

SCOPING DOCUMENT FOR WHO Treatment Guidelines on chronic non-malignant pain in adults

BACKGROUND

The initiative to develop these guidelines emerged from the findings of the Delphi study conducted (1) for the Access to Controlled Medications Programme which confirmed that experts and professional bodies related to pain are looking to the WHO to take a lead in this development.

These 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 would 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 adult patients with chronic non-malignant pain, such as low back pain, arthritis and fibromyalgia. WHO statistics show a high level of disability relating to these conditions (see table 1) although there are many more conditions which include or cause significant chronic non-malignant pain. (e.g. chronic pelvic pain, chronic post surgical pain, phantom limb pain, multiple sclerosis). Although fibromyalgia is not separately classified in the WHO data, its prevalence is estimated to be between 3-6% of the world population.

Some therapies which contribute to the improvement of the pain experience are beyond the scope of this document. These include specific disease-modifying therapies (e.g. anti-rheumatic therapies, joint replacement).

Patient population: these guidelines address adults and adolescents (i.e. people aged 11-18 years) with chronic pain related to non-malignant conditions like low back pain, arthritis and fibromyalgia. Since pharmacology for adolescents is similar to adult, management of chronic non-malignant pain in adolescents is included in this guideline.

The critical outcomes that should be considered include: effectiveness and maintenance of pain reduction, cost effectiveness, speed at which pain reduction may be achieved, effect on quality of life, effect on an individual's function, anxiety and mood, adverse effects, complications of treatments/interventions and risk-benefit analysis of interventions for pain reduction.

Table 1 Disability-adjusted Life Years (DALYs) in 2002

Source: *www.who.int*

Conditions	2002 ('000)
Low back pain	2320
Osteoarthritis	14,861
Rheumatoid arthritis	4866

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 adults. It also aims at policy makers and programme managers, who may not be involved directly in providing care, nevertheless play an important role in ensuring care of patients
- a clear statement on what is beyond the scope of this document
- a description of the biopsychosocial context in which these guidelines are contained - in particular the wider context of chronic pain and the importance of holistic care of patients and their caregivers

- the concept of total pain based on IASP and WHO definitions including the psychological, emotional, cultural and social sequelae of living with chronic pain over prolonged periods of time
- 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 limited availability of high quality clinical trials of medicines and other therapies in chronic pain over prolonged periods of time and the realization that many recommendations will be based on clinical experience and best opinion
- 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

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

- a definition and diagnostic features of the following:
 - nociceptive pain – including somatic, visceral and musculoskeletal pain
 - neuropathic pain
 - episodic pain
 - malignant vs. non-malignant pain
 - acute vs. chronic pain
 - pain at rest vs. pain on movement
 - mixed pain (nociceptive and neuropathic components together)
- the different causes of chronic non-malignant pain in adults
- the key investigations/actors which can be helpful in distinguishing between different causes/types of pain
- a recognition that chronic pain is a complex phenomenon where the intensity/ impact of the pain is not always directly related to pathology.

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, mood (anxiety, depression etc) and social impact
- a recognition that there is a need to evaluate, measure and monitor pain and pain control and that a variety of pain scales are available though not one has been shown to be superior to others across all settings

- a description of the evidence underpinning a selection of frequently used validated pain scales and the settings in which each has been validated for use (these pain scales to appear in annex)
- a recognition that patients often do not report pain – for a variety of reasons including religion, finance, fear, culture (see ref 2, annex 4)
- a recognition that health workers often underestimate and under treat patients’ pain and the role of skilled listening by health workers.

E. Treatment strategy

This should include a statement of the principles of treatment, e.g.:

- the underlying cause of pain should be treated whenever possible
- oral medicines are among the key components of pain management
- some medicines should be given regularly ("by the clock")
- a recognition that therapeutic regimes need to be individualised with attention to detail and combined with psychological support e.g. cognitive behavioural techniques
- the necessity to monitor and evaluate for therapeutic and unwanted effects.

This section should be divided into two main sections:

- Medicinal therapy: anti-neuropathics, non-opioid medicines, opioid analgesics, co-analgesics, rescue medicines, adjuvant medicines, routes of administration, efficacy, safety, cost-effectiveness, limitations, benefits, side effects.
- Non-medicinal therapy: explanation, beliefs, education, physical therapy, peripheral stimulation therapy (eg. transdermal electronic nerve stimulation (TENS), acupuncture), nerve blocks, psychological therapy (cognitive behavioural therapy), supportive therapy (occupational therapy, employment etc).

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. Specific Opioid Issues

There are a number of topics that are specific for opioids, including:

- When to start opioids? When to try stopping or reducing them? When to try to introduce an alternative?
- How to cease opioids in patients who have been on escalating doses but for whom there has been a lack of effect at any dose?
- How to cease opioids in people who have become tolerant on them and wish to cease them or for whom the use has become problematic?
- How to rotate between opioids in an ambulatory and clinical setting?
- How to organize a drug holiday as a strategy to treat tolerance phenomena?

Chronic use of opioids might result in tolerance to opioids, abuse and dependence on opioids. In addition, chronic pain and opioid dependence can overlap, resulting in specific management issues.

- How prescription of opioids in the use of pain should minimize these problems
 - how clinicians should detect people at risk of abuse and dependence on opioids prior to their commencement
 - how clinicians identify patients who are abusing or dependent on their chronic pain medication
 - how clinicians should detect opioid hyperalgesia versus tolerance
 - whether the administration of opioids for the treatment of pain be supervised at all
- how to treat pain in patients who are opioid dependent
- how to manage patients who have become dependent on their opioid medication and/or are abusing their prescription opioids.

G. 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 22 - 24 (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 recommendation on the skills required to prescribe treatment to adults with chronic non-malignant pain
- how health systems should balance the availability of prescription opioids for pain with prevention of prescription opioid abuse and dependence
- the key policy, legislative, regulatory issues that ensures opioid availability across all levels of care, including:
 - a statement about facts and myths about medical use of opioid tolerance, and dependence
 - 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 minimizing the risk of drug diversion.

H. Annexes

- Selection of frequently used pain scales, measuring pain intensity and pain relief, including those which are particularly suitable for specific groups, e.g. patients with dementia/learning disability.

- Opioid analgesic conversion table
- Opioid analgesic half-life table
- Evidence tables and other background materials
- Research agenda
- Membership of Expanded Review Panel (ERP) and Guideline Advisory Group and involved WHO staff.

CLINICAL QUESTIONS

Evidence should be sought, critically appraised and synthesised before recommendations are formulated in response to these questions. For each question, the term 'chronic non-malignant pain' is used as a generic term at this stage. At the time of gathering evidence, a separate search needs to be carried out for each of the top three aetiologies identified under Section D above in addition to the term 'chronic non-malignant pain'.

The outcomes that should be considered during evidence retrieval, evaluation and synthesis for each of the questions below include: effectiveness of pain reduction, speed at which pain relief may be achieved, maintenance of pain relief, functional capacity, effect on quality of life and adverse effects and complications of treatments/interventions.

The relative importance of each of these outcomes will depend on the clinical question being addressed. For issues of short term management of acute severe pain - time to effective pain relief is priority. For management of chronic pain - quality of life, functional capacity, potential severe adverse effects are the most important followed by perception of pain and speed to pain reduction. Also important is the time frame of outcomes. For chronic pain, the time frame of outcomes should be in the medium to long term if possible (i.e. months, not weeks).

A risk/benefit profile would then need to be prepared for each of the question. Each question and its related sub-questions should lead to a specific recommendation. Separate recommendations may be required for the three specific aetiologies if the evidence is found to support these.

Use of opioids in the treatment of chronic pain

1. Considering the potential adverse effects of opioids and the impact on quality of life, disability and long term pain, should the long term prescription of regular opioids be used in the treatment of chronic non-malignant pain?

Analgesic ladder

2. In patients with chronic non-malignant pain, what is the evidence for using the 2-step analgesic ladder compared to the 3-step analgesic ladder in order to achieve rapid, effective and safe pain control?

3. In patients with chronic non-malignant pain, what is the evidence to support the use of paracetamol as compared to aspirin and 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?
4. If the evidence supports the continuing use of a 3-step analgesic ladder, what is the evidence 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?

Choice of strong opioids

5. In patients with chronic non-malignant pain, what is the evidence 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?
6. In patients with chronic non-malignant pain, what is the evidence for the practice of opioid rotation or opioid switching as compared to continuing use of one opioid in order to maintain effective and safe pain control?

Administration of opioids

7. In patients with chronic non-malignant pain, what is the evidence 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?
8. In patients with chronic non-malignant pain, 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?
9. In patients with chronic non-malignant pain, what is the evidence for the benefit of using the oral route as compared to parenteral administration for opioids in order to achieve rapid, effective and safe pain control?
10. In patients with chronic non-malignant pain, what is the evidence for the benefit of using the subcutaneous or transdermal route as compared to the intramuscular and intravenous routes when the oral route for opioids is inappropriate (e.g. patients with diminished consciousness, ineffective swallowing or vomiting)?

11. What is the evidence for the recommendation that a double dose of immediate release morphine should be given at bedtime for those taking 4-hourly immediate release morphine during the day as their regular analgesic in order to maintain effective pain control?

Co-analgesic and adjuvant medications

12. In patients with chronic non-malignant pain, what is the evidence for the use of steroids as an adjuvant medication as compared to placebo in order to achieve and maintain effective and safe pain control?
13. In patients with chronic non-malignant pain where muscle spasm is a specific feature, what is the evidence for the use of muscle relaxants such as diazepam as compared to baclofen and to placebo in order to achieve and maintain effective and safe pain control?
14. In patients with chronic non-malignant bone pain:
 - 14.1 What is the evidence for the use of non-selective NSAIDs as an adjuvant medication in order to achieve rapid, effective and safe control of bone pain?
 - 14.2 What is the evidence for the use of bisphosphonates as an adjuvant medication, in order to achieve rapid, effective and safe control of bone pain?
15. In patients with chronic non-malignant neuropathic pain:
 - 15.1 What is the evidence for the use of amitriptyline and other tricyclic antidepressants as compared to SSRIs in order to achieve rapid, effective and safe pain control?
 - 15.2 What is the evidence for the use of second generation anti-epileptics such as gabapentin as compared to first generation anti-epileptics such as carbamazepine or sodium valproate in order to achieve rapid, effective and safe pain control?
 - 15.3 What is the evidence for the use of second generation anti-epileptics such as gabapentin as compared to first generation anti-epileptics such as carbamazepine or sodium valproate in order to achieve rapid, effective and safe pain control?
 - 15.4 What is the evidence for the use of second generation anti-epileptics such as gabapentin as compared to placebo in order to achieve rapid, effective and safe pain control?
 - 15.5 What is the evidence for the use of NMDA receptor antagonists (e.g. ketamine) as compared to placebo in order to achieve rapid, effective and safe pain control?
 - 15.6 What is the evidence for the use of local anaesthetic agents as compared to placebo in order to achieve rapid, effective and safe pain control?

Non-drug therapies

16. In patients with chronic non-malignant pain, what is the evidence for the use of nerve blocks and other interventional therapies as compared to placebo in order to achieve rapid, effective and safe control of pain?
17. What is the evidence for the use of cognitive behavioural therapy as compared to none to reduce pain and disability?
18. What is the evidence for the use of biofeedback as compared to none for chronic pain?
19. What is the evidence for the role of transcutaneous electrical nerve stimulation as compared to none in order to achieve rapid, effective and safe control of pain?
20. What is the evidence for the role of exercise as compared to none in the management of chronic pain?
21. What is the evidence for the use of physiotherapy as compared to none for chronic pain?

SYSTEMS QUESTIONS

22. In the management of chronic non-malignant pain, 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 non-malignant pain, 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

1. 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.
2. The AGREE Collaboration. Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument. www.agreecollaboration.org/pdf. Accessed 12 Nov 07.