SCOPING DOCUMENT FOR
WHO Treatment Guidelines on Chronic Pain in Children

BACKGROUND

The justification for developing these guidelines lies in the need to update existing
guidelines for cancer pain relief and palliative care in children, and to extend these to
non-malignant pain. Published in 1998 (1), some aspects are now out of date as new
drugs have come on the market whilst others have dropped out of common clinical
practice. Also, the appreciation of pain management in children, as distinct from adults,
has grown. The Delphi study conducted in June 2007 (2) confirms that experts and
professional bodies related to pain are looking to the World Health Organization (WHO)
to take a lead in this development.

The WHO regards palliative care for children as ‘the active total care of the child’s body,
mind and spirit, and also involves giving support to the family’
(http://www.who.int/cancer/palliative/en). Whilst recognizing that pain control is only a
component of the much wider scope of palliative care in children with cancer, HIV and
other chronic and progressive life-threatening illnesses, these pain treatment guidelines
could serve as a guide to health care professionals, policy makers and regulatory
authorities for facilitating legal access and ensuring proper use of analgesics and other
modalities to achieve rapid, effective and safe pain control. The guidelines will be jointly
developed by the Access to Controlled Medicines Programme, the Cancer Control
Programme, Management of Mental and Brain Disorders, Clinical Procedures and Child
and Adolescent Health and Development.

This scoping document sets out:
• the overall objective of these guidelines
• the types of patients to whom the guidelines apply
• the outcomes that are sought
• the proposed table of contents for the publication, and
• the clinical questions for which evidence needs to be sought and appraised so that
evidence-based recommendations can be made.

The full guidelines should be developed in accordance with the principles laid down by
the WHO Guideline Review Committee.

OBJECTIVES AND PATIENT POPULATION

The overall objective of these guidelines is to provide evidence-based recommendations
that, if followed, will improve the pain experience of children with chronic pain related to
malignant disease (cancer) and non-malignant conditions (e.g. HIV/AIDS, neurological and genetic disorders [e.g. cystic fibrosis, cerebral palsy, muscular dystrophy, mucopolysaccharidoses], sickle cell disease, etc).

These conditions were identified because they cause significant global burden, from among conditions that particularly cause chronic pain relative to all chronic conditions. See Table 1 for mortality statistics for some of these diseases by age. These guidelines do not include the management of procedural and acute pain as they will be addressed in another document.

Some therapies which contribute to the improvement of the pain experience are beyond the scope of this document. These include disease-modifying therapies (e.g. anti-cancer therapies, anti-retroviral therapies), and complementary therapies. Although these are important contributors to pain management they are excluded from this guideline because of difficulty of establishing a direct link between the specific intervention and pain relief or lack of published evidence for that intervention.

Patient population: these guidelines address children from 1-10 years of age with chronic pain due to malignant conditions (cancer), HIV/AIDS, non malignant conditions and other progressive diseases.

N.B. Since pharmacology for adolescent is similar to adult, chronic pain in adolescent will be addressed in WHO Treatment Guidelines on chronic pain in adults.

The critical outcomes that should be considered include: effectiveness of pain relief, speed at which pain relief may be achieved, maintenance of pain relief, effect on quality of life and risk-benefit analysis of interventions for pain relief.

**Table 1 Global burden of disease: mortality 2002 (3)**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mortality ('000)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-4 years</td>
</tr>
<tr>
<td>Malignant neoplasms</td>
<td>18,314</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>182,230</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>944</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>219,850</td>
</tr>
</tbody>
</table>

**PROPOSED TABLE OF CONTENTS**

A. **Executive summary**

The objective of these guidelines, the patients to whom they apply, the target audience and key recommendations should be stated. Acknowledgment would be included before the executive summary.
B. **Introduction**

This should include:

- a clear statement on the overall objective of these guidelines and the patients to whom these guidelines are meant to apply
- a statement on target audience: who will use these guidelines—physicians, nurses, physician assistants, clinicians, specialists, general practitioners, pharmacists, caring for children. It also aims at policy makers and programme managers, who may not be involved directly in providing care to children, nevertheless play an important role in ensuring care of children
- a clear statement on what is beyond the scope of this document
- a description of context within these guidelines sit—in particular the wider context of palliative care in the case of children with advanced or progressive disease, the importance of holistic care of children and their families, and the recognition of pain as only one of many symptoms and areas of concern for them (with reference to other key documents relating to palliative care: reference 1)
- the need to pay attention to children’s developmental needs and the active involvement of their parents/teachers and other care givers
- the recognition that much of pain management can be carried out in primary care and the community, with only a relatively small percentage of patients requiring specialist pain management
- the effectiveness of a coordinated team approach, in its broadest sense, i.e. depending on the resources available and the setting in which pain is being managed, teams may vary in composition (different disciplines, professions and combinations of professionals and non-professionals), complexity and size.

C. **Causes and classification of pain**

This should be a brief section (maximum one page) to state:

- definition and diagnostic features of the following:
  - nociceptive pain— including somatic, visceral and musculoskeletal pain
  - neuropathic pain
  - breakthrough or episodic pain (end of dose failure, pain at rest, associated with movement or other incident)
  - malignant vs non malignant pain
  - pain at rest vs pain on movement
  - mixed pain (nociceptive and neuropathic components together)

- a definition of chronic, acute pain, malignant, non malignant pain, total, mixed pain, breakthrough, episodic pain, etc will be included

- the age-appropriate key investigations which can be helpful in distinguishing between different causes of pain
D. **Evaluation of pain**

This should include:
- a reiteration of the concept of total pain
- a recommendation about the steps which should be taken in a holistic assessment and documentation of pain, including assessment of cause, severity, activity and sleep disturbance, emotional and social impact and the necessity to frequently reassess pain
- emphasis on the importance of evaluating the primary and secondary causes of pain
- a recognition that children experience pain in the same way as adults but express it differently, so there is a need to recognise, evaluate, measure and monitor pain and pain control using methods and pain scales that are age-appropriate
- a recognition that assessment of pain in children is especially difficult and require carers and professionals to be trained in techniques to assess and grade pain, as well as having ample time for evaluation
- a description of the evidence underpinning a selection of validated pain scales for children and the settings in which each has been validated for use (these pain scales to appear in annex) and relating these to suitability at different ages
- a recognition that children use a variety of coping mechanisms for pain, including play and sleep, which are different to adults and may not be easily recognisable to inexperienced carer or professionals
- a recognition that the presence or absence of anxiety, fear and stress must be included in pain assessment in children
- a recognition that functional ability and status must be included in pain assessment in children.

E. **Treatment strategy**

This should include a statement of the principles of treatment, e.g.:
- oral medicines, including liquid formulations, are often, but not always, the mainstay of pain management; topical preparation, rectal suppositories, and oral or intranasal sprays may be more suitable alternatives in younger children
- some medicines should be given regularly ("by the clock")
- therapeutic regimes need to be individualised with attention to detail
- the necessity to monitor for therapeutic and unwanted effects
- the necessity to address issues around withdrawal and weaning of opioid.

This section should be divided into two main sections:

- Medicinal therapy - non-opioid medicines, opioid analgesics, co-analgesics, reversal agents, rescue medicines and routes of administration
- Non-Medicinal approaches – including supportive, cognitive, behavioural, biofeedback, transdermal electronic nerve stimulation (TENS), nerve blocks, radiotherapy, exercise, psychological, occupational, or complimentary methods.
The recommendations should be based on evidence sought and appraised in response to clinical questions 1 – 21 (see below). The formatting of this section could be as follows: preamble or introductory paragraph, followed by tabulated evidence leading to statement of recommendation.

F. System issues

The content of this section should flow from the evidence-based recommendations in the treatment section as well as evidence sought and appraised in response to the systems questions 20 - 23 (see below).

This section should include:
• a specific recommendation (which flows from the treatment recommendations) listing the key medications which should be available for pain relief at primary, secondary and tertiary levels.
• a cost-analysis of the health system inputs that are required in order to achieve the critical outcomes for this patient population.
• a statement about who /what skills are required to provide care to children with chronic pain.
• a statement about the safeguards that are useful to enable opioids to be safely and reliably administered to those who require this for effective pain control, whilst minimising the risk of drug diversion.

G. Annexes

• Selection of frequently used and validated pain scales for assessing pain in children at different age groups
• Opioid analgesic conversion table
• Opioid analgesic half tables
• Evidence tables for treatment
• Membership of Expanded Review Panel (ERP). Guidelines Advisory group

CLINICAL QUESTIONS

Evidence should be sought, critically appraised and synthesised before recommendations are formulated in response to these questions. Each question and its related sub-questions should lead to a specific recommendation.

Analgesic ladder

1. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, for using the 2-step analgesic ladder compared to the 3-step analgesic ladder in order to achieve rapid, effective and safe pain control?
2. If the evidence supports the continuing use of a 3-step analgesic ladder in children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, to support the use of codeine as compared to tramadol at step 2 of the analgesic ladder, in terms of benefit balanced against adverse effects such as constipation, nausea and vomiting, sedation and confusion, in order to achieve and maintain rapid, effective and safe pain control?

3. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, to support the use of paracetamol as compared to NSAIDs at each step of the analgesic ladder in terms of benefit against adverse effects in order to achieve and maintain rapid, effective and safe pain control?

**Choice of strong opioids**

4. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, to support the use of morphine as the gold standard for strong opioids, in comparison to the use of other strong opioids (in particular fentanyl, hydromorphone, oxycodone and methadone), in terms of efficacy, adverse effects (such as constipation, nausea and vomiting, sedation and confusion) and cost-benefit in order to achieve and maintain rapid, effective and safe pain control?

5. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, for the practice of opioid rotation or opioid switching as compared to continuing use of morphine in order to maintain effective and safe pain control?

**Fears**

6. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the risk of hastening death, by age groups, compared to a similar group of patients who are not taking opioids, when strong opioids are properly prescribed for pain control?

7. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the benefit compared to risk, by age groups, of:
   - developing tolerance
   - developing dependence
   - developing respiratory depression
   - developing opioid induced hyperalgesia

from taking regular or intermittent morphine for pain control as compared to a similar group of patients who are not taking opioids?
8. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, for the use of opioids influencing a child’s development when taken regularly to achieve and maintain pain control?

**Administration of opioids**

9. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, for the benefit of administering modified-release morphine regularly as compared to immediate-release morphine on a 4-hourly or as required basis, in order to maintain effective and safe pain control?

10. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, for the benefit of using immediate release morphine as the top-up as-required analgesic of choice (in addition to regular background analgesia), as compared to other strong opioids in order to maintain effective and safe control of episodic or breakthrough pain?

11. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, for the benefit of using the oral medication as compared to the intravenous or intramuscular routes as the optimal route of administration for opioids in order to achieve and maintain rapid, effective and safe pain control?

12. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, for the benefit of using the rectal route as compared to the intravenous or intramuscular routes as the optimal route of administration for opioids in order to achieve and maintain rapid, effective and safe pain control?

13. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, for the benefit of using the transdermal route as compared to the intravenous or intramuscular routes as the optimal route of administration for opioids in order to achieve and maintain rapid, effective and safe pain control?

14. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, for the benefit of using the intranasal route as compared to the intravenous or intramuscular routes as the optimal route of administration for opioids in order to achieve and maintain rapid, effective and safe pain control?

15. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, for the benefit of using a subcutaneous route of administration as opposed to intravenous or intramuscular routes when the oral, transdermal or intranasal route for opioid administration is inappropriate (e.g. patients
with diminished consciousness, ineffective swallowing or vomiting) or unavailable in order to maintain effective and safe pain control?

**Co-analgesic and adjuvant medications**

16. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, for the use of steroids as an adjuvant medication as compared to placebo in order to achieve and maintain effective and safe pain control?

17. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, for the use of muscle relaxants from the class of benzodiazepines as compared to baclofen in order to achieve and maintain effective and safe pain control?

18. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups, for the use of non-pharmacological methods compared to anxiolytics such as benzodiazepines in order to achieve rapid and effective control of anxiety and stress associated with pain?

19. In children with chronic bone pain related to cancer, HIV/AIDS and non-cancer conditions:
   19.1. What is the evidence, by age groups, for the use of non-selective NSAIDs as an adjuvant medication in order to achieve rapid, effective and safe control of bone pain?
   19.2. What is the evidence, by age groups, for the use of bisphosphonates as an adjuvant medication, and in which specific subsets of patients, in order to achieve rapid, effective and safe control of bone pain?
   19.3. What is the evidence, by age groups, for the use of radiotherapy in order to achieve rapid, effective and safe pain control?

20. In children with chronic neuropathic pain related to cancer, HIV/AIDS and non-cancer conditions:
   20.1. What is the evidence, by age groups, for the use of amitryptiline and other tricyclic antidepressants as compared to SSRIs in order to achieve rapid, effective and safe pain control?
   20.2. What is the evidence, by age groups, for the use of Second generation anti-epileptic like gabapentin as compared to First generation anti-epileptics such as carbamezapine or sodium valproate in order to achieve rapid, effective and safe pain control?
   20.3. What is the evidence, by age groups, for the use of Second generation anti-epileptic like gabapentin as compared to placebo in order to achieve rapid, effective and safe pain control?
20.4. What is the evidence, by age groups, for the use of NMDA receptor antagonists (e.g. ketamine) as compared to placebo in order to achieve rapid, effective and safe pain control?

20.5. What is the evidence, by age groups, for the use of local anaesthetic agents as compared to placebo in order to achieve rapid, effective and safe pain control?

Non-drugs: psychological

21. In children with chronic pain related to cancer, HIV/AIDS and non-cancer conditions, what is the evidence, by age groups:

21.1. Of the use of cognitive behavioural therapy as compared to none to reduce and disability?

21.2. Of the role of exercise as compared to none in the management of chronic pain?

21.3. Of the use of physiotherapy as compared to none for chronic pain?

SYSTEMS QUESTIONS

22. In the management of chronic pain in children with cancer, HIV/AIDS and non-cancer conditions, what evidence is there to support the practice of shifting the task of prescribing, titrating and monitoring analgesics from medically-qualified professionals to other professionals in order to ensure that rapid, effective and safe pain control can be achieved for all those who need it?

23. If the evidence supports the practice of task-shifting, what are the safeguards that need to be in place, in particular training and continuing supervision, and the resources required to provide and maintain these safeguards?

24. In the management of chronic pain in children with cancer, HIV/AIDS and non-cancer conditions, what evidence is there about the level of pain management that can be provided at the primary care or generalist level, as compared to specialist level, in order to ensure that rapid, effective and safe pain control can be achieved for all those who need it?

REFERENCES

2. 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. Report prepared by Prof Neeta Kumar, WHO Geneva, 2007.

Other references: