. Given this, changes in legislative and administrative requirements could enable health services to meet the growing need for morphine or other strong opioids for medical use outside of health care settings. For example, in Uganda, legislative changes in 2004 made it possible for specially trained nurses and clinical officers to prescribe controlled substances, including oral morphine liquid for homecare patients. This change has been noted as being instrumental in expanding palliative care service to nearly 90% of the districts in Uganda (*38*). In Australia, an authorized nurse practitioner, upon approval, could prescribe opioids within their scope of practice and with certain prescribing restrictions, such as quantity and frequency. This policy has been refined over time to "ensure the safe and effective prescribing and use of opioids while maintaining access for patients who need them" (*39*).

Fig. 2.5. Main steps in the supply chain of morphine and other opioids



Source: Adapted from *(3)* citing (*37*).

3. Medical use of morphine: enablers and barriers determined from the survey

Access to morphine for medical use is influenced by a suite of system factors that interact with the supply–demand interplay as presented in Chapter 2. Fig. 3.1 lists the main system factors documented in the literature, which are broadly categorized as enablers: good governance, resource availability and capacity-building activities; and as barriers: overly restrictive legislation and policies, inadequate service provision, and misinformed attitudes and perception.

Enablers and barriers are inextricably linked. As such, each factor is essential but insufficient in its own to influence access to morphine. For this reason, health systems ought to consider these enablers and barriers in their totality, although the relative importance may vary according to context, as discussed further below.

3.1 Governance structures enable access but regulatory requirements could present barriers

Good governance is the bedrock of a balanced policy to ensure access to morphine for medical use while preventing misuse. Respondents to the WHO survey noted the existence of various structural elements of good governance in countries. These include a multidisciplinary body (e.g. regulatory, clinical, social care, consumer-representative, civil society) to coordinate government policies on use of controlled substances; medicines/therapeutics committees in districts and hospitals to oversee access and rational use of opioids; or other arrangements to ensure appropriate use of opioids (e.g. health worker training, clinical supervision, formal audit and feedback). More than 55% of WHO survey respondents reported the enactment of regulations or policies to facilitate medical use and prevent misuse of opioids in their contexts. Regulation and policies can provide clarity on government's objectives and guide all stakeholders towards delivering socially desirable outcomes.

However, more than a third of respondents across all regions also noted at least one barrier arising from legislative and regulatory factors. For example, significant proportions of responses from the Eastern Mediterranean (52.6%), Western Pacific (41.7%), South-East Asia (37.5%) and African (35.3%) Regions noted that legislations or policies had been unduly focused on preventing illicit use. Restrictions on importing, prescribing and dispensing could hamper access (e.g. limits on import quantity, requirements for permits and licence approval considered as more than necessary; restrictions in long-term care facilities and home-based care). Unduly restrictive administrative requirements could also impede the flow of supplies (e.g. limits on prescription validity, quantity or dosage restrictions, special prescription forms, record keeping requirements), as a survey respondent explained:

> *The regulatory controls are so many that the pharmaceutical industry doesn't find it [morphine] worth manufacturing as the profit is low and regulation is high. The regulators are more concerned about misuse than easing the pain of patients.*

While some restrictive requirements might have been implemented to mitigate potential risks of misuse or diversion, policy should focus on addressing the underlying causes, which include a lack of administration and health worker training regarding safe use and prescription of opioids.

Misalignment between administrative processes and clinical service provision can cause severe discontinuity of supply, as noted in the quoted example below:

> *The process to get morphine starts only after the hospital that has the licence exhausts all its available medicine. Now there's no morphine at the hospital, and you have to wait for months before the provincial health and Excise & Taxation departments process your request, which is then sent to the federal narcotics ministry for an NOC [no-objection certificate] (40).*

3.2 Financial resources and clinical guidelines not consistently available to support optimal use

Medicines, equipment, funding and knowledge are important resources to facilitate access to morphine for medical use. For example, supportive medicines (e.g. naloxone, anti-nausea products and laxatives) and equipment (e.g. security safes and safety boxes) must be available to support the appropriate and safe use of morphine. Financial resources should be predictable, stable and adequate to meet the demand for morphine and clinical services. Service providers should be supported by information materials to guide their clinical practice, including the listing of essential morphine products in the medicine formulary, and establishing practice guidelines and data infrastructure to help assure good quality of care. These materials could also support ongoing professional development.

The WHO survey suggests that all health systems included at least some enablers mentioned above. However, funding for supporting supply of morphine and associated services seems to be insufficient, particularly in the African, South-East Asia, Eastern Mediterranean and Western Pacific Regions.

Inconsistent funding could result in unreliable supply. Indeed, consistent with the statistics presented in sections 2.2 and 2.3, survey respondents from lower-income countries were more likely to report morphine and other strong opioids being not regularly available in health facilities (e.g. for morphine: low income 53%; lower-middle income 36%; upper-middle income 25%; high income 7%). For this reason, countries would need to increase modest financial commitments needed to secure supply.

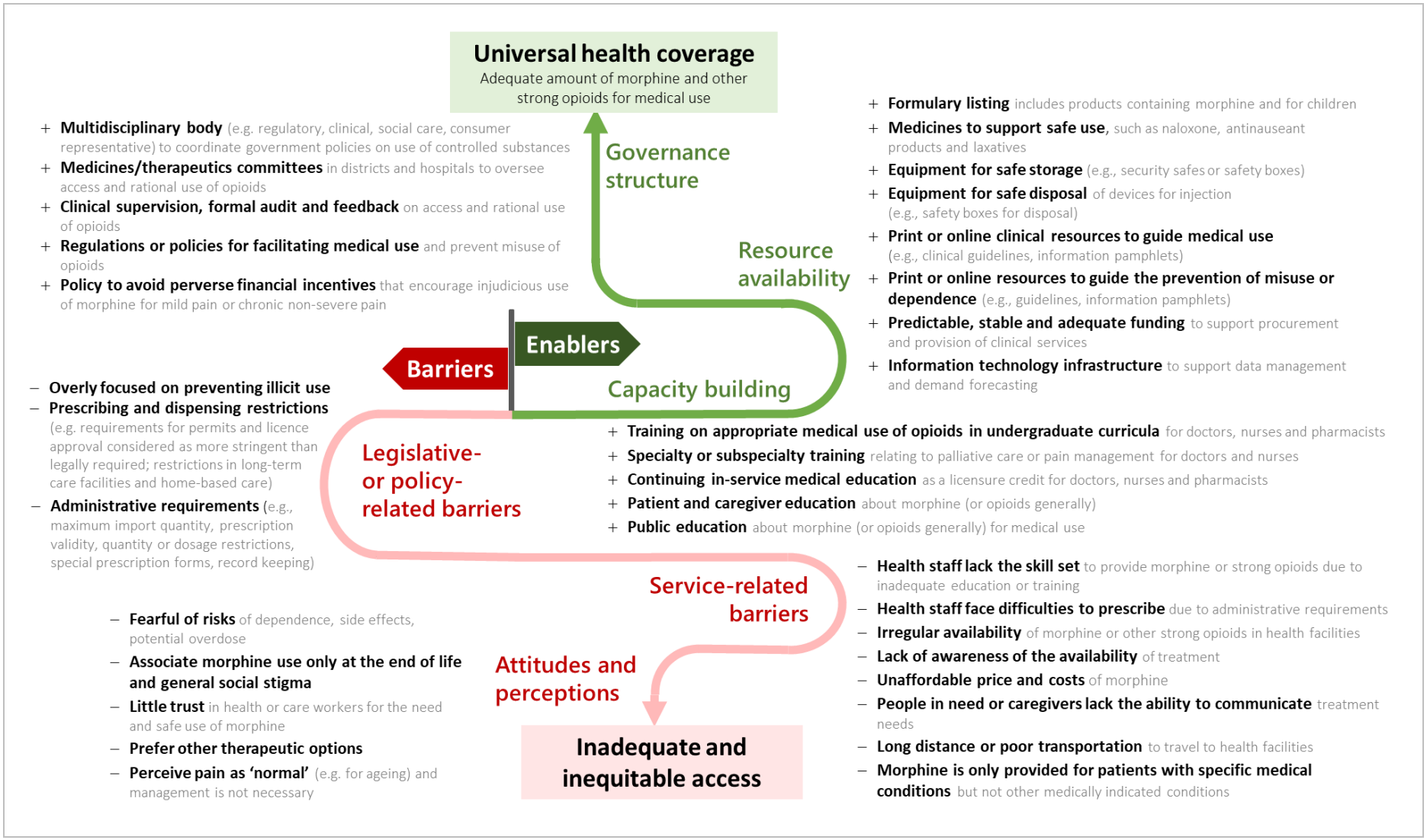
Countries in the African Region, Region of the Americas and South-East Asia Region, among others would benefit from additional resources to guide clinical services and harm prevention (e.g. guidelines and information pamphlets). Specifically, if well implemented, these resources could address a barrier relating to service providers' concern about patients developing opioid use disorder (see further discussion in section 3.4). Some respondents explained further:

> Pain patients are undermedicated by hospitals. Doctors who are educated in opioid substitution treatment for drug users are less fear stricken and more ready to prescribe medical morphine to other pain patients.

> Service providers are prescribing opioids of lower potency too long before changing to strong opioids. Many people are started on codeine or tramadol, and the switch to stronger opioids is not considered early enough.

The survey also suggests that all regions could benefit from building stronger data infrastructure. Through data analytics, such infrastructure could confer a range of benefits, including improving supply chain transparency, better demand projection and supply planning, and monitoring utilization patterns to detect any inappropriate medical use, illicit use or diversion of products.

Fig. 3.1. Enablers and barriers influencing access to morphine for medical use



3.3 Workforce capacity development remains a priority

A skilled health workforce is an indispensable component of any health system aiming to enable timely and appropriate access to morphine and other opioids, including at primary care settings *(41,42)*. Workforce capacity development could be achieved through appropriate academic and work-based training, and refinements to require pain control and palliative care as basic responsibilities of all doctors (and in some cases specially trained, non-physician health professionals) who treat children and adults with serious illnesses.

Respondents of the WHO survey indicated that training on appropriate medical use of opioids was inconsistently incorporated in undergraduate and postgraduate curricula in all regions, with training offered more often as part of specialty or subspecialty education for doctors and nurses (33% to 69%). Continuing in-service medical education as a licensure credit was much less common (less than 33% generally, except in the European Region for doctors and the Eastern Mediterranean for pharmacists).

Countries should continue to develop workforce capacity not only to meet the current demand for pain and symptom relief, but also in readiness for the growing demand due to ageing populations and chronic conditions. This is especially important for lower-income countries undergoing demographic transition due to ageing, and for health care professionals working in primary care and long-term care settings. As noted in section 2.6, countries may also consider changing legislative and administrative requirements to support the expanded role of trained, non-physician health professionals to facilitate greater access to opioids, which is particularly important in settings where doctors may have high workloads. Furthermore, given the risk of developing opioid use disorder, health care workers should be trained to prescribe and dispense morphine (and other opioids) in a fashion that lowers risk of opioid use disorder; such training also should include how to manage this disorder appropriately. Health workers must also learn to effectively communicate with patients and caregivers so that they are well-informed about the potential risks, discussed in section 3.4.

3.4 Addressing misconceived beliefs about pain and opioids could improve acceptance to morphine

Personal, societal and professional attitudes and perceptions play critical roles in health-seeking behaviour and the uptake of medicines, particularly for opioids. Some historical events, cultural beliefs, misinformation and disinformation about pain, and social stigma related to opioids use are known to have caused mistrust of opioids and contributed to fear of using them, for example, associating opioid use with imminent death, that opioids can immediately and definitely cause dependence and that opioids are always harmful or even lethal *(43–45)*.

> *Opioids used to manage pain in palliative care do not hasten death. Even when titrated to avoid distress in ventilation withdrawal, opioids do not shorten life (43).*

It is important to note that some concerns about the potential harmful effects of opioids are valid, such as their potential to lead to opioid use disorder. For this reason, a certain amount of caution about the potential harms of opioid use (e.g. in chronic non-cancer pain) is good for public health insofar as it is well-informed and proportionate to risks. Such concerns should not undermine the benefits of opioid use when clinically indicated and when used safely by trained professionals.

The responses from the WHO survey confirmed the presence of negative attitudes and perceptions towards the use of morphine and opioids. For example, significant proportions of respondents indicated being fearful of developing dependence, not only among people in need and their caregivers (responses ranged from 46% to 59%), but also service providers (36% to 53%). The only exception to this was the European Region, reporting 38% and 16%, respectively. Concerns about the risks of dependence were more commonly reported among service providers in lower-income countries (low income 50%, lower-middle income 37%, upper-middle income 34%, high income 23%) and in countries of the African Region (51%), Eastern Mediterranean Region (53%) and Western Pacific Region (42%).

Service providers should also be better informed about the risk of significant respiratory depression, which is uncommon or rare, and clinically manageable when internationally accepted dosing guidelines are followed (see Section 1.2).

Respondents of the WHO survey highlighted that people in need and their caregivers also commonly had a misconceived belief that morphine was only suitable for use in people near the end of life (Region of the Americas 62%, South-East Asia Region 50%, Eastern Mediterranean Region 41%). Countries in some regions may also need to address people's concerns about side-effects (e.g. drowsiness, nausea and constipation), because any negative impacts of such side-effects on daily activities could be minimized through appropriate management. For example, 64% of respondents from the South-East Asia Region were concerned about side-effects.

The root causes of these beliefs and social stigma are complex and could be entrenched in some settings. As a starting point, engaging the community and people in need of morphine is needed to better understand the basis of their views. Such engagement could also identify how service providers, via education and broader health promotion activities, can dispel any misperceptions about and build trust in the use of morphine or other opioids for medical purposes. Respondents to the WHO survey indicated that a greater emphasis existed in countries on patient and caregiver education about the medical use of morphine and opioids, with less emphasis on informing the broader public. In contexts where negative attitudes and low acceptance of morphine for pain management persist, patient, caregiver or public engagement and education are equally important. Engagement and education can build trust in the importance of morphine or opioids for medical use, addressing barriers due to cultural beliefs about pain, and removing social stigma.

In addition, effective communication skills and cultural sensitivity of health professionals must be an integral part of workforce capacity development, as discussed in section 3.3. The WHO survey found that people in need of morphine and their caregivers have high levels of confidence in their health care workers to administer morphine safely. Having more effective communication skills and cultural sensitivity will build this trust further.

3.5 Pain management services should be made known and accessible to all people in need

Bringing services closer to people in need of treatment and care is an important health system strategy for making progress towards universal health coverage, including improving access to pain management or pain control services. Closer in this context refers not only to physical proximity, but also awareness of the availability of services and a streamlined process for service provision.

The WHO survey indicated that service-related barriers were significantly less likely in the European Region (60% of respondents indicated no barriers) and

high-income countries (45% of respondents indicated no barriers), compared to all other regions (i.e. 11–29%) and country income levels (i.e. 24–29%). In addition to a lack of regular availability of morphine and strong opioids in health facilities (noted previously), respondents indicated that long distance or poor transportation to access health facilities where morphine was available could be a barrier (41% in low-income and lower-middle-income countries; 54% in the African Region, 34% in the Americas Region, 33% in the Western Pacific Region, and 29% in the South-East Asia Region). This observation is supported by various studies that have noted the geographic disparities in the provision of pain management or palliative care services in various countries, as well as utilization patterns *(46–49)*. While services are generally concentrated in urban centres, health systems should explore various modalities of service provision to facilitate better access in non-urban areas; such service provision should include integrating palliative care and symptom relief into primary health care *(42)*, and expanding the the capacity of health workers through training to provide morphine and other opioids in specific circumstances (section 2.6). Respondents to the WHO survey in some regions (e.g. 43% in the African Region and 33% in the Western Pacific Region) noted that people in need or caregivers lacked awareness of treatment availability. Respondents also noted difficulties in prescribing due to administrative requirements (e.g. specific prescription forms); this was noted as a barrier specifically in the Region of the Americas (42%), Eastern Mediterranean (35%) and African (31%) Regions.

4. Priority areas of action to improve safe access to morphine for medical use

This report has summarized the current understanding of the extent of variations in global access to morphine for medical use. Reaffirming the findings from previous studies, the supply of morphine products has been found to be persistently unequal and inequitable, particularly in lower-income countries where the supply is far below the estimated medical needs (Chapter 2).

Although various enablers have been instituted to facilitate safe access to morphine in countries, many barriers to timely access are due to inherently suboptimal supply and health system designs or market conditions. In some contexts, such barriers have also been compounded by the effects of misinformed beliefs and disproportionate fear of using morphine when genuine medical needs exist (Chapter 3). There is therefore an urgent need to amplify enablers and remove barriers, with a view to easing all the preventable suffering caused by poor medical access to morphine and other strong opioids.

To this end, a list of potential areas for action has been identified from the literature. This list was shared with those responding to the WHO survey to prioritize according to their respective contexts. Fig. 4.1 and Fig. 4.2 show the survey respondents' prioritization by WHO region and country income level. Given the different country contexts, actions identified as priorities vary. For example, as shown by the encircled number in Fig. 4.1, respondents from all six WHO regions identified developing small-scale or state-wide programmes and establishing regional or local manufacturing of morphine products as among the top five priorities to improve access to morphine for medical use. The latter can be implemented in countries in conjunction with the commitments and suite of actions noted in resolution WHA74.6 on *Strengthening local production of medicines and other health technologies to improve access* (*50*). It is important to note that any efforts to improve the availability of morphine products must be accompanied by a health workforce that is well-trained in the use of opioids for medical purposes through professional education. Without it, increased product availability cannot translate into safe and effective pain relief for patients, and can cause wastage *(51)*.

To improve safe access, survey respondents indicated the following actions as among the top five priorities (regions concerned in parentheses).

- Establish and implement a package of essential services and products to facilitate rational use of morphine (Americas, South-East Asia, Eastern Mediterranean Regions).
- Establish affordable pricing for morphine for medical use (Americas, European, Western Pacific Regions).
- Establish hub-and-spoke distribution networks (African, European Regions);
- Expand access for people with health conditions other than cancer and HIV and for children (Americas, European Regions).
- Expand access for long-term care facilities, home-based care and hospice institutes (Western Pacific Region).

It is important to note that many of these areas for action are complementary to one another. For example, small-scale or state-wide programmes on improving access to morphine for medical use should include a package of essential services and products, formulated according to accepted standards or guidelines, such as the WHO Model Lists of Essential Medicines (children and adults) and the WHO Essential Package of Palliative Care *(42)*. Such programmes

should also establish affordable pricing and ensure access for all people in need of morphine (e.g. people with health conditions other than cancer and HIV), in all service contexts (e.g. long-term care) and across all ages (e.g. children and elderly).

Furthermore, each of these areas for action should encompass a set of supporting policies and activities that are carefully planned, carried out and regularly monitored and revised, based on national and regional contexts. For example, in developing small-scale or state-wide programmes on improving access to morphine for medical use, policies and activities must be in place to address any barriers arising from the lack of supply chain coordination or efficiency because of legal or unduly restrictive administrative requirements (see section 2.5 and section 3.1). Government officials should work with relevant stakeholders (e.g. health care professionals, manufacturers or suppliers, UN agencies) to find ways to streamline the process of procurement and supply. Indeed, respondents from the South-East Asia and Eastern Mediterranean Regions as well as those from lower-income countries highlighted the importance of strengthening governance, including establishing interdisciplinary, inter-institutional, multi-stakeholder committees to provide overall governance in conjunction with the government; and to engage in policy and legislative design or changes.

Respondents from lower-income countries also indicated raising awareness among policy-makers and health care workers about the availability and safe use of morphine and patient needs as one of the priority actions.

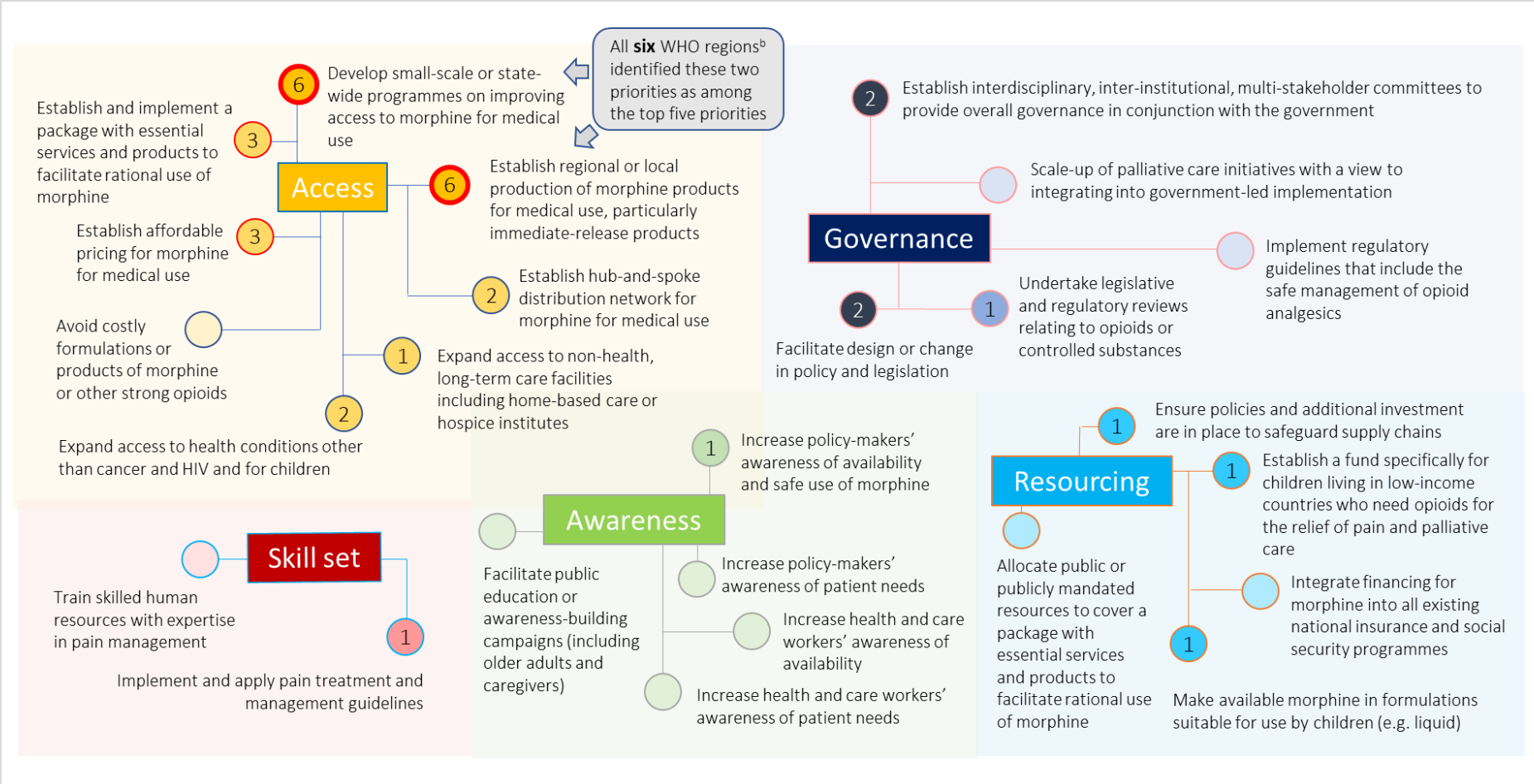
Respondents from most WHO regions suggested that developing skill sets to support the provision of morphine and other strong opioids was comparatively a lower priority, except for those responding from the Eastern Mediterranean Region, where further actions are needed to support the implementation and application of pain treatment and management guidelines. However, as indicated in section 3.3, workforce development should remain a priority for many countries, especially in view of the anticipated growing demand for pain management and palliative care due to an ageing population and chronic conditions. Workforce capacity development should also not be limited to clinical skills, but also effective communication skills and cultural sensitivity, as noted in section 3.4.

Resourcing is among the top five priorities noted by respondents from the African Region and low-income countries; this specifically included putting policies and additional investment in place to ensure safe supply chains, and establishing funding specific for children living in low-income countries who need opioids for the relief of pain and palliative care. Respondents in the Eastern Mediterranean Region indicated providing morphine in formulations suitable for use by children (e.g. liquid) is a priority.

At the international level, WHO will continue to work with Member States, INCB, the United Nations Office on Drugs and Crime and other related UN agencies, and other stakeholders to facilitate collective actions for addressing the priority actions noted above. Table 4.1 presents specific areas for action discussed in this section with suggested primary and secondary actors required to realize these actions in the short, medium and long term.

Finally, any policies and collective actions to achieving safe access to morphine globally must place health and human rights at the centre of activities, as the persistent disparity in access to morphine for medical use globally, and the associated suffering, is unacceptable.

Fig. 4.1. Priority areas for action[a] to improve safe access to morphine for medical use, as indicated by survey respondents

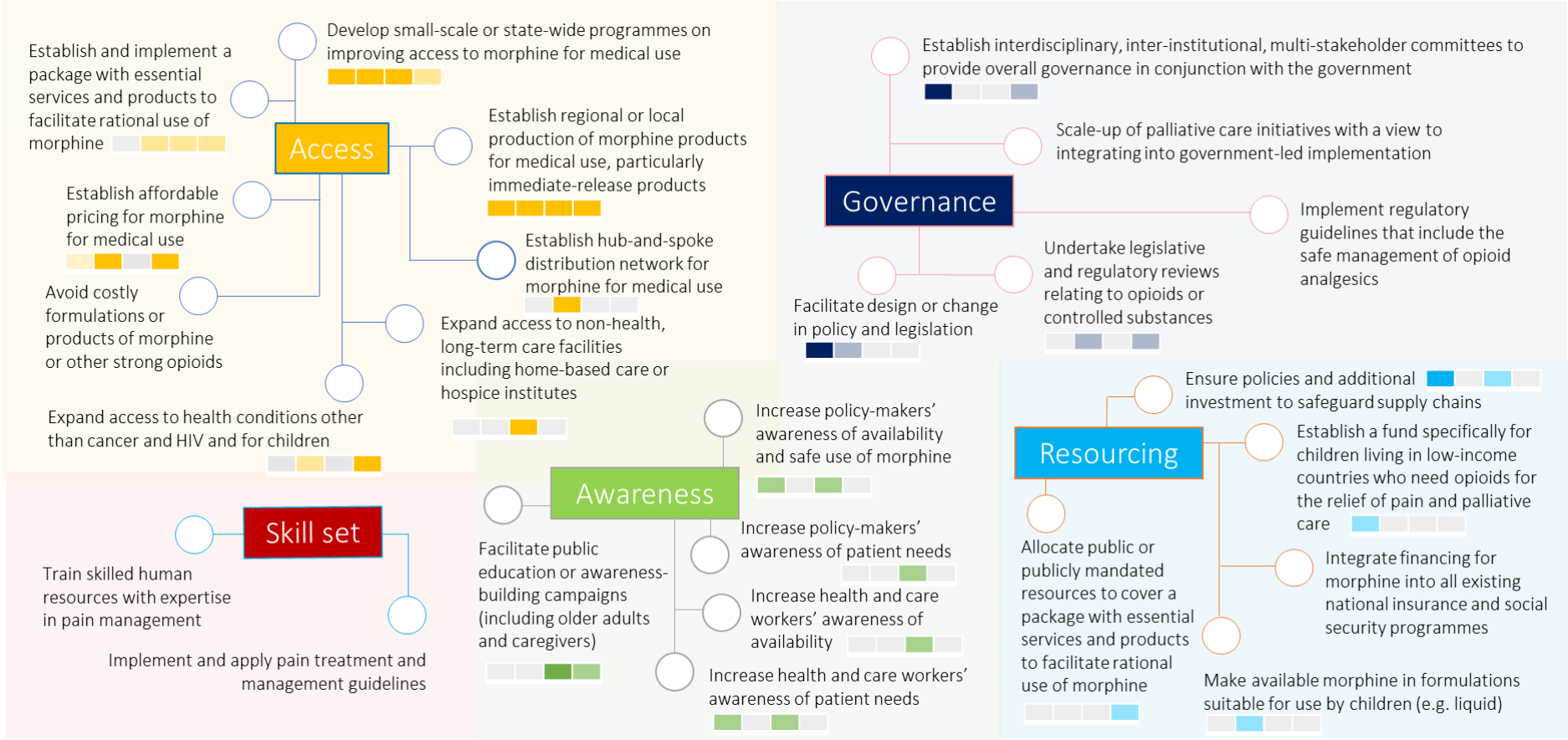


[a] Circled numbers show the number of WHO regions indicating that the action was among its top five priorities of those listed in the WHO survey. Refer to Web Annex B for details of priorities for each region. Empty circles mean that respondents did not identify the areas for action as a priority.

[b] WHO African Region, Region of the Americas, South-East Asia Region, European Region, Eastern Mediterranean Region, Western Pacific Region

Source: The WHO survey (Web Annex B).

Fig. 4.2. Priority areas for action indicated by survey respondents, by World Bank income group[a]



[a] Coloured cells correspond to the country income categories indicated in the order below. The brightness of the colour reflects the relative priority respondents from those income groups attributed to each action. Grey means not a priority for that income group.

Low income	Lower-middle income	Upper-middle income	High income

Source: The WHO survey (Web Annex B).

Table 4.1. Areas for action to improve safe access to morphine for medical use, with suggested stakeholders to be involved in taking actions

Option	Time frame for action[a]			Proposed actions taken by:						
	Short	Medium	Long	WHO and other UN agencies	Government[b]	Payer[b]	Industry	Health care professionals	People in medical need	NGO
a. Improving access to morphine and associated services										
(a.1) Develop small-scale or state-wide programmes on improving access to morphine for medical use	▭	▭		✶	✱	✱	✶	✱	✱	✶
(a.2) Establish and implement a package with essential services and products to facilitate rational use of morphine	▭	▭		✶	✱	✱	✶	✱	✱	✶
(a.3) Establish regional or local production of morphine products for medical use, particularly immediate-release products		▭	▭	✱	✱		✱	✱		
(a.4) Establish hub-and-spoke distribution network for morphine for medical use		▭	▭		✱		✱	✱	✶	✶
(a.5) Establish affordable pricing for morphine for medical use	▭				✱	✱	✱	✱		
(a.6) Avoid costly formulations or products of morphine or other strong opioids	▭				✱	✱		✱	✶	
(a.7) Expand access to health conditions other than cancer and HIV, and for children	▭				✱	✱		✱	✶	
(a.8) Expand access to non-health, long-term care facilities including home-based care or hospice institutes	▭	▭			✱	✱		✱	✶	

Option	Time frame for action[a]			Proposed actions taken by:						
	Short	Medium	Long	WHO and other UN agencies	Government[b]	Payer[b]	Industry	Health care professionals	People in medical need	NGO
b. Improving awareness										
(b.1) Facilitate public education or awareness-building campaigns (including for older adults and caregivers)	▭			✶	✱			✱		✱
(b.2) Increase policy-makers' awareness of availability and safe use of morphine	▭			✱	✱			✱		✱
(b.3) Increase policy-makers' awareness of patient needs	▭			✱	✱			✱		✱
(b.4) Increase health and care workers' awareness of availability	▭				✱			✶		✶
(b.5) Increase health and care workers' awareness of patient needs	▭			✶	✱			✶		✶
c. Improving governance										
(c.1) Establish interdisciplinary, inter-institutional, multi-stakeholder committees to provide overall governance in conjunction with the government	▭				✱			✱		✱
(c.2) Scale-up of palliative care initiatives with a view to integrating into government-led implementation	▭				✱	✶		✱		✶

Option	Time frame for action[a]			Proposed actions taken by:						
	Short	Medium	Long	WHO and other UN agencies	Government[b]	Payer[b]	Industry	Health care professionals	People in medical need	NGO
(c.3) Facilitate design of or change in policy and legislations		▭		✶	✱			✱		✶
(c.4) Implement regulatory guidelines that include the safe management of opioid analgesics	▭			✱	✱			✱		
(c.5) Undertake legislative and regulatory reviews relating to opioids or controlled substances		▭			✱	✶	✶	✱	✶	✶
d. Improving resourcing										
(d.1) Integrate financing for morphine into all existing national insurance and social security programmes	▭				✱	✱		✶		✶
(d.2) Establish a fund specifically for children living in low-income countries who need opioids for the relief of pain and palliative care		▭			✱	✱		✶		✱
(d.3) Make available morphine in formulations suitable for use by children (e.g. liquid)		▭		✶	✱	✶	✱	✶		
(d.4) Allocate public or publicly mandated resources to cover a package with essential services and products to facilitate rational use of morphine	▭				✱	✱				
(d.5) Ensure policies and additional investment are in place to safeguard supply chains		▭		✶	✱		✱	✱	✶	

Option	Time frame for action[a]			Proposed actions taken by:						
	Short	Medium	Long	WHO and other UN agencies	Government[b]	Payer[b]	Industry	Health care professionals	People in medical need	NGO
e. Improving skill set										
(e.1) Train skilled human resources with expertise in pain management	▭			✶	✱	✶		✱	✱	
(e.2) Implement and apply pain treatment and management guidelines	▭			✱	✱			✶	✶	

[a] Short term: within 1 year; medium term: 1–3 years; long term: more than 3 years.
[b] Government and payer may be the same.
✱: Primary actor; ✶: Complementary actor

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