WHO Normative Guidelines on Pain Management

Report of a Delphi Study to determine the need for guidelines and to identify the number and topics of guidelines that should be developed by WHO

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1. Executive summary

The correct diagnosis and proper treatment of pain is an important public health concern. Millions of people in the world with severe acute and chronic pain suffer because of the ignorance of doctors and the lack of a standardized scientific approach.

World Health Organization (WHO) is committed to facilitate the adequate treatment of pain by legitimate use of opioid analgesics. WHO through its *Access to Controlled Medications Programme* plans to assist Member States to achieve a balance between the use of controlled substances for legitimate medical purposes and the prevention of their abuse. WHO through normative guidelines on the treatment of all types of pain can provide guidance to governments, institutions and health care professionals for policy, legislation and practice.

A Delphi study was done to identify the topics to be included in WHO guidelines and the number of guidelines that need to be developed. Experts and office bearers of professional bodies related to pain were identified in order to get the views of the international medical and pharmaceutical communities on the best solution for the development of one or more guidelines. Fifty six experts were approached through e-mails, telephone or personal interview. Forty six (82%) responded.

All experts, including representatives of the professional bodies, urged that WHO should take a lead in this area. WHO has normative clinical and policy guidelines on opioid availability only for cancer related pain. These guidelines are widely used and have served as a major tool for policy change and as an educational tool on the appropriate use of opioids for pain management. Similar to the cancer pain relief guidelines, the new WHO guidelines could serve as a guide to health care professionals from all disciplines, in addition to policy makers and regulatory authorities, for legitimate use of opioids in pain management and facilitating their legal access.

The majority of experts favored that WHO should develop three distinct guidelines, keeping broad distinctions between acute and chronic pain: 1) Acute pain, 2) Chronic malignant pain (including pain in cancer and HIV patients) and 3) Chronic non-malignant pain. They should include recommendations for specific age groups, clinical situations and resource settings. Examples include pain assessment of patients who have difficulty communicating and the treatment of patients with co-morbidities, substance abuse, terminal stage (end of life), emergencies and who need home-based care.

The best option chosen was to have a total of three guidelines for adults, with specific issues for children and older adults mentioned as a chapter, paragraph or appendix. However, this option was not acceptable to many paediatricians. It remained an issue whether there should be separate guidelines for children since there are only a few types of pain, especially chronic pain, that are common in both adults and children (e.g. sickle cell pain, burns, cancer, HIV). In addition, the assessment of pain, types and doses of medicines, route of administration and adverse effects are different in very small children. The WHO Guideline Steering Group of the *Access to Controlled Medications Programme* should consider both options. Although widest acceptability by the medical community is the most important consideration for widespread use of guidelines, the final decision by WHO will also depend upon the cost involved in terms of money, time frame and expertise.

WHO should develop one guideline on pain in patients with cancer, HIV and other life-threatening conditions; this was considered to be the best option and had the highest net acceptability among experts. This should be in line with a holistic approach to palliative care for cancer and HIV/AIDS

patients by WHO cancer programme and could serve as input for the pain management part of field guidelines for palliative care.

The two existing WHO guidelines for cancer related pain relief in adults and children require updating to include newer opioid and non-opioid drugs, newer routes of administration, adjuvant drugs, different interventional approaches and non-drug modalities.

The experts commented extensively on many controversial issues, barriers and undesirable practices in optimal pain management. These are summarized in table 3 (annex 4). Addressing these issues and wider participation were considered important for the acceptance and ownership of WHO guidelines. Although taking account of recent advances, these guidelines should encourage cost effective practices in limited resource settings. WHO should also provide a guidance plan for implementation and adherence to these guidelines.

The experts suggested building on the available guidelines developed by different organizations, and where appropriate, developing new guidelines. WHO should contemplate the possibility of joining hands with other organizations like International Association for the Study of Pain (IASP), European Association of Palliative Care (EAPC) and International Association of Paediatrics (IAP) and with other experts who have offered support and expertise in developing WHO guidelines. WHO can take a lead and coordinate the efforts of these organizations for optimal utilization of resources and avoid duplication of efforts. It was considered necessary to involve health care professionals from all disciplines, including nurses and pharmacists, in the development of guidelines and define their clear roles, including the prescribing of opioids.

This report reflects the opinion of various experts and organizations active in the area of pain management on what is acceptable and not acceptable to the medical community. This can provide the basis to the WHO Guideline Steering Group for decision making on developing WHO normative guidelines on pain management. It may also be of interest to organizations active in the area of pain management who wish to support WHO in this endeavor by providing technical and/or financial assistance.

2. Background

Pain is a direct or indirect consequence of several diseases. However patients with moderate to severe pain are often under-treated in both developing and developed countries because opioids, which are the mainstay of pain relief in such cases, are mostly inaccessible. Opioids are categorized as *controlled substances* and therefore are subjected to stringent control. This poses a significant public health challenge. WHO is committed to promote maximum possible pain relief to every patient in pain.

WHO has developed the *Access to Controlled Medications Programme* [1], to address the adequate treatment of pain by legitimate use of opioid analgesics and provide uniform guidance to governments, institutions and health care professionals for policy, legislation and practice. Development by WHO of evidence-based treatment guidelines for the treatment of all types of moderate to severe pain (both acute and chronic) would be one of the steps towards achieving this goal.

A Delphi study was done to determine how many normative guidelines on pain treatment WHO needs

[1] Framework of the Access to Controlled Medications Programme, World Health Organization. February 2007

to develop, and which types of pain should be included in each of the guidelines. At the moment WHO has normative clinical guidelines for cancer related pain that include policy guidelines on opioid availability as separate documents for adults and children.

This report describes the process and results of broad consultation. It highlights the urgent need for WHO to develop guidelines that together cover management of all types of pain and promote their implementation in all Member States as well as facilitating the availability of essential drugs, including opioids. The recommendations on various types of pain that need to be included in these guidelines and the potential options regarding the format of the final document are provided in this report. The experts raised many controversial issues that need to be addressed in WHO guidelines; they are summarized in table 3 (annex 4).

WHO can play an important role in bringing this crucial topic to the agenda of policy makers and health planners and in raising awareness of the health care professionals.

3. Objective

The overall objective of the study was to determine which guidelines should be developed by WHO that would gain broad support worldwide from experts and various organizations active in the area of pain management.

4. Methodology

The study was done over a period of four months (February- May, 2007).

A brief review of literature was done that included Cochrane and systematic reviews. This was done through an internet search from various websites (Google, Pubmed and Cochrane library) to prepare a list of diseases and conditions in which pain is an important symptom and requires treatment with opioid analgesics. Based on this, the areas for discussion were recognized and various existing national and international pain treatment guidelines were identified.

An inventory of existing WHO guidelines on pain management was made through an internet search of the WHO website, a Google search and in-house consultations.

Professional and technical staff in different departments of WHO Headquarters (HQ) working in pain-related medical conditions were consulted (annex 7). The purposes were to identify and obtain various WHO documents having reference to pain management, to explore possibilities of collaboration and identify experts in different countries, organizations and professions who are active in pain management.

To produce suitable information for decision making, the Delphi method was used. This method is a structured process for collecting and distilling knowledge from a group of experts. [2] The experts were identified through referral by WHO HQ staff, participants' lists of WHO meetings reports, referral by other experts and professional organizations, published literature and internet searches from Google, Pubmed and Cochrane websites. Office bearers of professional bodies related to pain were also contacted to identify opinion leaders.

[2] http://www.ryerson.ca/~mjoppe/ResearchProcess/841TheDelphiMethod.htm accessed on 9 February , 2007

Fifty six experts, representing international and regional organizations working in the area of pain and medical care providers from various medical and related disciplines dealing with diseases and conditions associated with moderate to severe pain requiring use of controlled medication, were selected. These included pain physicians, general practitioners, family physicians, general surgeons, anesthesiologists, neurosurgeons, trauma surgeons, orthopedic surgeons, neurologists, pediatricians, palliative care specialists, hematologists, geriatricians, nurses and hospital pharmacists (annexes 7, 8). Efforts were made to include opinion leaders from both developing and developed countries from each of the regions of WHO.

The selected group of experts was consulted through e-mails or telephone. Those who were in Geneva for WHO meetings were consulted through personal interview. All were informed about the purpose of the study and selected open-ended questions (annex 1A) were asked. The aim was to ascertain the need for WHO to develop guidelines on pain management, explore the need to update existing WHO guidelines on cancer related pain relief, recognize the controversial issues, barriers and practices that need to be changed in pain management and consider the various types of pain for which treatment guidelines need to be developed.

The responses were reviewed at regular intervals and additional questions were identified for further discussion with external experts. New experts were included into the study at different stages depending upon whose opinion ought to be included. All of the comments from the 46 experts who responded are summarized and presented in the results below. The experts suggested many options and formats for the number and types of guidelines to be developed. In the next stage of the study, each of the 46 experts was provided with a summary of opinions and options using a second short questionnaire (annex 1B). They were asked to choose the best option and or to arrive at some consensus on the acceptability of the option chosen by WHO. The final analysis of responses from the 31 experts who responded is presented in table 1 in results section.

5. Results

5.1 The urgent need for WHO guidelines on pain management

At present many physicians from different specialities (e.g. neurosurgery, neurology, surgery, anaesthesiology, psychiatry and physiotherapy) are involved in the care of pain patients. There is a bias for surgeons to operate, anesthesiologists to do pain procedures, physiotherapist to emphasize function improvement and psychiatrists and physiologists to prescribe medication and behavior modification techniques. This reflects a particular physician's education and training. The medical curriculum does not have a common plan of pain management and uniform nomenclature of various pain states. Therefore there is a strong need for WHO to develop guidelines using a multidisciplinary approach.

WHO published extensive guidelines on the relief of pain related to cancer in adults in 1986, which was updated in 1996, followed by guidelines on cancer related pain relief and palliative care in children in 1998.[3,4] These have had major impacts, but they need to be updated in view of large clinical advances. More effort and focus on developing appropriate guidelines for the limited-resource settings are needed. International Association for the Study of Pain (IASP) considers that there is a

[3] Cancer Pain Relief with a Guide to Opioid Availability Second Edition 1996
[4] Cancer Pain Relief and Palliative Care in Children 1998

great need for focusing on the education of the WHO developed principles of cancer related pain management in the developing world.

Most experts in developing and developed countries informed that they follow the WHO analgesic ladder and WHO guidelines for cancer related pain relief. Different departments in headquarters and regional offices of WHO have addressed pain management and related issues in their respective areas (annex 2: Table 2). Some of them have addressed policy-related issues and others have provided treatment protocols without addressing policy issues regarding opioid availability. However there is a need to look at the problem of pain in a comprehensive manner as there are many cross-cutting issues across the sectors managing pain that can only be addressed by a comprehensive approach.

Many local, national and international professional bodies have developed their own guidelines (annex 3). The appropriate drug selection, dosage, alternative replacement of the drugs and changing the management program are included in the guidelines but are not uniformly agreed upon between the societies. WHO through these guidelines can help to promote adequate availability of opioids and other essential analgesics. Often the allowed dosages of opioids in policy guidelines from the governments do not consider the patient's pain status and the effectiveness of the treatment. Authoritative, clear and concise evidence-based guidelines from WHO could have a major impact on the correct use of these drugs. These will be very much welcomed by the medical communities, as well as regulatory authorities in all countries.

5.2 Types of WHO normative guidelines

Updating WHO guidelines on cancer related pain relief

Almost all the experts advised to update and revise the existing WHO cancer related pain relief guidelines. Although one expert from a developing country felt that he would rather see efforts focused on guidelines other than cancer.

The 3-step analgesic ladder has been an exceptional model that demonstrates a conceptual step-wise approach to the management of cancer related pain. The basic premise stands very useful, but many changes in pharmacotherapy need updating.

Recently new drugs, new formulations, different classes of drugs and different methods of administration have become available. There are a number of opioids that were not available then; including sublingual and transdermal buprenorphine, transmucosal and oral fentanyl etc. In addition, methadone has a much larger role now; the issue of prescription opioid drug dependence syndrome has become much more prevalent. There has been development of newer techniques of pain assessment and greater development of palliative care and hospice programs. More evidence is now available for the optimal use of opioids and the control of their adverse effects, such as the major problem of gastrointestinal dysfunction that occurs during opioid treatment for chronic pain.

Updating of WHO cancer pain relief guidelines should specifically address the following issues:

* Practice of waiting until curative care options are exhausted before initiating palliative care.
* **Usefulness of the second step** in the WHO analgesic ladder has been questioned by some experts. WHO should emphasize that the use of the analgesic ladder depends upon the type and intensity of the pain associated with the cancer.

- **Weak versus strong opioids,** as well as the relative potencies of each of the analgesics (e.g., does morphine belong to the second or third step?). Many physicians having access to strong opioids skip step II and use low doses of strong opioids instead of weak opioids. Transitions between steps II and III of the ladder need to be less rigid.
- The issue of using or not **using a double dose** at bed time while on immediate-release oral morphine (still relevant to most resource-poor regions where newer opioids or slow-release preparations may not be affordable).
- **Use of inexpensive drugs** in the context of the developing world (evidence is generated mostly for expensive drugs resulting in needless pain in the limited-resource settings) and the need of access to **low-cost opioid** analgesics for all patients. The new guidelines should take into account the recent advances and the limitations of poorer countries.
- The need to secure **alternative routes of opioid delivery** when patients are unable to continue taking opioids by mouth.
- **Opioid switching ("rotation")** (very useful in clinical practice but not supported by strong evidence yet); the role of second step (tramadol, codeine etc); the role of transdermal buprenorphine; the need of opioid titration before starting with fentanyl patches; the need of opioid titration by immediate-release opioids (morphine).
- Need to adequately assess and manage a patient who has cancer-related pain and **a history of drug dependence syndrome** because their life expectancy can often be similar to the non-malignant patient.
- There is no consensus for the management of cancer-related **neuropathic and incident pain.** Practical strategies for treatment of breakthrough pain in cancer needs attention in both the hospital and the home settings.
- There is confusion about regular use of bisphosphonates and radionuclides for **bone pain** in cancer. Bisphosphonates have been increasingly used in treatment of painful bone metastasis. While external beam radiation therapy remains the mainstay of pain palliation of solitary lesions, bone-seeking radiopharmaceuticals have entered the therapeutic armamentarium for the treatment of multiple painful osseous lesions.[5] This approach, however, should not be considered for terminal cancer patients.
- Provide practical strategies to reduce **side-effects** of opioids such as sedation (bolus vs. continuous infusion), pruritus, urinary retention, constipation etc.
- The **adjuvant drugs** are necessary to treat side effects, relieve **symptoms** like breathlessness, nausea, vomiting and other symptoms of advanced cancer or to provide additive analgesia. Antiemetics, laxatives, antidiarrheals, antidepressants, antipsychotics, antiepileptics, anxiolytics, corticosteroids, and psychostimulants are important and should be available. Special attention should be paid to the psychostimulants administered as adjuvant in association with opioids. Also, the use of gabapentin and pregabalin, alone or in association with NSAIDS or with opioids, should be dealt with.
- The WHO Model List of Essential Medicines, 14th Ed**.,** (2005) includes some but not all of the adjuvant drugs and analgesics. This needs to be revised.
- **Non-drug modalities** have been included in cancer guidelines. Interventional therapies as 4th step are not necessary. These can be used at each step depending on the patient need.
- **Pre-emptive pain management** for symptoms that occur with procedures or activity.
- Include practical alternatives for effective control of **pain in the outpatient setting**.

[5] Pandit-Taskar N, Batraki M, and Divgi CR. Radiopharmaceutical Therapy for Palliation of Bone Pain from Osseous Metastases. Journal of Nuclear Medicine 2004; 45 (8): 1358-1365

- WHO analgesic ladder **is not child or infant specific** and it does not include the management of anxiety, especially in young sick children. Perhaps an analgesic ladder for infants and children can be developed where options for anxiolytic agents are included.
- A more practical guide to support the dying child is needed with specific mention of the **dying infant and very young child**, for example, in settings with high language barriers or with cultural and religious differences. In addition, guidance is needed to support the child (and family) on chemotherapy, radiation therapy or post operatively.

Thus, it would be useful to expand the guidelines and the ladder to address the above controversial issues and to include new medications, newer routes and more interventional approaches.[6,7] Also it is important to provide updated information to new generations of clinicians who have not used opioids and it would be useful to keep this key topic visible.

One of the external experts raised a concern for a stand-alone publication to cover cancer related pain management without tackling other symptoms in palliative care in the same edition. In palliative care, for pain in particular, it is essential that all precipitating and maintaining factors, such as other symptoms and problems, are addressed in order to achieve good pain control.

Dr Sepúlveda, (Senior Adviser, Essential Practices and Palliative Care, WHO HQ) remarked that she strongly discourages guidelines covering cancer related pain management alone, without tackling other symptoms and palliative care as a whole. It would provide a contradictory signal as WHO Programme on Cancer Control has been promoting in the previous years that cancer palliative care is not only about pain relief, but is a much broader and holistic intervention. She suggested that if pain treatment guidelines are being developed as a single document including cancer related pain relief for adults and children, then this should include a reference to the main *updated* guidelines of cancer related pain relief and palliative care for adults and children available in separate WHO publications. (For the options provided by her, see annex 6: Note for record)

Chronic malignant pain

This category includes pain due to potentially life-limiting illnesses such as cancer, HIV/AIDS, amyotrophic lateral sclerosis, multiple sclerosis, end stage organ failure, advanced chronic obstructive pulmonary disease, advanced congestive heart failure and Parkinsonism. All of these are indications for similar pain management that focuses more on symptom control than function, as opposed to chronic non-malignant pain that has more of a rehabilitation focus. Pain therapy will require continuous adjustment in progressive conditions where the underlying disease is expected to advance.

Chronic non- malignant pain

Chronic non-malignant pain includes:

i) Chronic musculoskeletal pain (including spinal pain or low back pain, chronic degenerative arthritis, osteoarthritis, rheumatoid arthritis, myofascial, rheumatic), chronic headache, migraine and bone pain;

[6] Portenoy RK, Lesage P. Management of cancer pain. *Lancet* 1999; 353:1695-1700

[7] Grossman SA, Dunbar EM, Nesbit SA. Cancer Pain Management in the 21st century. Oncology (Williston Park). 2006, 20 (11) :1333-9; 1340-2

ii) Neuropathic pain (including nerve compression pain, post-nerve injury and post-amputation pain, diabetic neuropathy, complex regional pain syndromes (type I and type II), skeletal muscle spasm, post herpetic neuralgia and chronic post surgical pain);
iii) Visceral pain (like distension of hollow viscera and colic pain); and
iv) Chronic pain in sickle cell anemia

Low back pain is the most common musculoskeletal pain in the hospital, as well as in the clinics not dedicated to pain treatment alone. Chronic non-malignant pain is invalidating and less researched than cancer related pain. Over the past 15-20 years there has been a great amount of effort to improve the management of cancer related pain, but the need for the optimal management of non-malignant pain remains largely unrecognized. Cancer patients do benefit from the three-step WHO analgesic ladder, but those who do not have cancer related pain often do not receive the same benefits that this stepwise approach offers. Pain in about 70% of older patients is chronic non-malignant pain. They are not treated anywhere, whereas cancer patients do get treated at nursing homes. There are no established procedures and as a result, chronic non- malignant pain often goes untreated. Patients with chronic non-malignant pain need separate guidelines using a multimodality approach.

Thus, the greatest need for guidelines is in the area of chronic non-malignant pain as these patients are at the highest risk of having inadequately managed pain.

Acute pain

Acute pain includes nociceptive, somatic or visceral pain namely premedication, perioperative, post-operative pain, post-traumatic pain, burns pain, acute pain during child birth, spinal cord injury, acute headache, HIV/AIDS, sickle cell crisis, pain in trigeminal neuralgia (Tic Doloreux), interventional pain (diagnostic and therapeutic procedures), pancreatitis and other colic pain, myocardial infarction and other major cardiac events, acute on chronic pain. Acute and postoperative pains are the most extensive types of pain treated by the pain clinics.

Opioid analgesics play a major role in the relief of acute pain. Guidelines are certainly needed for the choice of drugs, administration methods, dosing, and treatment of adverse effects.

One expert said that pain in the emergency room should have its own guidelines and recommended to have them separately because when they are involved in another type of guidelines, they lose importance.

There is inadequate understanding among clinicians about the right approach to breakthrough pain. Failure to recognize the diverse type of breakthrough pain such as incident pain directly related to activity or spontaneous pain unrelated to a particular activity can lead to under-medication or overmedication.

Acute on chronic pain is the most difficult to treat. A multimodality strategy must be advised for this.[8] Obstetric Analgesia and Caesarian sections are other areas where definite guidelines on drug concentrations and combination therapies for special indications have to be specified.

[8] Olorunto WA, Galandiuk S. Managing the Spectrum of Surgical pain : Acute management of the Chronic Pain patient. *J AM Coll Surg* ,202 (1);171-175

Pain in burns

In burns, there are three types of pain: injury pain (immediate, severe, regressive), background pain which is prolonged until wounds are healed and procedural pain (dressing changes, physiotherapy, post operative) which is severe and repetitive. Paediatric burn pain management often focuses on procedural pain only, with limited support for back ground or breakthrough pain. Ketamine has special place for procedural pain in children but requires monitoring.

Sickle Cell Disease Pain

Patients with Sickle Cell Disease (SCD) experience acute pain associated with a crisis (common) and chronic pain associated with long-term bone and joint damage (less common but can cause significant pain management problems).

It would be possible to incorporate SCD specific acute pain management recommendations in the guidelines for acute pain in adults. The approach to pain assessment, monitoring, and the use of medications is not significantly different. There are issues relating to the management of SCD that need to be emphasized, for example the association between pain, acute crisis and sequestration - analgesics, especially strong opioids, should not be used without consideration of these issues. It would be valuable, but not essential, if SCD pain management could be separated into adult and paediatric cases.

Chronic pain in SCD is more difficult. A guideline might be helpful, but it may be difficult to create something that is specific to SCD. There is no need to have a separate guideline for SCD pain management in older people.

Pain Syndromes in HIV/AIDS

Pain syndromes encountered in HIV/AIDS patients are diverse in nature and etiology. These include sensory peripheral neuropathy, extensive Kaposi's sarcoma, headache, oral and pharyngeal pain, abdominal pain, chest pain, arthralgias and myalgias, and painful dermatologic conditions. Neuropathic pains comprise a large proportion of pain syndromes, pains of a somatic and/or visceral nature are also extremely common clinical problems. The pain can be directly related to HIV infection or consequences of immunosuppression; or due to AIDS therapies; or unrelated to AIDS or its therapies. Optimal management of pain requires a multidisciplinary approach.

The experts suggested that it needs to be considered whether pain in cancer and HIV patients can be discussed together in one guideline or separate guidelines. In contrast to pain in cancer, pain in HIV disease more commonly may have an underlying treatable cause. On the other hand, both conditions are life threatening and progressive in nature and may coexist in many patients.

5.3 Types of pain which need separate guidelines in children

There are misconceptions about the need for pain management in children. Specifically neonates, infants and very young children are still not managed for pain, due to misbelief that they are not able to feel pain as adults. Pain relief for neonates is largely ignored - there is some evidence for the use of sugar, but other treatments are needed. There are few specialists in developing countries to treat pain in children.

A researcher working on pain in children in South Africa wrote that there is very little support for paediatric pain management available in most South African and African hospitals, mainly due to a lack of knowledge and expertise. Pain management is not seen as a priority or necessity. WHO should acknowledge and support paediatric pain management. Lack of interest in clinical research in this sector should be addressed.

In children, particularly newborns and infants, there are differences in the mode of assessment of pain severity, types and dosages of drugs, routes of administration, personalized drug delivery (for example transdermal formulation might be removed by the child and fentanyl lollipop might be asked not only for pain relief) and side effects. The dosages should not be extrapolated from adults. Severity of illness or disease that may impact on drug metabolism should be included in the guidelines.

There is fear around the use of morphine in children. A nurse wrote that, in case of children the opioids are supplied only in cancer terminal stage in Mexico. Children cannot swallow tablets and may refuse bitter tasting liquids. Use of off-label and unlicensed drugs in paediatrics need to be stopped. Effective and safe dosages of analgesics and treatment of their side effects for the paediatric population should be provided.

Language barriers, cultural differences and development all impact on measurement and assessment of pain in children. Assessing pain is difficult in pre or nonverbal children. It is important to include the assessment of the presence and management of anxiety, stress and fear. Because pain and anxiety are difficult to differentiate in preverbal children, it is vital to assess whether pain treatment was adequate or sedatives or anxiolytic agents are required in addition to the pain treatment. Education of health professionals in the use of appropriate medication for pain and anxiety is required.

In South Africa, at Red Cross Children's Hospital, they have developed innovative approaches to comfort care, such as nursing children who are in respiratory distress in bean bags, using latex gloves filled with ice on itching areas and using frozen carrots or ice lollies for mouth ulcers. Touch Visual Pain Scale (TVP) and PEDHIV Scales have been developed.[9] The TVP scale cuts across all language and culture barriers. It uses touch and observation to assess not only pain, but also any anxiety or discomfort that may be present in a child.

In the acute pain states in children, one has to think about multiple episodes of trauma as children grow. Maintaining the function of the child is more critical than the intensity of pain relief. Children have the capacity to heal earlier and regain their normal function faster than adults. For these children with trauma in the acute phase, the guidelines should emphasize the need to reduce the intensity of pain from intolerable to a tolerable state. Drug use in the paediatric patient even at the acute pain stage is fraught with danger.

Interventional procedures are very rarely advocated and yet they may be most effective to reduce the pain in children, especially in post-operative pain management. [10] In recent literature, use of least invasive effective technique for level of pain anticipated is recommended in post operative pain management of children. The technique should be matched to complexity of procedure and adjusted for age, medical status and comorbidity. [11]

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[9] Touch Visual Pain Scale (TVP) and PEDHIV Scale developed by Dr Rene Albertyn, Red Cross Children's Hospital, Cape Town. http://www.health24.com/medical/Condition_centres/777-792-820-3507,36832.asp accessed on 14 March, 2007

[10] Raj, PP. Pain in Children. Practical Management of Pain 2nd edition. 2000

[11] Morton NS. Management of postoperative pain in children. *Arch. Dis. Child. Ed. Pract.* 2007;92;14-19 doi:10.1136/adc.2004.070888

Children do not want to decrease their function, even if the pain persists. Their behaviour changes when they cannot do the things that the other children do. They withdraw in isolation, seek attention from their loved ones and if they do not receive it, they become very disabled, irritable and cry for help. The guidelines should be developed for such a pain state to recognize this behavioral aspect in a child and recommend the appropriate treatment to correct the behaviour before it becomes intractable. This area is a specialized area and multi-modality treatment is essential. Some experts have observed significant differences in the behavioural response to "being ill" in sick children from predominantly disadvantaged communities as compared to developed countries.

It was suggested that guidelines for children would be helpful for acute pain (trauma including rape, procedural pain, burn pain and postoperative pain) and chronic malignant and non-malignant pain. In particular, management of sickle cell pain and pain in HIV/AIDS, paediatric migraine, juvenile rheumatoid arthritis, abdominal recurrent pain, neurological disorders, cancer related pain and palliative care, associated problems including life threatening trauma or illness, reflex sympathetic dystrophy in children should be addressed. Treatment of pain in neonates, infants and very young children needs special mention. Additionally, pain in children in intensive care units, pain assessment and management at home (i.e., oral opioids including methadone) and pain in children with neuro-cognitive impairment, preverbal or nonverbal states should also be addressed as special issues.

The majority of experts felt that children pain guidelines should be separate but largely following the same principles. One expert recommended not to have separate guideline publications for each topic but to include guidelines for all issues as part of a comprehensive single document that addresses pain management in children. The topic of pain management in children should not be covered as a secondary objective in a manual for pain management in adults. Children are not "little adults"; management of pain in this population deserves its own guidelines. A paediatric pain management training manual is greatly needed. Paediatric palliative care teams should also be trained in pain management.

However some experts felt that the issues of acute pain in children can easily be discussed within the guidelines for adults in acute pain as a separate chapter. On the other hand, chronic pain in children requires different assessment and management techniques and this should be the focus of an independent guideline.

5.4 Types of pain which need separate guidelines in older people

Older people are at a high risk of having their pain inadequately managed. Clinicians are afraid of treating pain in them.[12] In view of the aging (deteriorating bone, heart, renal and brain function, generalized muscular activity), they do not tolerate the common pain treatments advocated for adults. They are sensitive to drug-drug interactions, pharmacology of analgesics (different dose regimens for opioids and other drugs) and influence of co-morbidities (orthopaedic injuries such as fractured neck of femur, acute vertebral crush fracture). Acute *Herpes zoster* infection and post-herpetic neuralgia post-stroke pain, post-operative pain, and musculoskeletal (arthritic) pain are common in older individuals. Polypharmacy and indiscriminate use of NSAIDS is a major problem in the older people.

[12] Robinson CL. Relieving Pain in the Elderly. Health Prog 2007 ; 88(1) : 48-53

In a study by one expert (Geriatrics) it was shown that with treatment of pain with morphine using WHO ladder, the need for neuroleptics is decreased considerably in older patients.[13]

If oral medications are inappropriate or ineffective, alternative techniques should be utilized. They may require multiple interventional procedures. The older patients with non-malignant pain are treated similarly to terminal cancer related pain patients using the same guidelines. There are no coordinated programs such as hospice or palliative care for them. The problem is that the drug dosage for the older people having pain without cancer is very different than for cancer related pain. The guidelines should reflect the aging process and carefully consider the appropriate drugs and dosage.

Their cognition is impaired; they may have a memory loss and may require a support system for their daily living. If there is no support system, the older patients deteriorate. Guidelines should provide simple management so the older patients follow the protocol of their pain management. Sometimes the older people can manage the pain in a salvation spiritual way. It is important to give them the necessary information so they can easily accept the treatments of the persistent chronic pain with the opioids.

Thus older people have unique reasons for specialized management of their pain and require unique approaches to the management (assessment and treatment) of all types of pain.

Some experts said that the assessment and treatment of pain in older people could be stressed as a separate issue in the same book for pain in the adult population. A separate document for older people guideline overlapping with the other three guidelines for adults can lead to confusion if not fully integrated into the other existing ones. However other experts felt the need for separate guidelines for older people because many health care providers who treat this population don't have training in geriatrics and don't have training in pain management either and who are in small community hospitals without an easy access to consultation with a pain or geriatric specialist.

5.5 Role of nurses and pharmacists

Nurses are essential in pain diagnoses and treatment in all health care settings. They are closest to the patients and their families and provide constant emotional, spiritual and personal support. They have important role in assessing and monitoring pain management.

The nurses can first evaluate the pain and can recommend to the treating doctor whether the use of pain relief medication is appropriate. After using the medicines, nurses can evaluate the effect of the medications. They can guide the doctor about patient's condition and when to change the step of the ladder. Many of them act as the coordinators of different pain groups from different specialities.

One expert from a developing country informed that in their tertiary care facility, the nursing staff in acute pain service maintains records of various parameters and uses *Visual Analogue Scales.* The nursing staff also communicates to the pain team or doctor in charge the absence of pain control in the patient, if a treatment technique fails or any adverse effects that can not be properly managed. Nurses do not administer intravenous medications or epidural boluses and are not allowed to remove epidural

[13] P e r s o n n e s â g é e s Campagne «Vers un lieu de vie sans douleur» Un EMS valaisan se mobilize available at www.sans-douleur.ch/en/pdf/emsvsmetrailler.pdf

catheters. They are however taught to give subcutaneous medications and insert subcutaneous cannulae. The senior staff teaches pain management to the juniors.

The nurse is the patient's advocate and is the best communicator to the patient of what the physician plans to do. It is important to educate them to give drugs by the clock, day and night, and about the need for good pain control. The nurses should be educated about how they communicate to the suffering patient and explain treatments to them.

There are regions both in the developing and developed world where community nurses prescribe or dispense analgesics with no direct supervision by doctors. For example, nurses prescribe oral morphine in Uganda and Macmillan Nurses in the United Kingdom often write prescriptions and get them signed by General Practitioners. In most of the developing countries, only doctors are allowed to prescribe for any medications. In United States, registered nurses with bachelor's degrees cannot prescribe medications, but they can assess pain and make sure that patients are getting the correct pain treatment. Advanced Practice Nurses can prescribe medications including opioids. This group plays an important role in the overall pain management of patients, including pain assessment and therapy optimization for pain control. In Switzerland, assistant nurses are not allowed to give morphine or evaluate patients. They form 80% of the total professionals in nursing homes. They should be informed and educated to administer morphine and evaluate pain to improve pain management. Through them, we can have coverage of 90% of patients. Otherwise only few patients can be evaluated and treated.

A family physician from Nigeria said that the issue about their role in prescribing oral morphine is very delicate and should be decided after careful consideration. We can give them adequate training and they can be allowed to prescribe under strict supervision. However, this training should occur after they have attained some level of experience. The number of such nurses who are trained to prescribe oral morphine should be restricted.

Pharmacists have an important role both in the hospital setting and in the community setting. In many societies, the pharmacist is the most available health professional to the public and sometimes they are first one to talk to patients. They can be big advocates for pain relief as they discuss with patients the importance of pain treatment and direct them to the right doctor. Pharmacists should be educated to avoid changes of medication at the counter and educate people to avoid improper practices such as self-medication. Pharmacists have the best knowledge of the drugs that physicians have prescribed and they are able to detect if there are any irregularities in prescriptions, dosing frequencies, drug-drug interactions or polypharmacy.

One expert from a developing country wrote "in our institution our pharmacy could not cope with the heavy load of pre-mixed medications required every day, their storage and dispensation, as this would need a sterile environment with laminar flow. So our anaesthesia technicians prepare the pre-mixed syringes in the operating room using sterile gowns and techniques under the supervision of the pain team." None of them are allowed to prescribe drugs or administer without the doctors orders.

Pharmacists should be involved in developing pain management guidelines in view of their essential role in drug procurement, drug preparations, dosages and drug interactions, for preparing the weak morphine solution from morphine powder. It is also important to concentrate their contributions on the preparation of galenic formulations (principles of preparing and compounding medicines) for very cheap and effective drugs. Information from pharmacists such as drug characteristics, reversal agents, combinations of drugs, paediatric doses and drug side-effects should be included in the guidelines.

The nurses and pharmacists are hesitant to use or recommend opioids appropriately due to unfounded fears and biases that they will be prosecuted or investigated. This contributes often to the under treatment of all types of pain. Also, many of them are fearful that they may cause drug dependence syndrome by using, dispensing or suggesting opioids. In some developed countries, pharmacists are empowered to prescribe in a collaborative fashion with a licensed prescriber. There is need for a system of checks and balances.

The nurses and pharmacists can play an important role by understanding the current knowledge of pain management and the limits and advantages of various techniques available. Their consistent training regarding good analgesic practices may help decrease the diversion of prescribed drugs. They need to be educated and empowered to administer opioid analgesic drugs in those parts of the world where medical doctors are few and far apart. Otherwise, major parts of the population in need for relief of severe pain will never get much needed pain relief. These are major policy problems that WHO can hope to solve.

5.7 Issues to be addressed in the guidelines

Target group

The WHO normative guidelines will be formal guidelines reflecting the norms and minimum standards of pain management and will provide a policy framework to facilitate implementation of technical guidelines. The purpose is to provide uniform guidance to bring reasonable homogeneity in pain management by different groups and facilitate availability of opioids. It is evident that an immediate target audience for WHO normative guidelines would be national authorities (policy makers and legal authorities). These groups can use these guidelines as a tool to bring change in policy and legislation to address pain management. Professional bodies at national or regional levels can further adapt to the regional and national situation and develop treatment guidelines in line with WHO normative guidelines to be used by the health care personnel in health care facilities. This local adaptation should consider usability issues at a peripheral level.

Experts feel that rather than the palliative care specialist, it would be the general physicians who wish to incorporate pain management into their routine clinical practice. For a health care professional treating all kinds of pain in patients in all age ranges, the final document should be a single document with sections for each of the different situations. It should be usable for any single type or all types of pain. On the other hand, for professionals treating only a limited number of conditions (for example cancer) or age groups, separate documents may be preferable.

One family physician suggested that the guidelines should be in the format of a poster that can be posted on wall or a small sheet that can be put on the office table under glass for handy use. All guidelines need to be adjusted for conditions and parts of the world with limited medical and economical resources, as well as limited knowledge and skills of the health care system.

Assessment of pain

Assessment should be done in all cases of pain except when the pain is a presentation of major life threatening event, e.g. chest pain. Initial evaluation and ongoing reassessment are necessary. Pain

measurement is being standardised now using scales. Newer diagnostic tests are being developed for precise measurement of pain, including quantitative sensory testing and functional brain imaging. [14]

Psychosocial factors increase pain severity. It is important not only to assess the intensity and frequency of physical pain but also the presence and intensity of other suffering (Total pain). In *Total pain*, we consider not only the physical suffering but also the social, emotional and spiritual suffering. There is no amount of morphine that can alleviate such a suffering. This is an important message to send to nurses, physicians and other caregivers. Otherwise there is only an increase in the doses of opioids administered, which results in adverse effects and no response to the real suffering of the patients.

Pain management

It is important to recognize that pain is a problem in its own right, not "just" an indicator of an underlying disease or damage process, but one which extracts a great toll on individuals and society. Alleviation of pain itself, as a symptom, should be a therapeutic target. In order to improve the quality of life, the objective should be to avoid any unpleasant perception with an approach based on the right communication between the care giver and the patient.

According to some experts, in previous WHO guidelines, the use of drugs is over prescribed and over emphasized ignoring non-pharmacological methods of pain control. In both acute and chronic phase, for adequate pain relief and prevention of the side-effects of the oral morphine, the use of interventional procedures, surgical procedures, physiotherapy and other alternative treatments (including acupuncture, herbal therapy, meditation, and faith based treatments) should be recommended. For example, in the acute phase, pharmacologic management is vital and very efficient. On the other hand, in the chronic phase, pharmacological management is inefficient and may require a rehabilitative approach. Non-drug interventions need to be considered when there is no change in the pain state or when the patient has severe side effects due to the medications.

Pain management is moving towards a mechanism-based approach and molecular targeted pharmacological therapy. Treatment guidelines should consider the acute and chronic phase of the pain state, and recommend the appropriate treatment considering the recent advances and evidence base. They should also indicate when a single modality of treatment is appropriate and when multiple modalities are essential. Consider evidence-based practice for controversial issues; where there is no evidence regarding the treatment of those specific pathologies, the term "clinical practice recommendations" instead of "guidelines" may be used.

WHO guidelines should encourage research and use of inexpensive drugs in the context of developing world, specifically addressing the need of access to low-cost opioid analgesics for all patients. The new guidelines should take into account the recent advances and the limitations of poorer countries. Guidelines should encourage use and research on approaches that can reduce need for opioids; for example, neuromodulation for intractable visceral pain.

[14] Holdcraft A, Power I. Recent developments: Management of Pain. BMJ 2003;326:635-39. doi:10.1136/bmj.326.7390.635

Special consideration should be given in the guidelines for the management of pain in special patient groups and specific clinical situations, for example:

- Guidelines are needed in pediatric groups at all development stages (neonates, premature babies, infants, children and adolescents) for acute and chronic pain of all types.
- Guidelines for older people. At the moment, there is no United Nations standard numerical criterion, but the agreed UN cutoff is 60+ years to refer to the older population.
- Availability of drugs in suitable concentrations for these age groups is necessary.
- Guidelines for pain assessment in cognitively impaired patients, patients who have difficulties in communicating their suffering, feeble patients and patients with co-morbidities (depression, anxiety, insomnia, the debilitated, deaf, blind, displaced persons or refugees, terminal stage, dementia, and extreme old age).
- Management of pain that does not or poorly responds to opioid analgesics, such as neuropathic pain and bone pain.
- Treatment of pain in intensive care units, emergency rooms (abdominal or chest trauma and polytrauma) and at home.
- Management of adverse effects of pain medications (to include the issues of drug dependence and pain in patients with substance abuse, including opioid, disorders).
- Pain management in presence of substance abuse or in patients taking treatment for drug dependence (methadone, naltrexone, disulphiram).
- Deciding the duration for defining acute and chronic pain.
- Deciding the criteria for uncontrolled pain when on treatment with opioids. Scales cannot judge uncontrolled pain accurately. Patient's personal judgment is more crucial.
- Rescue medication should be included in all pain management protocols for breakthrough pain.
- Antidotes to opioids and benzodiazepines should be available.
- Weaning protocols and options are important to prevent the onset of withdrawal.
- The guidelines should give examples of case studies for different types of common pain.

To achieve wider applicability to the population, the guidelines must provide complete specifications of exceptions that may require deviations from the guidelines. (For detailed discussion on controversies, barriers and undesirable practices in pain management, see annex 4: table 3)

The guidelines also need to address the implications of adopting recommendations on costs and population health. These implication need to elaborated on for a number of possible settings, ranging from very limited to unlimited resources, including the resources required to carry out the recommended interventions.

5.8 Number and Types of guidelines WHO needs to develop

Most experts agreed that WHO needs to develop guidelines (keeping broad distinction in acute and chronic and specific clinical situations) on the following 3 categories of pain:

1. **Acute pain** (including pre- and post-operative pain, post-traumatic pain, burns pain, acute pain during child birth, spinal cord injury, acute headache, HIV/AIDS, sickle cell crisis, pain in trigeminal neuralgia (tic doloreux), interventional pain (diagnostic and therapeutic procedures), pancreatitis and other colic pain, myocardial infarction and other major cardiac events, acute on chronic pain).

2. **Chronic malignant pain** (including pain in patients with cancer, HIV/AIDS, amyotrophic lateral sclerosis (ALS), multiple sclerosis, end stage organ failure, advanced chronic obstructive pulmonary disease, advanced congestive heart failure, Parkinsonism).

3. **Chronic non malignant pain** including:
    i) chronic musculoskeletal pain such as spinal pain or low back pain, chronic degenerative arthritis, osteoarthritis, rheumatoid arthritis, myofascial, and rheumatic pain, chronic headache, migraine, bone pain;
    ii) neuropathic pain (including nerve compression pain, post-nerve injury and post-amputation pain), diabetic neuropathy, complex regional pain syndromes (type I and type II), skeletal muscle spasm, post herpetic neuralgia, chronic post surgical pain;
    iii) visceral pain (like distension of hollow viscera and colic pain); and
    iv) chronic pain in sickle cell anaemia.

Set A. The following four options were suggested to deal with guidelines for older people and children:

A1. Three guidelines on acute pain, chronic malignant pain (cancer, HIV and other life limiting conditions), and chronic non-malignant pain separately for adults, children and older people **(Total of 9 guidelines).**

A2. Three guidelines for adults and mention specific issues for elderly (as a chapter or paragraph or appendices) and make separate 3 guidelines for children **(Total of 6 guidelines).**

A3. Three guidelines for adults and mention specific issues for children and older people (as a chapter/ paragraph/ appendices) **(Total of 3 guidelines).**

A4. One guideline on acute pain for all age groups (as in option 3) and two guidelines for chronic malignant and chronic non-malignant pain separate for adults and children **(Total of 5 guidelines).**

Set B. The two options suggested by experts to deal with guidelines for patients with cancer and HIV related pain were as follows:

B1. One guideline on pain management in patients with cancer and HIV.
B2. Separate guidelines on pain management in patients with cancer and HIV.

The experts were asked to choose the best option in set A and B and indicate acceptability of various options included in the two sets. (see annex 1B, questionnaire 2). The final responses of experts in second round of discussion are summarized in table 1. Thirty one responded for set A options and thirty responded for set B options. The options A3 and B1 were chosen as the best by majority of experts, but net acceptability score was highest for options A2 and B1.

Table 1: Summary of responses on second questionnaire

	Options in set A				*Options in set B*	
Questions	*A1*	*A2*	*A3*	*A4*	*B1*	*B2*
Best options	2	8	**14**	7	**20**	10
Acceptable	16	**26**	22	16	26	25
Unacceptable	15	5	9	15	4	5
Net acceptability score	1	**21**	13	1	**22**	20

During second round of discussion, three more options (in set A) were offered by some experts:

5. Three guidelines for adults and mention specific issues for older people (as a chapter or paragraph or appendices) and make separate 2 guidelines for children on acute and chronic (malignant and non malignant) pain (**total 5 guidelines**).
6. Two guidelines on acute pain separate in adults and children and two guidelines on chronic pain separate in adults and children with chapter on palliative care **(total 4 guidelines).**
7. One guideline on acute pain, one on chronic malignant pain (for adults, older people and children), two guidelines on chronic non-malignant pain separate for adults and children (**total 4 guidelines**).

All paediatricians insisted that WHO should have separate guidelines for children. In view of that, the middle path between A2 and A3 was suggested by some of them (option A4 or A7). This is because there are only few types of chronic non malignant and malignant pain which are common in adults and children (e.g. sickle cell pain, burns, cancer, HIV).

6. Discussion

There was agreement among experts on the types of pain that guidelines should cover. However no consensus on how to deal with guidelines for children could be reached. The majority of the experts chose option A3 as the best option, which is to make total of **three guidelines** for adults and to mention specific issues for children and older people as a chapter, paragraph or appendix. However this option was also unacceptable to highest number of experts. On the contrary, option A2 which is to make **six guidelines** (three guidelines for adults, mentioning specific issues for elderly as a chapter, paragraph or appendix and separate three guidelines for children) was acceptable to a higher number of experts. Thus, this issue remained controversial after the second round of consultation as most paediatricians repeatedly stressed the need for separate guidelines for children. The assessment of pain, selection of medicines, dosing and to some extent, the route of administration and adverse effects, are different from adults particularly for newborn babies and infants. There are more differences in the guidelines for adults and children.

Wider acceptance by the medical and paramedical professionals of the choice on the number of guidelines is also a major consideration. However, from the production point of view, there are benefits to limiting the number of guidelines. Also, having many guidelines may restrain their widespread use in countries and updating frequency. The decision making in WHO guidelines will be

guided by what is most efficacious, cost effective, affordable and beneficial for the population. The final choice by WHO of the option A2 or A3 will be guided by many factors such as the operational process in the development of WHO guidelines and cost (money, time frame and expertise) involved. This can be addressed by the Steering Group of the *Access to Controlled Medications Programme*.

Cancer related pain is different from HIV related pains. It needs to be considered whether pain in cancer and HIV patients can be discussed together in one guideline or in separate guidelines. The majority of experts think it could be discussed together as these conditions may co-exist in many patients. The principals of the WHO analgesic ladder have been successfully applied clinically in AIDS patients. The ladder is considered equally appropriate for patients with HIV/AIDS. Although it has not been formally validated for patients with AIDS, it has been recommended for pain in HIV/AIDS patients by the authorities.[15] As per the guidelines of the Agency for Health Care Policy and Research (AHCPR), the principles of pain assessment and treatment in the patient with HIV/AIDS are not fundamentally different from those in the patient with cancer and should be followed for patients with HIV/AIDS.[16]

Thus, WHO should choose option B1 (one guideline on pain in patients with cancer, HIV and other life-threatening conditions), which was the best option with higher net acceptability than alternative option B2 (separate guidelines on cancer and HIV) among experts. The normative guidelines on cancer and HIV pain that will be developed in this way could serve as input for the pain management part of field guidelines for palliative care. This should be in line with a holistic approach to palliative care for cancer and HIV/AIDS patients by WHO Programme on Cancer Control.

WHO should contemplate the possibility to join hands with other organizations like IASP, EAPC and IAP and experts who have offered support and expertise in developing WHO guidelines (annex 5). WHO can take a lead and coordinate the efforts of these organizations for optimal utilization of resources in order to avoid duplication of efforts and to provide a uniform and consistent approach to pain management. This is necessary because the available guidelines from national and international organizations may not be uniform in their process of development and/or consistent in their recommendations.

It is also important for WHO to consider how many expert groups are needed to develop all of the guidelines on pain management. Usually a minimum of 4 groups, the Guidelines Steering Group (WHO staff), Technical guidelines development group, Task forces and Secretariat are involved in the development of WHO guidelines. There may be already existing expert groups, for example the groups who worked on guidelines for cancer related pain relief for adults and children. These groups were formed and met more than 10 years ago, and their membership will need to be updated. It needs to be considered whether these existing groups can be given the responsibility of new guidelines or updating existing guidelines. There may be a need to form a new expert group or a mix of new experts and experts from previous groups.

[15] O'Neill JF, Selwyn PA, and Schietinger H (eds.) A Clinical Guide on Supportive and Palliative Care for People with HIV/AIDS, 2003. http://hab.hrsa.gov/tools/palliative/chap4.html

[16] Jacox A, Carr D, Payne R, et al. *Clinical Practice Guideline Number 9: Management of Cancer Pain*. U.S. Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research, AHCPR Publication #94-0592:139-41, 1994.

7. Conclusions

From the responses received in this study, it can be concluded that the following opinions are supported most among pain experts:

1) All respondents agreed that it is appropriate and timely for WHO to take an active role in the development and revision of guidelines on pain management.

2) WHO guidelines on cancer pain relief in adults and in children are widely used guidelines. These have created awareness regarding the appropriate use of opioids for pain management among health professionals and have been a good advocacy tool for policy change. It is important to update these guidelines to include newer opioids and other analgesic drugs, newer routes of administration, adjuvant drugs, different interventional approaches and non-drug modalities.

3) There is an urgent need for change in attitude from society, medical professionals, policy makers and regulatory bodies towards improving public pain policy. Like cancer guidelines, the new WHO guidelines can continue to serve as a guide to health care professionals from all disciplines (including primary care physicians, general practitioners, nurses and pharmacists), policy makers, regulatory authorities on the legitimate use of opioids in pain management and administrative leaders for the adoption of better clinical practices. These can emphasize the need for an appropriate balance between controlling opioid analgesics and preventing abuse, trafficking, diversion and ensuring availability for these controlled substances for adequate pain management.

4) Specific and authoritative guidelines from WHO are needed to assist the governments in developing countries to make essential opioids and non-opioid analgesics and adjuvant drugs available. More efforts are needed by WHO and the International Narcotics Control Board (INCB) to ensure appropriate and legal availability of much needed analgesic medicines in large areas of the world.

5) WHO needs to develop guidelines considering the following:

   - **Types of pain**: guidelines for the treatment of all types of pains i.e. nociceptive, neuropathic and psychogenic considering *total pain* (physical, psychosocial, emotional and spiritual).

   - **Age group**: a target-oriented approach is recommended with three different sectors for pain management (neonates/children, adults and older people). These three age groups are very different for various reasons; the type of pain, pain assessment, effectiveness, and the choice of pharmacological or non pharmacological strategies.

   - **Categories of pain**: most experts agreed that WHO needs to develop guidelines on the three categories of pain (Acute, Chronic malignant and Chronic non-malignant pain), including guidance for specific clinical situations and limited resource settings.

   - **Number of guidelines**: the best option chosen was to have total of three guidelines for adults. Specific issues for children and older people can be mentioned as a chapter,

paragraph or appendix. However, developing separate guidelines on each of the three topics for children is more widely accepted. So both options should be considered by WHO Guidelines Steering Group.

- **Guideline for pain in patients with cancer and HIV:** WHO should develop one guideline on pain in patients with cancer, HIV and other life-threatening conditions. The normative guidelines on cancer and HIV pain that will be developed in this way could serve as input for the pain management part of field guidelines for palliative care. This should be in line with a holistic approach to palliative care for cancer and HIV/AIDS patients by WHO Programme on Cancer Control.

- **Operational process and cost for WHO**: the final choice by WHO of best option on which and how many guidelines to be developed will depend upon available resources such as the money, time frame and expertise and wider acceptability by the medical community.

- **Use of existing guidelines**: many national, regional and international guidelines are available on different aspects of pain management. Experts suggested that it would be more efficient to utilize the available information in guidelines developed by other organizations, if found appropriate, than to develop new guidelines. However, expanding the concepts to apply to other countries should be considered.

- **Final document**: the experts concurred that it should be a single document to facilitate use for any particular or all types of pain and for different age groups. It would stop the problem of the wrong volume being available when needed. It would also be better for adults who are very small or malnourished and paediatric doses may be more appropriate for them.

6) WHO guidelines should be updated periodically. The scope of WHO guidelines should be expanded to include advances in pain management, but should give flexibility to adapt to what is feasible in a certain situation according to the different levels of care, including community and home-based care. The guidelines should encourage cost-effective practices for limited resource settings such as use of low-cost opioids. WHO guidelines should encourage research on the use of inexpensive drugs in the context of developing world.

7) Involve health care professionals from all disciplines, including nurses and pharmacists in the development of guidelines for "wider ownership". The role of nurses and pharmacists in pain management is pivotal and must be clearly defined in WHO guidelines, including prescribing opioids etc. They need to be educated about good practices in pain management for pain assessment and pharmacological and non-pharmacological treatment.

8) Address barriers in implementation and offer practical solutions to overcome them. There are several barriers or challenges: lack of education, lack of recognition of the importance of pain management, language barriers, lack of knowledge and information, lack of resources such as books and journals, essential drug lists, cultural diversity, inability to measure and assess pain and treatment efficacy, inability to understand the development of children from different cultural backgrounds, inability to communicate with parents, diverse patients with many different pathologies, lack of trained staff and the need of access to low-cost opioid analgesics for all patients.

9) Address drug storage requirements for stability and safety. Provision of legal and safe distribution of controlled substances is important.

10) Plan strategy and tools for implementation and adherence. How norms and standards defined in WHO normative guidelines might be implemented where they are not routinely used, but where use would be appropriate? How leverage can be applied to practitioners, hospital administrators, and ministers of health? What tools might make the monitoring easier? Plan to monitor adherence to guidelines like clinical audit. Consider education of patients, family and care givers along with health care professionals and policy makers to achieve balance between preventing abuse and ensuring availability of narcotic drugs.

8. Recommendations

1. **WHO needs to develop distinct guidelines** on following three topics. (Refer 5.8 for the causes of pain in each category).

    i) Acute pain
    ii) Chronic malignant pain
    iii) Chronic non-malignant pain

According to the option that was chosen by the experts to be the best (i.e. to make **three guidelines** for adults and to mention specific issues for children and older people as a chapter, paragraph or appendix) a total of three guidelines on above topics can be developed. They should give guidance for treatment of all age categories. Specific issues for children, older people and specific clinical situations and resource settings (refer 5.7) can be mentioned as a chapter or paragraph or appendices.

As an alternative, WHO could develop **six guidelines**, three on each topic for adults, including the older people and three separate guidelines on each topic for children; the study showed this will be more widely accepted. Both options should be considered by the Steering Group of the *Access to Controlled Medications Programme.*

2. Guideline(s) on pain in patients with cancer, HIV and other life-threatening conditions could serve as input for the pain management part of field guidelines for palliative care of cancer and HIV/AIDS patients.

3. The guidelines also should include the definition, taxonomy, types of pain, criteria for defining acute and chronic, criteria for defining children and older people, drugs used in pain (NSAIDs, opioids, adjuvant drugs) and alternative and interventional treatments.

4. In the development of the guidelines, it is imperative to use the wealth of information provided by experts in this study on barriers, controversial issues, undesirable practices and technical advances in pain management (refer annexure 4: table 3). This will be helpful in providing the desired population perspective, scientific integrity and sensitivity to local contexts to WHO guidelines.

5. WHO should collaborate with other organizations like IASP, EAPC and IAP and individual experts who have offered support and expertise in developing WHO guidelines.

9. Acknowledgements

I wish to thank all external and internal experts who gave their valuable time and support in conducting the study and identifying issues to be addressed in WHO pain treatment guidelines.

Effort has been made to include the views and comments of all the experts we consulted. Inadvertent omission, if any, is regretted.

The opinions expressed in this report are those of experts consulted during the study and from literature as cited (annex 9). These are not necessarily endorsed or recommended by WHO.

Annexure 1A. Questionnaire 1

1. Which guidelines should be developed, and which pain types each guideline should address?
2. Do we need to update existing WHO guidelines on cancer related pain relief?
3. Which types of pain need separate guidelines for the treatment of children?
4. Which types of pain need separate guidelines for the treatment of older people?
5. What are the controversial areas/issues in pain management?
6. Any practices you wish to change in the clinical practice?
7. What are the barriers in your setting for optimal pain management?
8. Which are the existing guidelines in your area which are presently being followed? (Please provide an electronic copy if possible).
9. Is there a need to address role of nurses and pharmacists and defining what should be their role in these guidelines?

Annexure 1B. Questionnaire 2

Set A. Four options need to be considered for children and older people:

A1: 3 guidelines on acute pain, chronic malignant pain (cancer, HIV other life limiting conditions), and chronic non-malignant pain separately for adults, children and older people **(Total of 9 guidelines).**

A2: 3 guidelines for adults and mention specific issues for elderly (as a chapter or paragraph or appendices) and make separate 3 guidelines for children **(Total of 6 guidelines).**

A3: 3 guidelines for adults and mention specific issues for children and older people (as a chapter/ paragraph/ appendices) **(Total of 3 guidelines).**

A4: guidelines on acute pain for all age groups (as in option 3) and guidelines for chronic malignant pain in cancer and HIV other progressive incurable illnesses and chronic non-malignant pain separate for adults and children (as in option 2) **(Total of 5 guidelines).**

Questions	A1	A2	A3	A4
Q1. From the 4 options above, which single option do you favour most? (Put a cross (X) under one option only)				
Q2. For each of the 4 options, indicate if it is acceptable (A) or unacceptable (U). (Answer all 4 options)				

Set B. Two options need to be considered for cancer and HIV pain:

B1. One guideline on pain in patients with cancer, HIV and other life-threatening conditions
B2. Separate guidelines on pain in patients with cancer, and HIV

Questions	B1	B2
Q3. Which option do you favour most ? (Put a cross (X) under one option only)		
Q4. For each option indicate if it is acceptable (A) or unacceptable (U). (Answer both options)		

Annexure 2. Existing WHO Guidelines

Table 2. WHO guidelines inventory

No.	Existing WHO Guidelines	What is available	Gaps
1.	Cancer related pain relief (second edition) WHO1996	Clinical Algorithm and Policy guidelines to opioid availability Includes pain assessment and non medical methods	Update pain assessment methods and newer drugs, interventional methods
2.	Cancer related pain relief and palliative care in **children** WHO1998	do	Update pain assessment methods and newer drugs, interventional methods
3.	IMAI Palliative care: symptom management and end of life care (HIV care) IMAI Module 4 WHO 2004	Clinical Algorithm using WHO analgesic ladder (P11-P17)and Table on pain medication **dosing for children** (P42) Includes pain assessment by faces or fingers and non medical methods	Care for opioid dependence and tolerance, Adjuvant therapy and interventional methods not included. Policy guidelines to opioid availability not included.
4.	Quick Check and Emergency treatment module (IMAI) WHO 2004	Clinical Algorithm for treating severe acute pain in HIV	Policy guidelines to opioid availability not included.
5.	IMAI Complementary course on HIV AIDS. Module 4 Follow up and chronic care of HIV exposed and infected children. Geneva WHO 2006	Chapter 9.0 special, considerations in assessing and controlling pain in children (page 35) Clinical Algorithm using WHO analgesic ladder and Table on pain medication **dosing for children,** Includes pain assessment by faces or fingers and non medical methods	Care for opioid dependence and tolerance Adjuvant therapy and interventional methods not included Policy guidelines to opioid availability not included
6.	Comprehensive Cervical cancer control A guide to essential Practice WHO 2006	Clinical Algorithm: Practice sheet 18 on pain management (page 225) adapted from IMAI Palliative care	Policy guidelines to opioid availability not included
7.	Pocket Book of Hospital care for **children** WHO 2005	Clinical Algorithm in Brief Chapter 10 Supportive care 10.4 Pain control (page 275) Chapter 9. Common surgical problems 9.3 Injuries 9.3.1 Burns care includes pain management (page 242) 9.1.3 Post operative care includes pain management (page 233) Chapter 8.7 Palliative care (HIV) 8.7.1 Pain control in HIV (page 221)	Policy guidelines to opioid availability not included
8.	Surgical Care at District Hospital WHO 2003	Clinical Algorithm for Post operative Pain relief, Pain in burn, Trauma patients, Post op Pain in children Chapter 14 pain management and	Policy guidelines to opioid availability not included

		techniques (page 14.47)	
9.	Guidelines for Essential Trauma care WHO 2004	Chapter 5.12 Pain Control And Medicines : Provides a list of essential trauma care medicines including pain control medicines (table 12, Page 50) Refers to WHO Policy guidelines to opioid availability *	Clinical Algorithm not included
10.	Better Palliative Care For **Older People** WHO/ EURO 2004	Policy guidelines to opioid availability	Clinical Algorithm with appropriate dosages not included
11.	Nursing care of the sick WHO/WPRO	Chapter 13 care for the patient in pain focused on nursing care	Will be useful to include with main guidelines

*Achieving balance in national opioids control policy, Guidelines for assessment. Geneva, World Health Organization, 2000

Annexure 3. The existing national or international guidelines

1. Joint Commission for Accreditation of Health Organizations (JCAHO). Approaches To Pain Management: An Essential Guide For Clinical Leaders. JCAHO resources Http://Www.Jcrinc.Com/Generic.Asp?Durki=3873
2. American Academy of Hospice and Palliative Medicine (2007). US Clinical Practice Guidelines For Quality Palliative Care, The National Consensus Project 2007. www.aahpm.org
3. American Pain Society. Guideline for The Management Of Acute And Chronic Pain In Sickle-Cell Disease. : Http://Www.Ampainsoc.Org/Pub/Sc.Htm
4. The American Pain Society (2005). Cancer related pain Management Guideline.
5. American Pain Society Quality of Care Committee (1995). Quality Improvement Guidelines For the Treatment of Acute Pain And Cancer, , JAMA December 20, 1995, (Vol. 274, No 23)
6. The National Comprehensive Cancer Network (NCCN), the National coalition of cancer centers. Practice Guidelines in Oncology-Adult Cancer related pain V.1.2006. www.nccn.org
7. American Pain Society. Principles of Analgesic Use in the Treatment of Acute Pain and Cancer related pain 5th Edition. American Pain Society, Glenview, IL. www.ampainsoc.org.
8. JCAHO. Pain Current Understanding of Assessment, Management, and Treatments www.reliefinsite.com/downloads/Pain_Current_Understanding_of_Assessmenet_Management_and_Treatment_JCAHO.pdf
9. Management of Cancer related pain. Clinical Practice Guideline No. 9 Public Meeting On Clinical Practice Guidelines For Cancer-Related Pain. Www.Hospicepatients.Org/Clinicalpracticeguidelines1994.Html - 765k -
10. Ballas S, Carlos T, Dampier C. New Handbook For Clinicians - Guidelines For Standard Of Care Of Acute Painful Episodes In Patients With Sickle Cell Disease Http://www.Scinfo.Org/Prodbook.Htm
11. McLennon SM. Persistent pain management. Iowa City (IA): University of Iowa. Gerontological Nursing Interventions Research Center, Research Translation and Dissemination Core; 2005 58 p.
12. Wisconsin Medical Society Task Force on Pain Management. Guidelines for the Assessment and Management of Chronic pain. WMJ 2004, 103;(3)15-42
13. Royal College of Nursing 2001 Clinical Practice Guidelines: The recognition and assessment of acute pain in children. Implementation Guide. London RCN Publishing
14. Palliative medicine pain and symptom control in the cancer and/or AIDS patient In Uganda and other African Countries. A Book For Health Professionals. Fourth Edition 2006
15. Clinical Audit. Clinical Effectiveness Committee Guideline For The Management Of Pain In Adults (British Association For Emergency Medicine (Baem) Guideline): The BAEM Clinical Effectiveness Committee Standards For Emergency Departments, January 2006, UK
16. Consensus Statement from the Pain Society and Royal Colleges of Anaesthetists, General Practitioners and Psychiatrists. *Recommendations*, 2004. (UK)
17. Ontario Workplace Safety and Insurance Board. *Report of the chronic pain expert advisory panel.* Ontario (Canada): 2000.
18. Guidelines from regional and national chapters of International association on study of pain (IASP) :
    - Chile: Cancer related pain Relief and Palliative Care, Government initiative (Document provided), the others Acute Pain and Pain in the Older people) was locally developed by members of Chilean Chapter of IASP (ACHED).
    - The Chairman of a Task Force of Latinamerican Federation of IASP Chapters (FEDELAT) informed that in Colombia every hospital or pain clinic use their own guidelines. A combined committee with representatives of Ministries of Health from Colombia, Venezuela, Bolivia, Chile, Ecuador and Peru is looking to improve the currents Policies of Pain Education and management in Latinamerica.
19 University of Wisconsin Pain and Policy Studies Group (WHO Programme) documents opioid availability.
20 World Institute of Pain (WIP) has produced some guidelines for neuropathic pain, use of botulinum toxin in pain patients and the practice of radiofrequency in pain procedures published in *Pain Practice* journal.
21 The International Network for Cancer Treatment and Research (INCTR) Clinical Guidelines for Palliative Care
22 European Association of Pain Control (EAPC) guidelines. EAPC is now thinking about an update on the Opioids. The EAPC in collaboration with the EPCRC www.epcrc.org are working on a second publication for Older people. The EAPC taskforce for Children will create a publication about solid facts and "recommendations" for Children in Palliative care. The EAPC has published the curriculum of nurses.
23 Local bodies also have developed their own guidelines
    - Organizations like Floriani Foundation in Italy have developed pain guidelines.
    - Rainbow Children Hospice(USA) Guidelines for palliative care in children.
    - Red Cross Children's Hospital (South Africa) in collaboration with the Dutch team, are writing a Paediatric Pain Training Manual for African Health Care Professionals.

Annexure 4

Table 3: The issues (controversies, barriers, undesirable practices) in pain management

No	Issues	Opinions by Experts and literature review
1.	**Patients often do not report pain.** They simply bear pain for a religious or theological reason or consider part of aging. They are concerned about adverse effects, dependence, financial and occupational consequences. The patients with family problems and spiritual troubles, poor information on sickness and etiology of pain and the lack of control of the side effects of the opioids show poor response to the treatment.	**Educate the patients** and their families. Pain treatment is often goal oriented (like compensation in accident) and not curative. Therefore approach needs to be changed. Provide home-based care whenever possible besides hospital and hospice care. Good control of the side effects and follow up is needed.
2.	There is **poor assessment of pain** (intensity, causes etc) and poor daily re-assessment of the symptom. Respiratory rate and sedation scores are not documented in most centres. Inability to measure and assess pain and treatment efficacy is due to language and cultural barriers and lack of education. Pain rating scales (verbal, numerical and visual) are simple, efficient, and minimally intrusive but uni-dimensional and are less useful for chronic pain.	Documenting pain scores as the fifth vital sign should be made mandatory for all pain patients. Pain measurement should be done for measuring drug efficacy. Pain assessment is the objective basis of pain control and also helps in audit and research to evaluate the adherence to guidelines. Local adaptation of pain assessment methods is necessary. Multidemensional scales (for example Mc Gill pain questionnaire) are being developed. [17] One expert recommended the use of Doloplus 2 for older patients (a method of evaluation for pain in older people who have trouble in verbal communication. [18]
3.	**Limited availability of opioids** due to complicated licensing system or regulatory oversight or government policy is the main on going issue. There is a need for a formal initiative to identify and eliminate impediments for the use of controlled substances to treat the pain.	The **regulators** need to be educated to recognize but not interfere with medical use of opioids for pain relief and reassured that drug dependence syndrome will not result from proper use while they continue to address the issue of prescription that may contribute to drug abuse and diversion.
4.	There is resistance among **health professionals** to use morphine. They believe that strong analgesics such as morphine are meant for dying patients only or that pain control should be for cancer patients and may be post surgery. There is fear of disciplinary action for prescribing opioids, and confusion among dependence, dependence and tolerance among the public, doctors and the administrators. Health care providers are not adequately educated on the appropriate and rational use of opioids and their side effects (when and how should they be used). Poor	Consideration to a broad quality improvement project is necessary to change old practices and eliminate old fears associated with the use of opioids in the management of all types of pain. Provide regular training for morphine prescribers (doctors, senior nursing staff and clinical officers) in the appropriate use of morphine and about the regulations of opioids. They must not be afraid of the early use of opioids in moderate and severe pain, which is better than NSAIDs which cause gastric bleedings, kidney and liver failure etc. Fear of respiratory depression due to morphine is unwarranted as it is a temporary phenomenon occurs only in opioid naïve patients and is antagonized by pain. [19]

[17] Holdcraft A, Power I. Recent developments: Management of Pain. BMJ 2003;326:635-39. doi:10.1136/bmj.326.7390.635
[18] Lefebvre-Chapiro, S. & the Doloplus group. (2001). European Journal of Palliative Care, 8(5), 191. www.doloplus.com
[19] Wisconsin Medical Society Statement on the Use of Opioids for the Treatment of Chronic Pain
http://www.wisconsinmedicalsociety.org/physician_resources/guidelines/stratguide/opioidsmain.cfm

	understandings of pharmacotherapy and analgesic equivalences of the different analgesics for managing all types of pain are big barriers. Misbelieve that increased requirement of drug indicates tolerance instead of unrelieved pain. It was thought that development of tolerance limited the ability to use opioids on along term basis.	Experience in cancer related pain has shown that what initially appears to be tolerance is usually progression of disease.[20]
5.	**Fear of development of drug dependence and diversion** interferes with opioids prescription. Monitoring patients for drug dependence and diversion is required. This is particularly important in chronic non-malignant pain. All patients receiving opioids need to undergo a through assessment of the indication and need for dose escalation.	It is known that de novo development of drug dependence syndrome when opioids are used for treatment of pain is low.[21] Studies have indicated that the physician prescribed opioids are not the primary source of diversion.[22]The theft from drug distribution chain is an important source of diversion of pain medications in the United States.[23] "**Universal precautions" for pain management** includes careful assessment, ongoing evaluation, clear communication between patient and doctor, and careful documentation of the treatment process has been recommended to avoid drug dependence syndrome or diversion. [24]
6.	The **role of opioids in non-malignant pain** where a balance of drug dependence syndrome and adequate pain controls is required.	The opioids have been used for many years in the treatment of non-malignant pain in Denmark and the results are rather disappointing, informed an expert.[25] Prospective randomized studies on long term results of opioid treatment are still lacking. [26]
7.	**Usefulness of second step** in WHO analgesic ladder has been questioned by some experts. Many physicians continue to use it as a restricted matrix and many patient suffering from pain, let's say 6-8/10 still receive just paracetamol or Non Steroidal Anti Inflammatory Drug (NSAID), or some of them with neuropathic pain just receive NSAID without any opioid or adjuvant. The advisability of including NSAIDs and/or Paracetamol in all the three steps of the ladder, in view of the accumulating evidence on the adverse effects of NSAIDs and observations of good pain relief from opioids alone in many situations. (Not forgetting that there are situations like bone pain which most of the time require NSAIDs for relief).	Many clinicians find it is useful to have three steps and range of choices. Patients with severe pain can start with step 3. Morphine is still first choice for severe pain.
8.	The **WHO analgesic ladder** for usage in cancer related pain is not appropriate **for non-malignant pain**, largely due to the category of "weak" opioids such as pentazocine, dextropropoxyphene and codeine. Why would one use a "weak" drug, especially one with	In practice the decision should be based on individual patient's response to a particular opioid. A range of strong opioids are available now to treat severe pain. Choice should be according to the cost and availability. There is need for population based

[20] Portenoy RK, Lesage P. Mangement of Cancer Pain. Lancet 1999; 353:1695-1700
[21] Blake S,Ruel B, Seamark C, Seamark D. Experiences of patients requiring strong opioid drugs for chronic non-malignant pain: a patient-initiated study. Br J Gen Pract. 2007 ;57(535):101-8
[22] Kline AT, Smith MY, Haddox et al. Abuser reported sources of illegally obtained opioid medications. American Academy of Pain Medicine 23rd annual meeting, Feb 7-10, 2007, New Orleans, Louisiana, abstract 105
[23] Joranson DE, Gilson AM. Drug crime is a source of abused pain medications in the United States. Journal of Pain and Symptom Management. 2005; 30(4):299-301.
[24] Gourlay DL, Heit HA, Almahrezi A. Universal Precautions in Pain Medicine: A Rational Approach to the Treatment of Chronic Pain. Pain Medicine 2005; 6 (2), 107–112. doi:10.1111/j.1526-4637.2005.05031.x
[25] Hojsted J, Sjogren P Dependence to opioids in chronic pain patients: A literature review. Eur J Pain. 2006
[26] Antoin H, Beasley RD Opioids for chronic noncancer pain: Tailoring therapy to fit the patient and the pain. In: Symposium on Pain Management. Post Graduate Medicine 2004, 116 (3)

	a short duration of action, when the aim of analgesic therapy is to facilitate activity. This is in contrast to the cancer related pain, where the aims are to improve comfort and minimize adverse drug effects. It makes good pharmacotherapeutic sense to use agents such as morphine, oxycodone or methadone, whose effectiveness is more predictable than a "weak" opioid and whose duration of action is or can be made longer. One would argue for the elimination of the second step of the analgesic ladder in non-malignant pain.	studies to address which patients respond to what drugs and what doses. This range of opioids should be available for rotation. Efficacy and safety differ between drugs and individuals. Patient can switch to a different opioid if necessary to achieve better pain control and less toxicity.
9.	Role of **drug therapy in chronic non-malignant pain** (neuropathic pain, complex regional pain syndromes and sympathetically maintained pain). The drugs such as antidepressants and anti-epileptics are not as widely used as they should be. NSAIDs are used alone for many months (6-10 months) before starting the use of opioid analgesics. In patients with **neuropathic pain** the clinical practice is to add high doses of anticonvulsant drugs instead to increase the opioids till the maximum tolerated doses. We should change this practice.	NSAIDs are relatively ineffective in the management of chronic neuropathic pain. Combination therapy is necessary.[27] Use of adjuvant therapy like anxiolytics, antidepressants may be useful. Published trials recommend use of gabapentin, 5% lidocain patch, opioid analgesics, tramdol hydrochloride, and tricyclic antidepressants as first line treatments.[28]
10.	Use of **meperidine** for pain relief	Meperidine in the oral form has1/10 potency to that of morphine, which makes it less efficacious in most patients. The increase in dosing to get to morphine equianalgesic level on a chronic basis is associated with the risk of accumulation of the metabolite normeperidine produced by the liver. Both compounds cause CNS excitability and may result in frank convulsions especially in renally impaired and older people. Hence, the use of meperidine has been rapidly declining in the cancer patient population.
11.	**Role of Cannabinoids** for pain relief	Cannabinoids are still in the list of forbidden substances in most countries.
12.	**Sickle cell pain** Attitudes and beliefs like "sickle cell patients are drug sickers" need to be changed. Use of strong opioids, meperidine is controversial.	Acute sickle cell pain is more severe than postoperative pain and as intense as cancer related pain. Few patients also experience chronic pain. Morphine is the drug of choice for acute pain.[29],[30]
13.	**Ketamine** as a dissociative analgesic. This is good in acute trauma, field conditions but can have dissociative and other reactions. Risk of oversedation is there.	There should be decreased utilization of sedating medications (e.g. skeletal muscle relaxants) in chronic pain settings.
14.	There is **high prevalence of post-operative pain,** which is a risk factor for other complications, compromised rehabilitation and probably for the development of persistent pain. The post-operative pain relief for all surgical patients to be made mandatory. An area of concern is the **use of high concentrations**	Establishment of acute pain services is essential which are nonexistent in most of developing countries. Guidelines should emphasize that more than *one MAC* of inhalational agent is hardly required intra-operatively. Also hypotension is not a criterion for decreased analgesia intra- operatively. A good

[27] Forde G. Adjuvant analgesics for the treatment of neuropathic pain: Evaluating efficacy and safety profiles.J Fam Pract. 2007;56(2):3-12

[28] Vadalouca A, Siafaka I,Argyra E, Vrachnou E, Moka E. Therapeutic management of chronic neuropathic pain: an examination of pharmacologic treatment. Ann N Y Acad Sci. 2006;1088:164-86.

[29] Marlowe KF, Chicella MF Treatment of sickle cell pain Pharmacotherapy, 2002; 22(4): 484-491

[30] Dunlop RJ, Bennett KCLB. Pain management for sickle cell disease. Sickle Cell Pain .Cochrane Database of Systematic Reviews 2006, Issue 2, Art No CD 003350 The Cochrane library, 2007, issue 1

	of volatile agents intra-operatively which would mask the responses to pain leading to inadequate analgesia intra-operatively which in turn would lead to increased post-operative analgesic requirements.	loading dose of analgesic, whether intravenous or epidural and adequate plasma levels are essential for maintaining post-operative analgesia as all post-operative analgesic techniques are essentially maintenance therapies. **Most people start infusions without adequate loading doses and this leads to failure with that therapy.**
15.	The role of **interventional therapies** such as continuous epidural or intrathecal delivery of drugs, spinal cord stimulators for chronic neuropathic pain, treatment of pain associated with metastasis to the spine. (medication vs vertebroplasty/ kyphoplasty vs internal fixation), usefulness of different invasive procedures to treat low back pain: epidural blocks, facet blocks, etc.	The **different modalities of treatment** have their own advocates but lack consistencies as to when they should be applied and how long and when to stop if the management is ineffective. The guidelines should take into account the multiple modalities available to the physician, the indications for such procedures in a pain patient and the duration of the use of that procedure or technique and a consistent guideline as to when one has to stop those procedures and follow other treatment.
16.	For orthopaedics, the major recent change is the more liberal use of **regional blocks** to reduce anaesthetic requirements and provide **postoperative analgesia**. This type of technology could be of great use in developing countries as well.	This certainly slows down the operative schedule, and less surgical work gets done. Sometimes blocks take up to 45 minutes.
17.	We should recommend the **non-drug modalities** for example pyschological and rehabilitation approaches (physiotherapy), holistic procedures like herbal therapy, acupuncture, faith based treatment, reiki and jugizu, music-therapy, arts and dramatization in play-acting other distraction techniques may be used in the treatment of all pain patients.	The inclusion of learning of the **other dimensions**: biologic, psychological, social and spiritual in the curriculum. The experience shows that if we work in these dimensions with the patient, we can see a big difference in the dosage of opioids. Reassurance by nurse and doctor is paramount.
18.	**There is lack of coordination, multidisciplinary and multimodality approach**. The physicians are trained differently in different specialities to manage pain patients. The controversy arises as to the best management plan which the physician wants to adopt for the pain patient. For instance, for low back pain a neurosurgeon or a spine surgeon would like to operate, an anesthesiologist would like to inject steroids, the physiotherapist would either do a facet injection or exercise program and psychiatrist or psychologist would advocate the patient to cope with their pain.	**Team approach** is necessary in pain management involving different specialities including dependence specialists, psychologist to manage the behavior and mental status of a patient and help those who are drug dependent while the pain management is being provided by other physicians or pain specialists. A greater understanding by each other and inter-dependence in each other is necessary for an effective pain management program. All these treatments are appropriate by themselves but quite useless if they are not coordinated with other modalities as well.
19.	**Fragmentation of care** and loss of continuity throughout the illness trajectory and across the multiple settings in which children receive care is a big problem. While a separate pain team is helpful for the management of post-operative pain or in the care of complex pain syndromes, it is not recommended as a strategy for the management of pain in the care of patients suffering from complex disease. A pain team in this scenario is problematic. These patients should be management by their primary care doctor or specialist, such as the oncologist in the case of cancer patients. A separate pain team contributes to more fragmentation of care and adds more barriers to the rapid and effective response in pain control needed for these patients.	**Teaching primary care physicians or specialists** about pain management is a better, longer-lasting solution to the problem. Teaching about pain control should be included in all medical teaching curricula and there should be continuous medical education for the senior clinicians of all the countries. WHO should propose curriculum in pain management for the skill of the palliative care specialists. Educate the personal in the Emergency Room regarding pain diagnoses and treatment. The information about to control the pain should be available by the side of the doctors in charge, and the instruction of how to dilute the medicaments for the nurses in charge of care of the patients that suffer pain. In case a doctor doesn't manage the pain in a

		good way, proceed to give him the required information and the support of a specialist doctor in pain control, giving to the doctor in charge and the family a list of the specialists in the city. Continue giving the required psycho-emotional, spiritual and legal support.
20.	Some experts suggested that pain management should be a primary **specialized practice**. Other specialities by themselves do not and cannot have the knowledge or training to treat a pain patient. The pain team from the anaesthesia service can manage to avoid having more than one individual prescribing pain medications at the same time. This is an important **patient safety** issue.	The pain curriculum should be taught at many levels of medical education, during medical school years, during residency and further to have to have at least 2 years of fellowship training. This training should then be completed by an examination for the knowledge and competency in pain management.
21.	**Individual patient's needs** such as particular formulations (modified release or skin patch) require attention. Use of fixed combination analgesics have limited role. But may be convenient to reduce the overall quantity of tablets.	Drugs should be used upto full therapeutic and tolerated doses before switching to different agent.
22.	**Ethical issues of using opioids at the end of life.** Palliative sedation near end of life needs consideration. There is misbelief that opioids can hasten death in such patients or can cause respiratory distress.	Contrary to general assumptions, effective opioid use to control pain does not appear to hasten death.[31]
23.	**Prescription required as needed** (PRN) medication is often not given by the nursing staff due to ineffective training, misconceptions and the fact that pain is often not taken seriously.	Use of PRN medication should either be limited to situations where nurses are trained to administer PRN pain medication or avoided altogether.
24.	**Economic Barriers** Poverty results in poor affordability of sustained morphine and limited availability of other analgesics. WHO should ensure the availability of simple analgesics (paracetamol and brufen), mild opioids (codeine/ cocodamol) and strong opioids (oral morphine solution), with access to adjuvant analgesics including amitryptylline and anticonvulsants. Target the availability of immediate release morphine as the first step, and other inexpensive drugs like methadone as second. There should be increased access to effective intravenous and oral opioids for out-of-hospital use, such as high concentration morphine and or methadone.	**Securing Resources** The **policy makers** play an important role in the choice of priorities, services planning and allocation of resources. They should be encouraged in the dissemination of information and knowledge and problem solving measures, promotion of research and provision of adequate resources for pain management. Guidelines need to be developed on **cost effective prescription practices**. Prescribing expensive analgesics when cheaper alternatives are available should be avoided. In developing countries the first priority would be easier access to affordable drugs.

[31] Portenoy et al. Opioid Use at End of Life Does Not Hasten Death *J Pain Symptom Manage* 2006;32:532-540.

Annexure 5: Experts willing to extend support in developing WHO guidelines

Many experts and International and regional organizations have offered their support and expressed wish to collaborate with WHO in developing guidelines. To name a few, Dr Kathleen M. Foley (USA), Professor Mary Kurula (India), Dr YP Gupta (UK), Professor Milton L Cohen (Australia), Professor Herald (IASP), Professor Geoffry Hanks (IASP), Professor Dr. German Ochoa, (The Chairman, Task Force of FEDELAT, Latinamerican Federation of IASP Chapters), Dr Rapin (Geneva, Founding President of International Association " Together against Pain"), Dr Rene Albertyn (South Africa), Dr Blumhuber Heidi (EAPC), Dr Ddungo (African Palliative Care Association), Dr Olaitan Soyannwo (Nigeria) and Professor Prithvi Raj (WIP), Dr Ikeoluwapo Ajayi (Nigeria).

The Executive Committee of the IASP confirmed that IASP will help develop normative guidelines for treatment of pain, if WHO so desires. IASP Executive Committee is eager to help and can mobilize many people with knowledge and expertise to support WHO in this important undertaking. IASP could help by continuing and reinforcing its efforts to educate health care professionals throughout the world at all levels of the health care system, to provide better pain relief in many parts of the world that presently have very limited or no pain relief services.

EAPC in collaboration with the EPCRC are planning one or more updates in this field. (EAPC key persons for this are Geoffrey Hanks, Augusto Caraceni, Stein Kaasa, Franco De Conno). They are also working on a second publication for Elderly. The EAPC has a recently founded taskforce for Children. EAPC key people for this are Franca Benini, Huda Abu Saad, Chantal Wood. Dr Heidi Blumhuber on behalf of EAPC suggested that WHO should discuss with some of these persons for the guidelines on different topics and plan to **c**ollaborate.

World Institute of pain (WIP) is involved in the training of physicians in the pain management and publishes an official journal called *Pain Practice* to train and educate pain physicians. WIP also conducts International Pain Conferences including World Congresses, and provides a forum for the physicians from all over the world. Emphases are placed on raising the standard of pain management and evaluating the competency of pain physicians by providing an examination. The certificate is called FIPP (Fellow of Interventional Pain Practice). This examination has been endorsed by pain physicians and societies all over the world. This can be used for dissemination of WHO guidelines.

International Pediatric Association (IPA) and the International Union of Basic and Clinical Pharmacology (IUPHAR) children's group have started a collaborative Alliance for Better Medicines for Children. They would be happy to review WHO existing guidelines for pain in children or developing new WHO guidelines.

Annexure 6: Notes for Record

1. Inputs from Suzanne Hill, WHO/HTP/ PSM/PAR in a meeting with Willem Scholten and Neeta Kumar (HTP/PSM/QSM), 1 March, 2007

Guidelines to develop evidence-based guidelines

Prerequisites

- To maintain continuity, a coordinator could liaise between **WHO/ PSM/QSM** and different departments of WHO working in pain and related areas (HIV, VIP- Trauma, Cancer, Surgery, Child and Adolescent Health, RHR) and external experts from different fields of medicine.

- Guidelines should be developed with an orientation to include concerns and view points of both clinicians and policy makers so that they endorse the guidelines and willing to implement.

- An author is required to document all meetings discussions and write draft guidelines and final guidelines

- Format of guidelines should be decided in the very beginning according to the target audience and health care settings. Ideally it should be a small handy document not a big textbook type with addendums for advocacy to policy makers, laminated one page (aide memoirs) for clinicians for handy use.

- Resources and cost should be worked out for developing guidelines and for dissemination.

Process of developing evidence-based global protocols/ guidelines

Steps

1. Primary discussion among clinical group (ideally from a broad range of fields and not only specialists) on various issues to be addressed in guidelines for example controversial issues, undesirable practices which need to be changed, how many guidelines are required for which clinical conditions (trauma, HIV, acute pain , cancer related pain etc) and which patient groups (children, older people, pregnant etc). This can be done through e mails. Depending on the outcome of discussion, a consensus meeting may be required to provide recommendations as to what questions and concerns guidelines will address.

2. Expert Group meeting to review inventories on

    a. What guidelines already available at WHO
    b. What international guidelines already available
    c. What guidelines already available at National level are of good quality and widely accepted
    d. If any systematic reviews and or Cochrane reviews available
    e. If no reviews available , propose one, which may take 5-6 months

    - Based on above an evidence table is prepared for guidelines.
    - Clearly set the goals for guidelines

3. Draft Guidelines
    - First draft is prepared based on this evidence table and discussed in a closed group meeting/ Expert group consultation
    - We may require a second meeting if there are lots of discussions.
    - Redraft based on comments and suggestions from above meeting.

- Stakeholders meeting (professional bodies, specialists, …) one of the experts would present the draft in this meeting

4. Final document
5. Plan for dissemination

2. Inputs from Andre Griekspoor, DGO/IOS/AEP (griekspoora@who.int), in a meeting with Dr Neeta Kumar, 26.02.07

From his own field of work, he had no information or document. He suggested following documents / contacts for further guidance

- HAC mass casualty guidelines – to contact Pino Annunziata
- VIP Deptt – in document *Violence Against Women* may have some guidelines on pain
- RHR- Reproductive health kits may have some guidelines on pain in delivery (to contact Margarete Ushu Patel)
- Women commission for refugees- see documents on guidance on reproductive health services
- Trauma guidelines
- The material on MISP Minimal Initial Service package can probably be found at www.womenscommission.org. That document has many references to other Reproductive health guidelines made by the IASC and WHO

3. Inputs from Dr Lulu Mussa Muhe, and Dr Martin Weber, WHO/ FCH/CAH in a meeting with Dr Neeta Kumar, WHO/PSM/QSM , 23 March, 2007

* There is a very strong need for the WHO guidelines for children on chronic HIV pain and HIV related cancer related pain especially in developing countries. (Dr Lulu)

* These should be included in current practice and medical education curriculum to change the attitude and perception towards pain in developing countries.(Dr Lulu)

* The guidelines provided in WHO publication (*Pocket Book of Hospital Care for Children Guidelines for the Management of Common Illnesses with Limited Resources: chapter 8.7.1 on HIV and Chapter 10.4 on Supportive care)* can be further improved by WHO Department of Child and Adolescent health after normative guidelines on peadiatric pain treatment are developed by WHO Department of Medicines Policy and Standards. (Dr Martin Weber)

4. Inputs from Dr Cecilia Sepulveda (Senior Adviser, cancer Control) HQ/DG/NMH/CHP/CPM, 11 April, 2007

It is important to update the original WHO clinical guidelines for cancer related pain relief in adults and in children to address controversial issues and to include new medications, newer routes and different interventional approaches according to the different levels of care including community and home based care. But we need financial resources to do that. It can be discussed with Willem Scholten (Department of Medicines Policy and Standards) for collaboration.

I don't recommend having a stand-alone volume which covers cancer related pain management alone, without tackling other symptoms and palliative care as a whole. It would provide a contradictory signal as WHO cancer programme has been promoting in the previous years that cancer palliative care is not only about pain relief but is a much broader and holistic intervention.

I therefore strongly suggest if pain guidelines are going to be developed as a single document that they include cancer related pain relief for adults and children with a reference to the main *updated* guidelines of cancer related pain relief and palliative care for adults and children

There are different options to be discussed regarding the *updated* cancer guidelines for adults and children:

1. have separate guidelines on cancer palliative care and HIV palliative care for both adults and children. (= 4 publications)
2. have guidelines for adults and children that include PC for cancer and HIV in one edition (=2 publications)
3. have guidelines for adults and children that include cancer , HIV and other life threatening conditions (= 2 publications)

We need to consider the pros and cons of every alternative which include epidemiological, political , technical and economic factors - For example proportion of patients with HIV or cancer requiring palliative care may differ in countries, for some leaders it may be politically relevant to maintain clear disease identity regarding palliative care, etc.

These issues may be discussed with some key external experts working in the field to arrive on some consensus.

5. Inputs from Dr Charles Mock, Medical Officer, Injuries and Violence Prevention (VIP) HQ/DG/NMH/VIP, in a meeting with Dr Neeta Kumar, 28 March, 2007

The guidelines provided in WHO publication from Department of VIP *Guidelines for Essential Trauma Care* have policy guidance as per WHO Policy guidelines to opioid availability.[32]

WHO guidelines should cover acute pain in general including trauma and burn. This trauma manual can be updated in line with the new updated guidelines as and when developed by the WHO Department of Medicines Policy and Standards.

6. Inputs from Dr Meena Cherian, Medical Officer , Emergency & Essential Surgical Care Project, Clinical Procedures Unit (CPR), Department of Essential Health Technologies, HQDG/EHT/CPR, 8 May, 2007

Pain relief is essential part of the surgical and anesthesia services in the intra-operative and postoperative period. These include providing pain relief in trauma, obstetrics, burns, anesthesia, cancer, HIV, which are provided by the frontline health personnel at the first referral health care facilities and very often inadequate due to lack of training, irregular supply of drugs, inappropriate devices (lacking disposable injections, badly maintained patient controlled analgesia syringe pumps) particularly at resource limited health facilities.

The CPR/EHT has developed the WHO manual *Surgical Care in District Hospital (SCDH*) and the WHO *Integrated Management of Essential and Emergency Surgical Care (IMEESC)* toolkit to provide WHO recommendations on pain relief (drugs and safety of techniques). Best Practice protocols on post operative pain management are available on surgery website: www.who.int/surgery

Collaborations between EHT/CPR and QSM will assist in the development of policies on pain, palliative care and ultimately the joint document will be integrated in the WHO manual SCDH and WHO IMEESC toolkit.

[32] Achieving balance in national opioids control policy, Guidelines for assessment. Geneva, World Health Organization, 2000 .

Annexure 7: External experts consulted

Dr Henry Ddungu
Advocacy Manager
African Palliative Care Association
Kampala, Uganda

Professor Geoffrey Hanks
Chair IASP task force
Bristol Haematology and Oncology Centre
Department of Palliative Medicine
Bristol, United Kingdom

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Annexure 8: List of International Organizations Contacted

No	Organization	Person / contact
1.	**International Association for the Study of Pain (IASP)**	**Professor Michael Bond** Executive Officer Immediate Past-President and liaison officer for IASP to WHO **Professor Harald Breivik** MD, DMsc, FRCA Honorary Secretary of IASP (elected) Former WHO-IASP-liaison Professor of Anaesthesiology Faculty Division Rikshospitalet University of Oslo, Norway
2.	**Pain & Policy Studies Group**	**Dr James Cleary** Past president American Academy of Hospice and Palliative Care Pain & Policy Studies Group/WHO Collaborating Center for Policy and Communications, University of Wisconsin Comprehensive Cancer Center, Madison, Wisconsin, USA
3.	**International Pharmaceutical Federation (FIP)**	**Dr Ton Hoek** General Secretary and CEO, Federation Internationale Pharmaceutique (FIP), The Hague, The Netherlands
4.	**European Association for Palliative Care (EAPC)** http://www.eapcnet.org/	**Dr Heidi Blumhuber** Executive Officer, Secretary of the Research Steering Committee EAPC Head office Istituto Nazionale Dei Tumori Milano , Italy **Dr De Conno Franco** Palliative Care Specialist Member Research Steering Committee EAPC Director of the Rehabilitation and Palliative Care Unit National Cancer Institute of Milan,
5.	**European Federation of IASP Chapters (EFIC)** http://www.efic.org/	**Dr Serdar Erdine,** MD, President EFIP Istanbul Turkey
6.		

	International Council of Nurses (ICN),	**Ms Linda Carrier-Walker** Director of Communications and External Relations, Geneva, Switzerland **Mr Tesfamicael Ghebrehiwet** Geneva, Switzerland
7.	**UICC**,	**Dr Isabel Mortara** Executive-Director, International Union Against Cancer (UICC), Geneva, Switzerland
8.	**World Institute of pain** (WIP) www.worldinstituteofpain.org	**Paula Brashear** Executive Secretary **Dr .P. Prithvi Raj** Founder President WIP Lubbock, TX USA
9.	**International Association Hospice and Palliative Care** http://www.hospicecare.com/	**Liliana De Lima** IAHPC Executive Director Houston, USA www.hospicecare.com
10.	**International Association "Together Against Pain"** http://www.sans-douleur.ch/en/	**Professeur Charles-Henri Rapin** charles-henri.rapin@hcuge.ch Founding President Médecin chef, Responsable du programme transversal "Bien Vieillir" - HUG Directeur adjoint, Chargé des Relations avec la Cité, Centre interfacultaire de Gérontologie, Université de Genève Directeur, département "Ages, Santé et Société", Institut Universitaire Kurt Boesch, Sion Bureau et secrétariat : Hôpital de LoëxBernex, Switzerland
11.	**Cochrane Collaborative Group** **Pain, palliative and Supportive Care**	**Dr Philip J. Wiffen** Pain Relief Unit, Churchill Hospital, Oxford; and Coordinating Editor, Cochrane Collaboration Pain Palliative and Supportive Care Collaborative Review Group, Regional Pharmaceutical and Prescribing Adviser, Anglia & Oxford Region, National Health Service Oxford England
12.	**International Pediatric Association** http://www.ipachildhealth.org/ Administrative Office:IPA	**Dr Jane G. Schaller** Executive Director, International Pediatric Association Visiting Professor of Pediatrics, University of British Columbia

		Consultant, Center for International Child Health Karp Professor of Pediatrics Emerita, Tufts University Vancouver, BC Canada
13.	**International Society of Paediatric Oncology (SIOP)**	**Prof Tim Eden** President SIOP Professor of Paediatric Oncology Academic Unit of Paediatric Oncology Honorary Consultant Paediatric Haematologist and Oncologist Christie Hospital NHS Trust and Central Manchester and Manchester Children's University Hospitals Trust
14.	**The International Society for Burn Injuries - ISBI** - http://www.worldburn.org/executive.asp	**Dr Mehmet Haberal** Professor, General Surgery Chairman, Department of Surgery, Transplantation and Burn Institutes Founder and President, Baskent University Ankara TURKEY
15.	**MEDITERRANEAN COUNCIL FOR BURNS AND FIRE DISASTERS** Website: www.medbc.com	**Dr S. William A. Gunn** Head of the Centre La Panetière Bogis-Bossey, Switzerland
16.	**International Network for Cancer Treatment and Research (INCTR)** **http://www.inctr.org/about/**	**Dr Ian Magrath** President NCI Liaison to the INCTR, National Cancer Institute, Bethesda, MD, USA **Dr Stuart Brown** Chair of Palliative Care Guidelines INCTR
17.	**World Medical Association (WMA),**	**Dr Otmar Kloiber** Secretary-General, WMA, Ferney-Voltaire, France
18.	**Multinational Association for Supportive Care in cancer (MASCC)** **http://www.mascc.org/**	**Dr Matti Aapro (President)** Doyen IMO Clinique de Genolier Genolier Switzerland
19.	**International Society of Orthopaedic Surgery and Traumatology (SICOT)** http://www.sicot.org/?page=society	**Professor M. Hinskamp** Secretary General (SICOT) Appointed Head of Orthopaedic Surgery and Traumatology Dept. Erasmus Hospital

		Université libre de Bruxelles Brussels, Belgium
20.	**FEDALET (Latin American federation of IASP Chapters)**	**Professor Dr Germán Ochoa** Orthopaedic Surgeon. Spine and Pain Specialist Department of Orthopaedic Surgery Spine and Pain Unit. University Hospital Clínica San Rafael. Bogotá, Colombia.
21.	**Asia pacific Hospice Palliative care network (APHN)**	**Dr Cynthia Goh** Honorary secretary Senior Consultant Head Department of palliative medicine National cancer Centre Singapore Asia pacific Hospice Palliative care network (APHN) Singapore **Dr Enoch Yuen-Liang Lai** Chairman APHN http://www.aphn.org/Index.asp

Annexure 9: Related publications

1. Acute Pain Management: Scientific Evidence, Second Edition. Melbourne: Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine. 2005 www.Anzca.Edu.Au
2. Brennan F, Carr DB. Pain Management: A Fundamental Human Right. Anesthesia and Analgesia, 2007;105:205-221
3. Mcnicol E, Horowicz-Mehler N, Ruth A. et al. Management Of Opioid Side Effects In Cancer-Related and Chronic Noncancer related pain: A Systematic Review. *The Journal of Pain*, 2003, 4 (5), 231-256
4. Kathleen M. Foley, Judith L. Wagner, David E. Joranson, and Hellen Gelband. Pain Control For People With Cancer And AIDS. In : *Disease Control Priorities In Developing Countries.second edition*, 2006, New York: Oxford University Press, Chapter 52 , 981-994 Http://www.Dcp2.Org/Pubs/DCP/52/Section/7831
5. Carr DB The Development Of National Guideline For Pain Control: Synopsis And Commentary *Eur J Pain.* 2001;5 Suppl A:91-8.
6. Mary Jo O'Hara, Lynn Czarniecki. Pain Management In Children With HIV/AIDS. National Pediatric & Family HIV Resource Center, University Of Medicine And Dentistry Of New Jersey Http://www.Thebody.Com/Gmhc/Issues/Julaug97/Kidpain.Html
7. Rajagopal M. R., Mazza D, Lipman AG(Editors) Pain And Palliative Care In The Developing World And Marginalized Populations: A Global Challenge The Haworth Medical Press, Hong Kong,
8. Portenoy RK & Lesage P. Management of cancer related pain. *Lancet* 1999: 353: 1695–1700.
9. Prithvi Raj P, editor. Practical Management of Pain, 3rd Edition St. Louis: Mosby Inc., 2000. 1070 pp.
10. Puig MM. When Does Chronic Pain Become Intractable and When Is Pharmacological Management No Longer Appropriate? *Journal of Pain and Symptom Management*, 31(4), Supplement 1 , 2006, Pages S1-S2
11. Marlowe KF, Chicella MF Treatment of sickle cell pain. *Pharmacotherapy*, 2002; 22(4): 484-491
12. Holdcraft A, Power I. Recent developments: Management of Pain. *BMJ* 2003;326:635-39. doi:10.1136/bmj.326.7390.635. http://www.bmj.com/cgi/content/full/326/7390/635?etoc
13. Harati Y, et al Double-blind randomized trial of tramadol for the treatment of the pain of diabetic neuropathy. *Neurology.* 1998 Jun;50(6):1842-6.
14. Moussavou A, Vierin Y, Eloundou-Orima C, Mboussou M, Keita M. Sickle cell disease pain management following the World Health Organization's protocol. *Arch Pediatr.* 2004 ;11(9):1041-5
15. McNicol E et al Management of opioid side effects in cancer-related and chronic noncancer related pain: a systematic review. *The Journal of Pain* 2003 ,4,(5,), 231-256
16. Vickers A P, Jolly A. Naltrexone And Problems In Pain Management- How To Manage Acute Pain In People Taking An Opioid Antagonist Editorials, *BMJ*. 2006, 21; 332(7534): 132–133.
17. Graziotti PJ, Goucke CR. The use of oral opioids in chronic non-malignant pain. Management strategies. *Med J Aust* 1997;176:30-34.
18. Maddox JD, Joranson D, Angarola RT. The use of opioids for the treatment of chronic pain (position statement). *Clin J Pain* 1997;13:6-8
19. Kalso E, Allan L, Dellemijn PL et al. Recommendations for using opioids in chronic non-malignant pain. *Eur J Pain* 2003;7:381-386.

Cochrane Reviews on Pain Management

http://www.mrw.interscience.wiley.com/cochrane/cochrane_clsysrev_subjects_fs.html

1. Dunlop RJ, Bennett KCLB. Pain management for sickle cell disease Sickle Cell Pain Cochrane Database of Systematic Reviews 2006, Issue 2, Art No CD 003350
2. Huertas-Ceballos A, Macarthur C, Logan S. Pharmacological interventions for recurrent abdominal pain (RAP) in childhood. *Cochrane Database of Systematic Reviews* 2007 Issue 2,
3. Wiffen PJ, McQuay HJ, Moore RA. Carbamazepine for acute and chronic pain The *Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD005451. DOI: 10.1002/14651858.CD005451.
4. Jorgensen H, Wetterslev J, Moiniche S, Dahl JB. Epidural local anaesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, PONV and pain after abdominal surgery. *Cochrane Database Syst Rev.* 2000;(4):CD001893.

5. Nishimori M, Ballantyne JC, Low JH. Epidural pain relief versus systemic opioid-based pain relief for abdominal aortic surgery. *Cochrane Database Syst Rev.* 2006 Jul 19;3:CD005059.
6. Anim-Somuah M, Smyth R, Howell C. Epidural versus non-epidural or no analgesia in labour. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No.: CD000331. DOI: 10.1002/14651858.CD000331.pub2.
7. Young G, Jewell D Interventions for preventing and treating pelvic and back pain in pregnancy. *Cochrane Database Syst Rev* 2002;(1): CD001139.
8. Green S, Buchbinder R, Glazier R, Forbes A. Interventions for shoulder pain. The Cochrane Library, Issue 1, 1999.
9. Stones W, Cheong YC, Howard FM. Interventions for treating chronic pelvic pain in women (Cochrane Review) *Cochrane Database Syst Rev*. 2005,3.
10. Crawford F, Thomson C. Interventions for treating plantar heel pain. *Cochrane Database Syst Rev.* 2000;(3):CD000416.
11. Quigley C. Opioid switching to improve pain relief and drug tolerability. *Cochrane Database Syst Rev* 2004, CD004847. DOI: 10.1002/14651858.CD004847
12. Bellù R, de Waal KA, Zanini R. Opioids for neonates receiving mechanical ventilation. *Cochrane Database Syst Rev* 2004. CD004212. DOI: 10.1002/14651858.CD004212.pub2.
13. Eisenberg E, McNicol E, Carr DB. Opioids for neuropathic pain. *Cochrane Database Syst Rev 2006*.CD006146. DOI: 10.1002/14651858.CD006146.
14. Zeppetella G, Ribeiro MDC. Opioids for the management of breakthrough (episodic) pain in cancer patients. *Cochrane Database Syst Rev 2005*. CD004311. DOI: 10.1002/14651858.CD004311.pub2.
15. Jennings AL, Davies AN, Higgins JPT, Broadley K. Opioids for the palliation of breathlessness in terminal illness. *Cochrane Database Syst Rev 2001*. CD002066. DOI: 10.1002/14651858.CD002066.
16. Eccleston C, Yorke L, Morley S, Williams AC, Mastroyannopoulou K. Psychological therapies for the management of chronic and recurrent pain in children and adolescents. *Cochrane Database Syst Rev* 2003;(1):CD003968.
17. Edwards JE, Moore RA, McQuay HJ. Single dose oxycodone and oxycodone plus paracetamol (acetominophen) for acute postoperative pain *Cochrane Database Syst Rev* 2000;(4):CD002763.
18. Hollingshead J, Duhmke RM, Cornblath DR. Tramadol for neuropathic pain. *Cochrane Database Syst Rev*. 2006 Jul 19;3:CD003726.

WHO Documents

1. World Health Organization Briefing Note-Access to Controlled Medications Programme. Geneva., World Health Organization, 2007.
2. Achieving balance in national opioids control policy, Guidelines for assessment. Geneva, World Health Organization, 2000
3. Guidelines For WHO Guidelines: Global Programme on Evidence for Health Policy (EIP/GPE/EQC/2003.1), Geneva, World Health Organization, 2003.
4. WHO model list of essential Drugs. Geneva, World Health Organization,2005
5. Cancer related pain Relief and Palliative Care In Children. Geneva, World Health Organization 1998.
6. Cancer related pain Relief: With a Guide to Opioid availability. 2nd Ed. Nonserial Publication, Geneva, World Health Organization. 1996
7. PAHO/WHO - Comprehensive Care Guidelines For Persons Living With HIV/AIDS In The Americas, June 2000
8. Davies E, Higginson IJ.(eds) Better Palliative Care for Older People. World Health Organization Regional Office for Europe, 2004
9. The solid facts on palliative care. World Health Organization Regional Office for Europe, and EAPC. 2004
10. HIV/AIDS Care and Treatment: Guide for Implementation, World Health Organization Regional Office for The Western Pacific, 2004.
11. Guidelines For Essential Trauma Care , Geneva, World Health Organization 2004
12. Pocket Book of Hospital Care For Children (Guidelines For The Management Of Common Illnesses With Limited Resources. Geneva,World Health Organization 2004
13. Comprehensive Cervical Cancer Control - A Guide to Essential Practice. Geneva, World Health Organization 2006.

14. Surgical Care in District Hospital Manual, Geneva, World Health Organization 2003.
15. Neurological Disorders Public Health Challenges Nonserial Publication, Geneva, World Health Organization, 2006.
16. IMAI Complementary course on HIV AIDS. Module 4 Follow up and chronic care of HIV exposed and infected children. Geneva, World Health Organization 2006.
17. IMAI. WHO/CDS/IMAI/2004.4 Rev. 1: Integrated Management of Adolescent and Adult Illness (IMAI) four modules World Health Organization, 2004
    1. Acute care
    2. Chronic HIV care with antiretroviral therapy
    3. General principles of good chronic care
    4. Palliative care
    Full text: http://www.who.int/3by5/publications/documents/imai/en/index.html

18. World Health Assembly WHA resolution **A59/9** Sickle-cell anaemia