

A world map showing the continents in a light blue color against a white background. The map is centered on the Atlantic Ocean.

Access to pain relief – an essential human right

A report for World Hospice and Palliative Care Day 2007
Published by Help the Hospices for the Worldwide Palliative Care Alliance



About Help the Hospices

Help the Hospices supports over 240 local hospices across the UK. This support is provided through a wide range of services all aimed at helping hospices provide the very best care for patients and their families. These include training and grants for hospice staff and volunteers, national programmes of advice, information and support, special award programmes to fund new services and the coordination of national fundraising initiatives. We are also involved in supporting services around the world, especially in resource-poor countries. In all that we do, we aim to make a real difference to the care given to patients and their loved ones.

About the Worldwide Palliative Care Alliance

The Worldwide Palliative Care Alliance aims to promote universal access to affordable quality palliative care through the support of regional and national hospice and palliative care organisations.

The publishers and authors make no representation, expressed or implied, with regard to the accuracy of the information contained in this publication and cannot accept responsibility for any errors or omissions that may occur.

The views expressed in this publication may not necessarily be those of Help the Hospices. Readers should consult their professional advisers if they deem this to be necessary before entering into any legal commitments.

No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise without the prior permission of Help the Hospices.

The right of Vanessa Adams to be identified as the author of this Work has been asserted by her in accordance with sections 77 and 78 of the Copyright, Designs and Patents Act 1988.

© 2007 Help the Hospices

ISBN: 978-1-871978-67-4

Registered Charity in England and Wales, Help the Hospices No. 1014851

Company Limited by Guarantee registered in England No. 2751549. Registered office: Hospice House, 34-44 Britannia Street, London WC1X 9JG.

Acknowledgements

We would like to extend our grateful thanks to all those who have contributed valuable advice and information, and to all those who have offered case studies and photographs, not all of which we have been able to include. Without these contributions the publication would not have been complete. Thank you.

Below is a list of the main contributors:

Author: Vanessa Adams – Palliative Care and Oncology Specialist Pharmacist, Cardiff, UK

Dr Mariela Bertolino – Programa Argentino de Medicina Paliativa-Fundación FEMEBA

Dr Henry Ddungu – Advocacy Manager, African Palliative Care Association

Dr Liliana De Lima – Executive Director, International Association for Hospice and Palliative care

Lucy Finch – Founder and Director of Ndi Moyo Hospice, Malawi

Professor Reena George – Christian Medical College, India

Carolyn Green – Senior Technical Advisor, Care and Support, International HIV/AIDS Alliance

Dr Liz Gwyther – Chairperson of Hospice Association of South Africa

David E Joranson – Senior Scientist, Director, Pain and Policy Studies Group

Dr Anne Merriman – Founder and Director of Policy and International Programmes, Hospice Africa Uganda

Dr María Minatel – Programa Argentino de Medicina Paliativa-Fundación FEMEBA

Dr Daniela Mosoiu – National Clinical Development Director, Hospice Casa Sperantei, Romania

Dr Lydia Mpanga-Sebuyira – Clinical Director, Hospice Uganda

Dr Faith Mwangi-Powell – Executive Director of the African Palliative Care Association

Professor M. R. Rajagopal, Chairman, Pallium, India

Dr Maryna Rubach – Head of Chemotherapy Day Ward, Cancer Center – Institute, Warsaw

Dr Willem Scholten – Technical officer, Department of Medicines Policy and Standards, World Health Organization

Professor Olaitan Soyannwo – Department of Anaesthesia, College of Medicine, University of Ibadan/University College hospital, Ibadan, Nigeria

Dr Roberto Wenk – Programa Argentino de Medicina Paliativa-Fundación FEMEBA.

Contents

Key

Foreword

1. Introduction

- 1.1 Pain incidence
- 1.2 Opioid analgesics
- 1.3 The importance of being able to access palliative care, morphine and other analgesics
- 1.4 Unavailability of opioids

2. Help the Hospices' survey on access to analgesics

- 2.1 Survey results: access to analgesics

3. Why are opioids not accessible to palliative care patients?

- 3.1 National laws
- 3.2 Fear of addiction, tolerance and side effects
- 3.3 Poorly developed healthcare systems and supply
- 3.4 Expense
- 3.5 Lack of knowledge – healthcare workers, public and policy makers

4. Essential elements required to increase availability

- 4.1 Education
- 4.2 Addressing the fears
- 4.3 Accountability
- 4.4 Reviewing laws and policies
- 4.5 Strengthening health facilities

5. Recent advances in increasing access to analgesics

- 5.1 Individuals
- 5.2 WHO and INCB
- 5.3 Resolutions advocating for an increase in accessibility to opioid analgesics
- 5.4 Changes in national laws
- 5.5 Some regional initiatives
- 5.6 Some country initiatives
- 5.7 Proposed projects

6. Educational opportunities

7. What you can do

- 7.1 Advocacy
- 7.2 Education
- 7.3 Support for hospices through international organisations and directly
- 7.4 Research

8. References

9. Further resources

Key

APCA

African Palliative Care Association

AIDS

Acquired Immunodeficiency Syndrome

ART

Anti-retroviral therapy

ECOSOC

Economic and Social Council

EML

Essential Medicines List

HCWs

Healthcare workers

HIV

Human Immunodeficiency Virus

Hospice Information

Information service provided jointly by Help the Hospices and St Christopher's Hospice, London, UK

IAHPC

International Association for Hospice and Palliative Care

IASP

International Association for the Study of Pain

INCB

International Narcotics Control Board

MoH

Ministry of Health

NGO

Non-governmental organisation

NMDA

N-methyl-D-aspartic acid

NSAIDs

Non-steroidal anti-inflammatory drugs

PPSG

Pain and Policies Study Group

UN

United Nations

WHO

World Health Organization

WHO EML

WHO Model List of Essential Medicines

WWPCA

Worldwide Palliative Care Alliance

All quotations in blue tinted boxes within this document are comments made by HCWs in response to the Help the Hospices' survey on access to analgesics.

All information in yellow tinted boxes show the results from the survey.

Definitions for the purpose of this document

Available/availability – a drug can be available in a country or community but the patient may not be able to access it, eg there is a stock in the pharmacy but the patient cannot afford to buy it, or there are no qualified HCWs allowed to prescribe the drug.

Access/accessibility – is when a drug is able to reach a patient: a HCW is able to prescribe it; there is a stock from which a HCW is able to dispense it; the HCW is able to give the drug to the patient (transport, etc, is not a barrier).

Affordability – when an accessible drug can be paid for by the patient and/or their family.

Foreword

We are pleased to recommend this significant report that highlights the lack of pain control currently available around the world. Urgent government action is needed to ensure that all sections of society have equal and adequate access to pain control. It is estimated that 100 million people could benefit from basic palliative care every year. New data in this report shows that even in established palliative care units, patients lack access to pain control that they desperately need.

This report is launched to coincide with World Hospice and Palliative Care Day 2007. The first World Hospice and Palliative Care Day took place in 2005, with more than 1,100 events taking place in 74 countries. Archbishop Desmond Tutu described the day as “an important global event”. Activities are wide ranging from music and arts performances to seminars, conferences, TV documentaries and successful lobbying of state officials.

World Hospice and Palliative Care Day is coordinated by the Worldwide Palliative Care Alliance of national hospice and palliative care associations.

The secretariat for World Hospice and Palliative Care Day and the Alliance is provided by Help the Hospices, the UK charity for the hospice movement, which supports UK hospices in their vital work on the front line of caring for people who face the end of life.

To find out more and get involved in World Hospice and Palliative Care Day 2007, visit www.worldday.org or email worldday@helpthehospices.org.uk

For information on Help the Hospices visit www.helpthehospices.org.uk or for the Worldwide Palliative Care Alliance visit www.wwpca.net

Dr Cynthia Goh
David Prall
Co Chairs – The Worldwide Palliative Care Alliance

With this publication Help the Hospices gives an overview of the widespread lack of access to analgesia. If we do not work together to change this, many of us will discover, sooner or later, what it means to need good analgesia; if we personally do not encounter this lack of access, we will watch a relative or a friend that does.

In this publication you will find the results of a survey held among palliative care workers. The results picture a serious situation. It is noted that the survey population will give a positive bias of the situation, as palliative care workers are likely to have relatively good access to opioids and other analgesics compared to an average doctor.

My impression, mainly derived from the per capita statistics of opioid consumption, is that the situation is even worse than that found by the survey. The differences between the countries with the highest consumption and the remainder of the countries – the large majority – are very wide. These statistics show that only 10 to 15 countries have a reasonable per capita consumption, and even in these countries underuse for medical reasons are occasionally reported.

For many people, pain is part of their daily life. Every minute they are reminded of it; there is no means of escape. We can wonder why so many people do not have access to analgesia and have to suffer so much pain, when there is an excess of opioids in the world. One reason is the longstanding fear of drug dependence and drug abuse. This fear is, in my view, unfounded. In fact, the relation between drug abuse/drug dependence and licit medical use of controlled medicines is weak.

More importantly, our countermeasures against the diversion of drugs required for medical use are out of balance. Globally, several hundreds of millions of people will require analgesia at least once in their lifetime, whilst only a small fraction of this number misuses opioids. There are restrictions on the handling of opioids for licit medical use which aim to prevent any possibility of abuse. However, many countries impose stricter regulations than required by the drug conventions to give good accountability. Yet we know that the source of the majority of opioids used in abuse is from illicit cultivation and not from the medical circuit. Furthermore, we know that it is quite rare for licit opioid medicines to be diverted for abuse. Although it is important to remain on one's guard, we should not exaggerate but pay attention to the side of the balance where the feather is, and not to the side where the lead weight is already.

Fortunately, the international community agrees that we need change. Both the UN's Economic and Social Council and the World Health Assembly recently accepted resolutions that have provided the basis for further action by the World Health Organization. I have pleasure to work on this, and to experience strong support from many individuals, governments and also NGOs such as Help the Hospices. They are in support of improving cancer care, HIV care and palliative care for all.

Together we have a strong case, and together we will be able to make the change.

[Dr Willem Scholten](#)
[Technical Officer](#)
[Department of Medicines Policy and Standards](#)
[World Health Organization](#)



1. Introduction

One essential component of palliative care is pain relief. Freedom from pain allows the highest quality of life possible for as long as possible. As we are all aware, pain increases distress and anxiety not only in the patient but also their friends and family. Pain decreases the ability of a patient, their friends and family to sleep, carry out everyday activities, work, communicate effectively, concentrate, resolve any conflict and address many of the issues which, if thought through, allow peace as the end of life approaches (ie organising financial affairs, ensuring children are cared for, making a will, etc).

Access to pain relief has been promoted as an essential human right by the IASP, the WHO, and the European Federation of IASP Chapters, EFIC.^(1,2) (See www.iasp-pain.org for details and justification). Human rights refers to the concept of a universal right regardless of legal jurisdiction or other localising factors, such as ethnicity, nationality and sex.

The UN Universal Declaration of Human Rights conceptualises human rights as based on inherent human dignity. We all know from everyday experiences that one person's perception and expression of pain is very different to another person's. One of the essential concepts is to listen and believe the patient – only they know what the pain feels like to them.

The right to pain relief applies to all conditions where pain occurs (acute, chronic non-malignant, chronic due to degenerative progressive disease, etc). In some countries/states, oral morphine can only be prescribed by specialist palliative care or oncology doctors (Mongolia, Tamil Nadu, Peru, Honduras and Kyrgyzstan).⁽³⁾ In these areas, patients requiring pain relief for any other disease or condition will be denied access.

For the purpose of this publication the rights of patients with pain and who have progressive, incurable diseases will be addressed. Many of the points highlighted here are applicable to pain relief required for all circumstances.

“...in my 10 yrs experience... I have never seen a doctor suggest or prescribe opioids other than for cancer patients, and they dismiss out of hand suggestions to consider them for end term AIDS patients, or end stage patients with severe respiratory distress.”
Private communication with HCW.

1.1 Pain incidence

Pain is a common symptom of many advanced, potentially incurable diseases. It occurs in most cancer patients especially during advanced or metastatic disease. The prevalence of pain depends on the type of cancer and stage, but overall an estimated 70% of advanced cancer patients experience pain.⁽⁴⁾

In developing countries the incidence of pain is higher. A South African study of AIDS patients found a pain incidence of 98%⁽⁵⁾; 60% of patients present to Hospice Uganda (HIV/AIDS and cancer patients) with severe pain.⁽⁶⁾

More than 50% of patients with advanced AIDS, heart disease, chronic obstructive pulmonary disease and renal disease experience pain.⁽⁷⁾

In 2005:

- ~ 38.6 million (33.4 – 46 million) people worldwide were living with HIV
- ~ 4.1 million new HIV infections.⁽⁸⁾

In 2002:

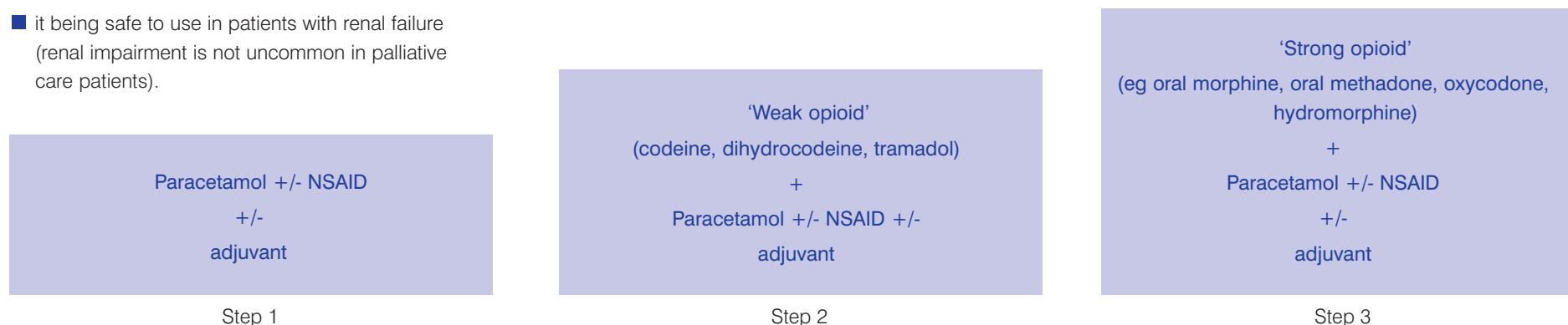
- ~ 10.9 million new cancer cases worldwide
- ~ 24.6 million people alive with cancer (within three years of diagnosis)
- Incidence of cancer was highest in North America for men and women whilst the risk of dying from cancer was highest in Eastern Europe for men and highest in Eastern Africa for women.⁽⁹⁾

1.2 Opioid analgesics

The majority of pain can be controlled with careful pain management, addressing psychological and social factors and using relatively inexpensive oral medicines. ‘Strong opioids’ are crucial to provide adequate pain relief. The WHO recommends oral morphine as the ‘strong opioid’ of choice.

Within Latin America oral methadone is often used in place of oral morphine, owing to:

- cheaper cost
- easier availability
- additional properties (antagonises NMDA receptor) which means it is better at relieving some neuropathic pains
- excellent oral absorption
- long half-life (leads to a smaller number of doses taken each day compared to normal release morphine)
- it being safe to use in patients with renal failure (renal impairment is not uncommon in palliative care patients).



WHO Analgesic Ladder: over 20 years, studies have found this to be effective in 45 – 100% of patients.⁽¹⁰⁾

Oral morphine and oral methadone:

- are 'strong' opioid analgesics (pain relieving drugs);
- have been proven to be very effective analgesics, wholly or partly relieving most types of pain;
- are cheap;
- are both established medicines with known, predictable and preventable side effect profiles;
- have a wide therapeutic index – the range of doses over which they can be effective without being toxic is exceptionally large; therefore doses can be individualised easily;
- are easy to administer;
- are easy to adjust (doses) for each individual and if analgesic requirements change.

Oral morphine has been included on the WHO EML since 1985.⁽¹¹⁾

Essential medicines are intended to be available:

- at all times in adequate amounts
- in the appropriate dosage forms
- with assured quality
- at a price the individual and community can afford.⁽¹²⁾

The WHO EML guides countries as to the drugs to include in their own essential medicines list, taking account of disease prevalence.⁽¹³⁾

Essential medicines are those that satisfy the priority healthcare needs of the population.⁽¹²⁾

Many patients are unable to access morphine, methadone or an equivalent opioid.

Based on INCB reports, the WHO estimated in 2006⁽¹⁴⁾:

- 80% of cancer patients have no access to the pain relieving drugs required
- ~7% of all people in the world will suffer from cancer pain that can be treated, but will not be treated.*

* Based on 80% of world population having no access to analgesia, 12% of all death causes being from cancer and 70% of cancer patients suffering pain – $(0.8 \times 0.12 \times 0.7) \times 100 = \sim 7\%$.

1.3 The importance of being able to access palliative care, morphine and other analgesics

At the age of 21, Mr AB was diagnosed with a giant cell tumour and underwent a midtarsal amputation in 1979. When it recurred, in 1985, he went through an above-knee amputation. He was able to have a reasonable quality of life with an artificial limb until 1992 when the disease recurred. He was in pain; radiotherapy helped only briefly.

His severe pain meant he lost his means of livelihood and life became a huge burden. He had to send three of his four children to an orphanage.

He was one of the first patients in the Pain and Palliative Care Clinic (PPCS) when it opened in 1994 in Calicut Medical College. By then Mr AB had been in pain for about two years. In the PPCS he was started on oral morphine and other medication. His pain was soon relieved. PPCS found him a livelihood by installing a coffee-vending machine in the hospital. It brought the means not only to get his children back from the orphanage but also to allow them all to be educated.

His disease is slowly progressive. His morphine requirement slowly went up to finally reach 1,000mg a day, and at that time a pathological fracture in his femur was found. Excision of the fractured bone brought down the pain and since 1999 (ie for the last seven years), his pain has been well controlled on a steady dose of 600mg of morphine a day.

He is 48 now. Recently he had a single fraction of palliative irradiation to the stump which has ulcerated. He is pain free on morphine and is able to work from morning to evening. His eldest son has a job and the other children are continuing their education.

Case study provided by Prof M. R. Rajagopal,
Chairman, Pallium, India



JM is 33 year old male with Kaposi's Sarcoma, a cancer occurring more frequently in HIV patients. He has a huge woody oedematous left leg. JM was one of the first cancer and HIV/AIDS patients to join the Ndi Moyo Palliative Care programme, Malawi, in August 2006.

However, he enrolled with me as a patient long before the Centre opened. JM lives with his wife and their four children. They are very poor and at first JM was living in denial of his condition.

JM noticed the swelling of his left leg in 1999 and went to traditional healers. His leg got worse. In 2000 he visited Salima District Hospital where Kaposi's Sarcoma was diagnosed. As he did not get relief from his symptoms, he alternated between the hospital and traditional healers until October 2002, when a friend referred him to me for pain relief at the Salima Parish home based care clinic where I was working as a volunteer nurse.

He presented with moderate burning pains, bone pain and extensive fungal infections. These were managed with amitriptyline 12.5mg bd, ibuprofen 400mg tds and antifungals with good effect. At this time he was tested HIV positive. We controlled his pain well and treated opportunistic infections until February 2004, when he developed severe pain and blisters all over his left leg.

As a result he became one of the very first patients in Salima to be given morphine, which he was only able to access from 'Lighthouse' in Lilongwe (over 100km from his home).

He started on 5mg of oral morphine every four hours with 10mg at night. He responded well and is at present pain free on oral morphine (7.5mg four hourly with 15mg at night). For a couple of months the dose needed to be increased to 10mg four-hourly and 20mg at night. Throughout he has continued to have ibuprofen, and since July 2004 has had free ART.

Access to analgesia and palliative care has really benefited JM; he is one of very many in Malawi who would benefit if they were able to access it. Besides medical treatment, we have provided him and his family with emotional support and used a comfort fund to assist them with transport and food at times of need. In addition, after a long advocacy fight by us, he and his family now benefit regularly from food aid distributed by the World Food Programme. He is now happy, able to walk, cycle, able to take care of his family, and we continue to travel with them on his journey.

Case study provided by Lucy Finch, Nurse and Founder of Ndi Moyo Palliative Care Centre, Malawi.



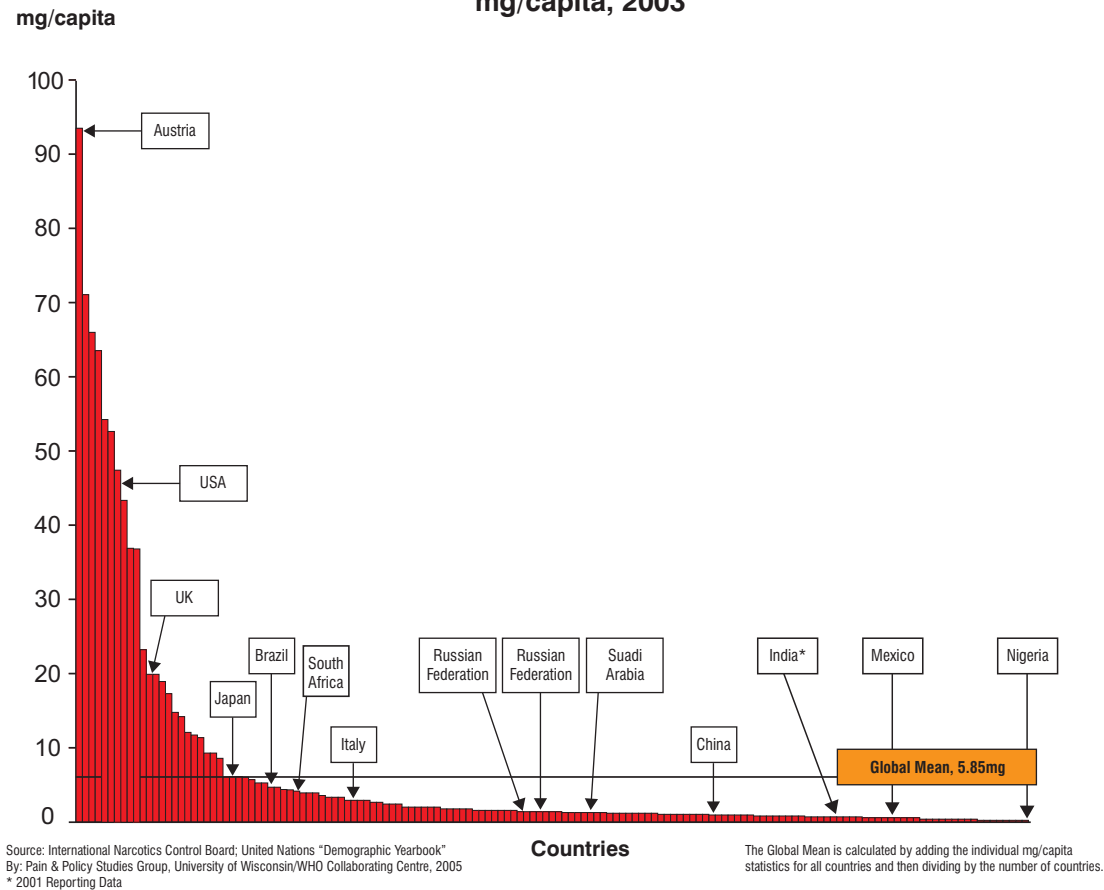
Mr GH was 56 years old when he was diagnosed with advanced colorectal cancer. He was referred to the palliative care team by the oncologists in June 2003, in severe pain. Oral morphine and adjuvant analgesics were started, and these controlled his pain allowing him to go home. He died nearly a year later at home in April 2004. The picture shows him preparing for his family Christmas.

Case study provided by Roberto Wenk, MD, Mariela Bertolino, MD, and María Minatel, MD.
Programa Argentino de Medicina Paliativa-Fundación FEMEBA, Buenos Aires, Argentina



1.4 Unavailability of opioids

**Graph 1: Global Consumption of Morphine
mg/capita, 2003**



The INCB collates information detailing each country's medical use of opioids. For a number of years the INCB has expressed concern that there is inadequate access to morphine and other opioids for pain relief in many parts of the world. The graph to the left details the amount of morphine used for medical reasons by a country divided by the population, ie the average medical use of morphine per person in each country. The huge variation illustrates how many people are being denied adequate pain relief – the majority (but not all) of these people are in developing countries.

UN ECOSOC Resolution 2005/25 'Treatment of pain using opioids'

- Medical use of narcotic drugs (opioids) is indispensable for the relief of pain and suffering.
- Morphine should be available at all times in adequate amounts and appropriate dosage forms for the relief of severe pain.
- Low national consumption of opioids is a matter of great concern.

2. Help the Hospices' survey on access to analgesics

In 2006 Help the Hospices, through the WWPCA, surveyed hospices, units and HCWs providing palliative care within Asia, Africa and Latin America to ascertain their ability to prescribe and dispense pain relieving drugs. All the palliative care providers listed on the Hospice Information website, contacts from the African Palliative Care Society, the Latin American Association for Palliative Care, the Asociación Argentina de Medicina y Cuidados Paliativos and those known personally to the researcher were contacted.

HCWs were asked about access to drugs recommended on the WHO EML (this is taken as the required minimum level of analgesics for palliative care – drugs which should be available at all times, in adequate amounts). In addition, drugs which are not currently part of the WHO EML but have been recommended to the WHO to be included in the next EML by an 'expert group' through the IAHPCC were included.^(15, 16)

Details of the questionnaires are available from Help the Hospices.

Sixty-nine questionnaires were returned – 24 from Asia, 28 from Africa and 17 from Latin America. This represented a 23% return rate from email addresses contacted which were not returned as invalid. Abbreviated results are shown in graphs 2 to 16.

Responses were from a range of types and size of organisations including:

- NGO networks, contacting 6,000 – 7,000 patients a month;
- free standing hospices with and without inpatient beds, with average patient numbers per month ranging from six to 1,000;
- hospice/home care teams attached to a hospital, with average patient numbers ranging from six to 1,000 per month;
- state hospitals with average patient numbers ranging from six to 400 a month.

When looking at the results note:

- The graphs are likely to greatly 'overestimate' patient access to opioids and other analgesics when considering the whole region.
- Questionnaires were completed by HCWs specialising in palliative care. In some countries there are only one or two palliative care providers listed on the Hospice Information website. In a large number of countries there are no palliative care providers on the website. Thus, if some of the respondents are unable to access the essential drugs, it is likely that the rest of the country is unable to access opioids and other analgesics (with the possible exception of a few private clinics or donations).
- The questionnaire aimed to capture information from rural as well as central palliative care providers; thus there are more questionnaires from some countries than others – and these are the countries where palliative care services are more developed.

The results, therefore, reflect reasonable access in some countries, but that in other countries access is at a bare minimum.

- Nine of the 28 questionnaires from Africa were from South Africa, reflecting the larger number of palliative care services there than in other African countries. Despite this, a report in the South African Sunday Times newspaper, October 2006⁽¹⁷⁾ (with quotes from Gareth Morgan, the governing Democratic Alliance Spokesperson), highlighted how many patients still cannot access analgesics:

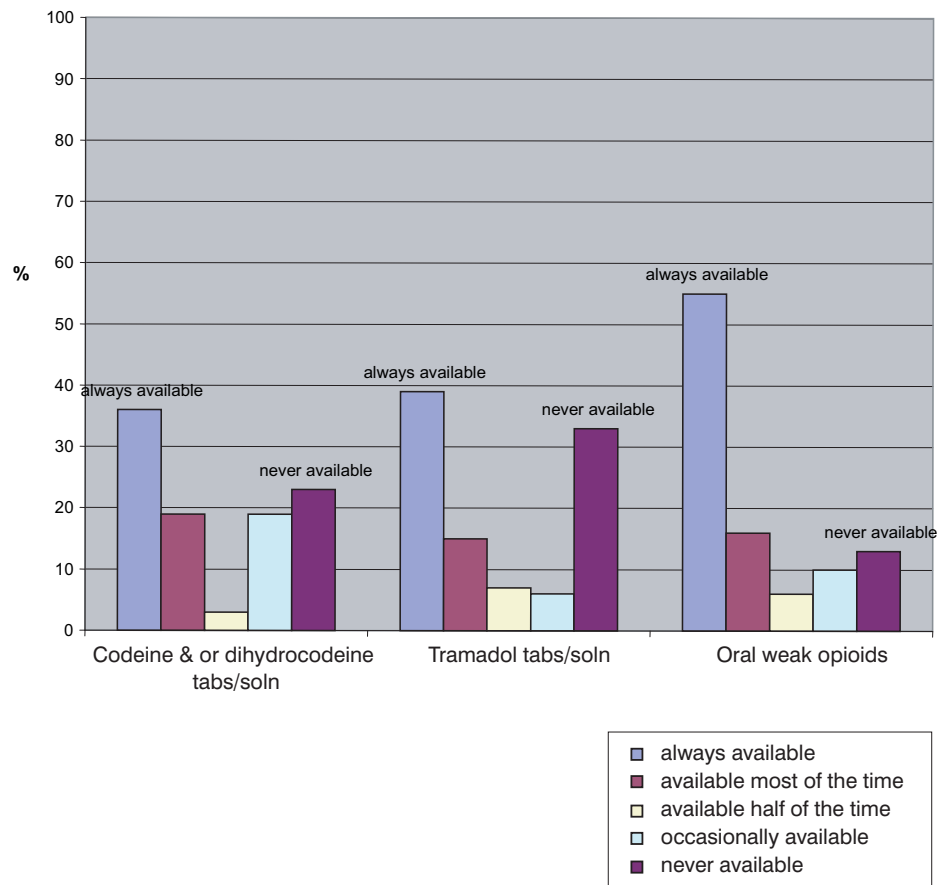
"...over 300,000 people died each year in South Africa from AIDS, and many thousands more from a range of other incurable illnesses. It was estimated that only five per cent of these people had access to adequate palliative care, mostly those treated in the private sector. This neglect, which saw thousands of South Africans left to die with unnecessary pain and fear, was inhumane".

- The 17 questionnaires from Latin America represented 10 countries.
- The 28 questionnaires from Africa represented 11 countries.
- The 24 questionnaires from Asia represented 10 countries (with six different Indian states – drug laws vary between the Indian states).

In one main regional hospital in Malawi aspirin is the only NSAID always available, with ibuprofen occasionally available and other NSAIDs 'never available'.

2.1 Survey results: access to analgesics

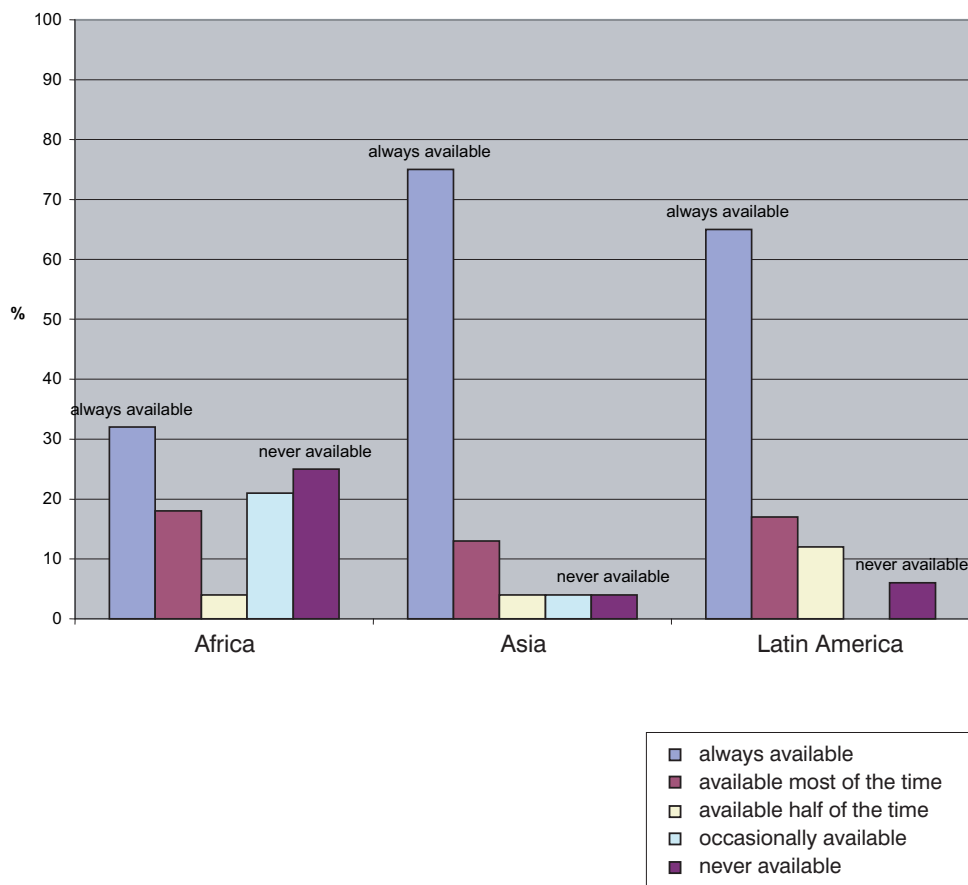
Graph 2: Access to 'weak opioids'



The WHO EML recommends codeine as a 'weak opioid'. For the purpose of this survey dihydrocodeine was included as being very similar in properties, strength and side effects to codeine. Tramadol was also included as this is more readily available in some areas owing to the different classification by the INCB and hence the different levels of accountability required. For this reason the recent 'expert meeting' to advise the WHO on the updating of the palliative component of the WHO list recommended the inclusion of tramadol as a 'core' drug.⁽¹⁶⁾

Only 55% of organisations providing palliative care had one of the weak opioids always available.

Graph 3: Access to 'weak opioids'

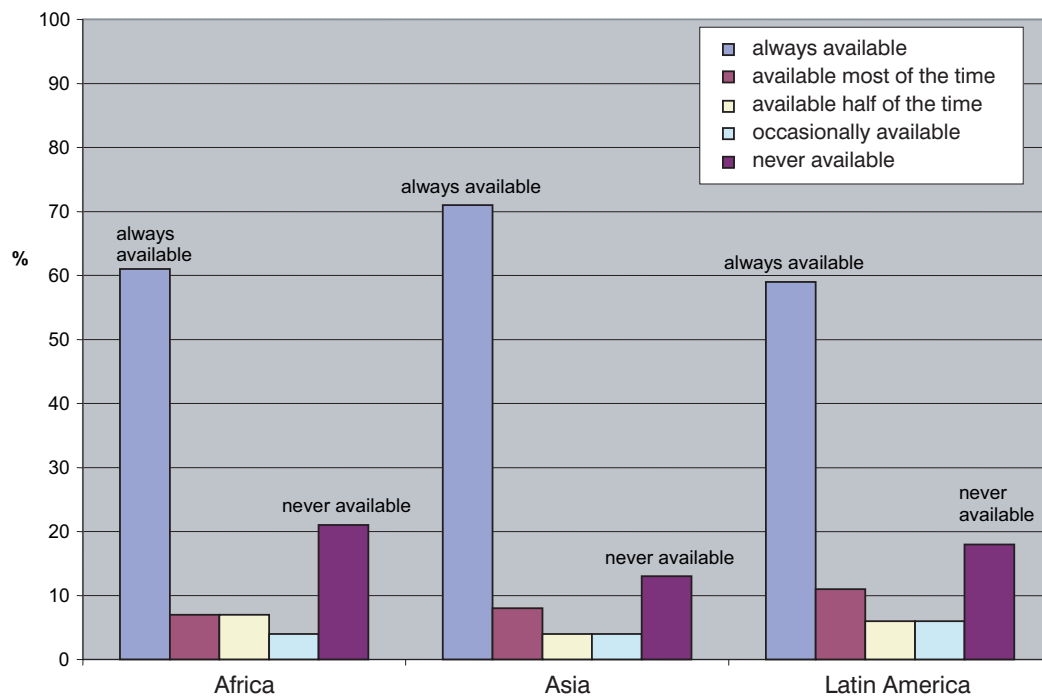


The availability of 'weak opioids' was markedly decreased in Africa compared to Asia and Latin America.

Note: In some places 'weak opioids' are expensive and hence the step of using a weak opioid is substituted with a smaller dose of a strong opioid. This is acceptable practice.

Twenty-five per cent of African Palliative Care Services never have a weak opioid available. Between 25 – 35% in Latin America and Asia do not 'always' have a weak opioid available.

Graph 4: Access to oral morphine normal release tablets or solution



Oral Morphine is the 'strong opioid' recommended on the WHO EML.⁽¹³⁾ Normal release preparations are preferable as they allow easier adjusting and individualisation of doses.

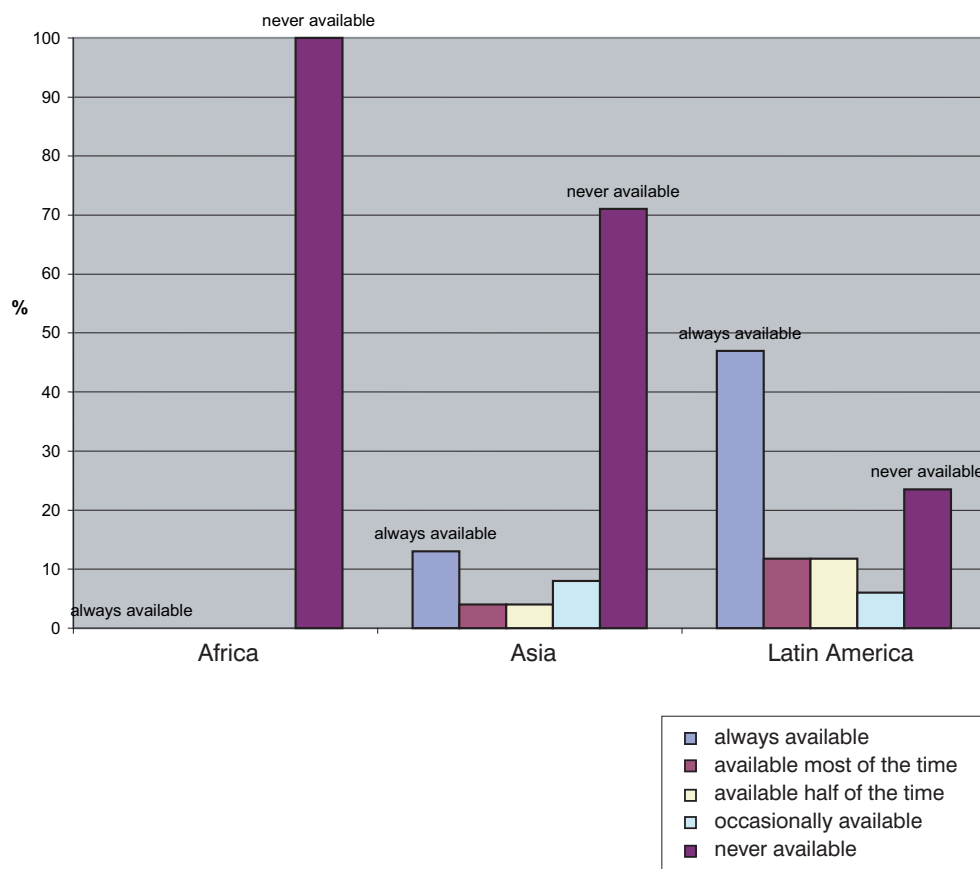
Note: In Latin America oral methadone is sometimes used instead of oral morphine. Reasons for preference of methadone over morphine include:

- additional analgesic properties (antagonism of NMDA receptor);
- longer half-life (less frequent dosing);
- safe to use in renal impairment;
- less expensive;
- less fear from patients and their families.

For 41% and 39% of palliative care providers in Latin America and Africa respectively, oral morphine is not 'always available', and for 18% and 21% respectively, oral morphine is 'never available'.

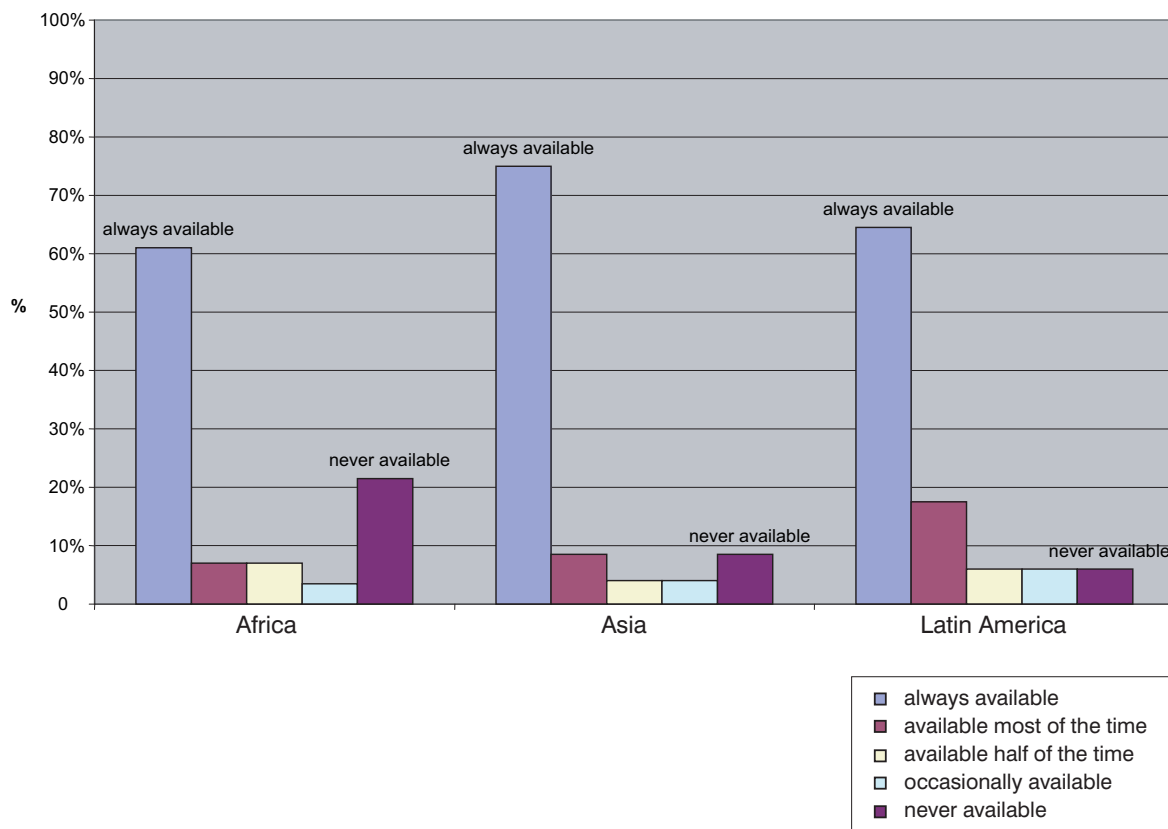
To prevent patients suffering pain it is important that supply is not interrupted.

Graph 5: Access to oral methadone



In some Latin American countries oral methadone is used in place of oral morphine. Oral methadone has an advantage in some neuropathic pains owing to its NMDA action. Neuropathic pain is common in AIDS patients and can be very difficult to control. Methadone can be more difficult to dose and has the disadvantage of accumulation. Despite the high incidence of AIDS in Africa, methadone was not available in any of the palliative care units. This may also be owing to its negative associations following its use to help decrease drug abuse, in addition to factors preventing access to all opioids, and the worry of accumulation. Its use in Latin America illustrates how, after appropriate training, it can be used effectively and safely. The 'expert advisory group'⁽¹⁵⁾ recommended methadone should be a 'complementary' drug in the next revision of the WHO EML.⁽¹⁶⁾

Graph 6: Access to one or more ‘strong opioids’



‘Oral or patch strong opioids’ included tablets, solution, normal and slow release preparations of:

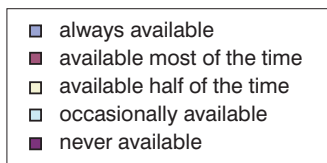
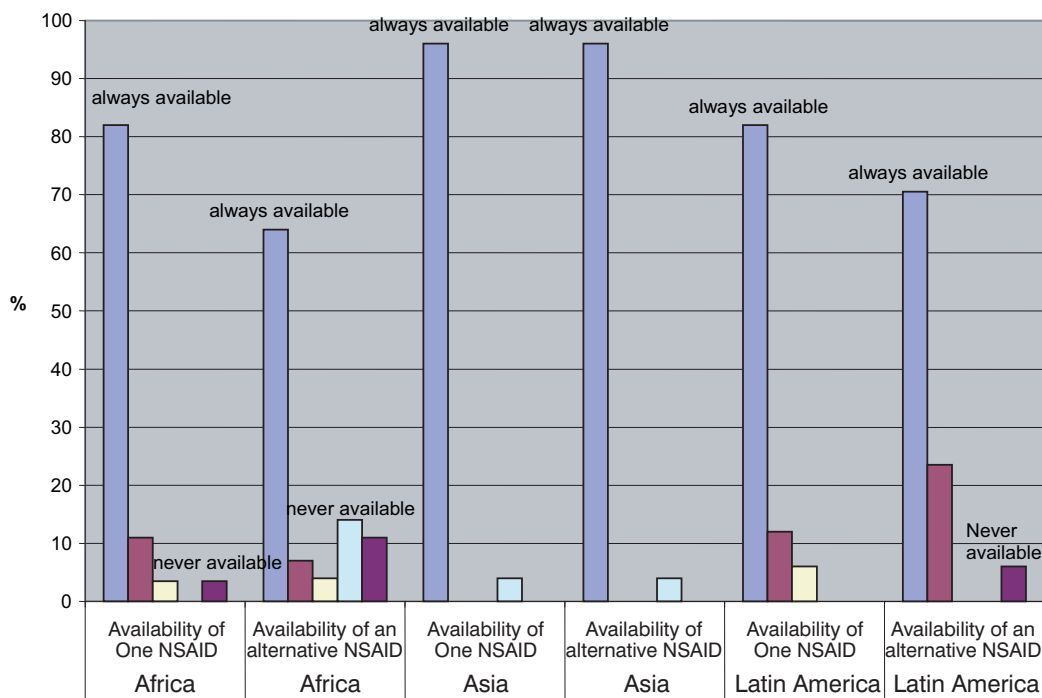
- oral morphine
- oral methadone
- oxycodone
- hydromorphone
- fentanyl patches
- and an option for ‘other’.

Pethidine was excluded from the analysis as it is not recommended in chronic pain relief owing to toxicity following accumulation.

Over 20% of palliative care providers in Africa can never access a ‘strong opioid’.

Thirty-five per cent of palliative care providers in Latin America and 25% in Asia cannot always access any ‘strong opioids’.

Graph 7: Access to NSAIDs



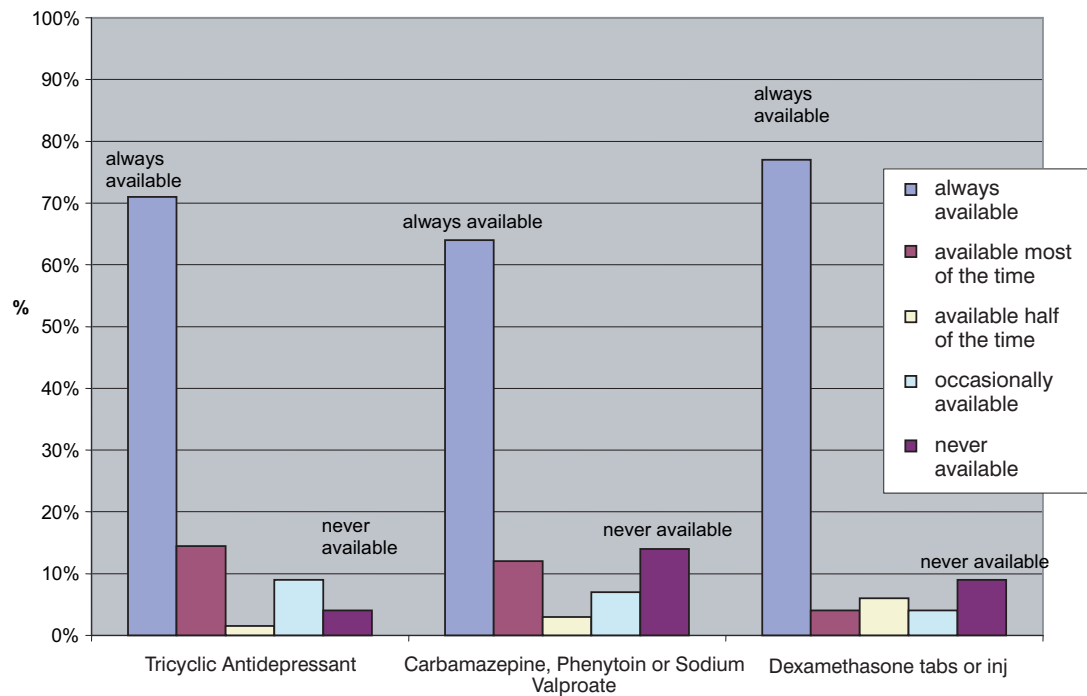
Graphs 7, 8, 9 and 10 illustrate the overall results for the availability of some of the other recommended analgesics. The variation in access to different drugs suggests multiple reasons for lack of access.

The current WHO EML⁽¹³⁾ includes one NSAID, ibuprofen.

The 'expert committee' has recommended to the WHO that the next revision of the EML should include two NSAIDs.⁽¹⁶⁾

NSAIDs do differ in properties, effectiveness and side effects. It is not known how to predict which NSAID a pain will be relieved by.

Graph 8: Access to neuropathic analgesics



'Neuropathic pains' covers a wide spectrum: some respond better to tricyclics whilst others respond better to anticonvulsants. No significant difference has been shown between different tricyclic antidepressants and different anticonvulsants in the control of neuropathic pain (with the exception of increased effectiveness of gabapentin compared to tricyclics in post herpetic neuralgia).^(18, 19)

The tricyclic amitriptyline and the anticonvulsants carbamazepine, phenytoin and sodium valproate are on the current WHO EML; all have different significant side effect profiles and drug interactions. Note: opioids can also be very effective in relieving some neuropathic pains. Opioids can be used in conjunction with tricyclics, anticonvulsants and dexamethasone.

Thirty-seven per cent of palliative care units do not have a constant supply of any drug from the 'anti-convulsant class'.

Nearly 30% do not have a constant supply of one of the tricyclics.

Twenty five per cent do not have a constant supply of dexamethasone.

Twelve per cent never have access to an anticonvulsant.

Dexamethasone is useful for relieving a number of symptoms common in palliative patients including:

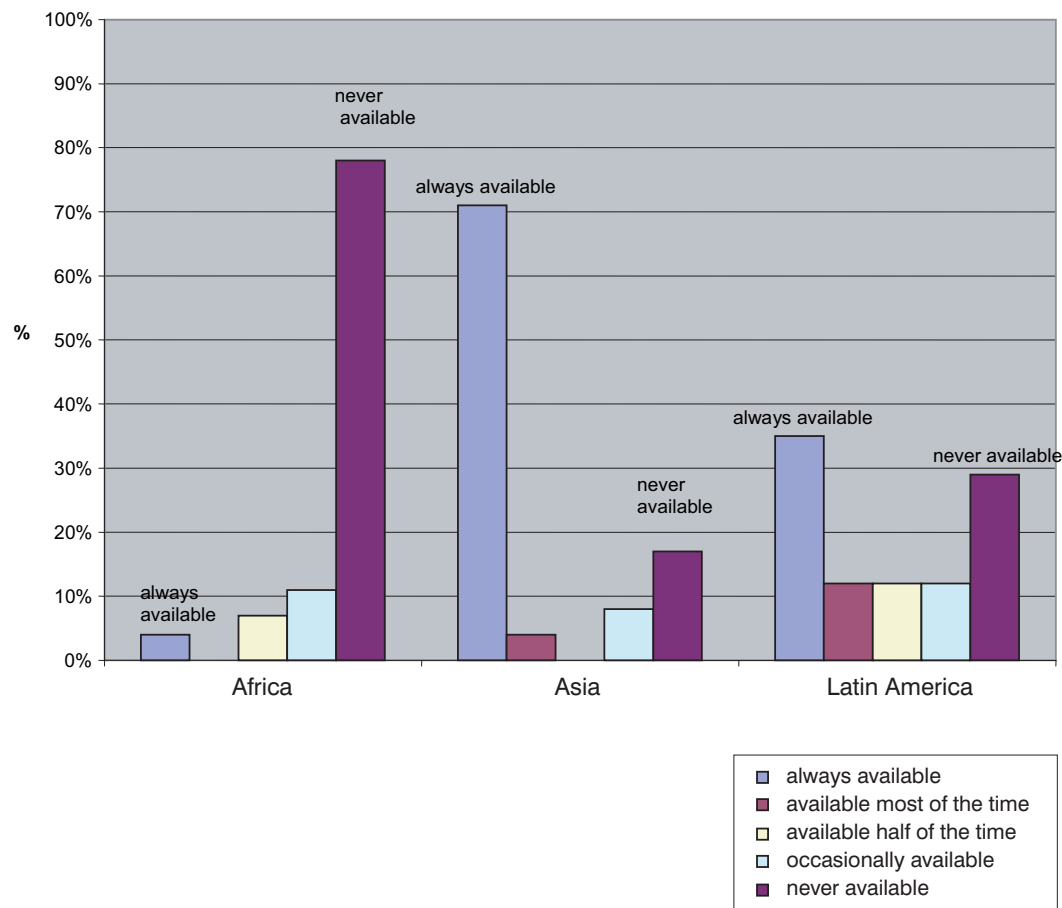
- pain – especially nerve compression pain and liver capsular pain
- aphthous ulcers
- raised intracranial pressure
- spinal cord compression
- intestinal obstruction
- ureteric obstruction
- large airway obstruction
- superior vena cava obstruction
- cerebral tumours
- hypercalcaemia in lymphoma
- sweating and hot flushes.

It can also act as an:

- antiemetic
- appetite stimulant.

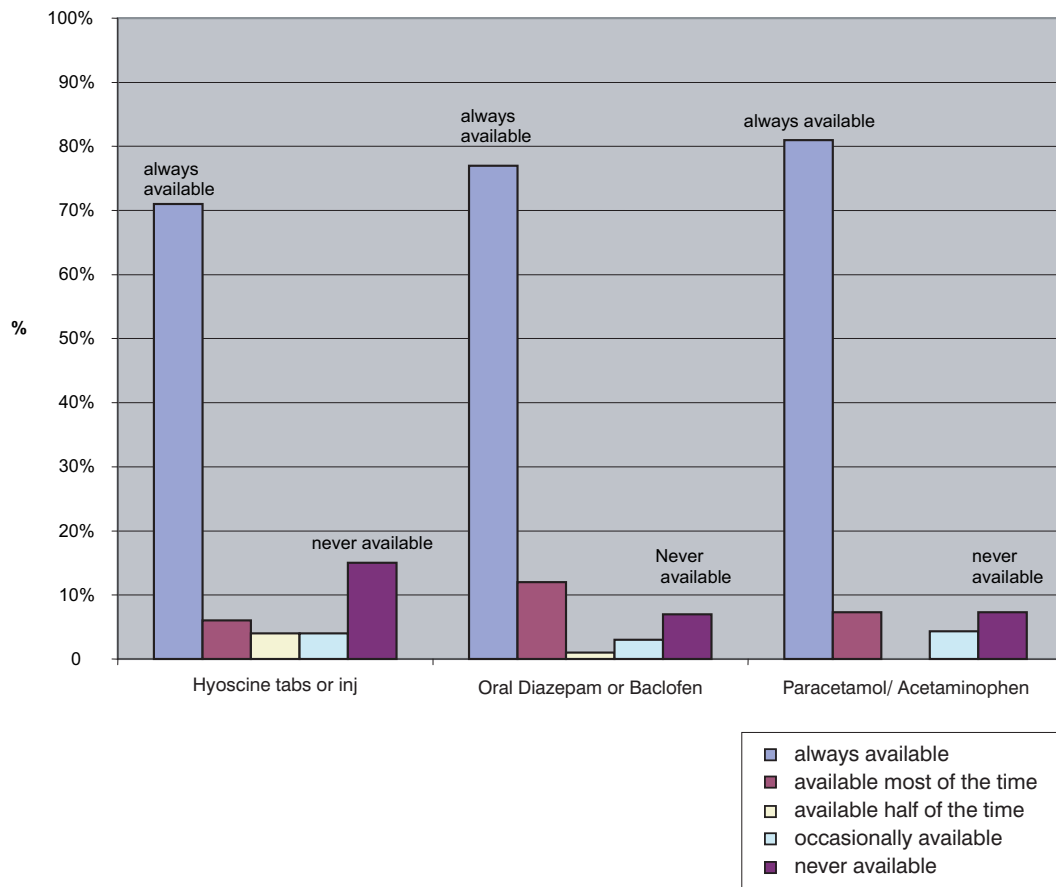
The current WHO EML⁽¹³⁾ recommends only the injectable form of dexamethasone; the 'expert group' advised the addition of the tablets.⁽¹⁶⁾

Graph 9: Access to gabapentin



Gabapentin was included in the recommended list of palliative care drugs to be added to the WHO EML.⁽¹⁶⁾ It has not been proved to be more effective than other anticonvulsants for neuropathic pain (except post herpetic neuralgia) but is usually better tolerated, with fewer side effects and drug interactions. Its cost is likely to be a factor decreasing access.

Graph 10: Access to other analgesics



Graph 10 illustrates the availability of some of the other analgesics currently on (diazepam and paracetamol), or recommended to be on (hyoscine), the WHO EML.^(13, 16) Baclofen is included as it is effective for muscle spasm in a similar way to diazepam but has fewer side effects.

Seven per cent of palliative care units never have access to paracetamol (acetaminophen).

3. Why are opioids not accessible to palliative care patients?

Help the Hospices surveyed palliative care providers to ask why they felt oral morphine* was not accessible to their patients (responses from 69 HCWs all in different organisations): 24 in Asia; 28 in Africa; and 17 in Latin America).

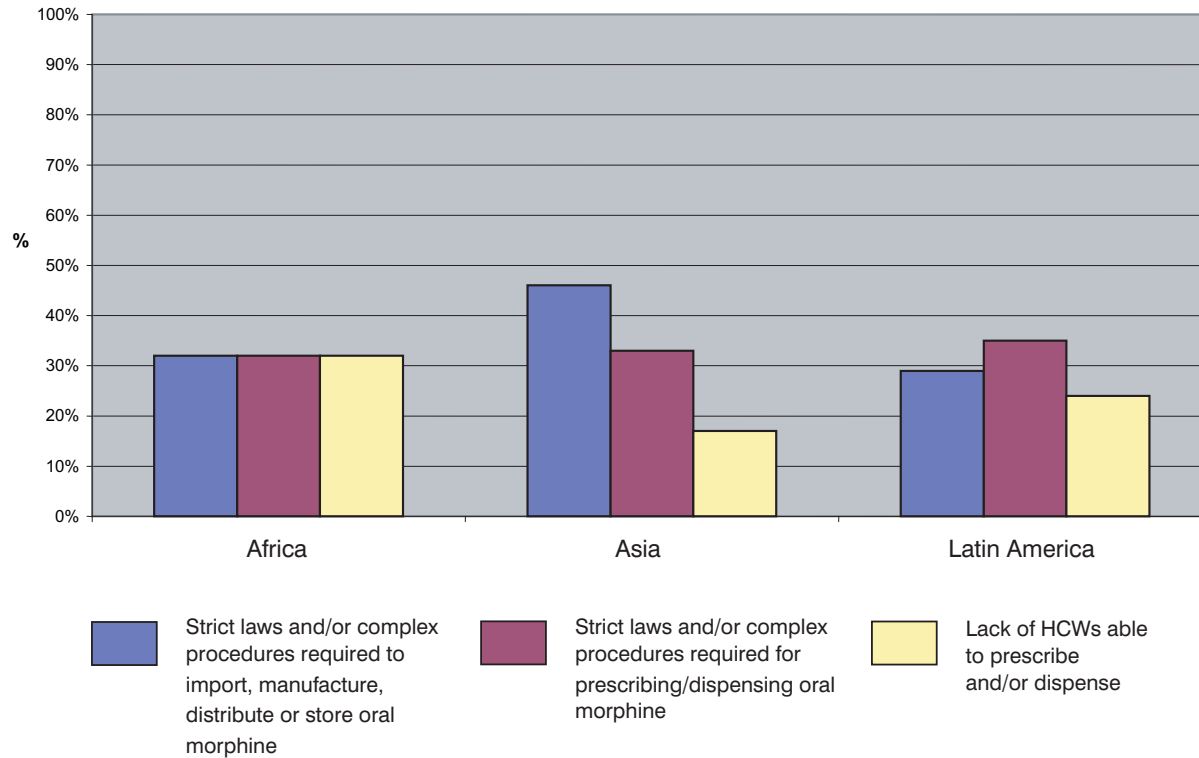
Reasons for the lack of availability could be categorised as:

1. Excessively strict national laws and regulations.
2. Fear of addiction, tolerance and side effects.
3. Poorly developed healthcare systems and supply.
4. Lack of knowledge – HCWs, public and policy makers.

* Oral morphine was used in the questions on reasons for lack of access, but it is assumed that many of the reasons are equally applicable to oral methadone and other 'strong/step 3' opioids.

3.1 National laws

Graph 11: Factors decreasing access: laws and regulatory barriers



In some countries laws governing the handling of morphine and other controlled drugs are impractical or so stringent that they prevent HCWs using morphine when they feel it appropriate. These laws were aimed at preventing misuse; they were adopted prior to advances in knowledge about pain and opioids, and were not intended to block pain relief. Other surveys have also highlighted this.⁽²⁰⁾

1. Process requires several forms, special licenses and/or authorisation stamps which are time consuming and/or difficult to acquire and thus deter HCWs from prescribing opioids.

“Palliative care doctors have a right to prescribe morphine but cannot obtain it if they work in a hospice which is not registered in the MoH as a medical organisation.”

“Drug companies are not willing to import oral morphine solution as they will not make enough profit due to spending months on legal papers.”

“Licences are hard to obtain. You need to write an exam then apply for a licence.”

“A supply of opioids is now available in the central medical stores but many practitioners are unaware, and even some of those who have the information have not accessed it as they are unwilling to follow the due process, which they regard as tedious.”

“I waited nearly one and a half years to get my first licence to prescribe oral morphine.”

“Licences are hard to obtain. This is to ensure that only genuine companies are allowed to import morphine as a way of ensuring that there is no misuse, and to ensure that the accounting bodies to INCB are not so many from one country.”

“Bureaucracy for collecting morphine delays work in the hospitals and centres.”

2. Length of supply allowed is short requiring repeated journeys – which are potentially expensive, a long way and difficult when ill – and repeated consultations with already busy doctors.

- a. In Honduras only a three day supply of oral morphine is dispensed.
- b. In Malawi only three days supply of analgesics are dispensed.
- c. Until the recent review of Romanian law, doctors could only prescribe three days supply of morphine (for a small number of specified diseases special authorisation from a government consultant could be obtained for 'long term prescribing' allowing 10 – 15 days supply on a repeated basis for three months).⁽²⁰⁾
- d. In Israel, unless the doctor confirms that the patient lives far from a pharmacy, supply can only be given for 10 days at a time. Opioids are only available from pharmacies with Health Sick Insurance. In some areas there are few or no pharmacies with Health Sick Insurance, meaning patients have to travel a long way for a few days supply. In addition, if any of the details required are omitted by mistake, the pharmacist will send the patient back to the doctor, which, when distances are far and patients' are ill, can deter patients from obtaining their drugs.

3. A maximum dose is stipulated. This does not account for patient variability and the fact that there is no maximum dose of morphine.

- a. Until reviewed recently, the Romania pharmacopeia stipulated that no more than 60mg per day should be prescribed^(20, 21)
- b. Drug laws in Israel state that no more than 60mg per day can be prescribed for non-cancer patients (confirmation that patient has cancer needs to be on prescription).

4. Lack of HCWs qualified to prescribe controlled drugs.

- a. In Honduras, Tamil Nadu, Mongolia, Peru and Kyrgyzstan only specialist palliative care and/or oncology doctors are allowed to prescribe morphine.
- b. In the Philippines only doctors with two special licences are able to prescribe morphine.
- c. Seventeen per cent of countries/regions were reported to require specific licences which were hard to obtain before being allowed to prescribe morphine.

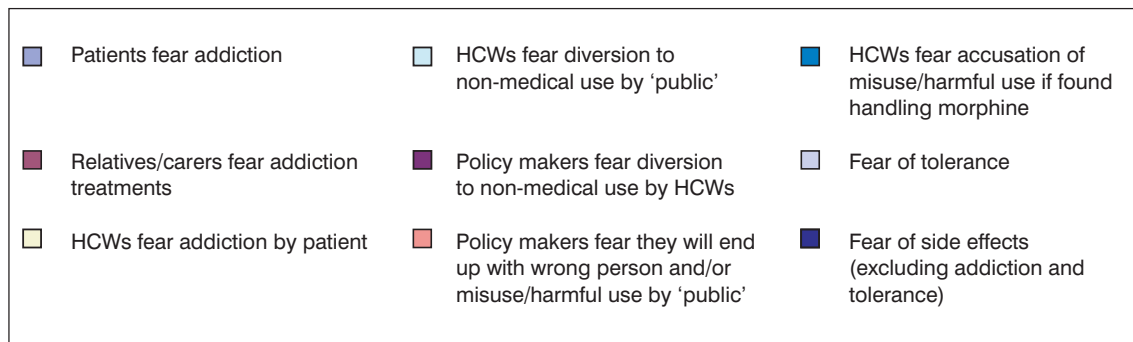
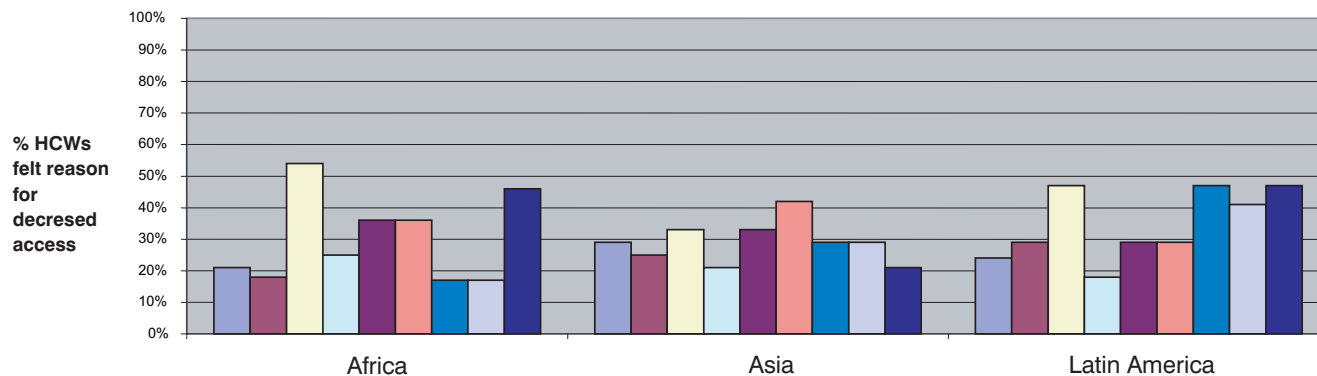
- d. In Malawi (where clinical officers and doctors can prescribe opioids) there is only one doctor for every 100,000 people.⁽²²⁾ Prior to a recent amendment, Ugandan laws allowed only doctors to prescribe opioids; in rural communities there is only one doctor for 50,000 people. Therefore, most people are unable to access a doctor. These figures compared to 164 doctors per 100,000 in the UK, where since May 2006 specialist nurses can prescribe opioids in addition to doctors.

5. Lack of HCWs able to dispense controlled drugs.

- a. Ugandan law allows only pharmacists to dispense oral morphine. In 2000 there were only 19 pharmacists outside the capital (ie 19 pharmacists to cover a population of just over 21million).⁽²³⁾
- b. In the Philippines only pharmacists with S3 licenses are allowed to dispense oral morphine.

3.2 Fear of addiction, tolerance and side effects

Graph 12: Factors decreasing access: fears of addiction, tolerance or side effects



The main reasons HCWs felt that oral morphine is not available are owing to fears of addiction, tolerance and/or other side effects. In Africa over 50% felt that other HCWs fear their patients will become addicted if given oral morphine. A high percentage also felt that HCWs fear accusation of misusing morphine if they prescribe/dispense it. The reasons why these should not be feared are addressed on pages 30 – 33.

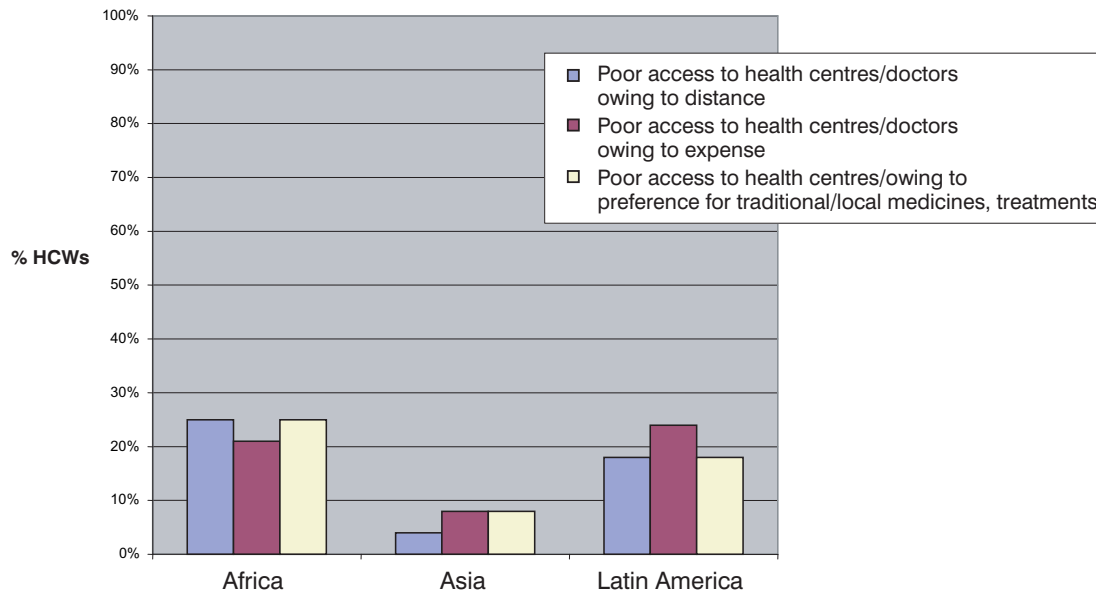
“Pharmaceuticals do not want to produce their own morphine due to myths and ignorance.”

“Patients fear its (morphine) use, because its use is related with close end stage of life.”

“Patients and relatives fear use of morphine thinking death is near.”

3.3 Poorly developed healthcare systems and supply

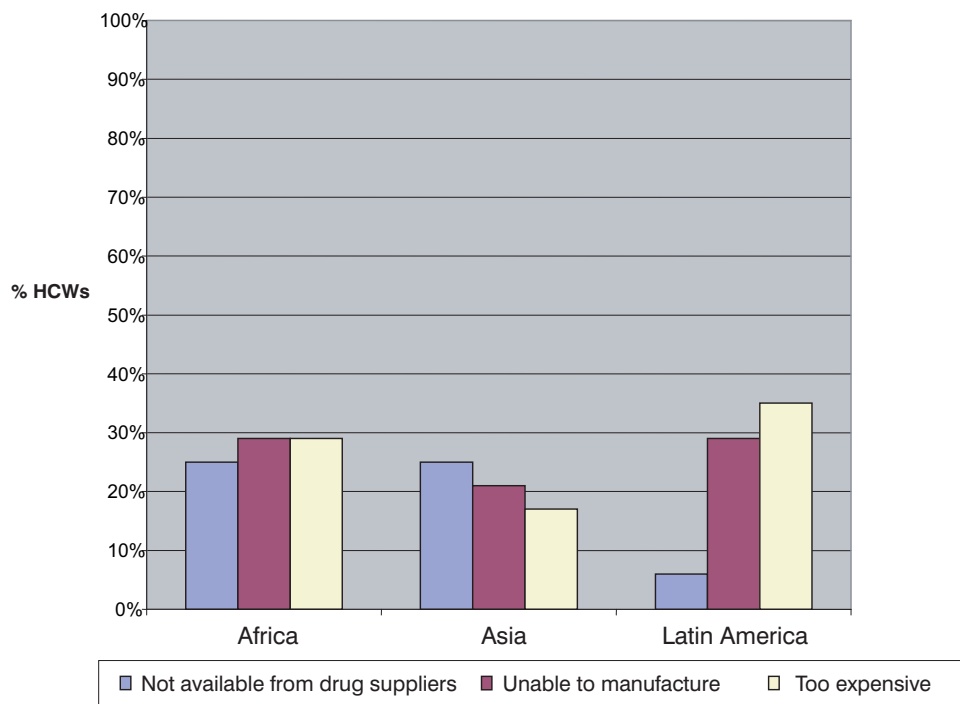
Graph 13: Factors decreasing access: poor access to healthcare



In some areas, lack of access to morphine simply reflects the difficulty for numerous people to access health facilities. The lack of HCWs able to prescribe and dispense opioids is discussed under 'national laws' (pages 20 – 22) This was felt to be more of a problem in Africa and Latin America than Asia – which is also reflected in the availability of some of the non-opioid drugs, eg NSAIDs. Comparing the availability of NSAIDs with the strong opioids indicates that this is not the only factor, as access to NSAIDs is still markedly higher.

“We are very aware that we do not provide adequate pain relief for our patients. We get our drugs from the local hospital and they only allow us basic pain analgesics. The hospital is not good on drug procurement, and there are often shortages so they don't give us what we order.”

Graph 14: Factors decreasing access: supply and expense



“Only small quantity used in a year compared to the fees required for importation.”

“Morphine is not available continuously. Small amount imported and next order placed after finishing and reporting previous supply. Drug importer does not inform the health centres about the arrival of the next supply. Thus there is a long period of drug absence because waiting for importing and informing.”

“Nobody prepares morphine in the city. It is prepared 600km away and delivery takes two days. Pharmaceuticals don’t want to produce their own morphine... The lab preparation costs US\$80 per litre. I have spoken to pharmaceuticals and in three years I have had no success.”

“Small budget for health centres does not allow morphine to be ordered in an adequate quantity. Thus only small quantities are ordered and imported.”

3.4 Expense

Oral morphine is an inexpensive drug. Slow release preparations can be more expensive due to patents but are not required to provide good pain relief. Normal release preparations should be inexpensive to make; oral solution can often be made locally very cheaply.

However, over one billion people live on less than \$1 a day.⁽²⁴⁾ Palliative patients often lose their ability to earn or grow food so that even inexpensive drugs become impossible to obtain.⁽²⁵⁾

Twenty-six per cent felt oral morphine was too expensive.

Examples include:

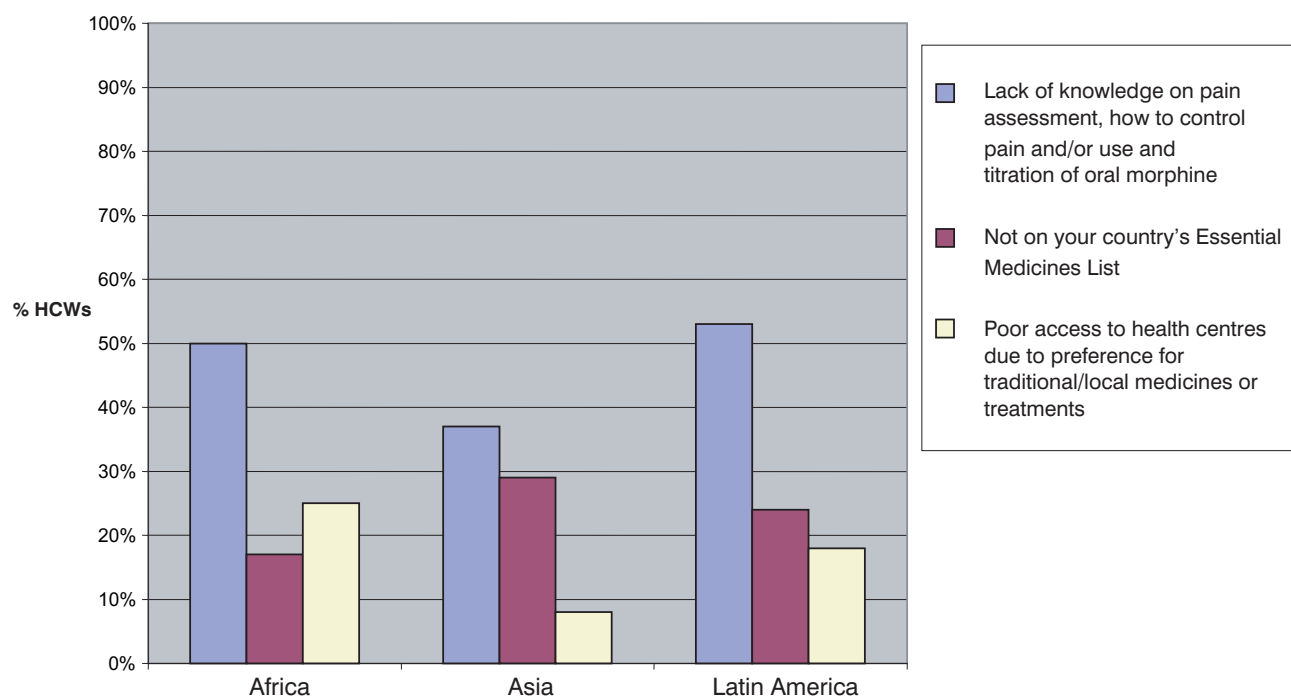
- a. One main hospice in Zimbabwe can only access normal release oral morphine for half of the patients who require it, as it is so expensive.
- b. In Honduras morphine (and all the other opioid analgesics, eg oxycodone, hydromorphone, fentanyl) is available readily to private patients but, owing to expense, only rarely available to non-private patients.

In 2004, a survey found that the relative cost of analgesics in developing countries was significantly higher than in developed countries. Another paper reported how the high costs of opioids in Argentina restricted their availability.^(26, 27, 28)

Promotion of non-generic forms (ie patented versions of the drug) has caused morphine to be unaffordable in some areas. When expensive formulations of opioids appear on the market, inexpensive immediate release morphine often becomes unavailable. Opioids are still poorly understood and underutilised in many developing countries. Promotion of expensive formulations disrupts the balance in their favour, as there is seldom any promotion or education on the cheaper formulations. For example, in India even at the moment there are institutions which have only sustained release morphine. There are others which have no morphine at all but have transdermal fentanyl, though the regulatory barriers are the same for both.⁽²⁹⁾

3.5 Lack of knowledge – HCWs, public and policy makers

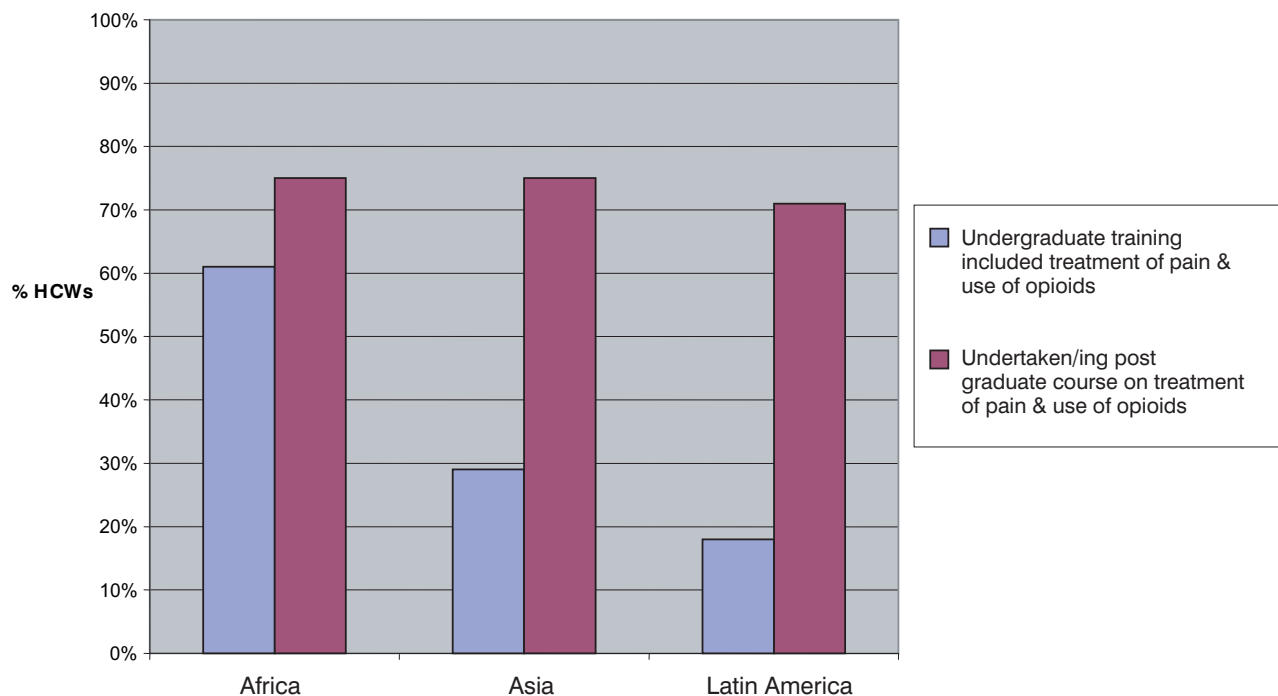
Graph 15: Factors decreasing access: lack of knowledge



“One of the main reasons in my state is the paucity of doctors prescribing morphine because of the lack of training/interest in palliative care.”

“It is simply irrational that oral morphine is not available in the country whereas expensive fentanyl patches can be made available for the rich patients. Lack of doctors training, awareness and cure orientated approach of the society as well as of the medical community makes palliative medicine an unknown field.”

Graph 16: Factors decreasing access: training



Exclusion from a country's essential drug list implies lack of understanding of the value of oral morphine in pain relief and possibly misunderstanding of fears by policy makers.

In Latin America and Asia less than 30% of the HCWs surveyed had pain management included in their professional training. However, the majority, more than 70%, of respondents had gone on to achieve further training for themselves.

As an undergraduate: 82% of HCWs in Latin America and 71% of HCWs in Asia had no training on pain or opioids.

“There seems to be poor knowledge of palliative care prescribing and fear at all levels of using opioids even when they are available, including amongst specialist doctors. For example, in my 10 years experience... when we have suggested using, or asked about knowledge of using, combinations of, for example, haloperidol/ hyoscine combos with or without opioids for terminal patients, it is negatively received.”

4. Essential elements required to increase availability

Simply providing a supply of any drug will not increase access; a number of interlinked factors need to be addressed.

4.1 Education

Education is fundamental, ensuring that HCWs are aware of:

- how to diagnose pain and other symptoms;
- which analgesics to use when, in what dose, how many times a day, and for how long before reassessment;
- how to prevent and minimise side effects;
- how to access advice and share knowledge;
- how to access local palliative care facilities;
- legal requirements and what, if any, records are necessary;
- where necessary drugs can be sourced;
- dispelling 'morphine myths'.

It also empowers patients, carers, volunteers and each community through knowledge:

- that pain and other symptoms can be relieved;
- of how to access palliative care facilities;
- of how to take drugs, minimise side effects, what to do if side effects occur (compliance is significantly higher when patients understand reasons for their medicines, and knowledge of potential side effects increases trust).

A survey in Uganda illustrated how educating communities can increase access and allay fears regarding morphine.⁽³⁰⁾

Finally, education is the key to ensuring that palliative care is supported and legislation is not restrictive by educating policy makers on:

- what palliative care is;
- the support INCB and international treaties give to ensuring opioids are available for medical purposes;
- how to account for movement of opioids and records required;
- the importance of integrating palliative care into cancer and AIDS policies;
- how current laws can be improved to allow access whilst preventing diversion.

Training is also vital for drug regulatory personnel and police, to ensure knowledge of who can possess and handle controlled drugs, and the records required.

It is important also to ensure donors and NGOs are aware of a country's priorities and requirements.

4.2. Addressing the fears

A number of HCWs, government officials and patients fear that having morphine available to relieve pain will lead to drug addiction (by HCWs, patients or through diversion to the general public).

Dependence on a drug can be divided into:

- Therapeutic dependence – analgesics do not remove the cause of the pain, therefore as long as the pain remains (eg the tumour is still pressing on a nerve) the patient will require the analgesic to remain pain free. Thus, patients may require morphine for the rest of their life in order to remain pain free.
- Pharmacological dependence – the body produces its own pain relieving substances, endorphins, a certain level of which are circulating around the body normally. These are chemically similar to opioids. When a patient is given morphine regularly their body 'senses' an increase in 'pain relieving' substances and responds by producing fewer natural endorphins. Consequently, if a patient suddenly stops taking morphine, they will have a lower level of endorphins than they had before they started taking morphine. This produces withdrawal symptoms. A similar reaction occurs with steroids. This can be simply avoided by slowly reducing the dose in patients that have been on morphine for a few weeks if the cause of the pain has resolved.

- Addiction (sometimes referred to as psychological dependence) – this is what is feared: abnormal, compulsive behaviour, including a desperation to obtain the drug in order to experience its psychic effects, characteristically having continued use despite harm.

Studies show addiction or psychological dependence is extremely rare when opioids are used for pain.^(31, 32, 33)

Availability for medical use does not go hand-in-hand with diversion for illegal purpose.⁽³⁴⁾

Twenty-one per cent of respondents felt that their colleagues fear that patients will become tolerant to morphine, resulting in the need for higher and higher doses to relieve their pain so that perhaps when pain becomes very severe morphine would no longer be effective. This can cause HCWs to delay starting morphine and other opioids, reserving them for 'exceptionally severe pain'.

Once a patient is on the correct dose of opioid to relieve a pain, the dose will not need to be increased, unless the illness progresses, causing further pain, or there is another source of pain or other factors increase the pain (social, spiritual, psychological). Then, when this pain is controlled, the dose will be kept stable again. It is also important to explain to patients and relatives that:

- the pain may not become worse;
- not all pains are 100% responsive to morphine, but there are other types of analgesics which can be tried.

“Morphine should not be withheld until the pain becomes unbearable.”

Note: a patient's pain requirement may increase even when there is no sign of disease progression.

- Pain is not only physical; psychological, spiritual and social factors impact on pain intensity.
- Pain may not be solely due to the 'main disease'.
- Disease progression may not be easy to detect.

In addition, remember:

- There is also no maximum dose of morphine. The dose should be increased to that required to relieve pain.
- Different pains respond to different analgesics.
- Some pains are only 'partly' responsive to opioids.
- Different opioids have different binding efficacies to different receptors, and therefore different analgesic properties and side effects.
- Everybody has different pain thresholds, and express and cope with pain in different ways.

“Only the patient knows how intense and frequent a pain is – a pain is what the patient says it is.”

Dispelling the fear of tolerance:

Ms CD, a 54 year old Argentinean nun, has had a locally advanced phaeochromocytoma with lung metastases since 1997. In November 1997 she was referred to the palliative care team and started with 30mg a day of immediate release morphine. In August 1998 the morphine was changed to 15mg a day of methadone. Until August 2006 her disease has been stable, and her pain well controlled. She now receives 10 mg a day of methadone.

During eight years on methadone she has had a very active life in her religious community; she is able to travel and performs several daily activities.

Case study provided by Dr Mariela Bertolino, Dr Roberto Wenk and Dr Guillermo Mammana, from the Palliative Care Unit , Tornu Hospital-FEMEBA Foundation.





Ms EF had advanced nasopharyngeal cancer. She received oncology treatment and was referred to the palliative care services in March 2003 with severe pain. The palliative care team started her on 12mg a day of methadone plus adjuvant analgesics. Her pain was well controlled, allowing her to enjoy two more years of active life. Here she is pictured with her husband, members of the palliative care team and two tango dancing teachers. She died at home in May 2005. At this time she was on 3mg of oral oxycodone PRN, (usually taken twice a day) plus adjuvants.

Case study provided by Roberto Wenk, MD, Mariela Bertolino, MD, and María Minatel, MD.
Programa Argentino de Medicina Paliativa-Fundación FEMEBA, Buenos Aires, Argentina

Thirty-eight per cent of respondents felt that fear side effects limited the use of oral morphine.

All drugs have side effects. The side effects of morphine and other opioids are known and can be easily minimised.

One side effect which many fear is respiratory depression – tolerance occurs to respiratory depression so that when the dose of morphine is increased gradually, respiratory depression does not occur. It is for this reason that patients are started on smaller doses of morphine which are titrated up until the pain is relieved (not because the patient has become tolerant to the pain relieving properties). In addition, pain is a respiratory stimulus, so the respiratory depressive effect is 'cancelled out' when morphine is used to relieve pain.

Other side effects such as sickness and drowsiness can also be minimised by increasing the dose slowly.

Tolerance to the constipating effect of morphine does not occur but can be anticipated and prevented using laxatives.

Not all patients will experience side effects

The following case study illustrates clearly how opioids do not render patients permanently drowsy, nor impair cognitive skills, nor are only used near the end of life – but how they can greatly enhance the life of the patient and their family.

Mr JK was a surgeon from Eastern Europe diagnosed with disseminated cancer of the oesophagus. On diagnosis he was given some palliative chemotherapy. Initially he experienced severe pain which limited him in his activities. Following referral to the palliative care team for pain control, his pain was controlled very satisfactorily with a 50 microgramme fentanyl patch and occasional immediate release morphine for breakthrough pain. Control of his pain allowed him to return to work, where he was able to perform operations. Sadly he passed away at the end of 2006, but until then he was very busy attending meetings throughout the country, giving short lectures as well as enjoying weekends away with his family.

How side effects can be managed:

Ms HI was a patient with ovarian carcinoma who was treated for four years by the palliative care team, after discontinuing chemotherapy. She had three enterocutanea fistulas during these years and severe abdominal pain related with the progression of the disease.

Her pain was soon controlled with opioids. Unfortunately, she initially experienced some neurotoxicity, but the palliative care team managed this successfully by rotation of class and doses of different opioids (morphine, oxycodone and methadone).

Successful control of her pain and the side effects meant she was able to greatly enjoy many parts of the next four years. She had an active life, she developed work projects and most importantly was able to take care of her two daughters. She was also able to undertake long-distance trips for some months to Spain to see one of her sisters.

Ms HI died in the palliative care unit in 2005, having developed brain metastases.

Case study provided by Dr Mariela Bertolino, Dr Roberto Wenk and Dr Guillermo Mammanna, from the Palliative Care Unit , Tornu Hopital-FEMEBA Foundation.



4.3. Accountability

Opioids are regulated under the 1961 UN Single convention on Narcotic Drugs (amended by the 1972 and 1988 protocols). The purpose of the regulation is to guarantee their availability for medical purposes, whilst preventing abuse. The INCB monitor implementation of the conventions. The INCB requires each country to submit:

- an estimate of the quantity of each specified drug (including opioids) it will require for medical use – the amount imported or produced by a country should not exceed its agreed annual estimate;
- quarterly forms detailing the medical use of the specified drugs (including opioids) within the country.

Time, resources and definition of responsibilities needs to be made within the drug regulatory authority for these activities, and to ensure accountability throughout the handling of these drugs.

Factors limiting access to opioids include:

- fear by government officials and/or HCWs that opioid abuse will occur;
- fear by HCWs that they will be accused of abusing opioids if they handle them.

By keeping accurate records of the movement of opioids and other restricted drugs, these worries can be dispelled and the INCB requirements fulfilled. It is recommended that records:

- are easy to complete;
- are kept throughout the whole supply chain (importation to patient supply or destruction or returned);
- include details of:
 - quantities acquired (imported/from wholesaler/main hospital)
 - supplier (eg wholesaler/doctor)
 - amount dispensed or supplied
 - whom it was dispensed/supplied to
 - separate running balance of the amount in stock for each form and strength kept (this should be verified with a regular physical count of the stock).

Seventy-five per cent of HCWs responded that they kept some form of record of handling morphine in their practice. Standardisation and provision of record books from a central government level, the INCB or the WHO would simplify this process.

HCWs should advise drug authorities how significant changes in palliative care services might alter the national requirements for morphine and other stipulated drugs. When estimating increases consider:

- the number of new patients likely to access the service(s);
- the percentage of these likely to require morphine (or other drugs);
- the average dose of morphine any patient requiring morphine is likely to require.

4.4. Reviewing laws and policies

Policy change will only occur if governments understand the importance of palliative care and the need to increase access to drugs for palliative care within their country. Thus, before changes to laws and policies can be addressed there is a need to:

- promote the benefit and role of palliative care, highlighting how many patients within the country could benefit;
- ensure all government individuals are aware of the ability of inexpensive medicines to relieve pain in the majority of people, including children;
- document areas where the requirement for palliative care is not met;
- develop leadership: workers within palliative care who are willing to help affect change.

National drug laws vary between countries. Drug laws need to be relevant and practical to clinical practice. For example, the drug laws were amended in Uganda recently to allow specialist palliative nurses as well as doctors to prescribe oral morphine, as the number of doctors would not allow access to all patients requiring pain relief.

There is a need to ensure palliative care is integrated into national HIV/AIDS and cancer policies, countries' EMLs and treatment guidelines (and that all these include children).

A recent INCB meeting called for relevant country authorities to consider and modify any restrictions in place which are not required by international law and which would potentially restrict access for medical need.⁽³⁵⁾

The PPSG has developed methods for evaluating national drug policies' suitability to allow access to opioids for medical purposes whilst maintaining regulation, in cooperation with the WHO, palliative care experts and government regulators. A tool has been published in conjunction with the WHO (2000) – *Achieving balance in national opioids control policy: guidelines for assessment*.⁽³⁶⁾ Details of this and further information on amending drug laws can be obtained from www.painpolicy.wisc.edu

“...consensus among all governments 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.”⁽³⁷⁾

4.5 Strengthening health facilities

Strengthening of many countries' health services is required to enable full access to palliative and other drugs. It is likely that different structures and approaches will work better in different countries. It is recommended when establishing or expanding services to:

- examine existing services, their effectiveness and disadvantages;
- ensure integration with existing models;
- encourage community participation;
- ensure cooperation with the private sector;
- communicate clearly to donors what is required.

4.5.1 Human resources

Lack of trained HCWs contributes to inaccess to palliative drugs in a number of countries. The number and skill mix of HCWs varies widely between countries. Ways in which to address this problem will also vary, perhaps, for example, utilising and paying lay counsellors, ensuring quality training and support of volunteers, and establishing guidelines nurses can follow, with a referral doctor available.

4.5.2 Drug procurement

Ensuring a reliable, timely, quality and inexpensive drug supply is important to ensure patients remain pain free and prevent withdrawal reactions. Accounting for opioid use will help estimate quantities required. There are a number of steps in the drug procurement process:

- Planning – ensuring sufficient supplies are always available but that stock does not expire, ascertaining what is the best form to use, finding a reliable importer or supplier, co-ordination with other organisations (it is often more cost effective to have a central source therefore collaboration is important).

- Importation – sufficient time needs to be given to allow for form filling and potential delays, and good communication between clinicians and procurement 'agents' is vital.
- Manufacture – is it cheaper to manufacture locally or in-house; who nearby has the capacity? Is the final formulation cheaper to import? For small scale manufacture (production of drugs from raw materials in your health facility) you will require:
 - reliable source of raw materials;
 - good water supply;
 - accurate weighing scales and measures;
 - funnels, bowls, pestle and mortar;
 - labels;
 - containers for final product;
 - verified formula;
 - trained staff;
 - appropriate storage for raw materials and final product;
 - quality control procedures in place.
- Transportation – who is allowed to collect controlled drugs from a wholesaler?

4.5.3 Drug costs

Establishing a reliable, quality assured and inexpensive drug supply and distribution is not always easy.

Many pharmaceutical companies are not interested in manufacturing morphine or in obtaining a licence for their formulation in countries where usage is thought to be low and bureaucracy potentially cumbersome.

Perhaps there should be a call to the WHO to establish reliable and inexpensive manufacturing of drugs on the WHO EML?

Morphine solution can be made cheaply from the powdered form. However, many smaller providers lack the scales, raw materials and qualified staff; only 32% of the respondents worked in units which had facilities for making morphine solution from the powder and then storing it in a secure place. Hence, establishing in-country central production and adequate distribution can be a good option. In some places a larger hospital or NGO organisation has agreed to manufacture morphine solution as a central supplier.

For example:

■ In Uganda in 2000 following advocacy by Hospice Uganda, the MoH commissioned a charitable procurement and manufacturing facility to produce morphine solution which could be distributed to hospitals, health centres and palliative care providers as requested. Commercial manufacturers had been approached but owing to the lack of profit they were not interested in manufacturing morphine solution.

■ In Nigeria supply of morphine through central importation had been erratic since 1993. Following advocacy by the Society for the Study of Pain and the Centre for Palliative Care, the University College Hospital pharmacy in Ibadan now prepares oral morphine from the morphine powder (5mg/5ml and 50mg/5ml) and supplies patients across the country (with over 130 prescriptions per month being dispensed for cancer patients from all over the country).

5. Recent advances in increasing access to analgesics

Over the last 10 years access to analgesics has increased substantially in a number of countries or regions within a country. A few of these are outlined below (this is not a comprehensive list).

5.1 Individuals

Numerous individuals have made significant steps in increasing patient access to analgesics in the last 10 years.

“I am instructor at the residence of general medicine in the hospital where I work, and I train residents annually in the formation of general palliative care, especially in the treatment of pain and opioid use. This has generated some changes for the better. Furthermore, I produced a basic guide that deals with the process of pain treatment and use of opioids, which is starting to be used by doctors and nurse interns, and hospital guards. We are currently creating a palliative care team.”

5.2 WHO and INCB

In 2005 the World Health Assembly (WHA) and ECOSOC adopted resolutions inviting the INCB and the WHO to examine the feasibility of assisting in projects to increase the availability of opioid analgesics (resolutions ECOSOC 2005/25 and WHA58.22). The INCB and the WHO agreed that the WHO would act as the focal point, with the WHO preparing the ‘Access to Controlled Medications Programme’. The programme, which will commence in late 2007 or 2008, aims to work with all involved, including governments and NGOs, addressing the situation in over 150 countries with bad or no access.

The PPSG has published 22 translations of the WHO publication *Achieving balance*⁽³⁶⁾ which provides a resource for governments and HCWs to evaluate and improve national laws on preventing access to opioids. www.painpolicy.wisc.edu

5.3 Resolutions advocating for an increase in accessibility to opioid analgesics

- ECOSOC 2005/25 – On treatment of pain using opioid analgesics.
- WHA 55.22 (25-05-2005) on Cancer prevention and control
“...to examine jointly with the International Narcotics Control Board the feasibility of a possible assistance mechanism that would facilitate the adequate treatment of pain using opioid analgesics”.

5.4 Changes in national laws

1. In February 2002 the PPSG, the Eastern European regional office of the WHO and the Open Society Institute (OIS) conducted a workshop on 'Assuring the Availability of Opioid Analgesics for Palliative Care within Eastern Europe'. From this, Bulgaria, Croatia, Hungary, Lithuania, Poland and Romania completed action plans to help address regulations which impeded access. Romania was chosen as a pilot country.

Hospice Casa Sperantei in Romania was commissioned by the Romanian MoH to review their opioid legislation and policy using the WHO guidelines. Recommendations were presented to the MoH in 2003 which would help increase access to opioids for patients, eg increasing the supply of opioids allowed to be given to patients from three days to 30 days. The recommendations were accepted and the new law, nr 339/Nov 2005, has been in action since July 2006, although it needs to be printed in the official journal before the regulation can be applied.^(20, 38)

2. In Kerala, India, advocacy and amendment of state drug regulations laws now allows more than 100 palliative care units around the state to have access to oral morphine. An audit demonstrated that increased use of oral morphine did not lead to diversion and misuse.⁽³⁴⁾

3. The Ugandan Government has recently amended drug laws to allow clinical officers and nurses who have completed a specialised course in palliative care to be able to prescribe oral morphine.⁽³⁹⁾ This follows the recognition of the shortage of doctors within the country. Zimbabwe also allows specifically trained nurses to prescribe oral morphine and the Democratic Alliance Government in South Africa has recently proposed that prescribing by specially trained nurses should be allowed in South Africa too.⁽¹⁷⁾

4. The PPSG has documented recent changes in laws aimed at improving access to morphine; these include increasing the length of supply which can be prescribed and dispensed:

1. France: 1995
Seven days increased to 28 days
2. Mexico:
Five days increased to 30 days
3. Italy: 2001
Eight days increased to one month; in addition simplified prescription format and allowed two drugs or dosage units on one form
4. Germany:
One day increased so there is no limit
5. Peru:
One day increased to 14 days
6. India:
Five licenses required decreased to two licenses for morphine
9. Romania:
Three days supply increased to 30 days supply
10. Colombia:
10 days increased to 30 days (for strong opioids)

5.5 Some regional initiatives

1. Pallium India (Trust), working with the PPSG and the National Cancer Institute (USA), has facilitated the creation of palliative care facilities in three cancer centres in three states, in which effective palliative care facilities did not previously exist. Working with the American Cancer Society and International Network for Cancer Treatment and Research, the trust has also catalysed the development of a palliative care training centre in Hyderabad.

2. Hospice Africa (Uganda) has been running a programme to help train HCWs in other African countries and help approach government officials and advocate the need for palliative care and morphine. To date, visits/courses for African countries have been held in Ethiopia, Tanzania, Malawi, Nigeria, Kenya, Ghana, Zambia, and for South Africa in Kampala and Uganda. Funding has come from the RAF (UK) grant and the Diana, Princess of Wales Memorial Fund.

3. The African Palliative Care Association (APAC) provides advice on the provision of affordable, culturally appropriate palliative care throughout Africa. Initial visits to Sierra Leone (2005) have led to advice to small initiatives as well as discussion with Ministry officials as to the importance of palliative care. APCA is currently working in collaboration with the PPSG to help a number of African countries examine their drug laws, to ensure they allow access. In 2006 a workshop was commissioned to help establish country plans and examine drug regulations.

info@apac.co.ug; www.apac.co.ug

4. Help the Hospices runs a Twinning programme for Hospices – a two-way sharing of ideas and experiences. See www.hospiceinformation.info/hospicesworldwide/twinning.asp

5.6 Some country initiatives

1. India

In 2005 the government of India appointed a task force of experts to assist it in formulating a strategy for the country's National Cancer Control Programme, a five year plan which is due to commence in 2007. The task force consisted of separate groups each for an individual area in cancer control and care. One of these groups was on 'Palliative Care and Rehabilitation'. The group had extensive discussions via email and met a couple of times. Its recommendations, which were submitted to the government in May 2006, included strategy for:

- the creation of palliative care facilities, or upgrading them where they existed, in all of 28 Regional Cancer Centres in the country;
- the upgrade of five centres to training centres;
- the creation of 100 other palliative care facilities in other oncology centres so that each state would have at least two palliative care services;

- the inclusion of palliative care in undergraduate medical and nursing curriculum, and in the postgraduate curriculum for oncology trainees;
- the simplification of narcotic regulations in all states in India (currently 15 of 28 states have complicated rules);
- community participation in palliative care delivery.

2. Romania

Hospice Casa Sperantei in Romania:

- has prepared a training curriculum (20 hours) and has educated 40 trainers to run a national training programme in the use and prescribing of opioids. This was funded by Help the Hospices and the Open Society Institute, New York;
- under the umbrella of the national postgraduate training centre, is running courses for doctors and pharmacists detailing the use and prescribing of opioid medication in 30 districts of Romania, in order to facilitate the implementation of the new opioid legislation. This is funded by the Open Society Institute New York and three drug companies: Janssen, Lannacher and Mundipharma.

cshospice@hospice.bv.astral.ro

3. Nigeria

Professor Olaitan Soyannwo and four colleagues from Ibadan began advocating for opioid availability in 1996. Their dedication and enthusiasm over the last 10 years has led to:

- the establishment of the Society for the Study of Pain, Nigeria (a chapter of the International Association for the Study of Pain);
- the creation of the Centre for Palliative Care, Nigeria.

Their inspiration has led to individual and group initiatives including:

- a home based palliative care service (supported by Hospice Africa, UK);
- training workshops;
- setting up a pain/palliative care clinic;
- the development of the National Palliative Care Guidelines adopted in 2006 by the Federal Ministry of Health (including the use of the WHO analgesic ladder and opioids for severe pain);
- the inauguration of a consultative committee for cancer care (including a sub-committee on palliative care) into the Nigerian MoH in October 2006. Formation of this committee has allowed Professor Soyannwo to guide other committee members about how their hospitals can access opioids; prior access was denied in many hospitals owing to a lack of knowledge about how to access opioids;

- symposia for healthcare practitioners;
- inclusion of palliative care and safe use of analgesics in undergraduate and postgraduate teaching, and input into curriculum review;
- the dissemination of information about opioid accessibility and safe use through the Nigerian Society of Anaesthetists, the West African college of Surgeons annual conferences, and in-service training units of hospitals, eg resident doctors, nursing, HIV and cancer centers.

4. Uganda

Dr Anne Merriman and dedicated colleagues set up a hospice in Kampala in 1993 after ensuring the government would allow oral morphine to be used for pain relief. Hospice Uganda has expanded and now includes three centres in Uganda, as well as serving as a model Hospice for Africa and aiding other African countries in establishing palliative care facilities.

Projects and initiatives include:

- three centres providing home care service for approximately 900 patients at one time;
- certified in-country training for healthcare professionals in palliative care, currently working closely with MoH to ensure training in all districts;

- providing special training for clinical officers and nurses to lead palliative care units in their hospitals or teams. These nurses and clinical officers are allowed to prescribe morphine following a recent change in Ugandan law;
- certified in-country training for volunteers in palliative care;
- training of trainers courses;
- advocacy leading to:
 - the inclusion of palliative care as an essential component in the MoH five year strategic plan in 2000 – this in turn led to increased access to oral morphine and amendments to Ugandan laws to allow specially trained clinical officers and nurses to prescribe oral morphine;
 - the inclusion of palliative care training in professional undergraduate courses.

5.7 Proposed projects

PPSG, a WHO collaborating centre:

- Internet courses on international pain policy.
- International Pain Policy Fellowship.
- New opioid statistics to allow the study of consumption (use) for medical purposes and estimated requirement:
 - to aggregate opioids for severe pain into one number (ie combine figures for use of oral methadone, oral morphine, oral oxycodone etc);
 - to estimate minimum country needs based on mortality.
- Guidance as to the essential elements of a balanced national drug law.
- Opioid availability profile for every country.
- Provision of support by international experts:
 - speaker support
 - data
 - collaboration.

6. Educational opportunities

1. Hospice Uganda – postgraduate multidisciplinary diploma in palliative care
2. Pallium Latinoamerica – distance learning advanced course in palliative care (multidisciplinary, postgraduate course in Spanish) www.pallium.org
3. Wisconsin fellowship
4. Programa Argentino de Medicina Paliativa-Fundación FEMEBA, Buenos Aires, Argentina – one hundred and sixty hours face to face (70% clinical practice in palliative care units) postgraduate courses in palliative care for physicians, nurses and psychologists. E-courses for physicians and nurses.⁽⁴⁰⁾ Both activities are in Spanish (paliativo_femeba@arnet.com.ar)
5. The IAHPCC website details a number of other diplomas and courses in palliative care - www.hospicecare.com/edu

7. What you can do

7.1 Advocacy

- Governments
- HCWs
- Public
- Call for provision of reliable and inexpensive source of EML drugs

7.2 Education

- Support initiatives

7.3 Support for hospices through international organisations and directly

- Volunteering
- Financial
- Coordination of services

7.4 Research

- How to increase access, demonstrating diversion is not a problem.

8. References

1. Lipman A.G. Pain as a human right: The 2004 Global Day Against Pain. *Journal of Pain and Palliative Care Pharmacotherapy* 2005; 19(3): 85-100.
2. Brennan F. Palliative care as an international human right. *Journal of Pain and Symptom Management* 2007; 33(5): 494-499.
3. Help the Hospices Survey on Access to Analgesics 2006
4. Hearn J. and Higginson I.J. Cancer pain epidemiology: a systematic review. In Bruera E.D. and Portenoy R.K. editor. *Cancer pain, assessment and management*. Cambridge: Cambridge University Press; 2003.
5. Norval D.A. Symptoms and sites of pain experienced by AIDS patients. *South African Medical Journal* 2004; 94(6): 450-454.
6. Merriman A (Personal communication 2006)
7. Solano J.P., Gomes B. and Higginson I.J. A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. *Journal of Pain and Symptom Management* 2006; 31(1):58-69.
8. UNAIDS. Report on global AIDS epidemic. Geneva: UNAIDS; 2006.
9. Parkin D.M. et al. Global cancer statistics 2002. *CA: A Cancer Journal for Clinicians* 2005; 55:74-108.
10. Azevedo Sao Leao Ferreira K., Kimura M. and Jacobsen Teixeira M. The WHO analgesic ladder for cancer pain control, twenty years of use. How much pain relief does one get from using it? *Supportive Care in Cancer* 2006; 14(11): 1086-1093.
11. World Health Organization. Comparative table of core medicines on the WHO Essential Medicines List from 1977-2005 [online]. Available from: http://www.who.int/medicines/publications/essential_medicines/compar_table_who_edls.xls [Accessed 21 August 2007].
12. World Health Organization. Essential medicines [online]. Available from: http://www.who.int/topics/essential_medicines [Accessed 21 August 2007].
13. World Health Organization. WHO Model List of Essential Medicines [online]. Available from: http://www.who.int/medicines/publications/essential_medicines [Accessed 21 August 2007].
14. Scholten W (Personal communication 2006)
15. De Lima L. The International Association for Hospice and Palliative Care list of essential medicines for palliative care. *Palliative Medicine* 2006; 20(7): 647-651.
16. De Lima L. Ensuring palliative medicine availability: the development of the IAHPCC List of Essential Medicines for Palliative Care. *Journal of Pain and Symptom Management* 2007; 33(5): 521-526.
17. Relax of morphine regulations. *Sunday Times (South Africa)* 2006 October 26.
18. Sindrup S.H. et al. Efficacy of pharmacological treatments of neuropathic pain: an update and effect related to mechanism of action. *Pain* 1999; 83(3): 389-400.
19. Colins S.L. et al. Antidepressants and anticonvulsants for diabetic neuropathy and postherpetic neuralgia: a quantitative systematic review. *Journal of Pain and Symptom Management* 2000; 20(6): 449-458.
20. Mosoiu D. et al. Reform of drug control policy for palliative care in Romania. *The Lancet* 2006; 367(9528): 2110-2117.

21. Joranson D (Personal communication 2006)
22. Oxfam. Healthcare in crisis: the shortage of health workers in developing countries. Oxfam; 2006.
23. Ugandan Ministry of Health estimate for 2000.
24. United Nations (UN). The Millennium Development Goals Report 2005. New York: UN; 2005.
25. Finch L. Fighting for food aid – the struggle to assist groups affected by HIV/AIDS. *The Lancet* 2004; 364(9446): 1650-1651.
26. De Lima L. et al. Potent analgesics are more expensive for patients in developing countries: a comparative study. *Journal of Pain and Palliative Care Pharmacotherapy* 2004; 18(1): 59-70.
27. Wenk R. et al. High opioid costs in Argentina: an availability barrier that can be overcome. *Journal of Pain Symptom Management* 2000; 20 (2): 81-82.
28. Bruera E.D., De Lima L. Opioid cost: a global problem. *Palliative Medicine* 2005; 19(6): 504.
29. Prof Rajagopal and Prof George (Personal communication 2006)
30. Kikule E. A good death in Uganda: survey of needs for palliative care for terminally ill people in urban areas. *BMJ* 2003; 327(7408): 192-194.
31. Sykes N. Morphine kills the pain, not the patient. *The Lancet* 2007; 369(9570): 1325-1326.
32. Passik S.D. et al. A pilot survey of aberrant drug-taking attitudes and behaviours in samples of cancer and AIDS patients. *Journal of Pain and Symptom Management* 2000; 19(4): 274-286.
33. Portenoy R. et al. Opioid use and survival at the end of life: a survey of a hospice population. *Journal of Pain and Symptom Management* 2006; 32(6): 532-540.
34. Rajagopal M.R., Joranson D.E. and Gilson A.M. Medical use, misuse, and diversion of opioids in India. *The Lancet* 2001; 358(9276): 139-143.
35. World Health Organization (WHO). WHO Expert Committee on Drug Dependence – Thirty-fourth report. Geneva: WHO; 2006.
36. World Health Organization (WHO). Achieving balance in national opioids control policy: guidelines for assessment. Wisconsin: Pain and Policy Studies Group; 2000.
37. United Nations (UN). Report of the International Narcotics Control Board for 1999. New York: UN; 2000.
38. Dr Mosoiu D (Personal communication 2006)
39. Jagwe J. and Merriman A. Uganda: delivering analgesia in rural Africa: opioid availability and nurse prescribing. *Journal of Pain and Symptom Management* 2007; 33(5): 547-551.
40. Wenk R. et al. E-teaching in palliative care: preliminary results of a pilot project. Proceedings of the UICC World Cancer Congress; July 8-12, 2006.

9. Further resources

Achieving balance in national opioids control policy: guidelines for assessment

World Health Organization, 2000:

www.painpolicy.wisc.edu/publicat/00whoabi/00whoabi.htm

Cancer Pain Relief

A quarterly WHO newsletter:

www.whocancerpain.wisc.edu

Help the Hospices website

Includes on-line education material, an international section and information on grants available:

www.helpthehospices.org.uk

Hospice Information

An international resource on hospice and palliative care provided by Help the Hospices and St Christopher's Hospice offering:

- Networking at regional, national and international levels
- Access to resources and training
- Electronic and print publications including:
 - Worldwide Hospice and Palliative Care Online,
 - Hospice Information Bulletin,
- International palliative care directories
- 'Starter packs' for people who wish to establish a service or develop links through volunteer placements or twinning partnerships

www.hospiceinformation.info

International Association for Hospice and Palliative Care website

Containing:

- Free monthly newsletter
- Under resources (not a comprehensive list):
 - Educational resources
 - Pain and palliative care assessment and research tools
 - Policy and advocacy tools
 - Standards for palliative provision
 - Treatment guidelines
 - Information for patients and relatives
 - Administrative and programme development tools

www.hospicecare.com

International Narcotics Control Board website

Containing:

- UN conventions relating to opioids
- Reports: Technical reports, Treaty Adherence, National Estimates
- List of drugs and substances covered by the conventions ('Yellow List')
- Guidelines for National Competent Authorities
- Forms required by INCB regarding opioids
- Guidelines for travellers
- Training materials:
 - Part 1 – general information
 - Part 2 – estimates system
 - Part 3 – statistical returns

www.incb.org

Médecins sans Frontières (MSF)

MSF's is campaigning internationally for greater access to essential medicines. Website includes press releases, reports and publications:

www.accessmed-msf.org

Pain and Policies Study Group, Wisconsin

Resources on opioid availability, conference presentations and monographs:

www.painpolicy.wisc.edu

Palliative Care Matters

Includes links to International palliative medicine journals and an electronic version of the Palliative Medicine Handbook by Ian Back: www.pallcare.info

palliativedrugs.com

Promotes and disseminates information about the use of drugs in palliative care: www.palliativedrugs.com

WHO Expert Committee on Drug Dependence – Thirty-fourth report

WHO, 2006:

www.who.int/medicines/areas/quality_safety/34thecddmeet/en/index.html

WHO List of Essential Medicines

Includes concept of essential medicines, current list, guidelines and how to submit suggestions for future lists:

www.who.int/medicines/services/essmedicines_def/en/index.html

WHO webpage on substances under international control, which links to UN conventions relating to opioids

www.who.int/medicines/areas/quality_safety/sub_Int_control/en/index.html

Access to pain relief – an essential human right

Help the Hospices
Hospice House
34–44 Britannia St
London WC1X 9JG
Tel: 020 7520 8200
www.helpthehospices.org.uk

Registered Charity in England and Wales,
Help the Hospices No. 1014851
Company Limited by Guarantee registered
in England No. 2751549.
Registered office: Hospice House as above.

Printed by Hobbs The Printers, Hampshire.

