NOTE: This guideline was replaced by the Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain in May 2010.

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Evidence-Based Recommendations for Medical Management of Chronic Non-Malignant Pain

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Facilitated by the College of Physicians and Surgeons of Ontario

November 2000

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Evidence-Based Recommendations for Medical Management of Chronic Non-Malignant Pain - Executive Summary

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Overview

This work is the product of a Task Force appointed by invitation from the College of Physicians and Surgeons of Ontario (CPSO) to certain physicians in November 1996 to develop evidence-based recommendations for the management of Chronic Non-Malignant Pain for the purposes of education, information and clinical guidance of the membership. The Task Force consisted of seven physicians practicing Pain Medicine, representing appropriate cross sections of disciplines and expertise. The Task Force recommended location and collation of an evidence-based resource that could be regularly revised, instead of creating another set of consensus guidelines.

The Task Force recommended that:

- prior to the establishment of an evidence-based resource, the needs of the CPSO physician membership be ascertained.
- published consensus guidelines should be reviewed/evaluated
- existing quality systematic reviews and meta-analyses should be searched and collated to provide evidence-based recommendations for the management of different kinds of Chronic Non-Malignant Pain, and that special reference to opioid use for Chronic Non-Malignant Pain should be made.

Limitations

Focus of the Task Force was limited by resources and by the findings of the needs assessment. Hence, the resulting document does not include all possible treatments relevant to chronic non-malignant pain. The Task Force chose as a focus some of the most important topics identified in the physicians' survey and the focus group. The current document deals with the medical management of pain. Other topics (neurosurgical management of pain, nerve blocks, management of addicts, etc) can be included in subsequent years.

Not all systematic reviews relevant to the work of the Task Force were located in the preparation period - however, they will be reviewed and included in subsequent years. It is significant that the Task Force reached essentially consistent conclusions to those reached by the Oxford group (McQuay and Moore, 1998).

The Task Force concentrated mainly on systematic reviews and meta-analyses, which tend to be more conservative estimates of efficacy. These types of studies tend to give greater weight to good quality RCTs. On the other hand, several of the systematic reviews made use of a similar sets of RCTs, so that the conclusions are not strengthened by multiple systematic reviews -- for example those on laser or Transcutaneous Electrical Nerve Stimulation (TENS). For some of these, the evidence level remains *Level II or Level III.*

Recent RCTs are not likely included in the meta-analyses reported in this project - hence some recent research may not be represented this year, but can be included in subsequent years.

The Task Force concentrated almost exclusively on chronic pain. Some procedures which show no significant efficacy in chronic pain do show efficacy in pain of shorter duration, for example, NSAID for low back pain. The conclusion of non-efficacy in this document resource does not mean that the procedures or treatments are never effective, but only that the efficacy in chronic pain populations has not been demonstrated. Patient selection and clinical experience will be factors in efficacious use.

General Outline

The work of the Task Force is divided in three volumes:

Volume I

Volume I includes discussion of :

- pain in general and pain disorder classification
- details of Task Force constitution
- types of searches used for retrieval of best available evidence
- a unified system for classification of strength or levels of evidence
- summary of project objectives
- availability of project resources
- costs and benefits associated with proposed modalities for treatment of Chronic Non-Malignant Pain
- consideration of peer review and piloting of the project
- methodology and timing of update of proposed resource
-

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- modes of dissemination/implementation of the resource recommendations
- monitoring and applicability of the project
- biases and limitations pertaining to proposed recommendations and relationship of evidence-based recommendations to professional standards of practice.

Details of membership survey method and results are provided. This volume also includes a detailed review and qualitative and content assessment of existing national and international guidelines for treatment of Chronic Non-Malignant Pain.

Volume II

Volume II includes details of the methodology for literature selection and quality assessment. Subsequently the reviewed literature focuses on:

- chronic daily headaches
- migraines
- neuropathic pain
- musculoskeletal pain
- opioid use in general for Chronic Non-Malignant Pain.

Each section includes definition of painful syndromes, details of the literature surveyed and summaries of available evidence regarding medical and non-medical management. When deemed necessary, review of pathophysiological mechanisms and general principles governing management are included.

Volume III

Volume III provides summaries of evidence retrieved and collated. In particular, specific attention is paid to opioid use for Chronic Non-Malignant Pain. The Task Force outlines principles of sound medical practice for use of opioids. For each recommendation regarding opioid use in Chronic Non-Malignant Pain, available evidence and strength of evidence is reported. Examples of good office practice are cited and checklists for side effects, drug abuse behaviours or behaviours suggesting opioid dependence are outlined. Consolidated summaries of reviewed evidence for all subjects covered by this resource, including recommendations, are presented in tables at the end of this volume.

References and Appendices

References are listed per chapter. The appendix includes several useful documents/tables/charts such as:

- Oxman and Guyatt's Index of the Scientific Quality of Research Overviews
- the focus group on "opioid" use in Chronic Non-Malignant {ain
- the summary of recommended use of opioids based on underlying pathophysiologic mechanisms of pain
- the general approach to history taking and diagnosis of Chronic Non-Malignant Pain
- a chart for Do's and Don't's when administering opioids for Chronic Non-Malignant Pain
- patient information sheets
- samples of opioid treatment contract, pain scale charts and narcotic flow sheet charts
- the role of methadone in the management of Chronic Non-Malignant Pain.

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Results - Recommendations Volume I

The survey of the membership was conducted by a specifically designed questionnaire mailed to a representative sample of physicians throughout the province. In summary, Ontario doctors proved to be aware of the importance of treatment of Chronic Non-Malignant Pain. The greatest clinical load in dealing with Chronic Non-Malignant Pain sufferers remains with family practitioners. The greatest interest of the physicians surveyed focussed on practice guidelines relating to different types of management of:

- chronic low back pain
- headaches
- neck pain
- chronic soft tissue pain
- neuropathic pain
- specific recommendations for the use of opioids in Chronic Non-Malignant Pain.

Review of existing consensus guidelines was performed on all currently published guidelines approved by a sponsoring body in Canada and the USA (7 in total). The consensus guidelines were rated by the best available instrument currently undergoing validation in Europe (Guideline Development Instrument by Cluzeau et al. 1997). The Task Force pointed to the common elements endorsed in these guidelines in detail. Strengths of existing guidelines were outlined. However, the need for creation of an evidence-based resource for the management of Chronic Non-Malignant Pain became evident, as the consensus guidelines displayed weaknesses primarily in the following areas:

- quality of evidence used
- potential of biases in the constitution/selection of the expert panels
- lack of peer review and feedback phase before final draft
- potential of obsolescence if guidelines are not regularly updated.

Volume II

Chronic Headaches

For Chronic (daily) Headaches little data seemed to emerge from meta-analyses or systematic reviews of drug treatments, with the exception of tricyclic antidepressants and selective serotonin-reuptake inhibitors (even in the case of non-depressed patients). Useful non-pharmacological treatments, however, included:

- behavioural
- cognitive
- relaxation
- biofeedback methods.

In general, useful treatments should address:

- depression and anxiety
- lifestyle changes
- limitation of analgesic intake to avoid rebound headaches
- limitation of dietary triggers such as caffeine and aspartame.

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Migraines

For Migraines, the definition of the International Headache Society was used. Recommended treatment approaches based on best available evidence include in rank order:

- ASA or NSAIDs,
- acetaminophen, combination acetaminophen/codeine

For non responders to above:

- Triptans (serotonin agonists, expensive but very effective)
- dihydroergotamine (DHE)
- ergotamine
- short-term combinations of abortive medication (with caution Fiorinal)

For severe episodes:

- parenteral metoclopramide followed by dihydroergotamine (DHE)
- chlorpromazine parenterally
- IM ketorolac
- intranasal lidocaine
- butorphanol nasal spray
- parenteral dexamethasone.

Cautions, risks for dependence and side effects were stressed in the use of these medications. For prophylaxis, the literature suggests:

- non-pharmacological approaches like removal of dietary and other triggers and relaxation/biofeedback techniques
- pharmacological approaches (beta blockers, calcium channel blockers, serotonin blockers, tricyclic antidepressants, and anticonvulsants).

Indications, contra-indications, risks and side effects are stressed.

Neuropathic Pain

For Neuropathic Pain, it was felt necessary to provide:

- definitions in order to distinguish nociceptive from neuropathic pain
- some basic understanding of the pathologic mechanisms underlying neuropathic pain phenomena
- general principles governing both pharmacologic and non-pharmacologic interventions.

In general, regarding pharmacologic treatments, *Level I* evidence exists in the literature for use of tricyclic antidepressants and anticonvulsants, and in selected cases local anaesthetic-type drugs. Indications, contraindications and systematic approaches to prescribing these drugs alone or in combination are discussed. Local capsaicin (the extract of chile peppers) has been proven beneficial in painful diabetic neuropathy. Other than the strong existing evidence for lack of efficacy of intravenous regional guanethidine blocks for reflex sympathetic dystrophy (currently called complex regional pain syndrome), there is lack of evidence to support other types of blocks.

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Chronic Musculoskeletal Pain

There is *Level V* evidence for the following approach. When musculoskeletal pain persists for three months or more, and no treatable cause is found despite adequate assessment, and when this persistent pain is unresponsive to apparently appropriate therapy a co-ordinated and more intensive approach is needed which should include the:

- patient's active participation
- practical goals for change and focus on problem areas
- patient's education including review of goals and progress, promotion of function and psychosocial intervention if appropriate
- closely co-ordinated approach by the treating physician/clinician.

Opioids in Chronic Non-Malignant Pain

Regarding opioid use in Chronic Non-Malignant Pain, existing survey data and available randomized controlled trials support the conclusion that sustained release opioids may benefit selected patients with chronic musculoskeletal and neuropathic pain. In these patients, history of substance abuse, is a relative contraindication for opioid prescription. Cognitive impairment can be minimized with individual titration of doses. Long term opioid therapy may or may not improve functional status. There is, however, some *Level V* opinion that treatment programs focusing only on analgesics can reinforce pain related behaviours at the expense of functional restoration. Therefore, opioid use should rather be part of a more comprehensive treatment program including gradual exercise and psychosocial/behavioural approaches to pain management. Such an approach, however, depends on underlying medical condition and clinical judgement is required. Detailed recommendations and step-by-step approach to administration, dosing etc. of opioids is separately outlined in Volume III.

Even when pain relief as a goal eludes the patient and his/her physician, patients are usually comforted by an empathic attitude, time to listen, and the offer of emotional support. Function can usually be improved through modification of methods or use of:

- aids
- changes of pace and rest periods
- exercise (strengthening and increasing range).

Occasionally referral may be necessary to a specialized multimodal rehabilitation program, but even then, the supportive stance of the primary physician is an important ingredient in the patient's progress.

Volume III General Recommendations

This contains a summary of the project, with tables, and bibliography.

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Appendices

Focus Group

The focus group on opioid use in Chronic Non-Malignant Pain consisted of community physicians. The focus group felt that opioid analgesics were an accepted form of treatment for selected patients. However, focus group members expressed the desire for guidance regarding those patients most likely to benefit versus those patients most likely to develop psychological dependence or addiction. The group expressed the need for a validated instrument to assess propensity for addiction, as well as the need for a central registry for opioid prescriptions to avoid "double-doctoring". The focus group felt it would be helpful if the CPSO could provide recommendations for use of opioids in Chronic Non-Malignant Pain, recognized that the recommendations would have to be revised and updated regularly to reflect advances in the management of Chronic Non-Malignant Pain, and expressed concerns that if the recommendations were too rigid, they would interfere with practice.

Finally the group indicated they would like to see more continuing medical education events to help guide the management of Chronic Non-Malignant Pain, as well as availability of more psychological services to assist in exploring non-pharmacological options in the management of Chronic Non-Malignant Pain.

Methadone

Note: ***Methadone use in Chronic Non-Malignant Pain is included in the appendices because it is not evidence-based; however, the appendix contains valuable information to guide the profession.***

Methadone use in Chronic Non-Malignant Pain is specifically discussed. The Task Force considered the available literature, the drug's limitations as well as advantages. Tables are provided for conversion to methadone from morphine/morphine equivalents. Cautions regarding side-effects (drowsiness, respiratory depression and toxicity), as well as the presence of certain medical conditions that increase the potential of serious side-effects, are outlined.

The Task Force recommends minimum standards for use of methadone as treatment for Chronic Non-Malignant Pain. From the regulatory point of view, the program for use of methadone for heroin addiction resides currently with the Substance Abuse Unit of the Ontario Ministry of Health, and the CPSO provides recruitment of physicians to the program and keeps a registry of physicians and their patients. Other regulatory bodies as well provide other input and support. However, regarding use of methadone for Chronic Non-Malignant Pain, the CPSO recognizes that use for analgesic purposes only is distinct from methadone for opioid addiction. In order to be permitted to prescribe methadone for non-addicted pain patients, physician must apply to the **Office of Controlled Substances in Ottawa (613) 946-5139.**

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Evidence-Based Recommendations for Medical Management of Chronic Non-Malignant Pain

Introduction

Volume I

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Chapter 1 Introduction

1.0 Definition

The definition of **pain** that has the greatest currency was proposed by psychiatrist Dr. Harold Merskey; "an unpleasant experience which we primarily associate with tissue damage, or describe in terms of tissue damage, or both" (Merskey and Spear, 1967). The Taxonomy Committee of the International Association for the Study of Pain (IASP) adopted the framework of this definition, with little change. The essence of the concept is that pain is an experience, and cannot be validated/invalidated on the basis of presumed underlying causes. For pain to be chronic, it must continue to persist beyond the usual trajectory of healing (usually several months), and/or be unrelieved despite treatment that would normally resolve the pain.

The concept of "**pain disorder**" has also been dealt with in the Diagnostic & Statistical Manual of Mental Disorders (DSM) manuals and in the International Classification of Diseases (ICD) system. "Pain disorder", either "with psychological factors" 307.80, or "with both psychological factors and a general medical condition" 307.89, evolved from an earlier concept of "somatoform pain disorder" or "psychalgia" which were used up to and including DSM-III, and are still used in ICD-10. This described the clinical problem of "psychogenic pain", or "pain without lesions" and/or "pain without adequate physical causes", and attributed to unconscious emotional problems and motives. The problem with the latter notions was that they were virtually indistinguishable from the concept of "conversion", and it was too restrictive in assuming that the pain must be "caused" by an underlying psychic factor, which implied a psychiatric diagnosis by exclusion.

The DSM-IV moved toward a descriptive categorization with independent dimensions of "medical factors, "psychological factors" and "acute versus chronic", with no assumptions about psychological or behavioural dynamics in the causation, but it kept the ICD and earlier DSM concept of a distinct "pain disorder associated with a general medical condition" in which psychological factors, if present, were "not judged to have a major role in the onset, severity, exacerbation, or maintenance of the pain." On the other hand, the ICD classification system has retained the "somatoform pain disorder" F45.4, which is a synonym for "psychalgia" or "psychogenic headache" or "psychogenic backache" concepts, and ICD distinguishes this from the medical conditions of "backache not otherwise specified (NOS)" (M54.9), "pain NOS" (R52.9), "acute pain" (R52.0), "chronic pain" (R52.2) and "intractable pain" (R52.1) which is often used to denote persistent cancer pain.
Recent DSM-IV focus on "association" of a significant presenting medical

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complaint/symptom with psychological factors which are judged to have an important role in the onset, severity, exacerbation or maintenance of the pain, and is not intentionally produced or feigned, and is not accounted for by other discrete psychiatric conditions, does not rule out the idea of "causation" but broadens the ways in which an apparent medical problem can depend on non-medical factors. To complete this diagnosis of pain disorder, the clinician is expected to specify which medical and/or psychological factors are present and to specify if the disorder is of duration less than six months (acute) or six months or more (chronic).

The upshot of all this is that in the DSM-IV thinking, a clinician does not have either to assume or try to prove that there are specific sufficient and necessary psychological "causes" for the "pain without adequate lesions", even if the clinician thinks these factors may be present - the descriptive category is enough to make the diagnosis. This avoids the fuzziness of psychodynamic speculations about symptom origins, which detracts from the cleaner empirical diagnosis of psychiatric categories.

1.2 Responsibility for Development of "Evidence-Based Recommendations" Document and Task Force Composition

On November 12, 1996, the College of Physicians and Surgeons of Ontario (CPSO), Clinical Quality Improvement Committee of Council, invited seven physicians to consider the feasibility of developing evidence-based recommendations for the management of chronic non-malignant pain. The College of Physicians and Surgeons of Alberta had already produced a set of guidelines in 1993, and these were subsequently adopted by the Colleges of Physicians and Surgeons of British Columbia and New Brunswick.

A Task Force was appointed by invitation of The College of Physicians and Surgeons of Ontario to define parameters for the management of chronic non-malignant pain for the purpose of education, information and clinical standards. The Task Force included specialists from an appropriate cross-section of disciplines and expertise. The Task Force elected to not attempt the creation of yet another set of consensus guidelines, but rather to locate and collate an evidence-based resource that could be revised on a regular basis according to new evidence, and that took into account quality-assessments of evidence. In order to create this resource, the Task Force conducted a needs assessment.

- membership survey by questionnaire
- focus group.

The priorities of the Task Force were focussed on the priorities reflected in this needs assessment.

The physicians who attended this meeting were people who were involved in:

- chronic pain management
- addiction management
- psychiatry
- rehabilitation

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- pain research
- education
- primary care and specialty practice.

This group, in discussion with CPSO staff, acknowledged the need for clarity in this difficult clinical area, but recommended that in order to address this problem properly, a careful and evidence-based process would have to be followed. It should be noted that external funding was not solicited. No grants, no honoraria, or expense accounts were made available to the group. Mailing, a portion of the literature searches, copying and distribution of documents, were provided by The College. Some individual members donated data analysis, further literature searches, part of the cost of conducting the survey and focus group, document preparation and write-up.

This committee recommended that the needs of the CPSO membership should be ascertained by questionnaire and a focus group. Existing consensus guidelines should be reviewed and evaluated. Evidence-based standards should be applied in any project to develop or to affirm evidence-based recommendations. The members who undertook to form the Task Force to accomplish the above objectives are all involved in the practice of Pain Medicine:

- Dr. Alejandro Jadad (Anaesthesiology and Research)
- Dr. Meldon Kahan (Family Medicine and Addiction Medicine)
- Dr. Angela Mailis (Physical Medicine and Rehabilitation)
- Dr. Michael Moore (Anaesthesiology)
- Dr. Dwight Moulin (Neurology)
- Dr. Eldon Tunks (Psychiatry)
- Dr. Lynn Wilson (Family Medicine and Addiction Medicine)

1.3 Types of Searches Used and Contents

The scientific and clinical research data bases were searched for relevant information pertaining to treatment options for chronic non-malignant pain. Two main systematic reviews were found to already exist, dealing with the efficacy issues in treatment of chronic non-malignant pain. These were authored by McQuay and Moore (1998), and by Tunks, Crook and Crook (1999) - both being systematic reviews that collate the results of other systematic reviews. Additional searches were added relevant to:

- chronic headache
- pain and addiction
- neuropathic pain
- use of opioids in non-malignant pain.

Note: *The Task Force lacked the resources to carry out a systematic review of surgical or invasive procedures, hence these are not discussed. The Task Force recognizes the importance of such procedures and recommends they be included in subsequent revisions.*

The results of these searches were used to select studies, based on quality

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assessments, and to prepare summary tables.

This data base was then used to annotate "treatment recommendations" for chronic non-malignant pain. A systematic review was also carried out with respect to "consensus guidelines" from various jurisdictions. These opinions were considered in preparation of this document, as a source of Level V evidence recommendations.

It is projected that this resulting resource will provide an authoritative resource for evidence-based practice, and will be useful for instructional purpose and for clarifying clinical standards.

Therefore the Task Force dealt with evidence-based parameters in Chronic Non-Malignant Pain in the following categories:

- Headache
- Neuropathic Pain
- Opioid Use
- Musculoskeletal Pain.

1.4 Levels of Evidence

A unified system was used to represent the levels of evidence for each conclusion. The source for this rating system was McQuay, H. And Moore, A. An Evidence-based Resource for Pain Relief, Oxford U. Press 1998.

1.4.1 Table #1 Levels of Evidence

Level of Evidence	Description
I	Strong evidence from at least one systematic review of multiple well-designed randomized controlled trials.
II	Strong evidence from at least one properly designed randomized controlled trial of appropriate size.
III	Evidence from well-designed trials without randomization, single group pre-post, cohort, time series, or matched case-controlled studies
IV	Evidence from well-designed non-experimental studies from more than one center or research group.
V	Opinions of respected authorities, based on clinical evidence, descriptive studies, or reports of expert committees.

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1.5 Objectives of the Project

The need in Ontario for a source for evidence-based practice for chronic non-malignant pain was viewed as necessary for the work of educational programs sponsored by or assisted by the CPSO, for clarification of clinical practice standards, and as a potential resource of physician members who seek guidance from the College.

It was intended that eventually a resource would be developed which would be based on:

- the best evidence available
- the evidence identified and in a form that could be regularly updated as new literature should become available, but that the resource would not be restricted to the nature of a "consensus report", of which several now exist in the literature.

The lack of financial support or grants required that the group should attempt to locate high-quality research that had already been done on the subject, and to organize this data in a meaningful and scientifically sound way. In order to responsibly and accurately reflect the needs of the membership of the profession, it was recognized that a needs survey of the membership would be necessary. It was intended that this resource should be authoritative, based on the best available quality standards in use for "guidelines" literature, and standards in use for "systematic review" and "Randomized Controlled Trials (RCT)" literature. In this way, educational programs, organizations and physician individuals using this eventual resource would have the confidence that recommended clinical parameters were consistent with validated standards. This resource with references will allow the reader to examine the level of evidence for many frequently-used treatments for chronic non-malignant pain conditions, to be informed about the alternatives, and to have authoritative literature references.

Note: *The Pain Task Force assumes that "non-malignant" signifies that pain does not arise from a progressive life-threatening disorder.*

1.6 Likely Costs and Benefits

Weir, et al. (1992) published the only known detailed study of costs and clinical benefits associated with chronic pain management. This was discussed recently in Chapter 34 by McQuay and Moore (1998). No studies have been done of the costs/benefits associated with treatment of specific diagnostic subgroups of non-malignant pain, or of the costs/benefits of individual treatment modalities. The reader is directed to the above references for discussion of the cost -benefits of organized pain clinic treatment of chronic non-malignant pain. The available literature supports a conclusion that this type of management is cost-effective both for patients as well as for the health care system.

Risks and harms that may occur as a result of chronic non-malignant pain management have been examined only with respect to adverse effects of some classes of medication. The reader is referred to the book by McQuay and Moore (1998) wherein adverse effects of NSAID, TCA, and anticonvulsants for chronic pain are compared in systematic reviews (Chapter 11, 30, 31).

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The Task Force depended on the above published works and did not conduct a separate study of costs and benefits.

1.7 Peer Review and Piloting

Peer Review was arranged at the end of the draft preparation. The recommendations were sent to 398 reviewers who included experts, users and consumers who were asked to provide feedback. The reviewers included the following:

- 200 Ontario physicians who had originally received the needs survey.
- 171 reviewers from the following areas:
  - 124 were reviewers in Ontario. This group included:
    - Physicians practicing pain management
    - Pain clinics
    - Members of the University of Toronto Pain Society
    - Deans of Medicine at Ontario Universities
    - OMA Sections on Anaesthesia, Addiction Medicine, Physical Medicine and Rehabilitation, Neurology, and Probationary Section on Chronic Pain Physicians
    - Chair or Heads of Sections at Ontario Universities
    - Pain Societies and Associations
    - Consumer Groups
  - 30 were mailed to Canadian National Societies, Associations and Universities outside Ontario, such as, Deans of Medical Schools, College of Physicians and Surgeons and The Migraine Association of Canada, the North American Chronic Pain Association of Canada, the College of Family Physicians of Canada, and The Canadian Pain Society.
  - 14 were mailed to USA Pain Societies, Associations, consumer groups and pain practitioners, for example the American Academy of Pain Management, The American Geriatrics Society and The National Headache Foundation.
  - Three were mailed to international societies and individuals, The International Society for Quality in Health Care Inc., The International Association for the Study of Pain and Dr. Henry McQuay from the University of Oxford.
- 27 Pharmaceutical Companies

The Task Force received a 24% response rate (95 responses) from the external review. The Task Force carefully deliberated and considered all of the suggestions of the reviewers. The revisions are included in the present version of the document.

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1.8 Updating

Given that the structure of this resource is evidence-based, it is projected that updating of the recommendations will occur approximately one year after the release of the current version. This will require:

- review of recent literature using the same search strategies and data bases
- review of included studies for quality ratings
- preparation of summary tables
- referencing the results into a document of updated recommendations.
- a systematic review of surgical and anaesthesiological procedures for chronic pain

As mentioned above, when the follow-up survey has been completed, data retrieved from the survey will also be included in subsequent updatings.

1.9 Local Protocol Development, Dissemination and Implementation

The resource will be disseminated by the CPSO in several ways:

- by publication in its' journal Members' Dialogue which goes to all members in the province
- by use in CPSO-sponsored educational programs
- by specific mailings to individuals who have participated in focus groups or "needs study"
- to other interested organizations
- on request to individuals asking for this type of information.

There is no need for "local protocol development" since the document is intended to be an evidence-based resource to be used in a variety of situations - not in a narrower application to one type of condition only, where local protocols would be necessary.

The Evidence-Based Recommendations will be used for a wide variety of activities, such as, sponsored educational activities, clinical quality improvement, quality assurance, complaints, patients relations, inquiries from individual physician members, and relations with other regulatory bodies.

Assessment protocols will be developed based on the recommendations. The College will carry out quality assessments based on the protocols in order to assist physicians to improve the quality of services physicians provide to patients.

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Feedback from assessments and the other activities and what can be learned from application of these guidelines will be brought back to the Task Force for consideration in future revisions of this document.

1.10 Monitoring of Recommendations, Quality Improvement and Incorporation into The College programs

This is mainly an evidence-based resource that may be used in clinical situations which may vary greatly with regard to:

- patient diagnosis
- mechanisms of illness
- mechanisms of treatment
- co-morbidities
- psychosocial circumstances.

Unitary dictums cannot be easily derived from this type of resource. It does not document singular criteria for monitoring compliance, since in most situations a variety of appropriate treatment options are likely to be available. There are some areas in which adverse effects have been well documented (see McQuay and Moore 1998; Chapters 11, 30, 31), but not enough is known to produce a comprehensive picture of contraindications based on risk factors, except perhaps with regards to the use of NSAID, TCAs, and anticonvulsants.

However, it does document a standard of practice that gives importance to quality-assessment of reports, and accurate extraction and interpretation of significant findings. This resource permits relative comparison of efficacy of common treatments with respect to chronic non-malignant pain. It would be assumed that ethical and knowledgeable clinicians would make an effort to be informed about the range of the most appropriate treatment alternatives for a given chronic pain problem, and it should be assumed that treatments used in a physician's practice should be generally consistent with evidence and standards of appropriate professional practices.

1.11 Standards of Practice

Standards of practice are always related to:

- maintenance of competence with regard to knowledge and skills
- habits of practice informed by knowledgeable use of evidence
- exercise of good interpersonal communication
  - informed consent
  - professional ethics
  - clinical documentation
- standards of professional conduct established in practice or regulation by peers
- accountability to the public and to the profession

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- the need for quality improvement.

The treatment guidelines resulting from the work of this Task Force will be incorporated into future College programs, including the carrying out of quality assessments

1.12 Applicability

The inclusion criteria for systematic reviews and meta-analyses and RCTs included in this resource were that the pain was "chronic" and non-malignant. Chronic was defined in most of the RCTs as persisting for at least several months, and in some cases years. In some reviews, the durations were unstated, apart from the implication that the pain was chronic. Presence or absence of psychological or other complications were not inclusion criteria. Children were not included in the included studies. There were no included studies that focussed specifically on male or female, or the aged, or other demographic subgroups. Several but not all of the studies included groups with probable behavioural or psychological complications, and managed with psychological or multimodal techniques. The majority but not all of the studies focussed on chronic musculoskeletal pains.

Therefore, the recommendations of this resource are applicable to the adult population with persistent non-malignant pain, with or without a definite diagnosis, and with or without psychosocial complications.

The circumstances in which treatment recommendations would be valid depend on patient characteristics. Particularly, if patients have indicators of psychosocial complications, and/or have been unresponsive to apparently appropriate treatments, intensive and multimodal and psychologically-oriented treatments would be recommended, based on the evidence of relative efficacy.

There are also certain treatments discussed in the resource which are more appropriate for certain diagnostic groups; e.g. anticonvulsants or TCAs for neuralgias or chronic headaches.

1.13 "Empowering" the Patient

When pain (irrespective of source of pathology) becomes persistent, good patient care dictates re-examination of the patient.

Depending on underlying pathology specialized treatment may be applied, but a focus on pain relief alone is likely to be inadequate. There are usually other important sources of distress such as fatigue, depression, and insomnia, and function may be more or less impaired. These other complaints may be as important as pain in the overall distress, and frequently are flags for co-existing emotional and social factors. These psychosocial factors in particular are:

- often important prognostically
- barriers to recovery
- along with pain an appropriate focus for intervention.

Hence, one should broaden the objectives from just "treating pain" to

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"rehabilitation of the pain sufferer". While working toward improving comfort where possible, the aim is always to help the patient to enhance his/her physical, psychological, and social functioning.

While the "medical model" of diagnosis and removal of the source of pain may fail to solve the problem, the rehabilitation model is oriented around goals toward which the patient is willing to work actively. This change in direction requires the awareness that prolonged and fruitless repeated investigations and trials of pain-relieving medications, procedures or surgeries are counterproductive for the patient as well as for the caregiver, whereas helping the patient to regain control of his/her life despite pain has a higher probability of success.

It also requires the willingness of the physician to form a relationship with the patient for the purpose of teaching, coaching, and supporting the patient, and co-ordinating the work of other health care providers who may be involved. Desirable outcomes include:

- reduction in distress and uncertainty
- increased participation in work and productive activity
- improved social and family relationships
- improved independence.

1.14 Comments on the Task Force's Recommendations

1.14.1 Biases

Many outcome measures found in some RCTs will not be reflected in systematic reviews because they were not used in other RCTs, and hence are not suitable for summarising the data across studies. Hence, some useful details from some RCTs have not be considered. However, the statistical power is effectively increased in measures which can be summarized across several RCTs, and this is the benefit of systematic reviews and meta-analyses.

Meta-analyses varied in the quality and numbers of studies they included, so that the levels of evidence of their conclusions are not equal.

1.14.2 Review Process and Patients' Preferences

This study has not yet included data with respect to patient preferences for particular approaches. However, in the peer review process which followed the completion of the draft document, the draft was sent to professional and consumer groups, and feedback was incorporated where appropriate in the final document.

1.14.3 Correct Understanding of this Evidence-Based Resource

When data are aggregated for the purpose of analysis, the means and distributions can be analysed meaningfully, but one must be careful in reasoning from the

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average to the individual case - because each sample is made up of a set of observations clustered about a mean. The evidence may show that NSAID is usually ineffective for chronic low back pain, but there will be a small minority of cases in which benefit will be reported. Hence, the evidence-based recommendations cannot be translated into a prohibition for certain approaches, but only a weighing out of the likely benefits or lack of same in a given population. This however is a very important consideration in the informed practice of every clinician, and contributes to the sound decision making in choice and preference of treatment approaches.

1.14.4 The Relationship of Evidence-Based Recommendations to Professional Standards of Practice

The purpose of an evidence-based resource is to provide recommendations based on the best available evidence and to cite the support for these opinions. This is not equivalent to standards of practice, but is one of several ingredients that help to measure standards of practice.

In a complex field such as chronic pain management, a variety of complementary skills and professions is needed. Professionals must be adequately trained, and must demonstrate competence in skills and knowledge adequately up-to-date. Physicians cannot be expert in all things but be informed and able to inform patients of the:

- efficacy
- limitations
- relative advantages
- cost benefits
- risks of the treatments they are able to practice.

Physicians should direct patients to other practitioners or clinics when it is in the best interests of treatment efficacy and patient benefit.

Treatments with lower demonstrated efficacy will not necessarily be avoided, but treatment choices will depend on:

- patient selection
- taking other appropriate modalities into account
- the priorities given should reflect known
  - efficacy
  - risk
  - cost-benefit
  - patient comfort
- the skills of the clinician to provide given treatment.

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Chapter 2 Survey of Membership

2.0 Survey of Membership

2.1 Aim and Objective

Part of the work assumed by this Task Force was the design, pretesting, and use of a questionnaire survey to be given to a representative sample of the membership. This survey was conducted in July and September 1997.

The objectives of the survey were to explore the attitudes, perceived needs, and concerns of physicians in Ontario with regard to the management of chronic non-malignant pain. From this, it was hoped to identify priorities to guide the work of the Task Force, with regard to specific clinical problems, and clinical treatment options, that should be addressed. The Task Force was also sensitive to the need for peer input into the process of defining recommendations for practice.

2.2 Methods

2.2.1 Design of Survey Instrument

A survey instrument was designed, incorporating 13 questions with sub-questions. The items were selected and constructed by the investigators based on the mandate of the Task Force, and on the clinical experience of the Task Force members. Two initial versions of the questionnaire were pretested by obtaining feedback from seven volunteer family physicians recruited by Task Force members. This feedback was used to refine the questionnaire.

The first six main questions captured demographic information including gender, duration of medical practice, specialty, solo vs group practice, and type of practice setting. The seven remaining questions addressed the following:

- The significance to the practice of the management of persistent pain (slight, moderate, great, and not applicable)
- The proportion of time dedicated to different areas (cancer, addiction management, or medical, psychological, or interdisciplinary management of pain).

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- The perceived need for guidelines for the diagnosis and management of various painful conditions.

- The perception of the need for guidelines regarding specific treatment methods (medication, exercise, rehabilitation, surgery, and alternative medicine).

- Problems evoking anxiety for the practitioner, such as medico-legal issues, lack of colleague support, clinical risks, and lack of guidelines for procedures during the treatment of pain.

- The type of resources that would be preferred by the respondents to provide them with information on the management of chronic non-malignant pain (courses, access to experts/computerized resources, and clinical practice guidelines from other jurisdictions).

- Potential concerns that practitioners have specifically in relation to clinical practice guidelines.

Note: *Six of the seven questions used Likert scales, and one used a checklist of alternatives.*

2.2.2 Participants

At the time of the survey, in Ontario there was 6,913 independent general practitioners, and 12,689 members listed as being in specialized independent practice. In order to adequately sample the membership, a formula was used to randomly select a convenience sample of 200 actively practising physicians and surgeons from the CPSO membership data base. This sample was designed to constitute a sample size of 1.02% of the membership, and was stratified to reflect the distribution of:

- physicians/surgeons by general practice vs specialty
- specialty by subspecialty
- gender
- location of practice (urban, suburban, and rural).

The sample identified was blinded - envelopes were addressed by a merge program, and no addressee names were available at any time to the Task Force or CPSO staff. The Task Force expected that the results from this sample would be generalizable to the population of physicians throughout Ontario.

2.2.3 Conduct of Survey

The survey questionnaire was sent to the sample of 200 physicians in July and September of 1997. This questionnaire was accompanied by a cover letter explaining the purpose of the survey, and asking for their participation. The potential respondents were reassured that their identities and individual responses would be kept confidential. One reminder letter with a copy of the questionnaire was sent to all participants two months after the first mailout. All questionnaires were sent with self-addressed stamped envelopes, with no identifiers that could reveal the identity of the respondents. As an incentive, the Task Force offered the

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respondents the opportunity to enter a draw for a photographic camera if they responded to the survey. We regarded, a priori, a response rate of more than 60% as adequate. The results indicated a response rate of 76%.

2.2.4 Statistical Analysis

The responses were coded and entered into a spreadsheet (Microsoft Excel, version seven for Windows 95). Descriptive statistics were produced to summarize the information in all the fields for all the questions, for all respondents, using cross-tabulation tables in SPSS. Chi-Square was used to compare the responses to the questions regarding sources of anxiety, and the concerns regarding the use of clinical practice guidelines, by years of practice, and type of specialty.

> ***Note:*** *In all cases, a p value of less than 0.05 was regarded as statistically significant.*

2.2.5 Results

The response rate to the survey was 76% (152/200). It was evident that one respondent sent in two completed questionnaires (both original questionnaire and second mailing reminder) - but because the responses were blinded, it was not possible to detect the redundant questionnaire, and hence an error of 1/200 was injected into the results, which we do not believe changes the results significantly.

In the sample who responded (75% of those who were sent questionnaires), the demographics were as follows:

- Ratios of male to female respondents was 80% / 20%
- Durations of practice were <5 years / 5-20 years / >20 years = 11%/ 43% / 45%
- Types of practice were Primary Care/Medical Specialty/Surgical Specialty = 48% / 32% / 20%
- 14% were university affiliated
- Urban/suburban/rural = 65%/ 23%/ 11%
- Solo/Group practice = 62% / 38%.

By comparison, the demographics for active independent licence holders in Ontario was the following:

- Male/Female= 72% / 27%
- Durations of practice = 10% / 56%/ 34%
- Types of practice were Primary Care/Medical Specialty/Surgical Specialty = 48% / 37% / 15%.

Hence, the respondents included:

- a 7% lower proportion of females
- a 13% lower proportion of "in practice 5-20 years"
- a 11% high proportion of "in practice more than 20 years"
- a 5% lower percentage of medical specialists
- a 5% higher percentage of surgical specialists.

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The sample was chosen randomly. The Task Force thought that there were no substantial discrepancies between the sample and the population from which it was derived.

The results regarding demographic of respondents stated interest for production of guidelines in:

- Chronic Non-Malignant Pain
- Types of resources considered useful
- Concerns experienced by the physicians are shown in Table #5

In summary, Ontario doctors are aware of the importance of the treatment of chronic non-malignant pain. The greater proportion of the clinical load in dealing with chronic pain sufferers remains with family doctors, who express the greater interest in all clinical issues concerning chronic non-malignant pain and its treatment. Recent medical graduates are probably more comfortable with questions regarding clinical practice guidelines, consistent with the growth of this type of study and publication in recent years, but the attitude in general of all Ontario doctors is one of faith in their colleagues and recognition of the importance of this sort of work in promoting a professionally better standard of practice.

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Table #2 Demographics of Respondents in CPSO Survey

The following indicates the demographics of respondents in the survey (N=153):

Sex F/M		20% / 80%
Duration in practice	<5 years	11%
	5-20 years	43%
	>20 years	45%
Practice Type	primary care/family practice	48%
	medical specialty	32%
	surgical specialty	20%
	urban	65%
	suburban	23%
	rural	11%
	solo	62%
	group	38%
Time devoted to chronic non- malignant pain management	none	17%
	occasional	53%
	frequent	30%
Time devoted to addiction management	none	55%
	occasional	40%
	frequent	4%
Time devoted to headache management	none	24%
	occasional	39%
	frequent	37%
Time devoted to nerve block	none	73%
	occasional	24%
	frequent	3%
Time devoted to palliative care	none	36%
	occasional	54%
	frequent	11%
Time devoted to behavioural or psychological treatment	none	51%
	occasional	35%
	frequent	13%

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Table #3 Interest in Practice Guidelines for Chronic Non-Malignant Pain

Type of Clinical Problem	All Respondents "moderate to great interest"	Primary Care Respondents only "moderate to great interest"
Acute/recurrent back pain	50%	58%
Chronic low back pain	64%	80%
Acute headache	50%	59%
Chronic headache	64%	85%
Chronic neck pain	58%	73%
Neuropathic pain	59%	71%
Chronic pain/psychological problems	54%	65%
Post-traumatic/post-operative pain	55%	59%
Chronic soft tissue pain	66%	82%
Work injury pain	59%	76%
Pain in addicts	63%	78%
Chronic pain in children	42%	60%
Chronic pain in elderly	54%	74%

Type of Clinical Treatment	All Respondents "moderate to great interest"	Primary Care Respondents only "moderate to great interest"
Antidepressants	60%	67%
Nerve blocks	44%	48%
Nonopioid analgesics	60%	70%
Opioids for chronic non-malignant pain	72%	81%
Patient-controlled analgesic systems	55%	63%
Headache prophylaxis	62%	77%
Physical exercise	54%	71%
Psychological techniques	47%	51%
Active rehabilitation/work hardening	57%	75%
Surgical methods	45%	35%
Alternative/complimentary therapies	48%	59%

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Table #4 Types of Resources that Would be Considered Helpful

Type of Preferred Resources	Percentage of Respondents
Access to expert peers who can provide advice	40%
Clinical practice guidelines from other jurisdictions	18%
Courses on non-drug management of non-malignant pain	34%
Courses on prescribing for non-malignant pain	37%
Computerized/electronic resources	35%

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Table # 5 Concerns Expressed By Ontario Physicians About Treating Chronic Non-Malignant Pain

Source of Concern	% of all respondents	% of primary care MDs	Years in Practice % of respondents		
			<5 yrs	5-20yrs	>20yrs
Anxious re: clinical risks	47%	57%	29%	52%	47%
Anxious re: medicolegal complications	64%	73%	59%	68%	62%
Anxious re: lack of guidelines for procedures	49%	52%	59%	45%	50%
Anxious re: lack of colleague support	40%	46%	24%	40%	43%
Concern that choice of experts making guidelines could be biassed	28%	28%	12%	25%	34%
Clinical practice guidelines might require me to change my practice	18%	16%	6%	22%	16%
Clinical practice guidelines could lead to a lack of professional freedom	21%	19%	12%	22%	16%
Clinical practice guidelines could create medicolegal risks	30%	28%	18%	33%	30%
We need more explicit clinical practice guidelines for our own protection	51%	57%	47%	46%	57%
There is not enough evidence for chronic non-malignant pain management guidelines	11%	6%	0%	7%	19%
Others are not competent to judge my specialized procedures	4%	1%	0%	3%	5%

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Chapter 3 Review of Existing Published Guidelines for Treatment of Chronic Non-Malignant Pain

3.1 Aim

The Task Force determined that views of interested parties among Ontario physicians, and other jurisdictions and special interest groups not among Ontario physicians, must be taken into account. It was known that other groups had prepared or were preparing "consensus guidelines" regarding the management of chronic non-malignant pain. In order that the work of this Task Force should be able to take into account the opinions and recommendations of other groups, this CPSO Task Force set the objective of locating other published and relevant practice consensus guidelines, and using a common yardstick to compare retrieved practice guidelines, on parameters relevant to "ideal attributes" of clinical practice guidelines. The work was to begin with a systematic search of electronic data bases for "guidelines" for management of "non-malignant pain".

3.2 Method

3.2.1 Selection of Background Evidence: Existing Guidelines Literature

The searches were performed in Medline/Pubmed, Ovid, and in the Cochrane Library. Additional information was obtained from the WebSite of "St. George's Hospital Medical School, Health Care Evaluation Unit", which is a unit in collaboration with other Research Centers in England and Scotland. Additional sources were sought from expert committee members, from retrieved bibliographies, and by searching the data bases of the Guideline Appraisal Project (GAP) project.

Selection criteria were that the guidelines were published, dealt with management of chronic and non-malignant pain, and the guidelines were approved by a

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sponsoring body or jurisdiction. Exclusion criteria were guidelines or drafts that had not been published, endorsed or approved by a sponsoring body or jurisdiction.

3.2.2 Quality Review of Retrieved Guidelines

Summary and review of retrieved guidelines was undertaken by E. Tunks and A. Jadad, using the following methods:

- Quality ratings were made for each guideline, using the Guideline Development instrument (Cluzeau et al., 1997) provided by Dr. A. Jadad. This instrument is the best available and is undergoing validation in the European Community. Each of the included guidelines was evaluated independently by two members of the Task Force; E. Tunks and A. Jadad. Following independent reviews, a consensus meeting was held to discuss discrepancies in ratings. Using this method, a high level of agreement was found between independent expert raters.

3.3 Results

The above search led to the identification of the following published guidelines:

- College of Physicians and Surgeons of Alberta, 1993
- Medical Board of California, 1994
- American Academy of Pain Medicine and the American Pain Society, 1997
- American Society of Anaesthesiologists, 1997
- Canadian Headache Society, 1997
- American Geriatrics Society, 1998
- Canadian Pain Society, 1999

Note: *After preparation of this report, the College of Physicians and Surgeons of Nova Scotia published guidelines, available at http:www.cpsns.ns.ca*

Guidelines that were excluded included the:

- Guidelines published as a draft document by the Probationary Section on Chronic Pain of the OMA (1998) because it was still a draft and not approved by the parent body

- British Columbia and the New Brunswick Colleges of Physicians and Surgeons because these were identical to the Alberta guidelines

- Manitoba College of Physicians and Surgeons because it was wholly derived from the Alberta guidelines

- Agency for Health Care Policy and Research (USA) guidelines (1994) on acute low back pain, because they only partly and non-systematically dealt with chronic pain.

The ratings according to the Cluzeau categories of the seven guidelines ranged from four to 16, out of a possible 46 points. Dimensions in which most or all of

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the guidelines were weakest included the following:

- identification of the responsible agency and the guideline development group
- the selection and quality-assessment of evidence used in the guideline development
- description of the process of consensus
- cost-benefit assessment
- peer review
- provisions for updating
- provisions for local development of protocols and provisions for monitoring of guidelines/clinical audits.

All of the published guidelines have strengths and weaknesses.

> ***Note:*** *Desirable attributes of guidelines include indications of the use of evidence and the process by which agreement is reached and by which guidelines approved and the methods by which this can be actualized and validated in clinical practice - such ratings are not a comment on the face value or clinical wisdom of recommendations in any given guideline, but rather provide a standardized and validated way to summarize and compare the ideal attributes of practice guidelines.*

Of the seven guideline documents located, two made an effort at a systematic review of the relevant literature - The American Society of Anaesthesiologists, and the Canadian Headache Society. The others adopted the strategy of forming a consensus group, which drafted the document based on opinions of the group members. Three of the seven guideline development groups sent the draft guidelines out for peer review.

All except the Canadian Headache Society guidelines dealt at least in part with the issue of prescription of opioid for chronic non-malignant pain. There was agreement among the guidelines that patients in need of pain control would be unduly disadvantaged by an overly restrictive use of opioid analgesia, based on fears that opioid analgesics are inherently addictive, and more harmful than beneficial. No guideline dismissed the possibility that opioids might in some circumstances be drugs of abuse, but the guidelines agreed on the principles of:

- comprehensive patient assessment
- good documentation
- appropriate procedures for documenting pain
- documenting analgesic effect and adverse effects
- adequate vigilance to ensure appropriate use.

The guidelines acknowledged that pain management requires appropriate use of a

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wide variety of interventions, according to their respective indications and the presenting clinical problems:

- rehabilitation
- psychological methods
- non-opioid and adjuvant medications
- local anaesthetics
- various physical therapies or anaesthesiological methods.

The implications of this are that there is an increasing choice of published consensus guidelines regarding the treatment of non-malignant pain generally, and the use of opioids in non-malignant pain in particular. It is noted that there is considerable agreement between the main recommendations made by these various consensus guidelines that:

- persistent pain is a multifactorial problem
- pain relief is an appropriate aim of treatment
- opioids constitute one legitimate treatment option, along with other medical and rehabilitation options.

Consensus guidelines provide an important source of *Level V* evidence *(please see Table #1 pg 7*). Despite the value of guidelines which are derived from a consensus panel, the weaknesses of a mainly consensus approach lie in factors such as quality of evidence (if the process does not entail a systematic search for and quality review of the evidence), the potential for bias in selection or sponsorship of the panel and/or from not employing a peer review and feedback phase, the potential for obsolescence if there is not a prescribed procedure and time-frame for including emerging evidence, and an uncertain cost/risk/benefit relationship if the latter variables are not considered systematically. The strengths of a mainly consensus approach lie in the experience and opinions of experts or acknowledged leaders in their fields, the tips and suggestions that experts can better provide for clinical procedures and practice management - these might not be evidence-based, but are helpful to practitioners *See examples of guidelines proposed by the Canadian Headache Society, 1997-8, the American Geriatrics Society, 1998 and the Canadian Pain Society, 1999.*

Evidence-based recommendations are a source for higher levels of evidence - *Level I, Level II or Level III* -- and include safeguards to:

- minimize biases
- increase peer influence
- create a renewable data base for future use
- document levels of evidence in support of various conclusions
- apply verifiable quality standards to the data that informs the conclusions.

These are much more difficult to carry out properly, and to date, represent a minority of the "guideline" literature.

There is a place for both types of resource -- consensus guidelines and evidence-based recommendations, and the advantages of each should be kept in mind. The Task Force was of the opinion that there already existed several usable sets of consensus guidelines, and that what was needed was a resource based on evidence, since the latter offers the only robust way to validate clinical opinions or

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impressions. The Task Force noted that the American Society of Anaesthesiologists had also produced a set of guidelines based on evidence and meta-analysis, but their document was tailored for anaesthetists in particular, and was from the USA. The Canadian Headache Society members published evidence-based guidelines for opioid and non-medication management of acute and chronic headache, which is pertinent to but does not cover most of the mandate of this Task Force. Thus, the Task Force undertook to develop a resource for recommendations for management of chronic non-malignant pain, with relevance to all physicians and specialists.

> ***Note:*** *The Canadian Headache Society was not included in the Consensus Opinion Chart because it did not address the issues below in Chronic Pain.*

The reader is advised to consult the other consensus guidelines for practical advice on pain management, particularly useful for this purpose are the Alberta guidelines, the Canadian Pain Society guidelines and the American Geriatrics Society guidelines.

In comparing the above consensus guidelines there is *Level V* evidence for the following opinions.

> ***Note:*** *This is not a digest of all opinions in all the above documents, but is a summary and comparison of the more important of these opinions.*

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Consensus Opinion Chart	AAPM/APS	ASA	CPS Alberta	MBC	AGS	CPS
Trial of long-term opioid is legitimate practice when other standard analgesic methods are insufficient	✔	✔	✔	✔	✔	✔
Iatrogenic addiction is rare with opioid use in acute or cancer pain. Careful screening of chronic pain patients can reduce risk of addiction	✔		✔		✔	✔
Tolerance or physical dependence are not in themselves evidence of addiction			✔			✔
Patients with a past history of addiction should not necessarily be denied a trial of opioid, providing there are safeguards (such as a consultant)	✔					✔
Repeated aberrant drug use, or decline in function despite opioid, are red flags to reassess or reconsider opioid			✔			✔
Chronic pain patients should have a comprehensive assessment	✔	✔	✔	✔	✔	✔
For chronic pain, multimodal treatment with a rehabilitation focus is appropriate		✔	✔	✔	✔	✔
Informed consent should be obtained. It may be verbal, but written is better if risk factors are identified	✔	✔	✔	✔		✔
Documentation of patient status, rationale for opioid treatment, consults, investigation, risk factors, and periodic review.	✔	✔	✔	✔	✔	✔
Only one doctor should prescribe opioids			✔			✔
Chronic pain patients taking opioids should be assessed at least every 9 weeks			✔			
A physician should not be expected to prescribe opioids beyond the dosages that that physician is comfortable with or thinks appropriate.			✔			
Opioids should not be the first line treatment of chronic non-malignant pain			✔	✔		✔
For continuous pain, (a) time contingent dosing and (b) probably sustained release opioid			✔		✔	✔ (a)
Acetaminophen for mild-moderate musculoskeletal pain. Intermittent short-acting opioid for intermittent pains					✔	
Presence of addiction or psychiatric disorder may require consultation with a specialist if opioid is used.	✔	✔	✔	✔		✔
Withdrawal of excessive medications and use of behavioural coping methods is a goal of chronic pain management	✔					

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Consensus Opinion Chart	AAPM/APS	ASA	CPS Alberta	MBC	AGS	CPS
In opioid-naive patients, failure to show partial analgesia with incremental dose titration may be evidence for opioid resistance						✔
In some patients, significant analgesia may not occur until a higher threshold dose is reached.						✔
Patients exhibit inter-individual variability in response and adverse effects to opioids, and dose requirements vary					✔	✔
Nociceptive pain warrants a trial of opioid. Neuropathic pain often requires higher doses than nociceptive pain. Idiopathic pain can be treated cautiously, if there are goals and monitoring			✔			✔
No direct risk of organ damage with long-term opioid						✔
Once stabilized, maintenance opioid does not interfere with cognition or with psychomotor function (such as driving)						✔
Opioid may be used concurrently with other treatments, but additive effects on cognitive function (especially with use of benzodiazepines) should be avoided.					✔	✔
Patients unresponsive or intolerant to one opioid may warrant a trial of another with different pharmacological profile						✔
Doses of opioid above the equivalent of 300 mg of morphine per day are unusual but not contraindicated			✔			
There is no "pharmacological" rationale for a dose ceiling for opioids						✔
Opioids should be given by the least invasive route			✔		✔	
For breakthrough pain, shorter-acting opioids can be used.					✔	✔
Tolerance is not common after the first 6 months of use						✔
Opioids should be tried before resorting to "destructive palliative pain procedures"						✔
Parenteral and IM dosing of opioids for chronic pain are to be avoided generally			✔			
With recommendations, these recommendations are applicable to children, adolescents, and the aged.					✔	✔

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Table #6 Comparison Ratings of Seven Guidelines for Managing Chronic Non-Malignant Pain

Parameter	AAPM/APS	ASA	CPS Alberta	MBC	AGS	CPS	CHS
Agency responsible/development group (max. =5)	2	2	2	2	5	. 2	5
Objectives/applicability/clarity (max. =8)	2	4	5	3	5	5	7
Evidence selection and assessment (max. =6)	0	3	0	0	0	0	3
Guidelines development group consensus process (max. =4)	0	0	0	0	0	0	0
Peer Review (max. =3)	0	0	0	0	1	1	1
Reference to other guidelines (max. =2)	0	0	0	0	2	2	1
Costs, risks, and benefits (max. = 4)	0	1	0	0	2	2	3
Provision for follow-up/updating (max. =3)	0	0	0	0	0	0	1
Summary (max. =2)	0	1	0	0	1	0	1
Application protocol development (max. =6)	0	2	0	0	0	0	0
Application guideline monitoring (max. =3)	0	0	0	0	0	0	0
Desired Attributes Rating (max. =46)	**4**	**13**	**7**	**5**	**16**	**12**	**22**

AAPS/APS = American Academy of Pain Medicine and American Pain Society
ASA = American Society of Anaesthesiologists
CPS Alberta = College of Physicians and Surgeons of Alberta
MBC = Medical Board of California
AGS = American Geriatrics Society
CPS = Canadian Pain Society
CHS = Canadian Headache Society

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Chapter 4 Review of the Literature

4.1 Rationale and Aim

The Task Force was of the opinion that it would be beyond the scope and resources of the Task Force to conduct an independent survey and analysis of the relevant literature in such a broad subject. It was considered more realistic to locate quality reviews on this subject, in order to distill the evidence-based parameters that had already been derived by previous researchers. The limitations of such an approach are that Randomized Control Trials (RCTs) generally have multiple outcome measures, making it difficult to meaningfully compare them in a narrative review. An alternative strategy for review is the use of systematic reviews and meta-analyses which compare research results by restricting analysis to outcome parameters that can be extracted in common across all the studies, which means that some useful data cannot be compared because it is not found in all studies and is not represented in the review, while the "power" of other conclusions can be increased by the meta-analytic process. Task Force members were aware that many meta-analyses or systematic reviews had already appeared, dealing with various aspects of management of chronic non-malignant pain.

A review of published systematic reviews offered the best and most economical strategy for distilling the literature and defining evidence-based parameters for management of chronic non-malignant pain.

4.2 Method

4.2.1 Selection of Evidence-Based Literature: Literature Search

In order to search for relevant publications, searches were performed in Medline/Pubmed, Ovid, and in the Cochrane Library. There was no specified time limit. Searches were performed with respect to:

- clinical disorder
- publication type
- intervention type
- "related articles".

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The search strategies included the following - categories for clinical disorder were:

- pain and chronic disease
- back pain
- neck pain
- cumulative trauma.

The categories for publication type were:

- meta-analysis
- systematic review
- randomized control trials.

The categories for intervention type were:

- pharmacotherapy
- cognitive therapy
- combined modality therapy
- multimodal
- manipulation
- chiropractic
- patient education
- psychotherapy
- behaviour therapy
- cognitive therapy.

The "related articles" option was chosen in the Medline/Pubmed. Language of choice was English. This data base was further augmented by sources known to the expert committee members. One was part of a British Columbia Royal Commission Report on Worker's Compensation Reform, June 1999, (chapter authored by E. Tunks, J. Crook, and M. Crook). In this report, inclusion criteria were systematic reviews or meta-analytic reviews of non-surgical treatment of non-malignant chronic musculoskeletal pain. Exclusion criteria were narrative reviews, reviews that did not include either natural or clinical course, or treatment. Some retrieved citations were rejected on the basis of published abstracts, and a few were rejected after the authors scanned the retrieved articles for inclusion criteria.

Other resources were provided by the Institute for Work and Health (Toronto), and subsequently the book by Henry McQuay and Andrew Moore - An Evidence-Based Resource for Pain Relief (Oxford Press, 1998) was used as a resource of systematic reviews and meta-analyses.

While the main strategy was to retrieve *quality systematic reviews and meta-analyses* in order to perform a review of reviews, the literature on injection therapies for "myofascial pains" and soft tissue pain, and opioid for chronic non-malignant pain, have only a few RCTs. Hence, a systematic review was conducted of these RCTs.

The bibliographies of retrieved articles were hand-searched for articles that may have been missed by the computer searches. Other experts were consulted for articles that might have been missed.

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4.2.2 Validity Assessment

Meta-analytic and systematic reviews were independently rated by two raters using the criteria of Oxman and Guyatt (1991). *See Appendix A Quality of Meta-Analysis - Oxman and Guyatt's Index of the Scientific Quality of Research Overviews*. There was complete agreement in the ratings on three-point scale of:

- acceptable
- borderline
- unacceptable.

Randomized controlled trials were rated by one author using the criteria of Jadad et al. (1996). Author blinding was not used. Systematic reviews (or meta-analyses) or RCTs that were rated unacceptable were not used in comparison tables. In this way, quality ratings were used to select the data on which the eventual "recommendations or parameters" were to be based. Tables were constructed to summarize the significant findings from this review or reviews. The systematic review studies retrieved were diverse with regard to outcome measures and designs. This did not provide a set of measures that could be used to extract common comparable outcome data. Instead, tables summarized the types of comparison, the type of outcome measure, and the direction of results. Hence, conclusions were dealt with in a narrative fashion and the tables summarize the direction and significance of the treatment effect - these are presented in *Chapter 12 Consolidated Evidence-Based Information Regarding Treatment Modalities*. The exclusion cutoffs were quality scores of two or less on a five-point scale in the criteria for RCTs (Jadad et al), and three or less out of seven in the quality scores for reviews (Oxman and Guyatt).

One should remember that "lack of evidence of efficacy" is not synonymous with "evidence of lack of efficacy". The former simply implies that adequate studies have not been done, therefore efficacy has not been vigorously documented. The latter, however, means that good studies have been done and the intervention under question has been found ineffective.

Given the fact that many or most of the interventions performed in chronic pain, have not been vigorously examined in high quality research, the clinician must employ judgement in order to combine:

- available best evidence
- knowledge of basic pathophysiologic mechanisms that can assist in judicious use of interventions
- personal experience
- expert opinion
- the particulars of each individual patient, for example:
  - age
  - cognitive and psychological functioning
  - other co-morbid conditions
  - psychosocial parameters including finances to support proposed treatment
  - patient's belief and preferences.

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Chapter 5 Chronic Headache

5.1 Overview

Results of the Needs Survey indicated an interest in help with the management of chronic headache and migraine. There are relatively few published meta-analyses or systematic reviews about chronic daily headache. This is surprising in view of the prevalence of chronic tension type headache of 2.2% to 3% of the population in epidemiological studies in the United States, Chile and Denmark. These numbers are actually underestimated as they ignored the other causes of chronic daily headache.

The Task Force looked at any meta-analysis of "chronic headache". We did not examine post traumatic headache or "whiplash" associated headache, though we could do so at a later date if there is sufficient interest. Rather than "re-inventing the wheel" with respect to migraine, we have relied heavily on the evidence-based recommendations published in the Canadian Medical Association Journal (Pryse-Phillips et al., 1997, 1998)

5.2 Definition

Chronic Headache (otherwise called Chronic Daily Headache) is understood to denote headache three days or more per week, continuously over six months. Most chronic headaches are a mixture of tension and vascular features. Many begin as intermittent headache and are perpetuated by:

- the effects of emotional factors
- rebound effects from excessive medications
- musculoskeletal factors.

Some begin suddenly, as with post-concussion headaches, and some evolve gradually. All represent chronic headache pain, and are the main concern of this review.

5.3 Meta-Analyses

Five meta-analyses were located and analysed, and the results of one, by Goodkin et al 1995, were excluded because the authors admitted none of the papers analysed met their criteria for inclusion. Of the remaining four analyses, two showed improvement with behavioural types of treatment, one suggested benefit

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with serotonin re-uptake inhibitors, and one showed improvement with tricyclic antidepressants.

Haddock analysed behavioural treatments with a comparison of home based and clinic based courses of treatment. There is no indication of frequency of headache, so this may not be applicable to daily headache. Migraine, tension and mixed headaches were included and analysed separately. Home based therapy implied the use of audiotapes and instruction books with little interaction with a therapist after the initial instructions.

Nine studies compared Home Based Therapy (HBT) to control, five compared Clinic Based Therapy (CBT) to control, and 13 compared HBT to CBT. Percentage improvement was calculated for each treatment as follows:

	HBT	**CBT**
Migraine	53.2%	52.5%
Tension	40.5%	41.5%
Mixed	51.0%	42.9%

As there is no advantage to results with Clinic Treatment, they conclude that Home based therapy is to be preferred as it takes:

- 1/3 of the visits
- 1/3 of the time with the Therapist and costs 1/5 as much.

Bogards set out to examine both behavioural and drug treatments for "recurrent tension headache" once again without defining frequency. Multiple types of treatment were examined as follows:

- relaxation
- biofeedback
- EMG-biofeedback
- cognitive
- combinations of the above
- pharmacological.

The drugs were a mixed bag including:

- antidepressants
- benzodiazepines
- analgesics
- anti-inflammatories.

In spite of the obvious diversity of these drugs, no attempt was made to distinguish their effects, they were simply lumped together as "pharmacological studies", and therefore the conclusions about drug therapy are meaningless.

Results of all types of treatment were expressed as percentage improvement, and were subdivided based on the use of a headache diary, or "other" methods of assessment.

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	Other Measures	Headache Diary [mean values]
EMG biofeedback	47%	48%
Relaxation	36%	36%
Biofeedback + relaxation	56%	59%
Cognitive	53%	53%
Pharmacological	39%	17%
Placebo	20%	16%

Note: *The results for improvement with relaxation ranged from a low of 17% to a high of 97%.*

All of the non-pharmacological treatments gave improvement, with the best being combined biofeedback and relaxation.

Jung examined the effects of serotonin re-uptake inhibitors in multiple painful conditions, including chronic headache. One study dealt specifically with daily headache and found improvement with fluoxetine compared to placebo. In the studies of chronic headache of unspecified frequency, both paroxetine and fluvoxamine were found better than baseline, though these were not placebo controlled. Citalopram was found to be no better than placebo.

Goodkin (1989) also looked for benefits from antidepressants and included studies of migraine, chronic tension headache, and mixed headache. One study showed Maprotiline superior to placebo, and two showed Doxepine better than placebo.

Conclusion

In summary, there is little data from meta-analysis or systematic review on drug treatment of chronic daily headache, but it seems that useful treatments which can be recommended based on the available data include cognitive, relaxation, and biofeedback methods, as well as pharmacological treatment with tricyclic antidepressants and serotonin re-uptake inhibitors. These recommendations are summarized, along with the level of evidence in Table #8.

The choice of drugs or behavioural methods will depend on a number of factors including the preference of the patient, availability of skilled therapists in the area, and cost, as many patients without private insurance will not pay the fees for behavioural therapy.

Many headache specialists believe that daily use of analgesics to treat headache causes rebound daily headache, though it is an awkward fact that people who use regular opioids for other types of pain do not usually develop daily headache. Almost all headache specialists agreed that continued use of daily analgesics in a patient with chronic daily headache will almost guarantee failure of any of the treatments outlined above. A useful treatment plan would therefore address issues:

- of depression or anxiety
- include lifestyle changes to ensure proper diet and sleep

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- limit intake of analgesics, caffeine, aspartame, and other potential environmental and dietary triggers.

Adding these steps to behavioural treatments or to tricyclics or serotonin re-uptake inhibitors should improve the results. Finally it should be noted that the antidepressants work for chronic headache even in patients who are not clinically depressed.

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Chapter 6 Migraine Headaches

6.1 Overview

It is recommended that physicians should read the *Guidelines for the Diagnosis and Management of Migraine in Clinical Practice* (CMAJ 1997 May; 156, pp 1273-1287) and *Guidelines for the Nonpharmacologic Management of Migraine in Clinical Practice* (CMAJ 1998 July; 159, pp 1273-1287) [both are available on the CMAJ website].

These guidelines include a description of the requirements for a diagnosis of migraine as well as an evidence-based review of drugs for both acute and prophylactic treatment. It has been acknowledged by the American Medical Association as the most comprehensive guideline document available, and the authors plan on updating it this year or next. The levels of evidence they quote have been adjusted to those used throughout our report.

> ***Note:*** *The CMAJ Guidelines did not have a category for "meta-analysis or systematic review" so their Level I is our Level II.*

Table #10 outlines the useful prophylactic drugs for acute attacks, together with suggested doses and major side effects.

6.2 Definition

The Task Force agreed that a definition of migraine was required, and the following is taken from the International Headache Society's classification. The diagnosis requires that:

- there have been at least five attacks.
- each attack, untreated or unsuccessfully treated lasts two to 72 hours
- at least two of the following criteria must be met:
  - Location - unilateral (occurs in 70% of patients)
  - Quality - throbbing (pulsating, pounding)
  - Intensity - moderate or severe (enough to interfere with daily activities)
  - Aggravated - by physical activity.

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- at least one of the following symptoms
  - nausea
  - vomiting
  - photo and phonophobia.

Finally, there is no other cause for headache suggested by history or physical examination.

6.3 Treatment Approaches for Migraine Headaches (Acute)

The approach to acute treatment should begin with aspirin or NSAIDs (*Level II* evidence), or if these are not tolerated then acetaminophen with or without codeine (*Level V* evidence). Patients with a lot of nausea usually benefit from metoclopramide 10 mg p.o.

For non-responders to these drugs the Triptans are excellent although expensive drugs (*Level II* evidence) and current choices are:

- sumatriptan
- naratriptan
- zolmitriptan
- rizatriptan.

Dihydroergotamine by nasal spray or by intramuscular injection is also useful in this group of patients (*Level II* evidence). Intravenous metoclopramide may be followed with intravenous dihydroergotamine, for a severe episode. Ergotamine by mouth or suppository has been in common use for many years, though evidence is only *Level III*, and side effects often severe.

The Canadian Headache Society guidelines (Pryse-Phillips et al., 1997) suggested that patients unresponsive to, intolerant of, or unable to afford Triptans, may benefit from combinations of ASA, caffeine, butalbarbital, +/- codeine (Fiorinal). Those guidelines also cautioned that such combinations should be for short periods and intermittently.

Note: *This CPSO Task Force commented that there is only Level V evidence for this suggestion, and notes that there is a risk of drug dependence in a minority of Fiorinal users.*

For patients who do not respond to any of the above there is *Level II* evidence for:

- ketorolac IM
- intranasal lidocaine (drops or soaked Q-tip)
- butorphanol nasal spray
- chlorpromazine or prochlorperazine IM, IV or suppository, *(Level V)*.

Note: *Caution is required with butorphanol (Stadol) because in spite of claims to the contrary this drug is addictive.*

Finally, there is *Level III* evidence for the use of Demerol IM, commonly used in Emergency Departments and for dexamethasone IV in very refractory migraine.

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6.4 Migraine Prophylaxis

Prophylaxis should be considered when attacks are so frequent or so severe as to cause significant dysfunction at home or at work. Looking for and avoiding triggers for the headaches is the place to begin. Commonly encountered triggers in the diet include:

- alcohol
- chocolate
- caffeine
- nitrates
- old cheese
- aspartame
- citrus fruits
- MSG.

Irregular meals and changed sleep patterns at weekends can be troublesome. Some triggers are hard to avoid, such as:

- perfumes
- fluorescent lights
- weather changes.

No method of prophylaxis works for all patients, and for some patients none of the methods seem to work. The patient may choose between medications or relaxation with biofeedback. There is *Level I* evidence that relaxation and biofeedback is equally as effective as propranolol, but limiting factors in choosing this method include availability of skilled practitioners in the area, and initial cost is high, although when it is successful drug costs are significantly lowered.

The use of prophylactic drugs always requires balancing effectiveness against side effects. There are five main categories of drugs used:

- betablockers
- calcium channel blockers
- serotonin blockers
- tricyclic antidepressants
- anti-epileptic drugs.
  Note: *Currently the only anticonvulsants recommended are the valproic acid derivatives, but evidence is accumulating for others.*

Evidence of why or where prophylactics exert their influence is generally lacking. It may be necessary to try several before finding one that is both effective and well tolerated. Initial selection should be based on a consideration of the patient's general health and other medications. For example, betablockers are well known to be contra-indicated for asthmatics, and some would avoid them in depressed patients too. There is co-morbidity between migraine and depression, and if this is found then a tricyclic might be a good choice, whereas flunarizine is contraindicated.

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Finally, it should be noted there is no evidence that specific serotonin re-uptake inhibitors are effective for migraine.

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Chapter 7 Neuropathic Pain

7.1 Definition

While nociceptive pain arises from the "normal operation of the pain sensory system", neuropathic pain is defined by the International Association for the Study of Pain (IASP) as "pain initiated or caused by a primary lesion or dysfunction in the nervous system."

An example of nociceptive pain is the pain arising from local tissue injury, followed by increased sensitivity of primary afferent nociceptors at the site of injury.

Examples of neuropathic pain include phantom limb pain, post-stroke and post-spinal cord injury pain, causalgia after nerve damage, etc.

Human neuropathic pain is associated with a variety of symptoms and signs. Spontaneous ongoing and continuous pains may be prominent in central pain syndromes and complex regional pain syndromes, while spontaneous paroxysmal pains can be seen in tic douloureux or post herpetic neuralgia. Evoked pains are produced upon application of certain stimuli, for example:

- touch (cutaneous allodynia)
- hyperalgesia after application of normally noxious mechanical, heat or cold stimuli
- kinesthetic allodynia (pain produced upon movement of a joint within the usually normal and painless range).

7.2 Pathologic Mechanisms Underlying Neuropathic Phenomena

Multiple abnormalities at several levels can exist and co-exist. They can be at the level of: (Mailis, A. & Bennett, G. 1999)

- primary afferent neurons subserving nociception (C and Aδ fibers) and other sensations such as large myelinated fibers like Aβ responsible for touch

  and/or

- central nervous system neurons.

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After local tissue injury primary nociceptors may become "sensitized" (peripheral nociceptor sensitization) and may acquire spontaneous discharges, lower threshold for activation, etc. "Central sensitization" may occur when C nociceptor barrages produce increased excitability in dorsal horn neurons. There is growing body of evidence that central sensitization involves activation of glutaminergic N-methyl-D aspartate (NMDA) synapses.

Furthermore, lesions of the central nervous system for example, after spinal cord or brain injury, produce hyper-responsiveness in CNS neurons and seem to be the basis of so called "central pains".

A puzzling phenomenon involving the expansion of spontaneous and stimulus-evoked pains beyond the site of the injury in areas not defined by dermatomes or nerve territories, has been traditionally considered one of the hallmarks of non-organic pain (Waddell signs). There is evidence from animal and human experimental work that these phenomena in *certain types of neuropathic syndromes* (complex regional pain syndromes or "CRPS" I and II, post herpetic neuralgia, etc.) are due to central mechanisms.

7.3 Basic Principles in Understanding the Pathophysiology of Neuropathic Pain

The basic principles in understanding the pathophysiology of neuropathic pain are listed below: (Mailis, A. & Bennett, G. 1999)

- similar clinical abnormalities may be produced by different pathophysiologic mechanisms
- more than one abnormality can co-exist in any given patient
- very frequently neuropathic and nociceptive pain co-exist
- initial tissue or nerve injury may produce one pathogenic mechanism which in turn may generate others peripherally or centrally in a domino effect
- while the original damage may heal, the secondary changes may acquire a "life of their own".

7.4 Principles Governing Interventions in General in Neuropathic Pain

In general one should:

- remove the cause when possible
- promote healing
- normalize nerve micromilieu and correct metabolic parameters
- normalize sensory input and nerve transmission
- modulate central pathways

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- reduce sympathetic over-activity if it exists
- treat the whole person in order to alter emotional and behavioural influences on pain interpretation.

7.5 Interventions for Neuropathic Pain

The range of interventions available for chronic neuropathic pain includes, in general: (McQuay & Moore 1998)

- Analgesics (conventional from NSAIDs to paracetamol and opioids and unconventional like antidepressants, anticonvulsants and others)
- Nerve transmission blocks (reversible via local anaesthetics +/- steroids or opioids, and irreversible via surgery and nerve destruction)
- Others
  - physical treatments and exercise
  - Transcutaneous Electrical Nerve Stimulation (TENS)
  - psychological and cognitive/behavioural treatments
  - neuro-augmentation, i.e. spinal and other stimulators.

Opioids are useful in selected patients. *(See Chapter 8, Dellemijn, P. 1999)*

Antidepressants have been classically used to relieve burning pain in different neuropathic pain syndromes while anticonvulsants have been used for shooting pain in nerve injuries and tic douloureux. Studies nowadays show that with very similar results, it is unclear which drug class is the first choice. Antidepressants may relieve neuropathic pain in much lower doses (about half) than the doses used for mood elevation, and their analgesic effect usually shows up much earlier than their mood elevating effect. However, high doses (within the antidepressant range) may still produce an analgesic effect, therefore the drugs should be titrated until desirable effect (analgesia) or side effects occur.

For anticonvulsants, pain relieving doses are close to anticonvulsant dosing range.

For other neuropathic pain syndromes like post-stroke pain, antidepressants and anticonvulsants may also work.

Mexiletine, an oral drug with local anaesthetic properties, may be effective in certain types of neuropathic pain syndromes at doses of 300-750 mg/day, but the higher doses may be associated with more side effects.

In general, these classes of medications should be tried in those syndromes that arise from injury of the peripheral or the central nervous system. CNS effects are commonly associated with both classes of medications and anticholinergic effects are mostly associated with antidepressants.

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7.6 Use of Injections/Blocks

Note: Strong evidence (Level I) demonstrates lack of effect of intravenous regional sympathetic blocks for reflex sympathetic dystrophy, therefore, these blocks are not recommended. (McQuay, H., and Moore 1998)

Systematic evidence for other types of blocks in chronic neuropathic pain syndromes in the form of RCTs or good clinical trials is lacking, however, anecdotal evidence and case reports exist regarding cervical, celiac or lumbar sympathetic blocks which are commonly used in pain clinics.

7.7 Local Application of Capsaicin

Local application of capsaicin (the extract of chile peppers) has been proven beneficial in diabetic neuropathy.

Note: Patients with other neuropathic pain syndromes particularly those with allodynia or touch evoked pain, may find the burning produced by the local treatment intolerable.

7.8 Summary of Effective Intervention in Neuropathic Pain

In summary, systematic literature search so far (McQuay, H., and Moore) demonstrates that in neuropathic pain effective interventions include:

- anticonvulsant and antidepressant drugs
- systemic local anaesthetic-type of drugs for nerve injury
- topical capsaicin in diabetic neuropathies.

Limited evidence exists for the use of opioids in post-herpetic neuralgia. Evidence for lack of efficacy exist for intravenous regional guanethidine blocks.

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Chapter 8 Opioid Analgesics in the Medical Management of Chronic Non-Malignant Pain: A Systematic Review of Controlled Clinical Trials

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8.1 Introduction

Despite the unquestionable value of opioid drugs in the management of cancer pain, the opioid literature on chronic non-malignant pain presents conflicting data largely due to uncontrolled retrospective studies. Some surveys report significant pain relief in response to long-term opioid therapy (Portenoy, R.K, and Foley, K.M., 1986) while others describe the additional benefit of improvement in performance status (Zenz, M et al., 1992). In contrast, surveys originating in multi-disciplinary pain programs with highly selected samples suggest that chronic opioid therapy leads to greater psychological distress, impaired cognition and poor outcomes (McNairy, S.L. et al., 1984).

The role of opioid analgesics in the management of chronic non-malignant pain is further clouded by the perceived risk of psychological dependence or addiction. However, survey data accumulated over the past twenty years does not support this view. In several studies involving almost 25,000 patients without a history of drug dependence, there were only seven cases of iatrogenic addiction (Portenoy, R.K., 1994). These data strongly suggest that overall risk of addiction among patients with no prior history of drug abuse is actually quite low. However, it is unclear whether these data can be extrapolated to a population of patients in which chronic non-malignant pain is associated with a higher prevalence of psychological comorbidity.

Perceived government interference may discourage physicians from using opioid drugs even when medical judgement clearly supports a therapeutic trial. Regulatory bodies have a responsibility to prevent the inappropriate use of medications such as the selling of controlled drugs, but should also support the legitimate use of opioid analgesics when the primary goal is pain relief.

8.2 Differentiating Between Physical and Psychological Dependence

Differentiating between physical and psychological dependence is crucial in understanding the role of opioid analgesics in the management of non-malignant pain. Physical dependence is a physiologic phenomenon characterized by the development of withdrawal symptoms following abrupt discontinuation of treatment, substantial dose reduction or antagonist drug administration. Abstinence symptoms are self-limiting and can be avoided entirely through 50% dose reductions of an opioid analgesic every 2-3 days. On the other hand, psychological dependence or addiction can be defined as:

- compulsive drug use despite harm
- an overwhelming preoccupation with securing a good supply and the tendency to relapse after withdrawal.

Addiction is a behavioural pattern of drug use in which medication is taken for its psychic effects rather than for its pain relieving properties. As suggested by survey data, addiction is uncommon if there is no prior history of substance abuse.

8.3 Methods

Clinical trials were consider eligible for this review if they met the following criteria:

- inclusion of patients of any age and gender with chronic non-malignant pain
- random and/or double-blind allocation of treatments
- administration of an opioid analgesic by any route to at least one of the treatment groups
- availability of information on pain assessments.

Studies were identified using a systematic search of MEDLINE (1976 to November 1998) and the Cochrane Library and a manual search of personal files. The key works used in the search were:

- chronic pain
- opioids
- narcotics
- non-malignant and non-cancer pain.

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Clinical trials that met the inclusion criteria were given to two observers who assessed the quality of each of the trial reports independently using a validated scale (Jadad, A.R., et al; 1996). The scores produced on the validated scale range from zero to five points and reflect the completeness of reporting of trial methodology and its likelihood of bias. Reports with scores of two points or less were regarded as having low quality and likely to yield biassed estimates of treatment effects and were excluded.

8.4 Results

Ten trials were identified as potentially eligible. Two trials were excluded (Mays, K.S. et al., 1987; Glynn, C.J., and Casale, R., 1993). The eight remaining trials were subjected to further analysis, *please see Table #7.*

Three trials found that chronic musculoskeletal pain responds to opioid analgesics (Kjaersgaard-Anderson, P. et al., 1990; Arkinstall, W et al., 1995; Moulin, D.E. et al., 1996). Three other trials concluded that neuropathic pain is also responsive to opioid analgesics (Rowbotham, M.C. et al., 1991; Dellemijn, P.L., and Vanneste, J.A. 1997; Watson, C.P., and Babul, N. 1998) and two trials concluded that neuropathic pain is not (Arner, S., and Meyerson B.A., 1988; Kupers, R.C., et al., 1991).

Only four studies involved oral agents with repetitive dosing. In a study of elderly patients with chronic pain due to osteoarthritis of the hip, acetaminophen 1 g. with codeine 60 mg t.i.d. was superior to acetaminophen alone but only in the first week of treatment (Kjaersgaard-Anderson, P. et al., 1990).

Another group reported on thirty patients with predominantly musculoskeletal pain who were treated for one week with sustained-release codeine or placebo in a crossover study (Arkinstall, W. et al., 1995). Using a mean daily codeine dose of 273 mg., there was an overall reduction in pain intensity of 29% and a reduction in the Pain Disability Index of an identical 29%.

A third group conducted a double-blind crossover trial where 61 patients with chronic musculoskeletal pain who had not responded to codeine, anti-inflammatory agents or anti-depressants were randomized to sustained-release morphine or active placebo (benztropine) for nine weeks (Moulin, D.E., et al. 1996). Forty-six patients completed the trial. The mean daily dose of morphine was 83.5 mg. The morphine group showed a statistically significant reduction in pain intensity relative to placebo, but the benefit was modest. The reduction in pain intensity relative to placebo was in the range of 15-20%. There were no significant differences in psychological features, disability status or cognition between morphine and active placebo, but there was no evidence of psychological dependence or addiction. The modest reduction of pain to morphine in this study may be related in part to the fact that the depression scores of the participants on standard psychological tests were almost two standard deviations above the mean of a control population although apparently representative of patients attending other multi-disciplinary pain clinics (Flor, H. et al., 1992). Patients derived from community-based clinics may have less psychological distress and may show a better response to morphine or other opioid analgesics.

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A fourth study evaluated controlled-release oxycodone versus placebo in patients with post-herpetic neuralgia. Oxycodone was increased weekly up to a maximum of 30 mg. q12h over a 4-week period. Opioid analgesics were withdrawn prior to the study, but patients were permitted to continue using anti-depressants and non-opioid analgesics that had been started three or more weeks prior to the study. Compared to placebo, patients receiving controlled-release oxycodone reported significant decreases in steady pain, brief lancinating pain and touch-evoked pain or allodynia. Reductions in pain-related disability were also noted. There were no significant differences between the two groups in depression or anxiety scores (Watson, C.P. and Babul, N. 1998)

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Table #7 Randomized Controlled Trials of Opioid Analgesics in the Management of Chronic Non-Malignant Pain

Author	Study Quality	Diagnosis	Mean Pain Duration (mo.)	Study Design	Intervention	Duration	Result Follow-up
Arner et al (1988)	3	Nociceptive, neuropathic and idiopathic	--	Double-blind crossover	IV infusions of multiple opioids vs saline	1hr.	Reduction in pain intensity for nociceptive pain only
Kjaersgaard-Anderson et al (1990)	4	Nociceptive (osteoarthritis)	--	Randomized Double-blind Parallel	Acetaminophen with codeine vs acetaminophen	4 wk.	Reduction in pain intensity in Week 1 only
Dellemijn et al (1997)	5	Neuropathic	--	Randomized Double-blind Crossover	IV infusions of fetanyl/diazepam vs fentanyl/saline	8 hr.	Reduction in pain intensity and pain unpleasantness with fentanyl
Kupers et al (1991)	3	Neurogenic and idiopathic	79	Double-blind Crossover	IV Morphine vs saline	1 hr.	Reduction of affective pain in neurogenic pain patients only
Rowbotham et al (1991)	3	Neuropathic (post-herpetic neuralgia)	46	Randomized Double-blind Crossover	IV Morphine vs lidocaine vs saline	3 hr.	Reduction in pain intensity with morphine and lidocaine
Moulin et al (1996)	5	Nociceptive (musculoskeletal)	49	Randomized Double-blind Crossover	Morphine vs active placebo (benztropine)	9 wk.	Reduction in pain intensity but no change in disability or psychological status
Arkinstall et al (1995)	5	Nociceptive (musculoskeletal)	73	Randomized Double-blind Crossover	Codeine vs placebo	1 wk.	Reduction in pain intensity and disability
Watson et al (1998)	5	Neuropathic (post-herpetic neuralgia)	31	Randomized Double-blind Crossover	Oxycodone vs placebo	4 wk	Reduction in pain intensity and disability

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8.5 Discussion

These controlled trials from our systematic literature search support the conclusion that sustained-release opioid therapy benefits selected patients with chronic musculoskeletal and neuropathic pain. A randomized controlled trial involving cancer-related pain suggests that there are no significant clinical or pharmacokinetic differences between sustained-release and immediate-release morphine preparations although sustained release opioid therapy might provide better compliance (Gillette, J. et al., 1997).

Significant pain relief can be achieved with a low risk of psychological dependence or addiction in the absence of a history of substance abuse. Cognitive impairment can be minimized or eliminated with an individualized dose titration program. A controlled trial involving cancer patients showed no significant difference in psychomotor driving skills between opioid-naive patients and patients on oral morphine (mean daily dose 209 mg.) (Vainio, A.et al., 1995). Other side effects such as nausea and constipation can usually be controlled with anti-emetics and bowel stimulants. However, long-term opioid therapy may or may not improve functional status and there is some evidence that a treatment program that focuses on analgesics can reinforce pain-related behaviour at the expense of functional restoration (Turk, D.C. and Meichenbaum, D., 1994). Opioid therapy should therefore be part of a comprehensive treatment program that includes a graduated exercise program and psychosocial and behavioural approaches to pain management. Such an approach, however, depends on underlying medical condition and clinical judgement is required.

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Chapter 9 Summary of Evidence from Included Studies: Chronic Musculoskeletal Pain

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9.0 Overview

In this "chronic musculoskeletal pain" we include chronic neck or back pain, and regional or diffuse soft tissue pain syndromes. Depending on one's point of view, chronic regional pain might be called "myofascial", and diffuse pain might be called "fibrositis " or "chronic fibromyalgia". Beyond this, the merits of "myofascial pain" or "chronic fibromyalgia" concepts are beyond the scope of the Task Force's mandate.

9.1 Multimodal Pain Management Programs

The greatest efficacy difference was seen in comparing multimodal with placebo/no treatment, and smaller differences were seen in comparing multimodal with physical therapy (Flor et al., 1992). Multimodal therapy combined with "patient education" was more effective than patient education alone with respect to improving pain and function (DiFabio, 1995; Koes et al., 1994). Studies of inpatient multimodal programs demonstrated greater effect sizes than comprehensive outpatient multimodal programs. Multimodal pain centers were significantly more effective in returning workers to full-time or part-time work, (*Level III)* whether or not the workers had been employed at the outset (Cutler et al., 1994). Return to work was considerably greater in multimodal treated patients, compared to study dropouts or untreated control patients (Flor et al., 1992; Cutler et al., 1994). The meta-analysis by Morley et al (1999) included 19 RCT's. Cognitive behavioural treatment was more effective on measures of pain experience, positive cognitive coping, and pain behaviour (*Level I)*.

Conclusion: There is at least *Level III* evidence that multimodal or multidisciplinary rehabilitation clinics were more effective than single-modality treatments, and greatest efficacy difference was seen in comparing multimodal with placebo/no treatment. There is *Level III* evidence that multimodal programs are more effective in measures of return to work than alternative treatments.

Recommendation: Multimodal therapy (multidisciplinary rehabilitation) is recommended for chronic pain, for both subjective outcomes as well as objective function outcomes (e.g. Return to work).

9.2 Unimodal Psychological Treatments

Outcomes significantly favour cognitive-behavioural therapy on subjective as well as functional measures, when compared to other treatment or no treatment. There are also advantages for operant behavioural therapy and for biofeedback and relaxation, but the effect is more evident with cognitive behavioural therapies due to the larger number of studies (Morley et al., 1999). Van Tulder et al. (1997) found evidence that behavioural therapy was effective when compared to no treatment, but the outcomes were contradictory when comparison was made to other conservative treatments or to other forms of psychological (behavioural) treatment. The evidence favoured the cognitive/behavioural therapies mainly on subjective measures such as pain report, self-reported pain behaviour, self-reported functional disability; more than in objective measures such as:observed pain behaviour, work hours, work absences, sick days, percent of workers re-entering employment or pensioned workers (Turner, 1996;Scheer et al., 1997).

Conclusion: There is sometimes contradictory *Level III* evidence that behaviourally-oriented psychological treatments are more effective than comparison treatments, especially on measures of subjective improvement, but also on functional improvement. Evidence for efficacy is not unanimous, but is greater in comparison to placebo controls.

Recommendation: Cognitive behavioural and behavioural therapies are more strongly recommended. There may be benefit in biofeedback and relaxation, but the evidence is less strong for these modalities.

9.3 Patient Education and Back/Neck School

Patient education or "back schools" are associated with short term benefits for short-term back pain (Spitzer et al., 1987; Koes et al., 1994; Cohen et al., 1994), and less certainly with recurrent, or chronic low back pain (Cohen et al., 1994; Gross et al., 1997). Benefits tend to be more in terms of subjective measures of distress than objective measures of function or ability to work (Scheer et al., 1997). Improvement is more likely if the education classes are given in conjunction with an intensive multimodal treatment program, or at least with exercise and active treatment (DiFabio, 1995; Cohen et al., 1994).

Conclusion: There is *Level III* evidence that patient education is effective when combined with multimodal rehabilitation therapy.

Recommendation: Education is strongly recommended as a component of a comprehensive treatment program. Although patient education plays an essential role in therapist-patient interaction, and results in subjective improvement, and is a standard part of most multimodal therapy, by itself education is an inadequate treatment for chronic neck and back pain.

9.4 Transcutaneous Electrical Nerve Stimulation (TENS)

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Transcutaneous Electrical Nerve Stimulation (TENS) can be effective in chronic musculoskeletal (MSK) pain according to some reviews (Spitzer et al., 1987; Gadsby and Flowerdew, 1996), while other systematic reviews have shown that TENS is no more effective than comparison or control treatment, or the evidence for effectiveness is contradictory (Malone and Strube, 1988; Gross et al., 1997a; van Tulder et al., 1997). The number of studies is small and the quality is poor.

Conclusion: The *Level III* evidence for TENS in chronic musculoskeletal pain is contradictory.

Recommendation: TENS might be worthwhile if in an individual case consistent benefits are clearly and repeatedly documented.

9.5 Acupuncture

The role of acupuncture in chronic MSK pain of more than three months duration is at best contradictory or equivocal *(Level III)*. (Ezzo, J.M., et al. In press. Pain; Patel et al, 1989; Ter Riet et al, 1990).

Conclusion: The *Level III* evidence for acupuncture in chronic MSK was contradictory.

Recommendation: Acupuncture might be worthwhile if in an individual case consistent benefits are clearly and repeatedly documented.

9.6 Manual Therapies/Manipulation

Manual therapies/manipulation are probably efficacious for pain and/or function, in chronic neck/back pain, but not necessarily better than other conservative treatment alternatives (Beckerman et al., 1993; Koes et al., 1991; Hurwitz et al., 1996; Shekelle et al., 1992; Aker et al., 1996 and Gross et al. (1997a); Van Tulder et al., 1997). For neck pain, Gross et al. (1997a) concluded that manipulation combined with other rehabilitation was probably efficacious, but there was not enough evidence to support manipulative therapies alone for this indication. Studies are mostly of poor quality.

Conclusion: There is *Level III* evidence for manual/manipulation therapies combined with other modalities.

Recommendation: Manipulation might be worthwhile if in an individual case consistent benefits are clearly and repeatedly documented, and may be more beneficial in the context of more comprehensive treatment.

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9.7 Passive Physical Therapies

In chronic musculoskeletal/spinal pain there is either no evidence or inconclusive evidence for the efficacy of most passive physical therapies for:

- chronic low back pain (CLBP)
- ultrasound (Beckerman et al., 1993)
- soft laser (Beckerman et al. 1993; Gam et al., 1993; Gross et al., 1997a)
- electromagnetic therapy (Beckerman et al., 1993; Gross et al., 1997a)
- traction (Gross et al., 1997a; van der Heijden et al., 1995)
- bed rest (Spitzer et al., 1987)
- corset/belt (Scheer et al., 1997)
- facet joint injections (Scheer et al., 1997)
- electromyographic biofeedback (van Tulder et al., 1997).

Scheer et al. (1997) found no convincing evidence that any single modality of treatment used in pain centers was significantly effective in returning injured workers to work. However, Cutler et al. (1994) found that an intensive multimodal approach was indeed effective in returning patients to work. This does not mean that these single modalities are unhelpful, but at least it serves as a warning that if single modalities of treatment are resulting in little change, and if several months have elapsed from pain onset, a change in approach is needed.

Conclusion: There is *Level II* evidence for lack of efficacy of passive physical therapies for chronic pain.

Recommendation: Passive physical therapy modalities are not recommended in chronic pain.

9.8 Exercise

Exercise and activity are generally assumed to be helpful, but prescribing "generic exercise" is no more appropriate than "generic surgery". Considering all types of exercise, active or passive, exercise in general is not significantly superior to other conservative treatment or physical therapy (Koes et al., 1991; Beckerman et al., 1993; Scheer et al., 1997; van Tulder et al., 1997). However, there is agreement that active exercise for chronic back/neck pain is more effective than less active exercise or passive treatment (Spitzer et al., 1987; Gross et al., 1997a; van Tulder et al., 1997).

Conclusion: There is *Level II* evidence that exercise is not significantly superior to other conservative treatment or physical therapy, but active exercise is more effective than less active exercise or passive treatment.

Recommendation: Active exercise is recommended as part of a comprehensive rehabilitation program.

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9.9 Systemic Medication

9.9.1 NSAID

NSAID was more effective than placebo for acute uncomplicated lower back pain (LBP), (Spitzer et al., 1987; Koes et al., 1997), but equivocal for acute and chronic back pain when compared to other conservative treatment (Koes et al., 1997). There is no evidence that one NSAID is superior to another in treatment of chronic low back pain (Koes et al., 1997; van Tulder et al., 1997; McQuay and Moore, 1998). Given the potential for toxicity increases with dose, one should be satisfied that the medication is producing significant benefit, that the minimum effective does is being used, and that adverse effects are being avoided and monitored.

Conclusion: There is *Level I* evidence for NSAID effectiveness in acute uncomplicated low back pain, but the evidence for effectiveness in chronic low back pain is equivocal.

Recommendation: NSAID might be worthwhile if in an individual case consistent benefits are clearly and repeatedly documented and if benefits outweight risks.

9.9.2 Antidepressants

There is fair evidence for efficacy of antidepressants in chronic headache and chronic neuropathic pain (Onghena and van Houdenove, 1992; Turner et al., 1993); (Goodkin et al., 1989 Goodkin et al., 1995), although individual controlled studies have often been of poor quality (Goodkin et al., 1989; Goodkin et al., 1995), whereas the evidence for efficacy in CLBP and mixed pain syndromes or soft tissue pain (fibromyalgia or myofascial pain) was considered to be equivocal.

Conclusion: Evidence for effectiveness in mixed chronic soft tissue pain is *Level III* and equivocal.

Recommendation: Although Tricyclic antidepressants are recommended in chronic headache and in chronic neuralgia, evidence in chronic musculoskeletal pain is equivocal.

9.9.3 Injected Cortisone for Other Musculoskeletal Pain

For lateral epicondylitis, there is a modest degree of short-term effectiveness over two to six weeks (Odds Ratio = 0.15) but on longer follow-up no differences are detected. (Assendelft et al., 1996).

For all shoulder disorders, the results were contradictory in comparing cortisone injections either against placebo or against other active treatments. In the specific studies of chronic subjects, no significant benefits were found (Van Der Heijden et al., 1996).

Conclusion: There is *Level II* evidence for a modest level of short term efficacy

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of cortisone injection for lateral epicondylitis, and there is *Level II* evidence for lack of efficacy for chronic shoulder disorders.

Recommendation: Injected cortisone may be warranted in some cases for lateral epicondylitis, and for chronic shoulder disorders, if consistent benefits are clearly documented..

9.9.4 Injections into Soft Tissue for Chronic Back and Neck Pain and Myofascial Pain

Note: *No meta-analyses were found for injection therapy for "myofascial pain" and other soft tissue pain conditions. Hence, the RCT literature on injection therapy was systematically searched and reviewed, and the results are presented in narrative format. RCT's satisfying criteria of chronic pain and injection therapy were the following: (Bourne, 1984; Byrn et al, 1993; Carette et al, 1991; Collee et al, 19991, Frost et al, 1980; Garvey et al, 1989; Hong, 1994; Lilius et al, 1989; Marks et al, 1992; Ongley et al, 1987; Sonne et al, 1985; Wreje & Brorsson, 1995)*

A minority of studies were of fair quality but there were no high-quality studies (Ongley et al., 1987; Sonne et al., 1985; Frost et al., 1980; Garvey et al., 1989). The results were contradictory and benefits short-term. Inconsistent results were found for injected saline vs lignocaine, and for saline vs sterile water. There did not appear to be any trend for either upper or lower back studies to reflect a greater success rate for experimental vs control condition. There did not appear to be a trend for shorter or longer duration pain to reflect a greater success rate of experimental vs control condition. One of the best studies (Garvey et al., 1989) failed to show an advantage of invasive treatment (either injection or acupuncture) over non-invasive treatment (vapocoolant and acupressure).

Conclusion: There is inconsistent and equivocal *Level III* evidence for efficacy of injection therapy for soft tissue pain.

Recommendation: Injection therapy for chronic neck and back and myofascial pain may be warranted in some cases if benefits are clearly and repeatedly documented.

Note: *Although a widespread clinical practice, the evidence for efficacy for injection of anaesthetic, saline, sterile water, or cortisone into painful soft tissues, is at best inconsistent and contradictory, and based on poor quality studies, usually on Level III evidence. This does not mean that patients should not receive a trial of injection therapy, but if patients show lack of clear progress using injection therapy, there is no evidence that would support continuation of the injection treatment.*

Our systematic review of specialized anaesthesiological procedures (such as peripheral nerve or facet joint blocks, epidural, or sympathetic blocks, etc) was not completed in time for publication and no systematic review of surgical procedures was done. Hence the conclusions of this review does not include these more specific anaesthesiological procedures or surgical procedures. This will be undertaken in future revisions of these recommendations.

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Evidence-Based Recommendations for Medical Management of Chronic Non-Malignant Pain

Summary

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Chapter 10 General Recommendations for Chronic Musculoskeletal Pain and Neuropathic Pain

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10.1 Chronic Musculoskeletal Pain

There is *Level V* evidence for the following approach (Tunks, Crook and Crook, 1999). When musculoskeletal pain persists for three months or more, and no treatable cause is found despite adequate assessment, and when this persistent pain is unresponsive to apparently appropriate therapy a co-ordinated and more intensive approach is needed which should include the:

- patient's active participation
- practical goals for change and focus on problem areas
- patient's education including review of goals and progress, promotion of function and psychosocial intervention if appropriate
- closely co-ordinated approach by the treating physician/clinician.

Even when pain relief as a goal eludes the patient and his/her physician, patients are usually comforted by an empathic attitude, time to listen, and the offer of emotion support. Function can usually be improvement through modification of methods or use of:

- aids
- modification of tasks
- changes of pace and rest periods
- exercise (strengthening and increasing range).

Occasionally referral may be necessary to a specialized multimodal rehabilitation program, but even then, the supportive stance of the primary physician is an important ingredient in the patient's progress.

10.2 Principles Governing Pharmacological Interventions in Neuropathic Pain

The principles governing pharmacological interventions in neuropathic pain are: (Mailis and Bennett, 1999 A,B)

- Have a basic understanding of:

  - underlying pathophysiologic mechanisms
  - the natural course of the disorder
  - the limiting medical contraindications

  This allows differential symptom classification, with each symptom possibly requiring specific management.

- Use a ladder approach starting from the least to the most adverse effect producing interventions

- First line approach includes:

  - specific adjuvant (neuropathic) medications (for example tricyclics and anticonvulsants)
  - mild analgesics
  - physical modalities, depending on the disorder and treatment always remembering that neuropathic and nociceptive pain may frequently co-exist.

  Concomitant sequelae of chronic pain (anxiety, depression, insomnia etc) may be separate targets for management.

- Opioids may be used when adjuvant (neuropathic) medications are ineffective or partially effective and residual pain is substantial.

  Note: *Be aware of contraindications to the use of each drug.*

- Look for desired **target effect** versus undesirable **side effect**

- In multi-drug pharmacotherapy, be aware of **drug to drug interactions**

- Multi-drug therapy should be instituted **sequentially,** not simultaneously, otherwise it will be impossible to tell what works

- **Time is of the essence.** Use each drug in adequate doses and sufficient time to reach effect or side effect. Be aware of the way drugs work. Some drugs may produce a graded effect with increasing response as the dose increases until the effect levels off (TCAs, carbamazepine, opioids etc.) Some others may work rather abruptly in a narrow window in high

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doses only, for example, gabapentin.

- **Monitor treatments** frequently by documenting changes in the basic condition. Be aware that improvement may be due to:

  - the natural history of disease with remission due to regression to the mean
  - placebo effect
  - actual effect of your intervention.

- Be aware that patients tend to complain of their most prominent pain. New complaint **may not mean** treatment failure but that the original pain may have been reduced and allow for unmasking of previously understated pain.

10.3 Caution and Clinical Judgement in Pharmacological Management

When administering oral medications for neuropathic pain, one should take into account:

- the age of patients (dizziness in the elderly particularly when living alone may lead to falls and severe morbidity)
- the degree of CNS effects (lightheadedness and dizziness, particularly for tasks requiring attention like driving or handling machinery)
- liver function tests (regular follow-up of liver function tests is required with carbamazepine)
- the presence of heart disease and arrhythmia (in case of antidepressants)
- glaucoma and prostatic hypertrophy (in case of antidepressants)
- kidney function (for drug excretion)
- patient's beliefs and expectations
- finances (for example, a drug not in the Ontario Drug Formulary with better efficacy or side effect profile, may not be afforded by the patient with limited finances)

Co-administration of CNS acting drugs (antidepressants and/or anticonvulsants together with opioids and/or benzodiazepines and other sedatives) may have a cumulative CNS effect. Recently gabapentin has been reported to have a better side effect profile than tricyclics or antidepressants.[1]

[1]The tables in this report contain only meta-analysis or systematic reviews, therefore, information on a new anticonvulsant medication (gabapentin) has not been included. Nevertheless, one multicentre RCT of substantial size demonstrated that gabapentin was effective on post herpetic neuralgia in doses up to 3600 mg/day (Rowbotham et al., JAMA, 280:21(1998) 1837-42). Similarly, another multicentre sizeable RCT demonstrated gabapentin efficacy in diabetic neuropathy again in doses up to 3600 mg/day (Backonja et al, JAMA 280:21(1998)1831-6).

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Chapter 11 Specific Recommendations for Opioid Use in Chronic Non-Malignant Pain

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11.1 Specific Recommendations for Opioid Use in Chronic Non-Malignant Pain

The recommendations for opioid use in chronic non-malignant pain include the following:

- The principles for opioid use in chronic non-malignant pain should be consistent with the "general principles of sound medical practice". An effort should be made to establish a clear diagnosis of the painful condition and of the associated medical and psychosocial conditions. Even if an exact medical diagnosis is elusive, an effort should still be made to identify the probable pain mechanisms, based on characteristic history and bedside criteria. Identification of possible mechanisms is useful since some treatments are more effective for certain mechanisms - e.g. TCA for headache or neuralgia (Goodkin et al., 1995).

  "Common sense" supports the recommendation that clinicians should exercise particular caution when evidence is lacking for the efficacy or safety of a given treatment for a given condition, or when the diagnosis or mechanism of a patient's illness is unknown. It should follow from this that caution should apply to use of opioids in patients for whom an organic diagnosis or cause is unknown, or when the pain is apparently due mainly to psychological factors. Caution does not mean contraindications; the two studies of Arkinstall et al (1995) and Moulin et al (1996) demonstrate *Level II* evidence that sustained release opioid can be used with a measure of success for pain relief in some chronic low back patients whose mechanism of illness was largely unknown and may have included psychological factors.

- Studies conducted in pain clinics suggest that the prevalence of opioid dependence in patients on opioid therapy for chronic non-malignant pain is low (Evidence Type IV; Portenoy, R.K. Opioid therapy for non-malignant pain: Current status, In. Fields: H, L., and Liebeskind, J.C. eds. Progress in Pain Research and Management, IASP Press, Seattle, 1994:247-287), although data on community prevalence is lacking. A history of dependence on opioids or other drugs is a risk factor for the development of dependence on prescribed opioids. Other factors may also play a role, such as the type and dose of opioid used and psychiatric co-morbidity. Physicians should prescribe opioids with considerable caution to patients with a current or prior history of substance dependence. Screening can identify patients at risk. Although evidence from controlled trials is lacking, certain prescribing practices may minimize the risk of opioid dependence particularly in patients in which there appears to be risk such as:

  - use of long-acting opioids
  - prescribing in small amounts and for short periods only
  - use of a treatment contract.

Effective treatments exist for opioid dependence.

- It has been recommended by some experts (*Level V* evidence) (Portenoy, 1996; the Alberta Guidelines, 1993; Levy, M.H. 1996) that before embarking on prescription of opioids for non-malignant pain, an adequate trial of non-opioid analgesics and adjuvant analgesics should have been carried out without success. This opinion is based partly on the concept of the World Health Organization "Analgesic Ladder". On the other hand, there is *Level II* evidence for the relative efficacy of opioid for some pain mechanisms (Jadad et al., 1992) -- suggesting that opioids might be chosen on the basis of serious pain and probable susceptibility to opioid analgesia.

- One physician only should prescribe opioids. The patient should be aware that this is the rule. A physician who consults on a patient who is receiving opioids from another practitioner should not prescribe an opioid unless this information is conveyed to the first prescriber of the opioid, and this should be followed by written documentation of the assessment and of the medication prescribed.

- In most cases, it will be best to proceed with analgesic therapy according to the principles of the World Health Organization "Analgesic Ladder", if there are no medical contraindications (*Level V* evidence). It is a matter of opinion that the WHO ladder is not appropriate for use in clear cases of neuropathic pain like:

  - Post-herpetic neuralgia (PHN)
  - Diabetic and other peripheral neuropathies
  - Peripheral nerve/root or plexus injury
  - Spinal cord injury and stroke.

  Instead, *Level I* evidence exists for use of anticonvulsants and antidepressants in different neuropathic pain syndromes (McQuay, H. and Moore, A. An evidence-based resource for pain relief. Oxford University

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Press, 1998). However, it is unclear which drug class is the first choice, since results are very similar for both classes or drugs. A summary of suggested use is included. (Evidence type V, Project CREATE; Use of opioids in chronic non-malignant pain, Kahan, M., Mailis, A., Moulin, D., Tunks, E., Wilson, L., Zalter, M., 1999).

One should keep in mind that NSAIDs can produce mild to moderately severe side effects and should be used with caution in the elderly. Side effects include:

- abdominal pain
- diarrhea
- fluid retention
- headache and fatigue.

Gastrointestinal perforation and haemorrhage are probably the most severe complications. One systematic review reported side effects in 0 to 31% of patients and there did not seem to be any clear difference in the reported number of severity of side effects between different types of NSAIDs (Koes, B.W., et al., 1997). McQuay and Moore (1998) recommended the alternative that acetaminophen offered a safer first step, before considering the more potent NSAIDs.

If combination acetaminophen and opioid is used (Percocet, Tylenol with codeine, and other generics), no greater than 12 tablets of the preparation should be taken per day because of risk of acetaminophen toxicity -- a risk which increases with age and with certain medical problems.

Meperidine is short-acting, which could lead to breakthrough of pain and/or escalation. Prolonged use in higher doses can lead to accumulation of the toxic metabolite, normeperidine. Anileridine is chemically related to meperidine, with the same caveat. The use of these two opioids in the management of chronic non-malignant pain syndromes is not recommended, except in extenuating circumstances (example: failure of all other oral or transdermal opioids) (*Level V* evidence) (Levy, M.H., 1996).

- Three randomized controlled trials have found that chronic musculoskeletal pain responds to opioid analgesics with variable improvement in functional status (*Level II* evidence) (Kjaersgaard-Anderson, P. et al. 1990; Arkinstall, W., et al., 1995; Moulin, D.E. et al., 1996). Three trials concluded that neuropathic pain also responds to opioid analgesics (Rowbotham, M.C. et al. 1991; Dellemijn, P.L., and Vanneste, J.A. 1997; Watson, C.P., and Babul, N. 1998) while two other trials concluded that neuropathic pain is not (Arner, S, and Myerson, B.A., 1988; Kupers, R.C. et al., 1991). However, the quality of the positive trials is much higher than the negative trials (Jadad, A.R. et al., 1996) so that on balance there is *Level II* evidence that neuropathic pain is responsive to opioid analgesics.

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Documentation of the treatment trial is important when prescribing opioids. Documentation should include:

- the investigation and documentation of diagnosis
- documentation of pain, preferably including a pain scale by which the patient can report changes in pain
- appearance of side effects
- changes in function.

This should be part of the patient's record. Effective therapy may be defined as determination of a dose and preparation associated with analgesia sufficient to reduce suffering and hopefully also improve function. No physician should feel compelled to prescribe a preparation or dose with which he/she is uncomfortable given that clinician's experience and training. Personal discomfort by the physician or concern about the adverse consequences of the treatment are valid reasons not to proceed. In some circumstances, the physician may elect to refer the patient to, or obtain consultation from, another physician who has more expertise in chronic pain management.

11. 2 Recommendations based on Level V Evidence

The following recommendations are taken from our systematic review of Pain Guidelines, based on *Level V* evidence. *See Chapter 3 Review of Existing Published Guidelines for Treatment of Chronic Non-Malignant Pain.*

- If trial of non-opioid analgesics is ineffective, one may try fixed opioid-analgesic combinations such as acetaminophen, caffeine, codeine. If the fixed combinations are ineffective, one may pass on to morphine syrup at a beginning dose of 10 mg every four hours, and titrate upwards once or twice per week by increments of 25% to 50%.

  Initial daily dosage of opioid must be chosen individually. Some patients, naive to opioids or elderly patients or those prone to adverse side effects, may need to start at much lower doses, for example at 5 mg q6h.

- One would hope to see initial analgesic effects beginning at relatively low dosages; without this, one must anticipate the possibility of ultimately opioid unresponsiveness [Portenoy, 1996]. Increasing doses should be accompanied by an increasing analgesic effect [Portenoy, 1996]. Megadoses of morphine (hundreds or thousands of mgs) may indicate:

  - non absorption leading to lack of efficacy
  - mechanisms of pain non responding to that opioid.
  - drug diversion

  Opioids may not be an effective treatment, and alternative interventions should be considered.

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- If short-acting morphine proves useful, and there are no features suggesting abuse, the patient should be switched to sustained-release opioid preparation.

  There is still a need for research in non-malignant pain treatment comparing the efficacy of sustained release opioids to regular release (short-acting) opioid, to determine if sustained release preparations reduce the risk of behavioural complications or reduce the chance of abuse or diversion. Sustained release opioids are more expensive, and some non-insured patients may not be able to afford them, whereas regular preparation morphine or codeine is relatively inexpensive. Approximate q4h dosing of regular release opioid would allow for adequate pain control in most patients. At higher dosages, or if breakthrough pain or opioid side-effects become a problem, sustained release preparations might have more of a clinical advantage.

  Doses of oral morphine or its equivalent above 300 mg daily are unusual, though not necessarily contraindicated, for chronic non-malignant pain.

- Parenteral dosing of opioids to treat chronic non-malignant pain should be strongly discouraged unless there are extenuating medical circumstances and oral or transdermal routes of administration are not available for medical reasons. In general, a physician converting a patient from oral to parenteral opioids (when oral opioid therapy has failed) should be able to justify that the benefits of this treatment outweigh the risks of high dose parenteral opioid therapy including local infection, sedation, myoclonus and seizures. However, even under these circumstances, daily IM or SC injections should be avoided except under a highly supervised environment for example, during an admission to the hospital or with regular outpatient follow-up.

- There should be an agreement between the patient and the prescribing physician which clearly delineates that there is to be no:

  - unsanctioned dose escalation
  - selling of opioids
  - injecting of opioids
  - seeking of opioids from another physician
  - buying "on the street" or obtaining from illegal sources
  - hoarding of opioids.

  This contract should clearly define consequences of violation, which could include a non-negotiable end to the prescribing relationship between the patient and physician. If the patient sees another physician and obtains opioids such as when the primary physician is not available, or when the patient has been seen in a consult, then the primary physician should be informed by the patient at the first reasonable opportunity.

  If warranted, this contract should be in writing - otherwise documentation in the physician's notes of the verbal agreement is also sufficient. *Please see Appendix F Sample Treatment Contract.*

- The patient should be seen and assessed at least every nine weeks and more

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frequently if needed, for example if there is a previous history of drug abuse.

The clinician should specifically evaluate the patient for several distinct aspects of therapy at each visit, including:

- analgesic efficacy
- adverse pharmacological events
- physical and psychological function
- the occurrence of apparent drug abuse related behaviour.

Documentation is a very important part of therapy, and physicians should keep careful records that include reference to these various aspects of therapy. Once a regular dose of opioid is established, the patient should not request a refill of the prescription earlier than the established duration for the prescription.

Examples of good office practices are as follows:

- To document analgesic efficacy pain diaries with use of pain scales (0-10) at set times during the day or prior to receiving pain medications can be used. It is advisable to establish pain ratings during a baseline period of three days prior to the initiation of opioids, so efficacy of analgesics can be documented by comparison of ratings to baseline period. The same "pain logs" assist in titrating the dose of opioids to the most efficacious levels. (Reference: Three day pain logs, Mailis, A., Comprehensive Pain Program, The Toronto Hospital, 1995.)

- A checklist of the following adverse effects should be documented during each visit:
  - constipation, sweating, nausea
  - exacerbation of sleep apnea, COPD
  - opioid bowel syndrome
  - rebound headaches
  - fatigue and confusion (particularly in the elderly)
  - reproductive effects (impotence in men and menstrual irregularities in women)
  - sensitization to pain (higher opioid doses may be required in acute pain)
  - neurotoxicity, seizures and hallucinations (for example with repeated administration of Demerol and Leritine).

    Reference: Project CREATE: Opioids in the treatment of non-malignant pain. Kahan, M., Mailis, A., Moulin, D., Tunks, E., Wilson, L., Zalter, M. 1999)

- Function (physical and psychological). An example of short checklist is as follows (use the same checklist or other similar during each visit to compare changes in function)
  - sleep
  - mood
  - libido

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- up time (time out of bed), ability to sit, stand
- activities within the house and outside (household chores, shopping etc)
- activities at work (return to, modified duties, trial employment etc.)

Reference: Mailis, A., Comprehensive Pain Program, The Toronto Hospital, 1995.

11.3 Apparent Drug Abuse Related Behaviours Checklist

Addiction is quite distinct from tolerance and physical dependence; true addiction resulting from appropriate medicinal use of opioids is uncommon *(Level V* evidence*)* [Portenoy, R.K., 1994].

Addiction is a state where a person takes a medication for its psychic effect, not for its pain relieving effect, and is characterized by:

- loss of control
- compulsive drug use
- continued drug use despite its harm.

Tolerance and physical dependency are different phenomena and can develop in patients who consume opioids chronically, are also part of the symptom complex of addiction, but of themselves are not pathognomonic of addiction (*Level V* evidence*)* [Portenoy, R.K. 1994].

Tolerance is a poorly understood phenomenon characterized by the need for higher doses to maintain opioid effects. Clinical experience in patients with chronic non-malignant pain managed with long-term use of opioids indicates that tolerance does occur initially, but tends to be less of an issue over the course of many years (*Level V* evidence*)* [Portenoy, R.K., 1994].

Physical dependence is a response to a drug characterized by the occurrence of an abstinence syndrome on abrupt dose reduction or administration of an antagonist.

More frequently seen is a "chronic pain disorder" (DSM-IV 307), in which a patient takes a large variety of medication with questionable benefit, and uses drugs inappropriately as part of the behavioural disturbances that characterize this state. Other behavioural traits of this syndrome include:

- physical inactivity
- inability to work
- social isolation.

Note: *Analgesic medication should only be used in this setting as part of a carefully controlled overall pain management program. (Level V* evidence*) [Portenoy, R.K., 1994].*

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11.4 Behaviours Suggestive of Opioid Dependence

Behaviours suggestive of opioid dependence include:

- on high and escalating doses of opioids
- frequently runs out of scripts early
- observed to be intoxicated or in withdrawal
- alters, borrows, steals or sells scripts
- accesses multiple sources of opioids (doctors, friends, relatives, the street)
- injects oral medications
- threatens or harasses staff for fit-in appointment
- reluctant to try alternatives
- angry, demanding, tearful if does not get drug of choice
- addicted to alcohol or other drugs
- deterioration of functional status while in receipt of opioid
- concurrent abuse of alcohol or illicit drugs
- multiple dose escalations or other noncompliance with therapy despite warnings
- multiple episodes of prescription "loss"
- repeatedly seeking prescriptions from other clinicians or from emergency rooms without informing prescriber, or after warnings to desist.

References: Project CREATE: Opioids in the treatment of chronic non-malignant pain. Kahan, M., Mailis, A, Moulin, D., Tunks, E., Wilson, L., Zalter, M. 1999. Portenoy, 1996.

Note: *Some behaviours could be misinterpreted as indicators of addiction. A person in serious pain may appear to be "drug-seeking" when seeking pain relief. In the presence of chronic non-malignant pain, "relapse" after withdrawal from the opioid and return to use of opioid, may be rationally expected sometimes [Portneoy, 1996].*

Flares of pain can be treated with small extra doses of opioid by mouth; each month a prescription should include a few extra doses for this purpose (*Level V* evidence) [Portenoy, R.K., 1994].

The goal of chronic opioid therapy is not the elimination of pain, which may be impossible, but rather to control pain to a tolerable level; there is a clear emphasis on level of function of the patient in social, work and personal life. (*Level V* evidence) [Portenoy, R.K., 1994]

The goals of a treatment program for chronic non-malignant pain include pain relief and functional restoration. A treatment program that focuses on analgesics without incorporating psychosocial and behavioural approaches may reinforce pain-related behaviour and undermine a rehabilitative program targeted to functional restoration (Turk, D.C., and Meichenbaum, D., 1994). Therefore, the focus of chronic opioid therapy should be on time contingent analgesic use rather than pain-contingent analgesic use. (*Level V* evidence)

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Chapter 12 Consolidated Evidence-Based Information Regarding Treatment Modalities

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Table #8 Chronic Headache Treatment Summary

	EMG Biofeedback	Relaxation	Relaxation & Biofeedback	Cognitive	Specific Serotonin re-uptake inhibitors	Tricyclic Antidepressants
Results **Results**	48% of patients improved	36% of patients improved	56% of patients improved	53% of patients improved	Fluoxetine better than placebo Paroxetine & Fluvoxamine better than baseline	Maprotiline & Doxepin better than placebo
Level of Evidence **Level of Evidence**	**III**	**III**	**III**	**III**	**II** Fluoxetine **III** Paroxetine & Fluvoxamine	**II**
Recommended or Not	**YES**	**YES**	**YES**	**YES**	**YES**	**YES**

Table #9 Recommended Medications for the Acute Treatment of Migraine Headaches

Medication	Main Side Effects
Aspirin, preferably soluble (e.g. Alka Seltzer up to 1000 mg)	Gastrointestinal pain, ulceration, bleeding
Ibuprofen 400-800 mg / Naproxen 275-550 mg	Gastrointestinal pain, ulceration, bleeding
Acetaminophen 625-1300 mg	No convincing evidence of efficacy
Sumatriptan 50-100 mg p.o., 20 mg nasal, 6 mg s.c. Naratriptan 2.5 -5.0 mg p.o. Zolmitriptan 2.5-5.0 mg p.o. Rizatriptan 10 mg p.o.	All may cause chest or throat tightness, tingling, tiredness, nausea. Contraindicated in Atherosclerotic heart disease.
Dihydoergotamine 1 mg IM or IV, or 1-2 mg nasally (2-4 puffs)	Chest pain, vomiting + + (needs to be combined with metoclopramide) Contraindicated in Atherosclerotic heart disease
Ergotamine 1-2 mg p.o. or suppository	Chest tightness, vomiting + + Contraindicated in Atherosclerotic heart disease
Acetaminophen + caffeine + butalbarbital +/- codeine	Drowsiness, habituation
Ketoralac 30-60 mg IM	Nausea, abdominal pain
Lidocaine 2% intranasal drops or soaked Q-tip	Bad taste
Chlorpromazine 50 mg IM, 0.1 mg/kg IV drip 50 mg suppository	Drowsiness, hypotension, extrapyramidal
Butorphanol 1 mg nasal spray	Nausea, dysphoria, addiction
Demerol 50-100 mg IM	Drowsiness, nausea, addiction
Dexamethasone 12-20 mg IV	Usual steroid effects if given too frequently.

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Table #10 Migraine Prophylactic Drugs

Medication		Limiting Side Effects
Beta Blockers		
Atenolol	50-150 mg/d	Fatigue, bradycardia, hypotension, depression, impotence, poor sleep, bronchospasm
Metoprolol	100-200 mg/d	
Nadolol	20-160 mg/d	
Propranolol	40-240 mg/d	
Calcium Channel Blockers		
Flunarazine	5-10 mg/d	Nausea, edema, headache, extrapyramidial [both] fatigue, weight gain, depression [flunarizine] bradycardia, hypotension, constipation [verapamil]
Verapamil SR	240-720 mg/d	
Serotonin Antagonists		
Methysergide [Sansert]	4-8 mg/d	Retroperitoneal, pulmonary, or pericardial fibrosis Weight gain, fatigue
Pizotyline [Sandomigran]	3-6 mg/d	Weight gain, fatigue
Tricyclic Antidepressants		
Amitriptyline	10-150 mg/d	Dry mouth, constipation, urinary retention, drowsiness, cardiovascular effects
Nortiptyline	10-150 mg/d	
Anti-Epileptics		
Valproic acid		Nausea, tremor, weight gain, alopecia, liver enzymes
Divalproex	500-1500 mg/d	
Sodium valproate		
NSAID		
Naproxen	550 mg bid no longer than 1 week/month	GI upset, ulceration, renal dysfunction
Relaxation & Biofeedback		No side effects, except cost. It was shown to be equally effective as propranolol in meta-analysis[6]

Note: *The Levels of evidence have been changed to comply with those used throughout our report.*
Reference for Column 7 is Holroyd & Penzien, PAIN, 1990; 42, 1-13.

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Table #11 Interventions for the Treatment of Neuropathic Pain

Condition	Anticonvulsants	Antidepressants	Oral Drugs with Local-Anaesthetic type properties	Opioids	Topical (Capsaicin)	Intravenous Regional Sympathetic Blocks (IRSB)
Trigeminal Neuralgia	Evidence: Yes Level I Effective* = 1:2.6 Recommended: Yes	No controlled trials	Evidence: Yes Level II Recommended: Yes	Evidence: may be effective Level V	No controlled trials	Not applicable
Diabetic Neuropathy	Evidence: Yes Level I Effective* = 1:2.5 Recommended: Yes	Evidence: Yes Level I Effective* = 1:3 Recommended: Yes	Evidence: Yes Level II Recommended: Yes	See general comments on Opioids (Chapter 8)	Evidence: Yes Level II Effective*: 1:4.2 Recommended: Yes	No controlled trials
Post-Herpetic Neuralgia	See page 65 re gabapentin Evidence: Yes Level II Recommended: Yes	Evidence: Yes Level II Effective* = 1:2.3 Recommended: Yes	Evidence: Yes Level II Recommended: Yes	Evidence: Yes Level II Sustained release opioids effective Recommended: Yes	Evidence: Yes Level II Effective: Yes, but effective minor Recommended: Maybe	No controlled trials

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Condition	Anticonvulsants	Antidepressants	Oral Drugs with Local-Anaesthetic type properties	Opioids	Topical (Capsaicin)	Intravenous Regional Sympathetic Blocks (IRSB)
Post-stroke Pain	Evidence: Yes Level II Effective*=1:3.4 Recommended: Yes	Evidence: Yes Level II Effective*=1:1.7 Recommended: Yes	No controlled trials	No controlled trials	No controlled trials	No controlled trials
Other **Peripheral Nerve Injury**	No controlled trials	No controlled trials	Evidence: Yes Level II Effective: Yes Recommended: Yes	No controlled trials	No controlled trials	No controlled trials
Spinal Cord Injury	No controlled trials	No controlled trials	Evidence: Yes Level II Effective: No Recommended: No	No controlled trials	No controlled trials	Not applicable
Post Mastectomy	No controlled trials	No controlled trials	No controlled trials	No controlled trials	Evidence: Yes Level II Effective: Yes, but effect minor Recommended: Maybe	Not applicable
Reflex Sympathetic Dystrophy	No controlled trials	No controlled trials	No controlled trials	No controlled trials	No controlled trials	Evidence: Yes Level III Effective: No Recommended: No

Note: **The denominator indicates the number of patients needed to treat with the active drug in order to obtain an effect not obtained with placebo.*

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Table #12 Medication for Chronic Musculoskeletal Pain

Area of Concerns	NSAID or Antipyretics	Anticonvulsants	Antidepressants	Opioids	Topical (NSAIDs or capsaicin)
Chronic Low Back Pain	Effective acute back pain in first week *Level III* Contradictory for CLBP	No systematic reviews found	Not effective *Level III* Not recommended	Sustained release opioid effective *Level II* May be attempted	No systematic reviews found
CLBP with sciatica	No systematic reviews found	No systematic reviews found	No systematic reviews found	Sustained release opioid Effective *Level II* May be attempted	No systematic reviews found
Neck with/without limb pain	No systematic reviews found	No systematic reviews found	No systematic reviews found	Sustained release opioid effective *Level II* May be attempted	No systematic reviews found
Chronic Generalized Soft Tissue Musculoskeletal Pain	*Level III* Not effective	No studies	*Level III* Contradictory	No studies	No studies

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Table #13 Role of Opioid Analgesics in the Treatment of Chronic Non-Malignant Pain

	Nociceptive Pain	Neuropathic Pain	Visceral Pain	Chronic Pain with Psychological Factors	Headache
Examples of Type of Pain	Severe Degenerative changes (multi-level or joint)	Diabetic neuropathy, causalgia, central pain (stroke, spinal cord injury)	Chronic pancreatitis Crohn's	Somatoform pain disorder, depression, conversion disorder	Tension, migraine
First Line Medications	WHO analgesic ladder; Acetaminophe n NSAIDs	Tricyclic antidepressants, Anticonvulsants e.g. carbamazepine Membrane stabilizers e.g. lidocaine	Smooth muscle relaxants, Antacids, H_2 blockers	Anxiolytics or anti-depressants in presence of clinically significant anxiety or depression	Prophylactic- Beta blockers, calcium channel blockers, serotonin receptor antagonists, tricyclic anti-depressants, anti-epileptics, NSAIDs, Acute - NSAIDs, DHE, sumatriptan, ketorolac, chlorpromazine, dexamethasone
Effectiveness of opioids in therapy	Often of value	Limited but definite value in selected cases	May be of value	Limited value	Tension: Rarely indicated. Migraine: Limited value
Caveats	Document significant organic pathology before long-term prescribing	Opioids less effective in neuropathic pain. Higher doses may be required but dosing limited by side effects.			Use combination meds (e.g. Tylenol #3) intermittently for short periods. May cause rebound headache.

Before prescribing opioids, physicians need to define and prioritize targets for treatment, bearing in mind that most chronic pain syndromes have a mix of mechanisms, and psychiatric co-morbidity is common. For example, in a depressed patient with diabetic neuropathy, treatment should be targeted towards depression, insomnia, and neuropathic pain. Tricyclic antidepressants would be the treatment of choice, because they are effective for all three targets.

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Table #14 Physical Therapy for Chronic Musculoskeletal Pain

Area of concern	Passive Modalities	Bed Rest	Corsets and orthotics	Manipulation	Exercise
Chronic Low Back Pain	Inconclusive *Level III* Not recommended	Ineffective *Level III* Not recommended	Inconclusive *Level IV*	Contradictory *Level III*	Contradictory *Level III* Active exercise recommended
CLBP with sciatica	Ineffective *Level III* Not recommended	Effective for acute *Level III* Doubtful otherwise	In conclusive *Level IV*	No systematic reviews but manipulation is contraindicated in presence of herniated disk	No systematic reviews
Chronic Neck with/ without limb pain	Inconclusive *Level III* Not recommended	*Level II* Not recommended	Not applicable	Contradictory *Level III*	Effective *Level III* Active exercise recommended
Headache from MSK Pain	No systematic reviews	No systematic reviews	Not applicable	Contradictory *Level III*	No systematic reviews
Generalized Soft Tissue Pain	Inconclusive *Level IV*	No studies	Not applicable	Inconclusive *Level IV*	Effective *Level III* Active exercise recommended

Note: *For TENS and Acupuncture there is Level III contradictory evidence for efficacy in a variety of musculoskeletal syndromes.*

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Table #15 Behavioural/Psychological Management for Chronic Musculoskeletal Pain

Area of Concern	Operant	Cognitive-Behavioural	Relaxation	Biofeedback	Education/ Back School	Multimodal
Chronic Low Back Pain	Effective *Level III* Recommended	Effective (on subjective measures) *Level III* Recommended	Probably effective *Level III* Recommended	Inconclusive *Level III*	Inconsistent Short-term Effective (on subjective measures) *Level III* Recommended if part of multimodal program	Effective *Level III* Recommended
Neck with/without limb pain	No systematic review	No systematic reviews	No systematic reviews	No systematic reviews	Not effective *Level III* Recommended if part of multimodal program	No systematic reviews Recommended on basis of efficacy with other chronic pain syndromes
Generalized Soft tissue pain	Effective *Level III* Recommended	Effective *Level III* Recommended	Effective *Level III* Recommended	Inconclusive *Level III*	Not effective *Level III*	No systematic reviews
Pain with psychological factors	Effective *Level V* Recommended	Effective *Level V* Recommended	Effective *Level V* Recommended	Effective *Level V* Recommended	Effective *Level V* Recommended if part of multimodal program	Effective *Level V* Recommended

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Table #16 Injection Therapies for Chronic Non-Malignant Pain (Based Partly on RCTs)

Condition	Local Infiltration
Chronic Low Back Pain	Inconsistent and equivocal Level III Possible short term benefit
Chronic Low Back Pain with sciatica	No systematic reviews
Neck with/without limb pain	Inconsistent and equivocal Level III Possible short term benefit
Chronic Headache	No systematic reviews
Neuralgia (post-herpetic or diabetic)	No systematic reviews
Soft tissue pain	Inconsistent and equivocal Level III Possible short term benefit

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Bibliography

Bibliography

Aker PD, Gross AR, Goldsmith CH, and Peloso P. Conservative management of mechanical neck pain: systematic overview and meta-analysis. Brit Med J 3313: 1291-1296, 1996

American Geriatrics Society Panel on Chronic Pain in Older Persons: The management of chronic pain in older persons. JAGS 46: 635-651, 1998

American Psychiatric Association Task Force on DSM-IV: Diagnostic and Statistical Manual of Mental Disorders. Fourth Edition. American Psychiatric Association Press, Washington, 1994

American Society of Anesthesiologists Task Force on Pain Management, Chronic Pain Section: Practice guidelines for chronic pain management. Anesthesiology 86:995-1004, 1997

Arkinstall W, Sandler A, Goughnour B, et al: Efficacy of controlled-release codeine in chronic non-malignant pain: a randomised, placebo-controlled clinical trial. Pain 62:169-178, 1995

Arner S, Meyerson BA. Lack of analgesic effect of opioids on neuropathic and idiopathic forms of pain. Pain 1988; 33: 11-23.

Assendelft WJJ, Hay EM, Adshead R, and Bouter LM. Corticosteroid injections for lateral epicondylitis: a systematic overview. Brit J Gen Practice 46: 209-216, 1996

Backonja, M., Beydoun, A., Edwards, K.R., Schawartz, S.L., Fonseca, V., Hes, M., LaMoreaux, L., Garofalo, E. Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetic mellitus: a randomized controlled trial JAMA 280(21) 1998 1831-6.

Beckerman H, Bouter LM, van der Heijden GJMG, de Bie RA, Koes BW: Efficacy of physiotherapy for musculoskeletal disorders: what can we learn from research? Brit J Gen Pract 43:73-77, 1993

Beckerman H, de Bie RA, Bouter LM, De Cuyper HJ, Oostendorp RAB: The efficacy of laser therapy for musculoskeletal and skin disorders: A criteria-based meta-analysis of randomized clinical trials. Phys Ther 72(7): 483-491, 1992

OUT-OF-DATE

Bogaards MC, & ter Kuile MM: Treatment of recurrent tension headache: a meta-analytic review. Clinical Journal of Pain, 1994 ; 10 : 174-190
Bourne IJH: Treatment of chronic back pain: comparing corticosteroid-lignocaine injections with lignocaine alone. The Practitioner 1984; 228: 333-338
Browman GP, Levine MN, Mohide A, Hayward RSA, Pritchard KI, et al: The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 13: 502-512, 1995

Byrn C, Olsson I, Falkheden L, Lindh M, et al.: Subcutaneous sterile water injections for chronic neck and shoulder pain following whiplash injuries. The Lancet 1993; 341: 449-452

Canadian Pain Society Task Force. Use of opioid analgesics for the treatment of chronic non-cancer pain – a consensus statement and guidelines from the Canadian Pain Society. Pain Research and Management 3:197-208, 1998

Cancer Pain: A monograph on the management of cancer pain, Health & Welfare Canada, Minister of Supply and Services, Ottawa, Canada, 1984, H42-42/5.

Carette S, Marcoux S, Truchon R, et al: A controlled trial of corticosteroid injections into facet joints for chronic low back pain. N Engl J Med 325:1002-1007, 1991

Cohen JE, Goel V, Frank JW, Bombardier C, Peloso P, Guillemin F: Group education interventions for people with low back pain: An overview of the literature. Spine 19(13):1214-1222, 1994

Collee G, Dukmans BAC, Vandenbroucke JP, and Cats A: Iliac crest pain syndrome in low back pain: A double blind, randomized study of local injection therapy. J Rheum 1991; 18: 1060-1063

College of Physicians and Surgeons of Alberta: Guidelines for the management of chronic non-malignant pain. CPSA, February 1993

Cluzeau G, Littlejohns P, Grimshaw J, and Feder G: Appraisal Instrument for Clinical Guidelines. Version 1. Health Care Evaluation Unit, St. George's Hospital Medical School, London UK, 1997

Crook, J., Rideout, E., and Browne, G. The prevalence of pain complaints in a general population. Pain 18: 299-314, 1984.

Crook, J., Tunks, E., Rideout, E., and Browne, G. Epidemiologic comparison of persistent pain sufferers in a specialty pain clinic and in the community. Arch. Phys. Med. Rehab. 67: 451-455, 1986.

Crook, J., Weir, R., and Tunks, E. An epidemiogical follow-up survey of persistent pain sufferers in a group family practice and specialty pain clinic. Pain 36: 49-61, 1989

OUT-OF-DATE

Cutler RB, Fishbain DA, Rosomoff HL, Abdel-Moty, E, Khalil TM, and Rosomoff RS: Does nonsurgical pain center treatment of chronic pain return patients to work? A review and meta-analysis of the literature. Spine 19:643-652, 1994

Dellemijn PL, Vanneste JA. Randomized double-blind active-placebo-controlled crossover trial of intravenous fentanyl in neuropathic pain. Lancet 1997; 349:753-758.

Dellemijn, P. Are Opioids Effective in Relieving Neuropathic Pain? A Review Article Pain 1999; 80:453-462.

DiFabio RP: Efficacy of comprehensive rehabilitation programs and back school for patients with low back pain: A meta-analysis. Phys Ther 75: 865-878,1995

Ezzo, J.M., Berman, B.M., Hadhazy, V., Jadad, A.R. Acupuncture for chronic pain: a systematic review of the literature. In press Pain.

Fainsinger R, Schoeller T, Bruera E. Methadone in the management of cancer pain: A review. Pain 1993; 52: 137-147.

Flor H, Fydrich T, Turk DC: Efficacy of multidisciplinary pain treatment centers: A meta-analytic review. Pain 49:221-230, 1992

Frost FA, Jessen B, and Siggaard-Andersen J: A control double-blind comparison of mepivacaine injection versus saline injection for myofascial pain. The Lancet 1980; 8167 :449-501

Gadsby JG, Flowerdew MW: The effectiveness of transcutaneous electrical nerve stimulation (TENS) and acupuncture-like transcutaneous electrical nerve stimulation (ALTENS) in the treatment of patients with chronic low back pain. In: Bombardier C, Nachemson A, Deyo R, de Bie R, Bouter L, Shekelle P, Waddell G, Roland M, Guillemin F (eds.) Back Review Module of the Cochrane Database of Systematic Reviews, [updated 01 Sept. 1997]. Available in the Cochrane Library (Database on Disk and CD-ROM). The Cochrane Collaboration; Issue 4, Oxford: Update Software; 1997 (updated quarterly).

Gam AN, Thorsen H, Lønnberg F: The effect of low-level laser therapy on musculoskeletal pain: a meta-analysis. Pain 52:63-66, 1993

Gannon C. The use of methadone in the care of the dying. European J Palliative Care 1997; 4(5): 152-158.

Gardner-Nix JS. Oral methadone for managing chronic non-malignant pain. J Pain and Symptom Management 1996; 11(5): 321-328.

Garvey TA, Marks MR, Wiesel SW: A prospective randomized double blind evaluation of trigger-point injection therapy for low back pain. Spine 14:962-964, 1989

OUT-OF-DATE

Gillette JF, Ferme C, Moisy N et al. Double-blind crossover clinical and pharmacokinetic comparison of oral morphine syrup and sustained release morphine sulfate capsules in patients with cancer-related pain. Clin Drug Invest 1997; 14 Suppl 1: 22-27.

Glynn CJ, Casale R. Morphine injected around the stellate ganglion does not modulate the sympathetic nervous system nor does it provide pain relief. Pain 1993; 53:33-37.

Glynn C, and O'Sullivan K: A double-blind randomized comparison of the effects of epidural clonidine, lignocaine and the combination of clonidine and lignocaine in patients with chronic pain. Pain 1995; 64: 337-343

Goodkin K, and Gullion CM: Antidepressants for the relief of chronic pain: do they work? Annals of Behavioural Medicine, 1989 11:83-101

Goodkin K, Vrancken MAE, and Feaster D: On the putative efficacy of the antidepressants in chronic, benign pain syndromes: an update. Pain Forum 4:237-247, 1995

Gross AR, Aker PD, Goldsmith CH et al: Conservative management of mechanical neck disorders: A meta-analysis. Online J Clin Trials, 1996

Gross AR, Aker PD, Goldsmith CH, Peloso P: Patient education for neck pain: Conservative management of mechanical neck disorders. Part four: Patient education.

In: Bombardier C, Nachemson A, Deyo R, de Bie R, Bouter L, Shekelle P, Waddell G, Roland M, Guillemin F (eds.) Back Review Group For Spinal Module of The Cochrane Database of Systematic Reviews , [updated 02 December 1997]. Available in The Cochrane Library [database on disk and CDROM]. The Cochrane Collaboration; Issue 1. Oxford: Update Software; 1998. Updated quarterly.

Gross AR, Aker PD, Goldsmith Ch, Peloso P: Physical medicine modalities for neck pain: Conservation management of mechanicl neck disorders. Part two: Physical medicine modalities. In: Bombardier C, Nachemson A, Deyo R, de Bie R, Bouter L, Shekelle P, Waddell G, Roland M, Guillemin F (eds.) Back Review Group For Spinal Module of The Cochrane Database of Systematic Reviews, [updated 02 December 1997]. Available in The Cochrane Library [database on disk and CDROM]. The Cochrane Collaboration; Issue 1. Oxford: Update Software; 1998. Updated quarterly.

Haddock CK, Rowan AB, Andrasik F, Wilson PG, et al. Home based behavioral treatments for chronic benign headache: a meta-analysis of controlled trials. Cephalalgia, 1997 ; 17 :113-8

OUT-OF-DATE

Haddox JD (committee chair), et al.: The use of opioids for the treatment of chronic pain. A consensus statement from the American Academy of Pain Medicine and the American Pain Society. Clin J Pain 13: 1-2, 6-8, 1997

Holroyd KA, Penzien DB: Pharmacological versus nonpharmacological prophylaxis of recurrent migraine headache A meta analysis of clinical trials. Pain 42:1-13, 1990

Hong C-Z: Lidocaine injection versus dry needling to myofascial trigger point: the importance of the local twitch response. Am J Phys Med Rehabil 1994: 73: 256-263

Hurwitz EL, Aker PD, Adams AH, Meeker WC, Shekelle PG: Manipulation and mobilization of the cervical spine. A systematic review of the literature. Spine 21(15):1746-1760, 1996

Jadad AR, Carroll D, Glynn CJ, Moore RA, and McQuay HJ. Morphine responsiveness of chronic pain: double-blind randomised crossover study with patient-controlled analgesia. Lancet 1992;339:1367-1371

Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJM, Gavagnan DJ et al. Assessing the quality of reports in randomised clinical trials: is blinding necessary? Controlled Clinical Trials 1996;17:1-12

Jung AC, Staiger T, and Sullivan M: The efficacy of selective serotonin reuptake inhibitors for the management of chronic pain. J Gen Intern Med 12:384-389, 1997

Kahan M, Mailis A, Moulin D, Tunks E, Wilson L, Zalter M: Opioids in the treatment of chronic non-malignant pain. Project CREATE, 1999.

Kahan M, Mailis A, Wilson L. CPSO Skills Prescribing Course. 1998

Kjaersgaard-Andersen P, Nafei A, Skov O et al. Codeine plus paracetamol versus paracetamol in longer-term treatment of chronic pain due to osteoarthritis of the hip. A randomized, double-blind, multi-centered study. Pain 1990; 43:309-318.

Koes BW, Assendelft WJJ, van der Heijden GJMG, Bouter LM, PG Knipschild: Spinal manipulation and mobilisation for back and neck pain: a blinded review. BMJ 303:1298-1303, 1991

Koes BW, Bouter LM, Beckerman H, van der Heijden GJMG, and Knipschild PG: Physiotherapy exercises and back pain: a blinded review. BMJ 302:1572-1576, 1991

Koes BW, Scholten RJPM, Mens JMA, and Bouter LM: Efficacy of non-steroidal anti-inflammatory drugs for low back pain: as systemic review of randomised clinical trials. Ann Rheum Dis 56:214-223, 1997

Koes BW, van Tulder MW, van der Windt DAWM, and Bouter LM: The efficacy of back schools: a review of randomized clinical trials. J Clin Epidemiol 47:851-862, 1994

OUT-OF-DATE

Kupers RC, Konings H, Adriaensen H et al. Morphine differentially affects the sensory and affective pain ratings in neurogenic and idiopathic forms of pain. Pain 1991; 47:5-12.

Large R, Peters J. A critical appraisal of outcome of multi-disciplinary pain clinic treatments. In Bond et al.: Proceedings of 6th World Congress on Pain, 1991, Elsevier Science Publishers, p. 417-427.

Levy MH. Pharmacologic treatment of cancer pain. New Eng J of Med 1996; 335:1124-1132.

Lilius G, Laasonen FM, Myllynen P et al: Lumbar facet joint syndrome. J Bone Joint Surg 71-8:681-684, 1989

Mailis, A. & Bennett, G. Painful neurological disorders: From Animals to Humans. In Aronoff, G.M. (Ed) Evaluation and treatment of chronic pain, 3rd edition, Williams and Wilkins, 1999, pp. 81-92

Mailis, A. & Bennett, G. Painful neurological disorders: Clinical aspects. In: Aronoff, G.M. (Ed). Evaulation and treatment of chronic pain, 3rd edition, Williams & Wilkins, 1999, pp. 93-113.

Malone MD, Strube MJ: Meta-analysis of non-medical treatments for chronic pain. Pain 34:231-244, 1988

Marks RC, Houston T, Thulbourne T: Facet joint injection and facet nerve block: A randomised comparison in 86 patients with chronic low back pain. Pain 49:325-328, 1992

Mays KS, Lipman JJ, Schnapp M. Local analgesia without anesthesia using peripheral perineural morphine injections. Anesthes Analges 1987; 66:417-420.

McNairy SL, Maruta T, Ivnik RJ et al. Prescription medication dependence and neuropsychological function. Pain 1984; 18: 169-177.

Medical Board of California: Guideline for prescribing controlled substances for intractable pain. Medical Board of California Action Report 51: 8, 1995

McQuay H, and Moore A. An evidence based resource for pain relief. Oxford: Oxford University Press, 1998

Chapter 11: Comparing analgesic efficacy of non-steroidal anti-inflammatory drugs given by different routes in acute and chronic pain. pp 94-101

Chapter 26: Intravenous regional sympathetic blockade (IRSB) for reflex sympathetic dystrophy. pp 212-215

Chapter 30: Anticonvulsant drugs. pp 221-230

Chapter 31: Antidepressants in neuropathic pain. pp 231-241

Chapter 34: Chronic pain: conclusion. pp 251-257

Merskey H, and Spear FG: *Pain: Psychological and Psychiatric Aspects*. Balliere,

OUT-OF-DATE

Tindall & Cassell, London, 1967

Morley S, Eccleston C, and Williams A. Systematic review and meta-analysis of randomized controlled trials of cognitive behavior therapy and behavior therapy for chronic pain in adults, excluding headache. Pain 80 (1999) 1-13

Moulin DE, Iezzi A, Amireh R, et al.: Randomised trial of oral morphine for chronic non-cancer pain. Lancet 347:143-147, 1996

Onghena P, Van Houdenhove B: Antidepressant-induced analgesia in chronic non-malignant pain: A meta-analysis of 39 placebo-controlled studies. Pain 49:205-219, 1992

Ongley MJ, Klein RG, Dorman TA, et al: A new approach to the treatment of chronic low back pain. Lancet 18:143-146, 1987

Oxman AD, Guyatt GH: Validation of an index of the quality of review articles. J Clin Epidemiol 44:1271-1278, 1991

Patel M, Gutzwiller F, Paccaud F, and Marazzi A: A meta-analysis of acupuncture for chronic pain. Int J Epidem 18:900-906, 1989

Portenoy RK. Opioid therapy for chronic non-malignant pain: Current status. In Fields et al.: Progress in Pain Research and Therapy, 1994, ISAP Press, p. 247-287.

Portenoy RK. Opioid therapy for chronic nonmalignant pain. Pain Res Manage 1996;1:17-28

Portenoy RK. Opioid therapy for chronic nonmalignant pain: current status. In: Fields HL, Liebeskind JC (eds), Progress in Pain Research and Management: Vol 1. Pharmacological Approaches to the Treatment of Chronic Pain: New Concepts and Critical Issues. Seattle: IASP Publications, 1994, pp 247-287

Portenoy RK, Foley KM. Chronic use of opioid analgesics in non-malignant pain: Report of 38 cases. Pain 1986; 25: 171-186.

Pryse-Phillips WEM, Dodick DW, Edmeads JG, et al. Guidelines for the diagnosis and management of migraine in clinical practice CMAJ 156:1273-1287, 1997

Pryse-Phillips WEM, Dodick DW, Edmeads JG, et al. Guidelines for the nonpharmacologic management of migraine in clinical practice. CMAJ 159:47-54, 1998

Rowbotham MC, Reisner-Keller LA, Fields HL. Both intravenous lidocaine and morphine reduce the pain of postherpetic neuralgia. Neurology 1991; 41: 1024-1028.

Rowbotham, M., Harden, N., Stacey, B., Bernstein, P., Magnus-Miller, L. Gabapentin for the treatment of postherpetic neuralgia: a randomized controlled trial.
Scheer SJ, Watanabe TK, and Radack KL: Randomized controlled trials in

OUT-OF-DATE

industrial low back pain. Part 3. Subacute/chronic pain interventions. Arch Phys Med Rehabil 78:414-423, 1997

Shekelle PG, Adams AH, Chassin MR, Hurwitz EL, and Brook RH: Spinal manipulation for low-back pain. Ann Intern Med 117:590-598, 1992

Sonne M, Christensen K, Hansen SF, et al: Injection of steroids and local anaesthetics as therapy for low-back pain. Scand J Rheumatol 14:343-345, 1985

Spitzer W (chair) and Task Force: Report of the Quebec task force on spinal disorders. Spine (Supp.) 12(7S), 1987

Ter Riet G, Kleijnen J, and Knipschild P: Acupuncture and chronic pain: a criteria-based meta-analysis. J Clin Epidemiol 43:1191-1199, 1990

Tunks E, Crook J, and Crook M. Natural history and efficacy of treatment of chronic pain arising from musculoskeletal injury. In: Injury and the New World of Work. Sullivan T (Ed.), (Chapter, in press, U. of British Columbia Press, 1999)

Turk DC, Meichenbaum D. A cognitive-behavioural approach to pain management. In Wall et al.: Textbook of Pain, 1994, Churchill Livingstone, p. 1337-1348.

Turner JA: Educational and behavioral interventions for back pain in primary care. Spine 21:2851-2859, 1996

Turner JA, and Denny MC: Do antidepressant medications relieve chronic low back pain? J Fam Practice 37:545-553, 1993

Van der Heijden GJMG, Beurskens AJHM, Koes BW, Assendelft WJJ, de Vet HCW, and Bouter LM: The efficacy of traction for back and neck pain: A systematic, blinded review of randomized clinical trial methods. Physical Therapy 75:93-104, 1995

Van der Heijden GJMG, Van der Windt DAWM, Kleijnen J, Koes BW, Bouter LM. Steroid injections for shoulder disorders: a systematic review of randomized clinical trials. Brit J Gen Practice 46: 309-316, 1996

Van Tulder MW, Koes PW, and Bouter LM: Conservative treatment of acute and chronic nonspecific low back pain. Spine 22:2128-2156, 1997

Vainio A, Ollila J, Matikainen E et al. Driving ability in cancer patients receiving longterm morphine analgesia. Lancet 1995; 346: 667-670.

Vigano A, Fan D, Bruera, E. Individualized use of methadone and opioid rotation in the comprehensive management of cancer pain associated with poor prognostic indicators. Pain 1996; 67: 115-119.

Watson CP, Babul N. Efficacy of oxycodone in neuropathic pain: A randomized trial in post-herpetic neuralgia. Neurology, 1998; 50: 837-841.
Watts RW, Silagy CA: A meta-analysis on the efficacy of epidural corticosteriods in the treatment of sciatica. Anaesth Intens Care 23:564-569, 1995

OUT-OF-DATE

Weir R, Browne GB, Tunks E, Gafni A, and Roberts J: A profile of users of specialty pain clinic services: predictors of use and cost estimates. J Clin Epidemiol 45(1992) 1399-1415

World Health Organization: Pocket Guide to the ICD-10 Classification of Mental and Behavioural Disorders. Churchill Livingstone, Edinburgh, 1994

Wreje U, and Brorsson B: A multicenter randomized controlled trial of injections of sterile water and saline for chronic myofascial pain syndromes. Pain 1995; 61: 441-444

Zenz M, Strumpf M, Tryba M. Long-term oral opioid therapy in patients with chronic non-malignant pain. J Pain Symptom Manage 1992; 7: 69-77.

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Appendix A Quality of Meta-Analysis - Oxman and Guyatt's Index of the Scientific Quality of Research Overviews

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Overview

The purpose of this index is to evaluate the scientific quality (i.e. adherence to scientific principles) of research overviews (review articles) published in the medical literature. It is not intended to measure literary quality, importance, relevance, originality, or other attributes of overviews.

The index is for assessing overviews of primary ("original") research on pragmatic questions regarding causation, diagnosis, prognosis, therapy or prevention. A research overview is a survey of research. The same principles that apply to epidemiologic survey apply to overviews: a question must be clearly specified, a target population identified and accessed, appropriate information obtained from that population in an unbiased fashion, and conclusion derived, sometimes with the help of formal statistical analysis, as is done in "meta-analyses". The fundamental difference between overviews and epidemiologic surveys is the unit of analysis, not the scientific issues that the questions in this index address.

Since most published overviews do not include a methods section it is difficult to answer some of the questions in the index. Base your answers, as much as possible, on the information provided in the overview. If the methods that were used are reported incompletely releative to a specific item, score that item as "partially". Similarly, if there is no information provided regarding what was done relative to a particular question, score it as "can't tell", unless there is information in the overview to suggest either that the criterion was or was not met.

- Were the search methods used to find evidence (original research) on the primary question(s) stated?

  ☐ yes ☐ partially ☐ no

  Yes is given to meta-analysis reporting categories of sources, including years (e.g. databases-medline) used, and whether these categories were explained. Partial points are given for the category of sources and how many of the categories (e.g. electronic, hand, register) are named.

- Was the search for evidence reasonably comprehensive?

  ☐ yes ☐ can't tell ☐ no

  Yes is given if at least three categories, one of which must be electronic with key words stated, and any two others (e.g. hand, register) are reported. Key words and/or MESH terms must be stated.

- Were the criteria used for deciding which studies to include in the overview reported?

  ☐ yes ☐ partially ☐ no

  This item was thought to be reasonably explicit.

- Was bias in the selection of studies avoided?

  ☐ yes ☐ can't tell ☐ no

  Yes is given if at least two reviewers independently assess for inclusion. A consensus must be reached.

- Were the criteria used for assessing the validity of the included studies reported?

  ☐ yes ☐ partially ☐ no

  It was felt that the issues relating to publication bias should not be included in the assessment of this. Yes is given to those meta-analysis reporting "a priori" methods of validity assessment.

- Was the validity of all studies referred to in the text assessed using appropriate criteria (either in selecting studies for inclusion or in analyzing the studies that are cited)?

  ☐ yes ☐ can't tell ☐ no

  This item relates to validity assessment. Yes is given if there is a description of any criteria (either internal or external) used.

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- Were the methods used to combine the findings of the relevant studies (to reach a conclusion) reported?

  ☐ yes ☐ partially ☐ no

  This item was thought to be reasonably explicit.

- Were the findings of the relevant studies combined appropriately relative to the primary question the overview addresses?

  ☐ yes ☐ can't tell ☐ no

  For question 8, if no attempt was made to combine findings, and no statement is made regarding the inappropriateness of combining findings, check "no". If a summary (general) estimate is given anywhere in the abstract, the discussion or the summary section of the paper, and it is not reported how the estimate was derived, mark "no" even if there is a statement regarding the limitations of combining the findings of the studies reviewed. If in doubt mark "can't tell".

- Were the conclusions made by the author(s) supported by the data and/or analysis reported in the overview?

  ☐ yes ☐ partially ☐ no

  For an overview to be scored as "yes" on question 9, ***data*** *(not just citations) must be reported that supports the main conclusions regarding the primary question(s) that the overview addresses.*

- How would you rate the scientific quality of the overview?

Extensive flaws		Major flaws		Minor flaws		Minimal flaws
–	☐	☐	☐	☐	☐	☐
1	2	3	4	5	6	7

  The score for question 10, the overall scientific quality, should be based on your answers to the first nine questions. The following guidelines can be used to assist with deriving a summary score. If the "can't tell" option is used one or more times on the preceding questions, a review is likely to have minor flaws at best and it is difficult to rule out major flaws (i.e. a score of 4 or lower). It is "no" option is used on question 2, 4, 6 or 8, the review is likely to have major flaws (i.e. a score of 3 or less, depending on the number and degree of the flaws).

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Appendix B Focus Group on "Opioid" Use in Chronic Non-Malignant Pain

OUT-OF-DATE

Aim

To hear the concerns and obtain the advice of community physicians regarding the management of chronic non-malignant pain.

The Task Force representing The College (CPSO) conducted a focus group to assess the attitudes of community physicians regarding the use of opioid analgesics for the management of chronic non-malignant pain. The focus group consisted of seven family physicians from Southwestern Ontario who volunteered to discuss this issue, an academic family physician who acted as the moderator and observers from the Task Force. The format was an informal focus group discussion over two hours with anonymous transcription of the entire proceedings.

The Focus group was asked to comment on the major issues or concerns in the prescribing of opioid drugs for chronic non-malignant pain, the direction that they would like to see The College provide to address these issues and concerns and the changes they would like to see in their own practices to facilitate the management of chronic non-malignant pain.

Results

The Focus group generally felt that the use of opioid analgesics was an acceptable form of treatment for selected patients in their own practices who had failed conventional treatment for chronic non-malignant pain. They felt that family practitioners should be the primary caregivers with support from consultants in pain management and addiction as required. However, focus group members expressed a desire for guidance regarding those patients that are most likely to benefit and those patients most likely to develop behaviour suggestive of psychological dependence or addiction. They felt that a validated instrument to

assess the propensity to addiction would be valuable. They also expressed concern about the risk of "double-doctoring" and felt that a central registry for opioid prescription use would be helpful. This could be through a computerized data base through the pharmacies or through the use of triplicate prescription pads as utilized in Alberta.

The Focus group felt that it would be helpful for The College to provide recommendations for the use of opioid analgesics for chronic non-malignant pain.

However, concern was expressed that, if the recommendations were too restrictive or rigid, they could be intrusive and could actually interfere with the management of this patient population. The Focus group also recognized that any set of recommendations would have to be revised over time to reflect advances in the management of chronic non-malignant pain. The Focus group would also like to see feedback from The College regarding the use of opioid drugs for non-cancer pain.

Community physicians would like to see more CME events to help guide them in the management of chronic non-malignant pain. Finally, the Focus group would like to see more psychological support services available to explore non-pharmacologic options in the management of chronic non-cancer pain.

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Appendix C General Recommendations for Medical Management of Chronic Non-Malignant Pain

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General Recommendations for Management of Chronic Non-Malignant Pain

The general recommendations for the management of chronic non-malignant pain are outlined as follows:

- Establish a diagnosis and rule out serious causes of pain.
- Assess degree of distress and functional disability caused by pain (inquire about activities altered by pain such as work, home, leisure, ADL). Obtain pain ratings at the outset, and then at regular intervals to monitor progress. A suggestion is a follows:

My present pain is:

0	1	2	3	4	5
(No pain)	(mild)	(discomforting)	(distressing)	(horrible)	(excruciating)

My worst pain today was:

0	1	2	3	4	5
(No pain)	(mild)	(discomforting)	(distressing)	(horrible)	(excruciating)

My least pain today was:

0	1	2	3	4	5
(No pain)	(mild)	(discomforting)	(distressing)	(horrible)	(excruciating)_

- Identify aggravating and relieving factors.

- Conduct a mental status examination to rule out depression, anxiety and other conditions that might contribute to pain.

- Take alcohol and drug history. In particular, inquire about alcohol, benzodiazepines, prescription opioids, over-the-counter drugs containing opioids like Tylenol #1 and 222s, barbiturates like Fiorinal, and illicit drugs such as cannabis and cocaine.

- Inquire about psychosocial history

- Obtain records from previous physicians in order to avoid delays and duplicate investigations

- Conduct a detailed physical examination and pay attention to behaviours and findings under confrontation (direct examination) and under distraction (indirect examination). Document consistency of findings and behaviours and record pain behaviours.

- Request a pain consultation from qualified physicians if you feel you need it.

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Appendix D Do's and Don't's of Prescribing Narcotics for Chronic Non-Malignant Pain

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"Do's" of Prescribing Narcotics for Chronic Non-Malignant Pain

DO:

- Screen for current and past alcohol and drug problems.
- If in doubt, get a consultation from a specialist, colleague, or peer.
- Try first-line non-opioid medications and adjuvant treatments first.
- Focus on improving function, not complete pain relief.
- Implement a treatment contract with your patient, specifying:
  - one prescriber
  - amount to be dispensed
  - no early refills
  - consequences for breaking the contract.
- Titrate opioids carefully, looking for analgesic effectiveness, functional status, and adverse effects.
- Switch to long-acting opioid.
- Use breakthrough doses sparingly.
- Keep a narcotic prescription flow sheet on the patient's chart.

- Reassess the patient at appropriate intervals - we suggest at least every six to nine weeks.

- Make your prescriptions tamper proof - blue ink, legible, quantities in numerals as well as script and keep a carbon copy.

Use care and monitoring especially when:

- prescribing short acting opioids
- a prescription for opioids earlier than the expected or agreed time
- prescribing injectable opioids for home use (in exceptional circumstances in which other routes are unavailable and contraindicated).
- prescribing two or more different opioids at the same time
- prescribing two or more drugs with abuse potential, e.g., opioids and benzodiazepines.

"Don't's" of Prescribing Narcotics for Chronic Non-Malignant Pain

DON'T

- Prescribe large quantities of short acting opioids

- Continue to prescribe opioids when there is evidence of non-compliance, escalation, misrepresentation, or fraud, e.g. double-doctoring or forgery.

- Feel compelled to prescribe opioid or any drug if it is against your honest judgement or if you feel uncomfortable prescribing the drug.

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Appendix E Types of Opioid Analgesics

Overview

The types of opioid analgesics used for the treatment of chronic non-malignant pain include:

Full mu-opioid Receptor Agonists

Alkaloids including:

- morphine
- codeine
- hydromorphone
- oxycodone
- oxymorphone
- heroin
- hydrocodone
- dihydrocodeine

Synthetic Opioids including:

- morphinan derivatives
  - levorphanol
- phenylipiperidine derivatives
  - fentanyl
  - sufentanil
  - alfentanil
  - meperidine
- diphenylheptane derivatives
  - methadone
  - propoxyphene

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Partial mu-receptor Agonists

Partial mu-receptor agonists including

- semisynthetic alkaloids
  - buprenorphine

Mixed Agonists - Antagonists

Antagonists for mu, agonists for other opioid receptors

- semisynthetic alkaloids
  - nalbuphine
- synthetic opoids including benzomorphan derivatives
  - pentazocine

  and

  morphinan derivatives
  - butorphanol.

Opioid Receptor Antagonists

Opioid receptor antagonists include:

- naloxone
- naltrexone

Routes of Administration

The following contains a list of the routes of administration of opioid medications:

- oral
- sublingual
- rectal
- transdermal
- subcutaneous via intermittent injection or continuous infusion
- intramuscular via intermittent injection
- intravenous via intermittent injection or continuous infusion
- spinal epidural via intermittent injection or continuous infusion
- spinal subarachnoid via intermittent injection or continuous infusion
- intraventricular.

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Appendix F Information for Patients - Opioid (Narcotic) Analgesics for Non-Cancer Pain

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FOR: _____

FROM: **Dr.**_____

DATE: _____

Making Pain Tolerable

The main reason for using an opioid (narcotic) analgesic for chronic non-cancer pain is to make the pain tolerable - not to eliminate it. This treatment is usually only considered after more standard treatments such as anti-inflammatory drugs have failed. If you are agreeable, your physician will prescribe an opioid analgesic for you in gradually increasing doses to minimize side effects. It is extremely important that you follow the directions exactly. Your physician will be the only one prescribing this medication to you. If you increase the dose without your physician's permission, give the medication to another person or obtain this medication from another physician without the consent of your primary physician, the physician may stop prescribing the opioid analgesic for you.

Pain medication is only part of your chronic pain treatment program. Equally important is a gradual exercise program that will increase your activity level despite ongoing pain. You and your physician should agree on specific ongoing treatment goals.

What is My Risk of Addiction?

There is increasing scientific evidence that strong painkillers can relieve some pain in selected patients without causing addiction. It is important to be careful, however, when defining what "addiction" is. Addiction, or psychological dependence, is a pattern of drug use in which the patient craves a drug for its ability to produce a "high" rather than for its pain-relieving properties. This can lead to the selling and injection of drugs and attempts to obtain drugs from multiple physicians - activities generally referred to as "drug abuse". Studies have shown that if a person has no past history of drug abuse and the pain is physical in origin, the risk of addiction is extremely low. If you are placed on an opioid analgesic for a period of weeks, however, and then are suddenly taken off the medication, it is possible to experience a short withdrawal reaction. Although this can be prevented by withdrawing the drug slowly, it does not mean that you have developed a craving for the drug or developed a drug addiction.

What are the Side Effects?

Although opioid analgesics can produce side effects (drowsiness, confusion, nausea, constipation), these can be minimized by slowly increasing the dose of the drug and by using anti-nausea drugs and bowel stimulants. Pain medication as prescribed will not depress your respiration or prevent you from breathing normally.

Remember Your Follow-up

If you seem to benefit from the pain medications, your physician will see you about every 4 to 6 weeks for the first few months and about every two to three months thereafter. During each visit, you and your physician will assess pain relief, any side effects from the pain medication and your ability to meet your established activity goals.

Other Instructions: _____

_____

_____

_____

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Appendix G Sample Treatment Contract

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Treatment Contract

I understand that I am receiving opioid medication from Dr. _____ to treat my pain condition. I agree to the following conditions under which this medication is prescribed:

- I will not seek opioid medications from another physician. Only Dr._____ will prescribe opioid for me.
- I will not take opioid medications in larger amounts or more frequently than is prescribed by Dr. _____.
- I will not give or sell my medication to anyone else, including family members; nor will I accept any opioid medication from anyone else.
- I will not use over-the-counter opioid medications such as 222's and Tylenol #1.
- I understand that if my prescription runs out early for any reason (for example, if I lose the medication or take more than prescribed), Dr. _____ _____will not prescribe extra medications for me; I will have to wait until the next prescription is due.
- I understand that if I break these conditions, Dr. _____ may choose to cease writing opioid prescriptions for me.

Patient's Signature:_____

Physician's Signature:_____

Date:_____

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Appendix H Sample Pain Scale

Sample Pain Scale

Please circle the number which best describes where you pain level is right now:

0	1	2	3	4	5	6	7	8	9	10
No pain										**Worst possible pain**

Sample Pain Diary

Write down you pain level in the diary at the same hour every day.

Day	Morning	Afternoon	Evening	If You Get Up at Night

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Day	Morning	Afternoon	Evening	If You Get Up at Night

OUT-OF-DATE

Appendix I Sample Narcotic Flow Sheet

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Sample Narcotic Flow Sheet

Patient Name:_____

Chart Number:_____

Prescribing Physician:_____

Date	Medication	Dose	Direction	Number Dispensed	Comments

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Appendix J The Role of Methadone in the Medical Management of Chronic Non-Malignant Pain: Specific Considerations

OUT-OF-DATE

Overview

This chapter deals specifically with oral methadone in the management of chronic non-malignant pain. *See Chapters 8 and 11 for General Guidelines for Opioid Use for Chronic Non-Malignant Pain*

Although the literature on methadone for non-malignant pain is scanty and based on case studies, the increasing use of Methadone for this indication requires recommendations to guide practice. Recommendations in this chapter therefore were arrived at by a consensus vote among Task Force members. Hopefully in future revisions there will be enough good literature to permit evidence based recommendations.

The use of oral methadone as outpatient maintenance therapy for opioid drug addiction is well known. There is also extensive literature on the use of methadone as a potent analgesic agent for cancer pain (Fainsinger, R. et al., 1993; Gannon, C., 1997). The potential role for methadone in the management of chronic non-malignant pain is less well known, but is being realized by an increasing number of clinicians despite the relative lack of literature support.

Methodology of Literature Searches

MEDLINE (1976 to November 1998) and the Cochrane Library were searched for randomized controlled trials involving methadone in the management of chronic non-malignant pain and none were found. A single report details one author's experience in the use of methadone for chronic non-malignant pain using case studies (Gardner-Nix, J.S., 1996). Therefore, recommendations for the use of methadone in the management of chronic non-malignant pain must be extrapolated from the cancer pain literature.

Methadone: Pharmacological Properties

Methadone is a synthetic opioid analgesic with excellent oral bioavailability and a duration of action of at least eight hours with repetitive dosing (Fainsinger, R. et al., 1993). These qualities make it an attractive drug for outpatient pain management. However, experience in the use of methadone for cancer pain has revealed that methadone is far more potent as an analgesic agent than has been suggested by equianalgesic tables derived from single dose studies (Cancer Pain, Health and Welfare Canada, 1984). With repetitive dosing, methadone is approximately ten times more potent than indicated in these standard tables (Vigano, A. et al, 1996). The main reason for this is probably the long elimination half-life of methadone (24-36 hours) which allows for much higher drug levels to be reached than could be predicted from single dose studies. This has obvious clinical implications for analgesic and side effects since methadone takes 5-7 days to reach steady state at any particular dose. The side effect profile of methadone is similar to that of other opioid analgesics and includes:

- cognitive changes
- nausea and vomiting
- constipation
- urinary hesitancy
- itching
- rarely respiratory depression.

Dose titration is critical given the potential for peak effects after 5-7 days at each dose level. Therefore, the use of methadone as an analgesic agent requires the same pain assessment skills as for any other opioid drug, but even greater scrutiny in patient monitoring of analgesic and side effects.

Potential Advantages of Methadone

Methadone has potential advantages as an analgesic agent relative to other opioid drugs. In the management of cancer pain, methadone has become popular in opioid rotation where switching from one opioid analgesic to another frequently results in improve pain control with reduced side effects (Vigano, A. et al, 1996). There are several reasons why methadone might provide a more favourable analgesic profile in a patient previously treated with morphine or hydromorphone (Gannon, C., 1997). Methadone has high affinity for delta receptors which might provide renewed analgesia in a patient whose *mu* receptors have become tolerant

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to morphine or hydromorphone. Methadone also has N-methyl-D-aspartate (NMDA) antagonist activity which may make it useful in the management of neuropathic pain. Methadone has no known active metabolites and therefore may be useful in a patient who has developed confusion and myoclonus due in part to the active metabolites of a drug like morphine. Finally, opioid rotation to a more lipid soluble drug like methadone may provide analgesia with fewer side effects such as nausea and vomiting.

Recommendations for Methadone in the Medical Management of Chronic Non-Malignant Pain

In Canada, methadone is provided as an elixir which is usually made up at a concentration of 1 mg/ml. It has a rather bitter taste and is commonly mixed with fruit juice. The low cost of methadone makes it more accessible. At equianalgesic doses, oral methadone is frequently 5-10% of the cost of other opioid analgesics (Gardner-Nix, J.S., 1996), but the lower base cost may not be reflected in the compounding fee at the pharmacy.

Opioid Naive Patients

In opioid-naive patients or patients taking codeine preparations, methadone 2.5 mg. q8h is safe and usually well-tolerated. Dose increments are 2.5 mg. q8h every five to seven days. Acetaminophen 325 mg. with codeine 30 mg. (Tylenol #3) can be used q4h as required for breakthrough pain.

Patients Receiving Major Opioid Analgesics

For patients already on a major opioid analgesic like oxycodone (e.g. acetaminophen 325 mg. with oxycodone 5 mg. "Percocet") or morphine, a reasonable starting dose of methadone is 5 mg. q8h with dose increments of 5 mg. q8h every five to seven days. A general rule is to provide careful dose titration until adequate pain relief is achieved or side effects limit further dose escalation. However, one should look for a graded analgesic response to incremental dosing. The absence of a graded analgesic response may mean that the patient is not opioid-responsive. An oxycodone preparation like Percocet can continue to be used q4h as required for breakthrough pain during the titration process. Patients should be seen weekly during the titration phase and every month or two during the maintenance phase.

Patients Who Are Switched from Relatively Large Doses of an Opioid

For patients being switched from relatively large doses of an opioid analgesic (>200 mg. oral morphine or morphine equivalents daily) Table #19 should be used to calculate equianalgesic doses. For patients taking more than 500 mg. oral morphine or morphine equivalents daily, the conversion to methadone should be staged with a third of the anticipated methadone dose being introduced every five days so that the entire conversion takes fifteen days. The dose of the previous

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opioid is decreased by a third every five days in inverse fashion (Vigano, A. et al., 1996).

Patients and co-habitants should be warned about potential side effects (especially drowsiness and respiratory depression) and the possibility that side effects can continue to evolve for five to seven days after each dose adjustment. The spouse or significant other should be available at least twice daily to monitor for toxicity. Since drowsiness commonly precedes respiratory depression, they should be instructed to call the prescribing physician if drowsiness develops to obtain advice about further dosing. This obviously requires physician availability 24 hours a day during the titration phase. Elderly patients (over the age of 65), patients with severe lung disease and patients who cannot be adequately monitored at home should be considered for inpatient initiation of methadone treatment.

Table #17 Equianalgesic Doses of Common Opioid Analgesics Relative to Oral Methadone with Repetitive Dosing

Drug	Per Os (PO)	Intramuscular/Subcutaneous
Methadone	2 mg	
Morphine	30 mg	10 mg
Hydromorphone	8 mg	2 mg
Oxycodone	15 mg	

Summary

As a minimum standard for analgesic use, it is recommended that:

- physicians be familiar with the above principles of opioid and methadone use
- physicians demonstrate and document appropriate patient work-up and selection
- documentation of the efficacy or lack of efficacy of drug trials is performed
- appropriate safeguards and supervision for opioid and methadone used in each case are in place.

In order for a physician to prescribe methadone in Canada, they must be granted an exemption under the *Controlled Drugs and Substances Act* by the Minister of National Health and Welfare. The requirement that a physician hold a special designation to prescribe methadone has been in place for several decades. The exemptions issued to prescribe methadone fall into three general categories:

- analgesia and pain management
- temporary exemption for emergency treatment and hospital admissions

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- for treatment of opioid dependence.

For exemptions which fall into the first two categories, the physician need only make application through the **Office of Controlled Substances in Ottawa**. For the treatment of opioid dependence, there are criteria which have been set by the College which must be met prior to the issuance of exemption to prescribe. Further, the College is also required to provide a recommendation to the Bureau of Drug Surveillance to support the exemption.

Regardless of the type of exemption issued to a physician by the National Minister of Health, notification is provided by the **Office of Controlled Substances in Ottawa** to the College. Generally exemptions for analgesia purposes are issued in three year intervals and renewable on request by the physician. The College of Physicians and Surgeons provides a list of exempted physicians to the College of Pharmacists in order that pharmacists can verify who is able to prescribe methadone in Ontario.

Note: *The CPSO involvement in the opioid dependence program mentioned is unrelated to the use of Methadone for analgesic purposes. If a physician wishes to obtain a permit to prescribe Methadone for analgesic purposes, he or she needs to apply to the* ***Office of Controlled Substances in Ottawa (613) 946-5139***

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Appendix K Chronic Non-Malignant Pain Evidence-Based Recommendations Task Force

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