Prescription Opioid Policy

Improving management of chronic non-malignant pain and prevention of problems associated with prescription opioid use

The Royal Australasian College of Physicians

FPM
FACULTY OF PAIN MEDICINE
ANZCA

The Royal Australian College of General Practitioners

The Royal Australian and New Zealand College of Psychiatrists

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April 2009

In 1980, the Australian Royal Commission of Inquiry into Drugs, commissioned by the Honourable Justice Williams, concluded:

...that any rational community action to limit the abuse of drugs must embrace all drugs, not merely those classified as illegal. The case for including legal drugs in any overall strategy aimed at minimising drug abuse is based not only on the seriousness of the problems associated with the abuse of these drugs, but also on the fact that the abuse of any one drug tends to be 'all of a piece' with the abuse of all drugs, legal and illegal alike.[1]

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Further copies are available from:
Policy and Advocacy, RACP
145 Macquarie Street
Sydney, New South Wales 2000, Australia
Tel +61 2 9256 5444, Fax +61 2 9256 9610
Email: mary.osborn@racp.edu.au
Website: http://www.racp.edu.au/page/health-policy-and-advocacy

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Associate Professor Robert Ali
Chair, Australasian Chapter of Addiction Medicine, (RACP, 2006-7)

Associate Professor Milton Cohen
Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists

Dr John Collins, Paediatrician
Paediatrics and Child Health Division (RACP)

Dr Malcolm Dobbin
Australasian Faculty of Public Health Medicine (RACP)

Dr Richard Hallinan
Australasian Chapter of Addiction Medicine (RACP)

Ms Mary Osborn
Policy and Advocacy (RACP)

Dr Alex Wodak (Chair)
Australasian Faculty of Public Health Medicine (RACP)

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Ms Kirra Atkinson
Health Issues Centre

Associate Professor Michael Baigent
Section on Addiction Psychiatry, the Royal Australian and New Zealand College of Psychiatrists

Dr Michael Bolton
Australasian Chapter of Palliative Medicine (RACP)

Ms Kanan Gandecha
NSW Health Department Pharmaceuticals Branch

Dr Robert Graham
Australasian Chapter of Addiction Medicine (RACP)

Dr Rhys Henning
The Royal Australian College of General Practitioners

Ms Jennie Houseman
Community Pharmacy

Associate Professor Peter Lowthian
Australasian Faculty of Rehabilitation Medicine (RACP)

Associate Professor David Reith
Paediatrics and Child Health Division (RACP)

Dr Alun Richards
Australasian Chapter of Addiction Medicine (RACP)

Professor Paul Seale
NSW Therapeutic Assessment Group

Dr Ian Scott (New Zealand)
Australasian Chapter of Addiction Medicine (RACP)

Dr Tom Solano
Joint Faculty of Intensive Care Medicine (of the RACP, Australia and New Zealand College of Anaesthetists)

Dr Michael Tedeschi
Australasian Chapter of Addiction Medicine (RACP)

Mr Tony Trimingham
Family Drug Support

Dr Lynn Weekes
National Prescribing Service

Dr Hester Wilson
Australasian Chapter of Addiction Medicine (RACP)

Contents

List of figures and tables

Figures

Tables

Foreword

This policy document is an initiative of the Australasian Chapter of Addiction Medicine. It is the final of four policies on addiction medicine, and has three broad aims:

1. Improving prescription and dispensing of opioids for people with chronic non-malignant pain (CNMP);
2. Improving management of pain in people with pre-existing drug and alcohol problems; and
3. Reducing unsanctioned use of pharmaceutical opioids, including over the counter (OTC) and prescription opioids.

The medical management of CNMP and the prescription of pharmaceutical opioids are two neglected policy areas in Australia and New Zealand, and the evidence base for policy in these areas is comparatively weak. Moreover, while much has been achieved in the reduction of heroin related harms in Australia and New Zealand in recent years, there are disturbing indicators of a steeply increasing supply of pharmaceutical opioids and related harms, including illicit use and injecting.

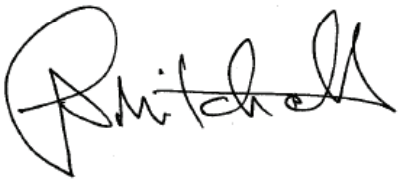
This document differs from previous policies in addiction medicine which have included tobacco, alcohol, and illicit drugs in reflecting the greater need to gather together the existing data and identify areas where further evidence is most needed. A further difference is that pharmaceutical opioids are usually supplied by pharmacists, most commonly on prescription by doctors for management of CNMP, a situation which does not resemble the legal or illegal marketplaces for tobacco, alcohol and illicit drugs. The policy document thus entails an especial element of self-scrutiny for medical practitioners, and may be correspondingly controversial. It is ironic that the group of psychoactive drugs over which the medical profession has the most control should be one about whose use so little is known.

The first target audience for this policy document is medical professionals whose responsibility is to safely prescribe and dispense effective opioid medication for people who have CNMP. Secondly, this document is aimed at health departments and professional organisations responsible for the development, implementation and dissemination of evidence-based guidelines for the treatment of CNMP and for monitoring key indicators.

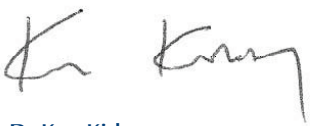
Each Medical College must work alongside clinicians and regulatory groups in all areas of healthcare to improve the treatment and management of people with CNMP. This is the first report for many years on opioid use and CNMP in Australia and New Zealand. It is anticipated that this report will spark renewed interest and activities in policy development and research in this area.

Associate Professor John Kolbe
President Elect, Royal
Australasian College of Physicians

Dr Penny Briscoe
Dean of the Faculty of Pain Medicine of the Australian
and New Zealand College of Anaesthetists (FPMANZCA



Dr Chris Mitchell
President of the Royal Australian
College of General Practitioners



Dr Ken Kirby
President of the Australia
and New Zealand College of Psychiatrists

Summary of recommendations

The issues in this summary are part of a framework required to adequately improve the management of CNMP and prevent the unintended consequences of prescribing opioid analgesics.

1. National expert advisory group to develop a coordinated approach to improve the management of CNMP and to reduce the unsanctioned use of pharmaceutical drugs

The policy document covers a number of important areas along the pathway of opioid prescribing for people who have chronic non-malignant pain (CNMP). The unintended consequences of opioid use are also a key area within this document. The document and all the components must be considered when attempting to deal with the recommendations.

2. Develop a set of guidelines that are primarily appropriate and useful for general practice

The guidelines need to incorporate a nationally standardised decision-making process for the assessment and management of patients with CNMP. They will also integrate non-pharmacological elements of treatment with a pharmacological approach in a biopsychosocial framework. An evaluation and monitoring component needs to be integrated into the development process.

3. Enhance clinical practice particularly at the primary health care interface

Most people with CNMP will have their first medical encounter in a primary health care setting. In addition to the guidelines there is a need for better coordination between the management of pain, addiction in a primary care setting.

4. Improve information systems

To monitor the prescription of drugs of dependence for the treatment of CNMP requires a system that is web based, confidential and real time. This will enable prescribing doctors and dispensing pharmacists to monitor prescriptions, to provide more effective, safer and cost-effective health care, and for government to monitor the overall use of these medications and evaluate the effectiveness of policy and other interventions.

5. Regulation and control

Regulatory strategies need to be standardised across jurisdictional boundaries in collaboration with relevant government bodies and agencies.

6. Minimising unmet demand for opioid substitution therapy (OST)

There needs to be support for an adequately sized, appropriately resourced variety of OST options for the treatment of heroin and other opioid dependence. This will reduce the diversion of pharmaceutical opioids on to the black market.

7. Training and research

The Medical Colleges need to ensure there is a strong commitment by medical practitioners for continuing medical education (CME) to enable them to engage in best practice management of CNMP and opioid prescribing.

The document identifies a number of gaps in service provision, regulation, attitudes and practice that require adequate funding and resources to undertake high quality research and to ensure the results are actioned.

Executive Summary

The aims of this report are to review the prescription of opioids for chronic non malignant pain (CNMP) in Australia and New Zealand, to consider what is known of the nature and extent of present and possible future unintended negative consequences of prescription of opioids for CNMP, and to suggest ways towards improvements in the management of CNMP and reducing adverse effects of prescription opioids.

Scope of the problem

There has been a substantial increase in prescription opioid use in Australia and New Zealand in recent years: in Australia, there was a 40-fold increase in oral morphine supply between 1990 and 2006, and a nearly 4-fold increase in oxycodone supply between 1990 and 2003.

Much of the supply of prescription opioids is in the context of treatment for CNMP. CNMP in Australia and New Zealand is common, with estimates ranging as high as 20 per cent of the population, and prevalence likely to increase with aging of the population.

Increased use of prescription opioids may be due to a number of factors, including: increasing prevalence of chronic pain; developments in pharmaceutical opioid preparations (especially the introduction of sustained release morphine and oxycodone) that have enhanced the safety and effectiveness of opioids in treating chronic pain; and consequently, a greater willingness by the medical profession to prescribe opioids, in part reversing a trend of 'under-treatment' of chronic pain of many decades. Opioids are an option for the management of some people with CNMP, when prescribed appropriately and used in sanctioned ways.

There are increasing concerns regarding problematic and/or unsanctioned use of prescription and over-the-counter opioids. There is good evidence of an increase in the number of people injecting pharmaceutical opioids, and some evidence of increased prescription fraud, however only very limited secondary data are available on service utilisation as indicators of harm. While there have been increasing numbers of deaths due to overdose of prescription opioids in USA, there is no reliable data for Australia and New Zealand.

In some parts of Australia, prescription opioids are the main opioid used illicitly, reflecting scarcity of heroin, poor regulatory control of pharmaceutical opioids and/or inadequate provision of treatment for dependent opioid users. Illicit use of pharmaceutical opioids entails risks of overdose, adverse events from injecting pharmaceutical drugs (e.g. systemic infections, respiratory fibrosis, and loss of limbs or digits) and blood borne virus (Hepatitis C Virus (HCV), Hepatitis B Virus (HBV), Human Immunodeficiency Virus (HIV)) transmission.

There are three areas of particular concern:

1. The development of dependence on prescription opioids with subsequent drug seeking behaviour by a proportion, probably small, of individuals taking prescription opioids for CNMP;
2. The use of prescription opioids by individuals with other drug and alcohol problems, often instead of illicit heroin or other drugs; and
3. The management of CNMP in opioid dependent individuals.

The data available on these populations in Australia and New Zealand is limited. Dependent heroin users (or those on substitution treatment with methadone or buprenorphine) may have a higher prevalence of CNMP than the general population. This problem may be under diagnosed, and the treatment of pain is often difficult in this population.

Gaps in Knowledge

There are still considerable gaps in our understanding of the scale of the issues, specifically:

- The extent of inappropriate prescribing and unsanctioned use, including injecting, of pharmaceutical (prescription and over the counter) opioids;
- The extent of black market diversion and illicit use of pharmaceutical opioids, including prescription forgery, internet supplies and theft (from pharmacies or warehouses); and
- The extent of harms associated with pharmaceutical opioid misuse, including the impact upon individuals and communities in terms of health, social and economic costs.

It is currently not possible accurately to quantify the extent of, and adequately to deal with, problematic prescription opioid use in Australia and New Zealand because:

- Existing monitoring systems cannot identify and track opioid prescriptions to the individual patient level;
- Inadequate monitoring systems make fraudulent presentation for opioid prescriptions difficult to identify and respond to in health settings (e.g. general practice, community pharmacies and emergency departments);
- Regulation of pharmaceutical opioids varies among jurisdictions, which impedes implementation of strategies to deal with problematic opioid use, and facilitates individuals seeking these drugs across State/Territory borders;

- The internet is further weakening regulatory controls of prescription opioids and other medications; and
- Research into these matters in Australia and New Zealand has been very limited.

Clinical research is also needed to fill gaps in the evidence on effective management of people with CNMP including:

- Is opioid therapy beneficial in the long term?
- If so, what factors predict benefit and how can benefit be maximised?
- How should opioids be prescribed optimally to achieve treatment goals and minimise adverse events?
- What is the realistic probability of dependence (addiction)?
- How can the risk assessment of problematic opioid use be improved?

Responding to the problem

There are two main causes of unsanctioned prescription opioid use and related harms -new problematic opioid use and dependence arising out of the use of pharmaceutical opioids (both prescription and over the counter) for CNMP, and the use of prescription opioids by individuals dependent on illegal opioids such as heroin, partly as a result of substantial unmet demand for treatment of opioid drug dependence. Strategies are required that deal with each of these factors.

The variety of ways in which pharmaceutical opioids may be obtained indicate that prevention of problematic use will require action at several levels, including engaging national and state regulatory bodies, professional boards and organisations, and implementing responses through law enforcement, health and community services.

Improving clinical management of CNMP

Strategies to optimise treatment of CNMP and minimise harms from pharmaceutical opioids include:

Improved and integrated primary care and specialist services for managing CNMP. Strategies for improving management of CNMP must recognise the essential role of general practitioners, facilitate the provision of multidisciplinary services at the primary care level, and enhance access to specialist pain and addiction medicine services. Multidisciplinary models of care, both in primary and specialist settings are important to optimise pharmacological and non-pharmacological management of CNMP. There is currently a substantial unmet need in the population with CNMP for services specialising in pain medicine and addiction medicine.

Clinical guidelines for managing CNMP in individuals with problem drug use and/or aberrant drug behaviours. While there are a number of guidelines in Australia and New Zealand for opioid use in CNMP, these do not specifically deal with the management of people with CNMP who use illicit drugs and/or alcohol or who engage in other high-risk behaviours. More effective treatment of CNMP involves attention to both pharmacological and non-pharmacological aspects of care. The Quality Use of Medicine (QUM) framework is an appropriate way of improving management and achieving better clinical and population health outcomes.

The development and implementation of guidelines regarding the management of CNMP and drug dependence require collaboration of multiple professional groups, including general practitioners (GPs), pain specialists, addiction medicine specialists, psychiatry, pharmacy, allied health professionals and consumer groups. The role of GPs is crucial in the implementation of guidelines, as most patients with CNMP are managed largely in primary care settings. Further, at present there are few mechanisms that examine professional compliance with existing guidelines. Provision should be made for compliance with guidelines to be monitored, and for effective and reasonable sanctions on medical professionals who repeatedly or substantially breach the guidelines.

Universal precautions in opioid prescribing. There is a need to improve the capacity of medical practitioners and other health professionals (including pharmacists) to identify patients at risk of developing opioid dependence and related problems, and increased awareness of aberrant drug behaviours that may appear during therapy, including the diversion of opioids. The conceptual framework 'universal precautions in pain medicine and opioid prescribing' has potential for prevention and early identification of problematic opioid use as well as appropriate 'triage' into levels of specialist care as needed, including pain, addiction medicine or psychiatry.

Regulatory controls and monitoring the use of prescription opioids

A key barrier to effective responses to this problem is the current inability of doctors and pharmacists to monitor their patients' use of prescription medications. Improved systems for collection of complete data regarding prescription and use of opioids are needed in Australia and New Zealand.

Prescription monitoring programs have the following potential benefits:

1. Enabling doctors to identify patients whose behaviour is problematic (e.g. doctor shoppers, dose escalation and use of other psychoactive prescription drugs);
2. Providing feedback to doctors about their practice compared with other doctors (the National Prescribing Service (NPS) does this for GPs in Australia);

3. Identifying doctors whose practice may be aberrant, and seek to rectify this through professional development, including counseling, education or other interventions.

Technological advances enable electronic data management of prescribing and dispensing, and provide for encryption and secure electronic data transmission. Such data can be provided in real time to doctors at the time of prescribing, and to pharmacists at the time of dispensing. Prescription of opioids should require robust identification of the patient at the time of medical consultation or at the pharmacy. Data collection systems should provide privacy safeguards and establish an audit trail to identify every time the patient's record is opened.

Role of pharmacists. Pharmacists, like doctors, have among their professional responsibilities an important role in monitoring and questioning the use of prescription opioids, and advising patients on the most effective and safe way to take their medications. There should be an emphasis on increasing pharmacists' ownership of issues related to opioid control, and improving pharmacists' screening of prescriptions and patients. Pharmacists should be recognised as key stakeholders in a multidisciplinary group to implement and evaluate policy.

Responding to problematic use of pharmaceutical opioids

Limited access to good quality, affordable and attractive Opioid Substitution Treatment (OST) for heroin dependent persons may be contributing significantly to the increasing diversion of opioids by increasing the price of black market prescription opioids. It is important to minimise unmet demand for opioid substitution therapy, by increasing the range of treatment options for heroin and prescription opioid dependent people and providing OST as attractively as possible. This can be achieved by making it easy to access, providing good quality care and providing OST free, or charging minimum fees.

The provision of sterile injecting equipment to reduce the spread of blood borne viruses should remain a public health priority, with efforts to reduce remaining obstacles to access. Injecting drug users should be encouraged to use filters, especially where pharmaceutical opioids containing particulate matter may be injected.

Novel pharmaceutical products which may discourage the injection of prescription opioids (such as the combination of buprenorphine-naloxone already licensed in Australia), should be considered based upon their safety, effectiveness and cost effectiveness. These approaches have the potential to increase treatment accessibility without the dispensing restrictions of traditional opioid substitution medications (e.g. methadone).

Training and research

To ensure patients receive evidence-based care for the treatment and management of CNMP, there must be a long term commitment to research, particularly by health professionals who are dedicated to this area of medicine.

Research is also needed into effective public education and early intervention measures to reduce problematic use of opioid medications.

Increased collaboration of the Australasian Chapter of Addiction Medicine (AChAM), the Faculty of Pain Medicine (FPMANZCA) and the Royal Australian College of General Practitioners is needed in training, research, and clinical practice and in developing, with the NPS feedback, audit and other professionals behaviour change interventions informed by clear treatment guidelines.

Recommendations

The working group recommends the following strategies and actions and suggests that it is reasonable to expect these to be achieved across Australian states and territories and New Zealand by 2020.

1. Establish an expert advisory group to develop a national strategy to improve the management of CNMP and to reduce the unsanctioned use of pharmaceutical drugs

Governments should establish a national expert advisory committee to develop a national strategy that:

- Reviews the available information on improving health, social and economic outcomes for people with CNMP and those with opioid dependence;
- Engages community groups, consumers, key organisations and experts in the area of pain and addiction management;
- Provides a framework for a coordinated and integrated approach to inappropriate prescribing and problematic use of opioids in the Australian and New Zealand communities; and
- Monitors and evaluates the implementation plan.

Key stakeholders should be identified by the Australian Department of Health and Ageing (DoHA) and the New Zealand Ministry of Health ensuring strong ownership by a multidisciplinary group that represents clinical experts, pharmacists, patients, communities and the pharmaceutical industry.

2. Improve endorsement of and compliance with guidelines for the assessment and management of patients with CNMP

Develop a nationally standardised decision-making process for the assessment and management of patients with CNMP.

Integrate non-pharmacological elements of treatment with a pharmacological approach in a biopsychosocial framework.

Develop guidelines for prescribing opioids for CNMP that are:

- Based on the best available evidence, cost effective and observe the basic ethical rights for people to receive the best quality of care;
- Widely owned and strongly endorsed across the medical profession;
- Accompanied by resources to assist in a thorough implementation strategy, including a plan for monitoring;
- Evaluated to identify adherence with best practice prescribing of opioids for CNMP; and
- Readily accessible to health professionals using widely available sources such as the Australian Medicines Handbook (AMH), and relevant professional training materials.

Ensure GPs have a leading role in the design and implementation of clinical guidelines for the management of CNMP. This process will have a number of separate strategies including:

- Supporting GPs through their professional organisations to accept ownership of CNMP guidelines;
- Developing attractive and effective programs to improve GP management of CNMP;
- Ensuring guidelines for CNMP are integrated into clinical software systems used in general practice; and
- Increasing collaboration between the sections of the medical profession and other health authorities involved in CNMP clinical policy and practice.

3. Improve information systems

Develop a best practice system for monitoring the prescription of drugs of dependence for the treatment of CNMP. This system should be web based, confidential and real time. This will enable prescribing doctors and dispensing pharmacists to monitor prescriptions, to provide more effective, safer and cost-effective health care, and for government to monitor the overall use of these medications and evaluate the effectiveness of policy and other interventions.

The Colleges recommend and will advocate for improved systems for collection of data regarding the prescription and use of opioid analgesics and other prescription drugs of dependence. Such systems could have the following features:

(i) Robust identification of the patient, similar to evidence needed to establish, for instance, a bank account, with photo ID or biometric ID;

(ii) Online, real time medication history available to potential prescribers at the time of prescribing, and to pharmacists at the time of dispensing;

(iii) Protected PIN held by the patient or accessible via a secure mechanism;

(iv) 24 hours per day, 7 days per week access by prescribers and pharmacists to prescription shopping information systems or the New Zealand equivalent, to identify unsanctioned use;

(v) Privacy safeguards; and

(vi) An audit trail to identify when patient's record are accessed.

It is also recommended that strategies to monitor compliance with guidelines for opioid prescriptions for CNMP be developed, including monitoring and surveillance of opioid prescriptions to include all Pharmaceutical Benefits Scheme (PBS) / Veterans Affairs and 'private' prescriptions.

4. Enhance clinical practice

The Colleges should work in partnership with clinicians in primary healthcare and other appropriate settings to ensure that there is a best practice system for prescribing opioids by:

- Ensuring there are evidence-based guidelines for safe and high quality management of people with CNMP;
- Developing an effective, consistent national process for monitoring the prescribing of opioids for management of CNMP;
- Increasing the capacity of services specialising in pain and addiction medicine to meet the unmet demand in the population with CNMP;
- Providing opportunities for interdisciplinary teams to work in clinical settings where patients present with CNMP and prescription drug dependence;
- Providing training for allied health professionals to deliver non-drug treatment modalities for people with CNMP;
- Developing indicators that identify improved delivery of care for people who have CNMP;
- Reducing prescribing that is inconsistent with CNMP clinical guidelines and/or jurisdictional legal requirements, especially for people who have problem opioid use; and
- Developing effective responses, including professional development and, where necessary, sanctions, for medical professionals who repeatedly prescribe opioids in breach of CNMP clinical guidelines for prescribing opioids.

5. Minimising unmet demand for opioid substitution therapy (OST)

The Colleges recommend, and will encourage governments and professional groups to support, an adequately sized, appropriately resourced variety of OST options for the treatment of heroin and other opioid dependence. This will reduce the diversion of pharmaceutical opioids on to the black market. Treatment should be improved by:

- Increasing the range of OST options for heroin and other opioid dependent people; and
- Providing good quality care OST as accessibly and attractively as possible, and at a minimum cost to the patient.

6. Training

The Colleges, through their specific education programs for training and Continuing Professional Development (CPD), will:

- Work in partnership to commission a series of learning modules, teaching materials and assessment tools to complement professional training programs, such as those of the RACP, AChAM, AFPHM, Faculty of Pain Medicine (ANZCA), Royal Australian College of General Practitioners (RACGP) and Royal New Zealand College of General Practitioners (RNZCGP), Royal Australian and New Zealand College of Psychiatrists (RANZCP), Australian and New Zealand College of Anaesthetists (ANZCA);
- Ensure there is a strong commitment by medical practitioners for continuing medical education (CME) to enable them to engage in best practice management of CNMP and opioid prescribing; and
- Develop processes for AChAM, ANZCA and other professional bodies to work together in training, research and clinical practice.

7. Research

The Colleges will advocate that research funding bodies identify and prioritise gaps in evidence on effective management of people with CNMP. Such projects may include:

- Research into the attitudes of medical practitioners to CNMP, to the use of opioid analgesics in its population, to the use of guidelines and to regulation;
- Research examining the prevalence and harms associated with pharmaceutical (prescription and over the counter) opioid use by different populations, including alcohol and other drug dependent populations;
- Research examining the morbidity attributed to pharmaceutical opioids, including opioid related deaths;
- Research examining the prevalence, impact and response to CNMP in individuals with mental health and substance use disorders, and the prevalence of mental health and substance use problems in individuals with CNMP;
- Research examining the impact of regulatory changes, guidelines and training initiatives upon patterns of prescription opioid use and related harms;
- Clinical research examining optimal treatment responses and interventions for individuals with CNMP and substance use or mental health disorders;
- Translational research to identify the best strategies at the practice level to ensure consistent approaches; and
- Research examining professional development issues in the management of pharmaceutical opioids, including regulatory and training initiatives and the use of clinical guidelines.

8. Regulation and control

The Colleges advocate that regulatory strategies be standardised across jurisdictional boundaries in collaboration with relevant government bodies and agencies, by:

- Comparing relevant jurisdictional legislation to identify the optimal systems;
- Reviewing the principles underlying PBS / the Pharmaceutical Management Agency of New Zealand (PHARMAC) subsidisation of controlled drugs; and
- Coordinating the monitoring of opioid supply across jurisdictional boundaries.

1. Introduction

1.1 Scope and Aims

Representatives from the Royal Australasian College of Physicians (RACP), the Royal Australian and New Zealand College of Psychiatrists (RANZCP), the Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists (FPMANZCA), the Royal Australian College of General Practitioners (RACGP), the Joint Faculty of Intensive Care Medicine (JFICM), Community Pharmacy, NSW Health Department Pharmaceuticals Branch, the National Prescribing Service (NPS), the NSW Therapeutic Assessment Group (NSW TAG) and consumer groups have worked together on this policy document.

The policy document is an initiative of the Australasian Chapter of Addiction Medicine. This is the fourth policy on addiction medicine and deals with three broad issues:

1. Improving prescribing and dispensing of opioids for people with chronic non-malignant pain, with a special emphasis on reducing problematic opioid use including dependence;
2. Improving management of pain in people with a pre-existing drug and alcohol problems; and
3. Reducing unsanctioned use of pharmaceutical opioids, including over the counter and prescription opioids.

The first target audience for this policy document is medical professionals whose responsibility is to safely prescribe and dispense effective opioid medication for people who have CNMP. Secondly, this document is aimed at health departments and professional organisations responsible for the development, implementation and dissemination of evidence-based guidelines for the treatment of CNMP and for monitoring key indicators.

In 1980 the Australian Royal Commission of Inquiry into Drugs, commissioned by the Honourable Justice Williams, concluded,

> *... that any rational community action to limit the abuse of drugs must embrace all drugs, not merely those classified as illegal. The case for including legal drugs in any overall strategy aimed at minimising drug abuse is based not only on the seriousness of the problems associated with the abuse of these drugs, but also on the fact that the abuse of any one drug tends to be 'all of a piece' with the abuse of all drugs - legal and illegal alike.* [1]

People who develop problems from their use of pharmaceutical opioids for pain relief, as well as their friends and families, face an array of complex problems when seeking help. Often healthcare services are not easily identified or available for this group of people. Health professionals are often not well trained or experienced to prevent, manage and treat these complex problems and at times have to make difficult clinical and ethical decisions. [2] For this reason, a wide range of health professionals was brought together to assist in developing a policy which would arrive at an agreed set of recommendations to deliver better health and social outcomes.

1.2 Background

Prescription opioid use in Australia and New Zealand

Information on trends in opioid use for CNMP is more readily available in the United States of America (US) than in Australia and New Zealand. US data indicates the supply of prescription opioids has increased over the past two decades, with increasing use of prescription drugs, primarily opioids, for non-medical purposes, particularly by young people.[3] There are also increasing reports of deaths from prescription opioid overdose. [4 5 6 7] Prescription drugs are now reported as the second most commonly abused category of drugs after cannabis, ahead of cocaine, heroin, and methamphetamine.[3] Despite the limitations of surveillance in Australia and New Zealand, similar trends in consumption of prescription opioids are becoming apparent in these countries.

It is not clear from current the data sources how many people in Australia and New Zealand have CNMP and have been prescribed opioids. Nor is it clear how many people have CNMP, are dependent on prescription opioids, whether legally or illicitly obtained, and need further and improved treatment for their pain.

The replacement of oral, shorter acting and injectable opioids by longer acting orally well absorbed opioids is a welcome development because of their superiority in maintaining therapeutic plasma levels throughout the dosing period. However, in Australia in recent years the injection of prescription oral opioids has been increasingly reported.[8] [9] Increasing unsanctioned prescription drug use may reflect a large and possibly growing unmet demand for opioid substitution therapy (OST).[9]

Chronic non-malignant pain

Studies in Australia, New Zealand and Europe show that 5-10 per cent of the population have severe persistent pain. [10 11] In 2002, an Australian study reported that up to 20 per cent of the population suffer pain and that pain is strongly associated with markers of social disadvantage. CNMP is associated with elderly populations, retirement and inability to take part in the paid workforce. [10] The reported prevalence

of opioid dependence among CNMP patients varies between clinical settings. [12] A review of studies conducted in tertiary care pain clinics in the US found that prevalence ranged from 3 per cent to 19 per cent or more. [13 14]

In Australia and New Zealand the prevalence of chronic pain is projected to increase as the population in these countries ages. [11 15]

Little information on the management of pain is available at a population level. The literature on CNMP has frequently cited the need for more complete and comprehensive epidemiologic data on pain (See chapter 3). [16 17]

Management of CNMP

The effective management of CNMP is a challenge for clinicians. Although pharmacological aspects of CNMP management are usually emphasised, non-pharmacological aspects are also very important. Despite extensive research into treatment options for CNMP, particularly in relation to opioid prescribing, there are still considerable uncertainties and a lack of consensus about what constitutes effective care. Under-prescribing of opioids for CNMP often results from a reluctance to treat CNMP with opioids in the first place. Inappropriate prescribing and over-prescribing would be less prevalent if there were better compliance with guidelines.[18]

Opioids in CNMP

The role of opioids in the management of CNMP is still being defined. There are surprisingly few studies evaluating the benefits and side effects of opioids in CNMP particularly their effectiveness in the long term. However, most pain specialists consider that opioids play an important role in alleviating CNMP.[19] Recent research suggesting that prolonged use of high dose opioids may reduce pain tolerance is not yet universally accepted, and the clinical implications of these studies are unclear.

There is now widespread evidence for the view that opioid management of CNMP can avoid the analgesia and euphoria of plasma peaks and the return of pain and dysphoria associated with low troughs. Short acting opioids are more strongly reinforcing than longer acting opioids and are best avoided in the management of CNMP.

In Australia and New Zealand there has been persistent advocacy by a group of concerned medical professionals and community groups for greater monitoring and quality use of opioid prescribing. [20 21] This concern extends to the diversion of opioids through general practitioners and pharmacies. [22] Current guidelines on managing patients with CNMP, including the prescription of opioids, are broadly consistent in their messages. However, the uptake and influence of these guidelines has been generally poor. A consistent finding in policy and research is the gap between evidence and practice. Up to 40 per cent of patients do not receive care according to present scientific evidence, and up to 25 per cent of care provided is not needed or potentially harmful. [23] This policy will outline strategies needed for greater ownership and more successful implementation of appropriate guidelines.

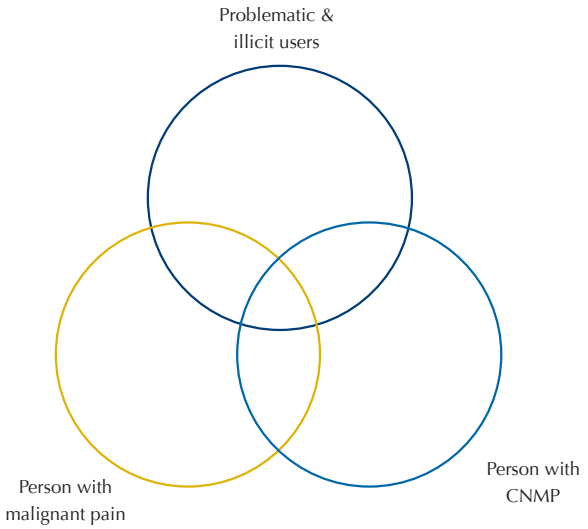
A number of factors can discourage primary care doctors from managing CNMP patients with opioids. Some fear the cognitive, respiratory, and psychomotor side effects of opioids. Others may be concerned about the risk of creating problematic opioid use, or contributing to diversion of prescription drugs to the black market. [24 25]

The risks of treating patients with a known history of a substance use disorder [26] are generally acceptable if clinicians are encouraged and supported by colleagues, professional bodies and departments of health. In Australia and New Zealand there are a number of guidelines on management of CNMP, all with differing levels of compliance by medical practitioners. One of the benefits of having widely accepted and implemented CNMP guidelines would be to distinguish between doctors doing their best in very difficult clinical circumstances and those whose practice was aberrant.

Legal and unsanctioned opioid use and dependence

Three overlapping markets for prescription opioids are patients who have malignant pain, patients who have CNMP and people who use opioids in unsanctioned ways, (both problematic and illicit users). In Australia over a 12 month period in 2004, 3.1 per cent (0.6 million) of the population aged 14 years and over reported that they had used pain killers for non-medical purposes.[27] Figure 1 illustrates the cross-over that exists between three groups of people who may require opioid treatment: if one of these three areas is being inadequately managed there may be flow on effects.

Figure 1: The three main groups of people who experience pain and require opioid treatment



There is now good evidence that treatment of opioid dependence, whether arising from street heroin or prescription opioids, with opioid substitution treatment (OST) is generally effective. Well managed OST reduces illicit opioid drug use, achieves excellent treatment retention, decreases criminal activity, reduces the risk of blood-borne virus transmission, and improves social functioning. [28 29]

Some people may become frustrated with the logistics of getting access to OST, and consequently purchase opioids on the black market or feign pain to get prescription opioids. This is illustrated in Figure 2 through a set of steps for interaction between the different groups of people who require OST and the flow-on effects.

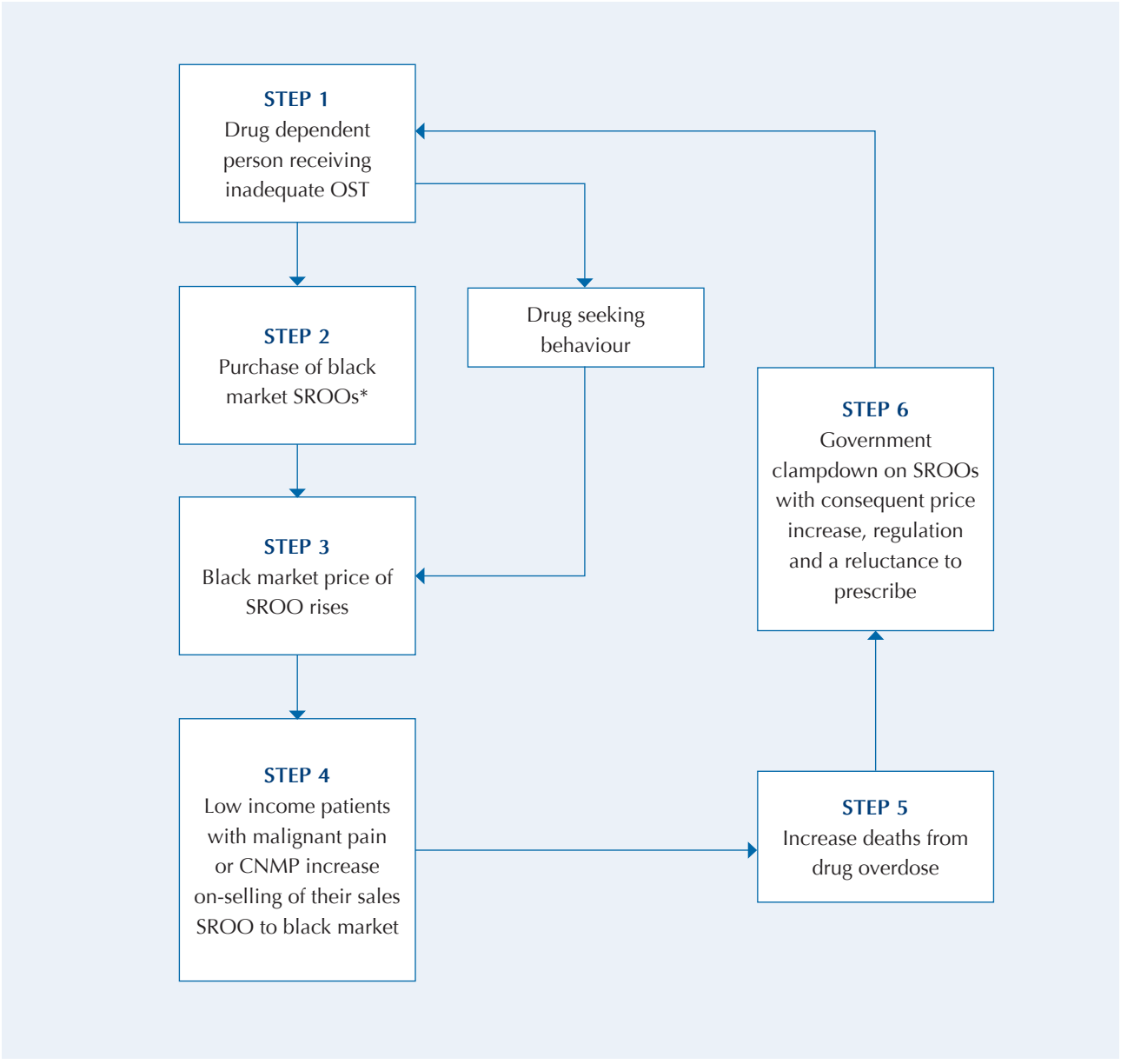
1.3 Conceptual framework for this policy document

Harm minimisation

Most of the measures described in this report are aimed at reducing inappropriate demand for and supply of prescription opioids. However, as some level of unsanctioned use of these medications is likely to continue, measures for reducing harms, especially those associated with injecting of prescription opioids are also considered.

Harm minimisation forms the conceptual framework of the Australian National Drug Strategy and its various subsidiary and derivative documents, as well as the first three of the suite of four policies on addiction of the RACP.

Figure 2: Postulated steps for interaction between the different groups of people who require opioid treatment



*SROOs (sustained release oral opioids)

'Harm minimisation encompasses:

- Supply reduction strategies to disrupt the production and supply of illicit drugs and the control and regulation of licit substances;
- Demand reduction strategies to prevent the uptake of harmful drug use, including abstinence-oriented strategies to reduce drug use; and
- Targeted harm reduction strategies to reduce drug-related harm for individuals and communities.' [30]

The harm minimisation concept developed out of the need to reduce harms of illicit drug use, with the recognition that some drug use will continue and that a greater good is served by considering the total harms associated with drug use rather than merely considering the incidence and prevalence of drug use. This idea has been usefully extended to alcohol and tobacco smoking, both legal drugs where use is more or less socially sanctioned.

The question in relation to this document is whether the concept of harm minimisation can be extended to legal medications generally available only by doctor's prescription? There are several reasons for believing this may be so:

- the psychoactive properties of opioid analgesics;
- overlap between illicit opioid and prescription opioid use; and
- potential flow on effects of policies relating to opioid prescription to the use of other substances, including alcohol, benzodiazepines and illicit drugs (heroin, cannabis) (see Figure 2)

Some qualification of the concept may be needed in considering prescription opioids, where supply usually arises out of a clinical relationship of medical practitioners with patients (or clients). Although supply is ultimately regulated by medical practitioners, they may also have a role in regulating demand, thus not bearing easy comparison with the suppliers of illicit substances and of tobacco and alcohol. Opioids have a therapeutic purpose not bearing simple comparison with the perceived benefits of tobacco, alcohol and illegal substances. With these caveats and appropriate modifications, the principles of harm reduction will be used as conceptual framework for this policy document.

Harm minimisation has potential for reducing the burden of morbidity and mortality for people with CNMP. It was estimated that in 2002/2003 the federal and state governments in Australia [31] spent AUD3.2 billion responding to illicit drugs. Most of the direct spending was on law enforcement (56 per cent), with 23 per cent allocated to prevention strategies and only 17 per cent spent on treatment.

In most countries, authorities have imposed restrictions on the supply of prescription opioids. However, this is unlikely to be effective in the absence of an adequately sized, appropriately resourced variety of opioid substitution treatment options for the treatment of opioid dependence. The importance of harm reduction policies (considered in Section 6.6) is all the greater given the likelihood that future supply controls will be weakened by the increased availability of prescription drugs through internet pharmacies.[32]

Decisions about the use of analgesic drugs subject to diversion and harmful use need to balance the potential benefits of control of pain against the risks of diversion and harmful use and trafficking of these drugs. Unless measures are taken to prevent large scale diversion and harmful use of these drugs, reluctance to use them, because of fear of diversion or scrutiny by authorities, may deter appropriate use.

Biopsychosocial models for opioid dependence and for chronic pain

Many of the harms associated with opioid use are associated with opioid dependence: this document is based on an understanding of both pain and dependence through a biopsychosocial model. Such a model recognises the complex interaction among biological processes (including the actions of a drug), the psychology of the individual and wider societal factors.[33]

Similarly patients in pain present with both physical and psychological symptoms, often reflecting social and environmental influences. Chronic pain is currently viewed as a biopsychosocial phenomenon that can have a profound impact on people's lives. [34 35]

Co-morbid illness in chronic pain and in addiction

The World Health Report 2002 [36] estimated that 8.9 per cent of the total burden of disease is attributable to the use of psychoactive substances, defined as follows: 'A psychoactive substance is one that, when ingested, alters mental process – that is thinking or emotion.'[37] Further, there is higher prevalence of substance use problems, including dependence, in individuals with mental illness compared to individuals without any mental disorder. [19 20]

There are several hypotheses that may explain why mental illness and substance dependence tend to co-occur: [38 39]

1 There may be a similar neurobiological basis;
2 Substance use may help to alleviate some of the symptoms of mental illness or side effects of medication; or,
3 Substance use may precipitate mental illness or lead to biological changes that have common elements with mental illnesses.

Psychological co-morbidity is also common in people with chronic pain (See Ch3.5).

There is thus often a strong relationship between severe dependence on pharmaceutical opioids and other substance use and mental health problems. Many people who use opioids problematically experience problems in family, physical and mental health, legal, financial and other lifestyle domains. Problematic drug use may be inextricably linked to problems that existed prior to drug use (for example, sexual abuse, mental health problems) and to current quality of life issues. Effective interventions are often those that enhance, or are associated with improvements in, quality of life subsequent to any change in drug taking behaviour. Thus, relapse risk is higher if a person gives up harmful drug use and his or her quality of life remains poor. [40]

While substance use in men accounts for 33 per cent of the mental health burden in Australia, [41] there is also significant social effect for the women and children in the lives of men with substance use problems. Although women's use of illicit drugs is less than that of men, the health impact of problematic use of prescription medicines can be greater for women. [42]

Conceptual model for integrating management of pain and addiction

There has been an historical tension between acceptable and unacceptable use of opioids, and over where the boundaries lie between them, reflected in the history of opioid control in Australia, (see Chapter 5, Regulation of opioid prescribing). In contempory medical practice the use of opioids is largely defined by the existence of pain. This is reflected in the development of the distinct specialties of pain medicine and addiction medicine. One result has been a separation of facilities for pain and addiction management, such that a patient may cross from one world to the other, or falls between the two worlds. This has a parallel in the historical disjunct between mental illness and addiction, so called 'dual diagnosis.'

The collaboration of medical colleges in this document is an acknowledgement of the need to integrate the perspectives of pain medicine and addiction medicine. Harm minimisation and a biopsychosocial model for addiction together provide a conceptual basis for unifying these perspectives in a way that can go to the core of good medical practice. This is discussed in Chapter 4(Universal Precautions in Pain Management).

1.4 Definitions used in this document

Definitions relating to pain

Pain can be defined as 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage'. [43]

Chronic pain is conservatively defined as continuous or recurrent pain that persists past the normal time of healing, most commonly about three month's duration.

Opiates and opioids

Opioids are drugs that have actions similar to those of morphine. Opiates, a term commonly but incorrectly used synonymously with opioids, are substances that are derived from opium and strictly speaking include only codeine and thebaine. For the purposes of this document 'opiates' refers to drugs derived from the opium poppy: morphine, heroin, codeine and thebaine; 'opioids' refers to drugs that have actions similar to those of morphine including the opiates, but also synthetic and semi-synthetic drugs including pethidine, hydromorphone, fentanyl, methadone, buprenorphine, oxycodone, dextropropoxyphene, dextromoramide, pentazocine, tramadol and others (see Appendix three), all of which are 'prescription opioids' in Australia and New Zealand.

The term 'opioid analgesic' is preferred to 'narcotic analgesic'. Narcotic has lost its precise pharmacological meaning and connotes illicit or illegal use.

Terminology relating to substance use

Healthcare professionals and others often use terminology related to substance use problems inconsistently. Therefore there is a need for caution when interpreting publications especially for developing policy. The International Classification of Diseases (ICD) produced by WHO is the most widespread system used in health epidemiology. [44] However the Diagnostic and Statistical Manual of Mental Disorders (DSM) is commonly used for mental health problems including substance use problems.

In common parlance the terms 'drug dependence' and 'drug addiction' are often used interchangeably. 'Harmful Use' (ICD) and 'Abuse' (DSM) refer to non-dependent patterns of substance use causing problems for the person. Appendix One illustrates the range of different definitions that may be used when referring to drug dependence.

Substance dependence is a pattern of maladaptive behaviours, including loss of control over use, craving and preoccupation with non-therapeutic use, and continued use despite harm resulting from use (with or without physical dependence or tolerance) [WHO, DSM].

This and other terms adapt poorly to the situation where prescription opioids are used to treat CNMP (Appendix One).

The terminology used in this field is constantly under review and may change in the future. This document uses the following terms as indicated:

(a) 'Inappropriate prescriber behaviour' which refers to physician behaviour;

(b) 'Problematic opioid use' which refers to patient behaviour; and

(c) 'Illicit or illegal use of prescription drugs' which refers to the possession or consumption by anyone other than the person to whom they were initially prescribed.

Furthermore, this document uses the term 'unsanctioned use' to subsume (b) and (c) above. (See conceptual table below.)

Appropriate prescriber behaviour refers to prescription decisions based on the best available current evidence at the time of assessment and taking into account the patient's perspective.

Inappropriate prescriber behaviour refers to persistent prescribing of opioids despite absence of sustained improvement in function, deterioration of function and/or the development of unacceptable side effects.

Problematic opioid use refers to patient behaviour defined as 'deviating from an appropriately prescribed program' of opioid treatment for CNMP. It is usually unsanctioned, but may be associated with inappropriate prescriber behaviour.

In general the term 'problematic drug use' may be clearer, more descriptive and less judgemental than terms such as 'drug misuse' or 'abuse'.[45] The AAPM/APS/ASAM consensus (see Appendix One)[46] defines 'problematic opioid use' as a pattern of overwhelming focus on opioid issues arising in the therapeutic context of prescribed opioids and impeding progress with other issues, with:

- early refills or escalating drug use;
- frequent accounts of lost, spilt, stolen medications; and/or
- use of supplemental sources of opioids

This policy document uses a wider definition of 'problematic opioid use' to include the above and other behaviours such as:

- use of oral medication parenterally by injecting or snorting;
- use to excess and/or in combination with other psychoactive drugs or alcohol to produce intoxication; and/or,
- diversion to or from the black market.

Notes to this definition:

1. Problematic use and dependence are distinct but overlapping concepts.
2. Problematic opioid use is usually unsanctioned. However, in circumstances where such behaviours are tolerated by the prescriber (i.e. sanctioned), the problem becomes one of inappropriate prescriber behaviour. (See conceptual table below.)
3. The term 'iatrogenic opioid dependence' is not used in this document except when quoting studies, as this may imply medical negligence.

Illicit or illegal use of prescription drugs refers to their possession or consumption by anyone other than the person to whom they were prescribed.

Sanctioned use of opioids is use, according to instructions, by a person to whom they were prescribed.

Unsanctioned use of opioids is use by the person to whom they were prescribed but not according to instructions (problematic use) or any use by someone other than the person to whom they were prescribed (illicit use).

Sanctioned opioid use	Unsanctioned opioid use	
(patients)	Problematic use (patients)	Illicit use (third parties)
Use, according to instructions, by a person to whom they are prescribed	Use by a patient 'deviating from a prescribed program'	Any use by someone other than a person to whom they are prescribed

2. The epidemiology of legal and illegal use of prescription opioids

1. Since 1990 there has been a substantial increase in the utilisation of opioids in Australia and New Zealand (and in the UK and US). In Australia, total morphine base supply has risen 4 fold since 1991; total oxycodone base supply 10-fold, mainly since 2000.
2. In Australia and New Zealand, there is little data on:
   - The prevalence of unsanctioned use of prescription opioids;
   - The numbers of problematic users of alcohol and other drugs including poly drug users who obtain opioids for CNMP - legally or illicitly; and
   - The prevalence of CNMP in populations on OST programs.
3. There is evidence in Australia of high demand for oral formulations of morphine and oxycodone, (especially slow release oxycodone) and that these drugs are commonly diverted. Possible reasons for this include:
   - Shortage of heroin;
   - Underfunding and consequent unmet demand for opioid substitution therapy systems.
4. Fraudulent presentation for opioid prescription is difficult to identify.

The following information has been gathered from a number of different data sets which together may contribute to understanding the extent and nature of opioid prescribing in CNMP, dependence on and diversion of prescription opioids. Before attempting to describe the patterns of unsanctioned prescription opioid use, it is important to present the extent of legitimate use. Furthermore, as opioids which are used problematically or illicitly are often diverted from the chain of legitimate manufacture, supply, prescription, dispensing, and finally use, it is important to review the data on the size of the licit opioid supply and use market.

2.1 Data sets in Australia and New Zealand describing the use of prescription opioids

Medical use

In Australia, the Health Insurance Commission (HIC) data set was intended to be used for administrative purposes: recording payments to pharmacists for dispensing prescriptions and to medical practitioners for providing medical services. The data set was not intended to be a source of data for audit and monitoring performance. Almost all services provided by clinicians generate a record in a Medicare file.

Purchase of Pharmaceutical Benefit Schedule (PBS) subsidised medication also generates a Medicare file.

However the publicly available HIC data do not attribute a prescription to an individual patient, so there is no information on the age or sex of the patient, no information on co-prescribed medications and no information on the indication for treatment with that drug. If a patient pays the entire cost of a medication, no PBS subsidy occurs, and no information is included in the PBS record. Therefore PBS data cannot be used as a complete measurement of opioid prescription or consumption.

The absence of clinical information (including patient characteristics and diagnosis) is a major impediment. The National Prescribing Service (NPS) provides prescribing feedback at an individual GP level. This aggregated data set allows an individual GP's patient demographic and prescribing profile to be matched against all GPs nationally. The limitation of this within the context of opioid prescribing is that such a comparison may unfairly disadvantage some GPs, particularly those working in areas of socioeconomic disadvantage with high clinical morbidity and large numbers of patients who use drugs problematically and/or are dependent on drugs.

New Zealand data

New Zealand has a unique illicit drug market with home-baked morphine and long acting morphine preparations partially acetylated to heroin.[47] Polydrug use is common with drug users seeking a wide range of prescription

medications, [48] and there is anecdotal evidence of an increase in prescription drug dependence. [49] One explanation offered was the increase in prescriptions for pain management and palliative care in New Zealand between 1998 and 2001.[50]

In New Zealand all those presenting for health care in public facilities, or for whom government subsidies are claimed, receive an individual identifier (the National Health Index).Thus most New Zealanders already can be identified. This could provide the basis for a national register but there is considerable resistance to any suggestion of the establishment of such a register on the grounds of confidentiality. New Zealand operates a 'Restricted Persons Register' where individuals with a history of doctor-shopping can be legally restricted to obtain medications of a specified class (for example: 'any opioids' or 'any opioids or benzodiazepines') from one named doctor or service (usually an addiction treatment service). The practical drawbacks associated with this are the difficulty in identifying the restricted person, especially if an alias is used. In Australia, the Repatriation Pharmaceutical Benefit Scheme (RPBS), administered by the Commonwealth Department of Veterans' Affairs (DVA), further provides subsidy for medications for entitled veterans and war widows.

The total numbers of both PBS and RPBS prescriptions for all pharmaceutical opioids, including morphine tablets and capsules, are recorded by the Drug Use Monitoring System (DRUMS), part of the Treaties and Monitoring Team of the Office of Chemical Safety, Therapeutic Goods Administration, Commonwealth Department of Health and Aging (TGA). However, if a patient pays the entire cost of a medication, i.e. no PBS or RPBS subsidy occurs, no information is included in the PBS or RPBS records. Therefore PBS/RPBS data cannot be used as a complete measurement of opioid prescription or consumption.

Non-medical use

In Australia, 7.6 per cent (1,026,300 individuals) of people aged 14 years and over had used pharmaceutical drugs (analgesics, tranquilisers, barbiturates or steroids) for non-medical purposes at least once in their lives; 3.8 per cent in the past year (658,300 individuals) and 2 per cent in the past month (259,400). Males (8.2 per cent) were more likely than females (7.0 per cent) to have ever used these drugs, but roughly equal proportions of males (3.6 per cent) and females (3.9 per cent) had used them illicitly in the past 12 months. People between 20 to 29 years of age were the most likely to have used these drugs for non-medical purposes in their lifetime, and in the past 12 months or the past month. [27] This is also the peak age for high risk and risky consumption of alcohol, tobacco smoking and illicit drug use.

In New Zealand the Illicit Drug Monitoring System (IDMS) captures trends but not particular opioids in its sample of injecting drug users.[51] In 2008 an estimate of the size of the population of daily or near daily users of illicit opioids obtained by multiplier estimation was 9,800.[52] While a proportion of this use is methadone diverted from OST programs, the majority is morphine or methadone prescribed for pain. Heroin is virtually unknown, oxycodone is not yet commonly used and 'home baking' conversion of codeine products to heroin is now rare. Thus if all the morphine used has been prescribed for pain, and (as an estimate) half the methadone, then about 6,000 – 8,000 of these 9,800 people are maintained on opioids nominally prescribed for pain. Taking average daily morphine use as 100 mg, gives a total estimate of illicit prescription opioid use as in the order of 250 kg morphine equivalent per annum for New Zealand.

Changing patterns of prescription opioid use

Since 1990, there has been a substantial increase in the utilisation of opioids in Australia, New Zealand, the United States of America and United Kingdom, based on a number of indicators such as community prescriptions. There has also been a decrease in the use of short acting injectable opioids and an increase in the use of orally well absorbed, long acting opioids. The introduction of sustained release formulations of opioids, which provide less fluctuation in plasma levels of analgesics, have offered an improvement in the ability to control chronic pain with fewer effects of excessively high or low opioid levels during treatment.

Although much of this increased opioid supply may reflect increasing population size and aging of the population, better pain management and other improvements in treatment for a range of conditions, there is also the possibility of a corresponding increase in problematic opioid use, and an increase in the total supply potentially available for diversion and non-medical use.[53]

Australian data on use of opioids reveal major differences between jurisdictions. This is due partly to different prescribing patterns, different formularies used and the difference in regulations for prescribing authorisation. The use of OxyContin (80 mg) and MS Contin (100mg) is more prevalent in Tasmania [22 54 55] and the Northern Territory possibly due to the lack of availability of heroin.[56] These two drugs are among the most commonly prescribed drugs in Australia and are sometimes diverted to the black market.[57]

Morphine

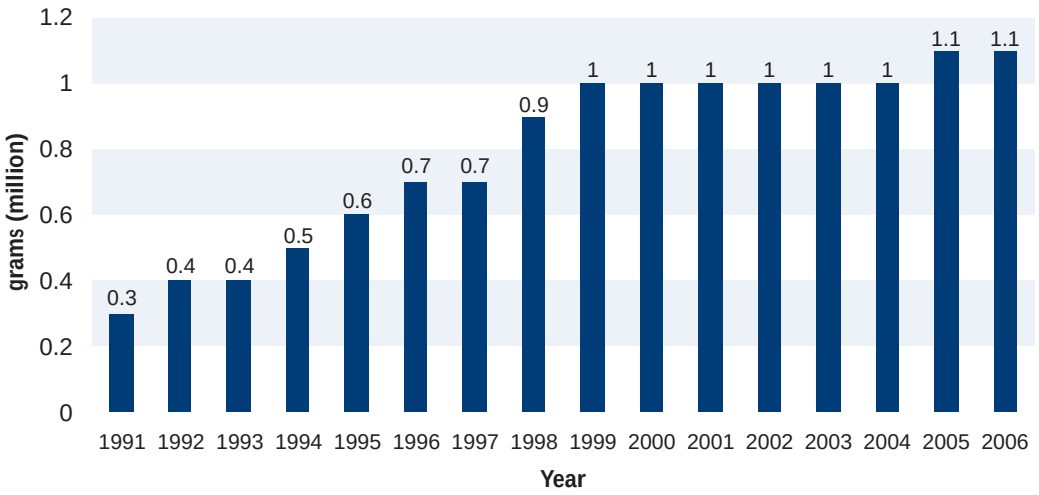
During the period 1986 to 1995, the total amount of oral morphine consumed in Australia was estimated to have increased from 117 to 578 kg. Almost all of this increase occurred from 1990-1995, probably reflecting the impact on morphine prescribing of the introduction of slow release oral morphine formulations: morphine mixtures accounted for less than 20 per cent of total oral morphine consumption by 1995. [58]

In Australia, controlled release morphine tablets (MS Contin®) were introduced in 1991 and capsules (Kapanol®)

in 1992. Over the period 1990 to 2006, the total number of morphine tablets and capsules provided in Australia increased from 651,360 to 32.8 million, representing a 40-fold increase, and consisting almost entirely of increase in slow release preparations. [22] The steep increase of supply of base morphine in tablet and capsule form (Figure 3) continued until about 2000, since when it has remained relatively stable. Total morphine base supply in Australia increased about 4-fold from 1991-2007 (Figure 4).

Similar trends are shown in DRUMS recorded PBS/RPBS data, with the rate of morphine prescription per person aged 15 - 54 years increasing by 89 per cent on average across Australia between 1995 and 2003. [8]

Figure 3: Supply of Morphine base tablet and capsules, Australia 1991-2006

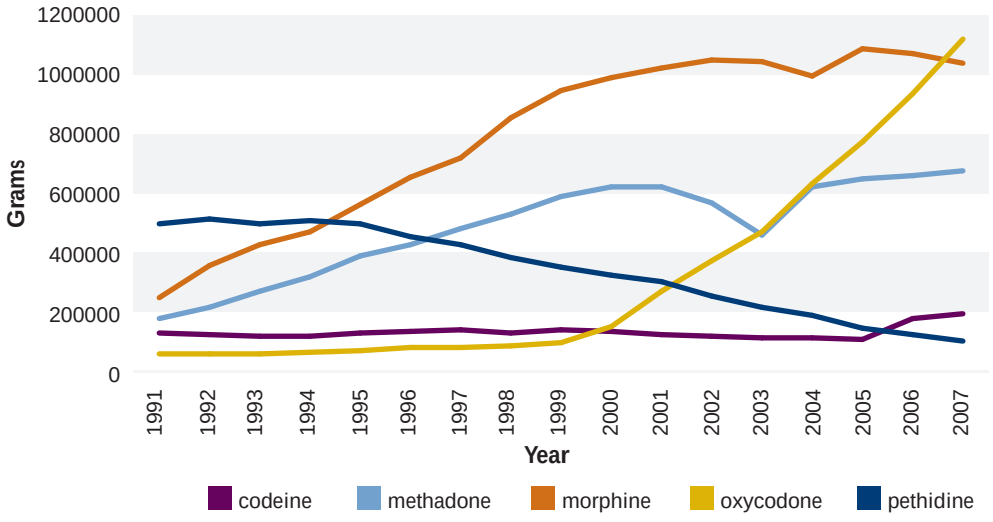


Source: Dobbin 2006, Morphine, Unpublished paper provided to the Drugs and Crime Prevention Committee. Data extracted from the National Drug-control System (NDS) domestic transaction data by the Commonwealth Department of Health and Ageing.

Oxycodone

The total number of oxycodone capsules, tablets and suppositories supplied in Australia increased from 8.4 million in 1990 to 31.4 million in 2003, representing a 3.75-fold increase.[20] However, total oxycodone base supply in Australia increased about 10-fold from 1991-2007 (Figure 4), with most of the increase occurring since the introduction of oxycodone hydrochloride modified release tablets (OxyContin) in 1999.

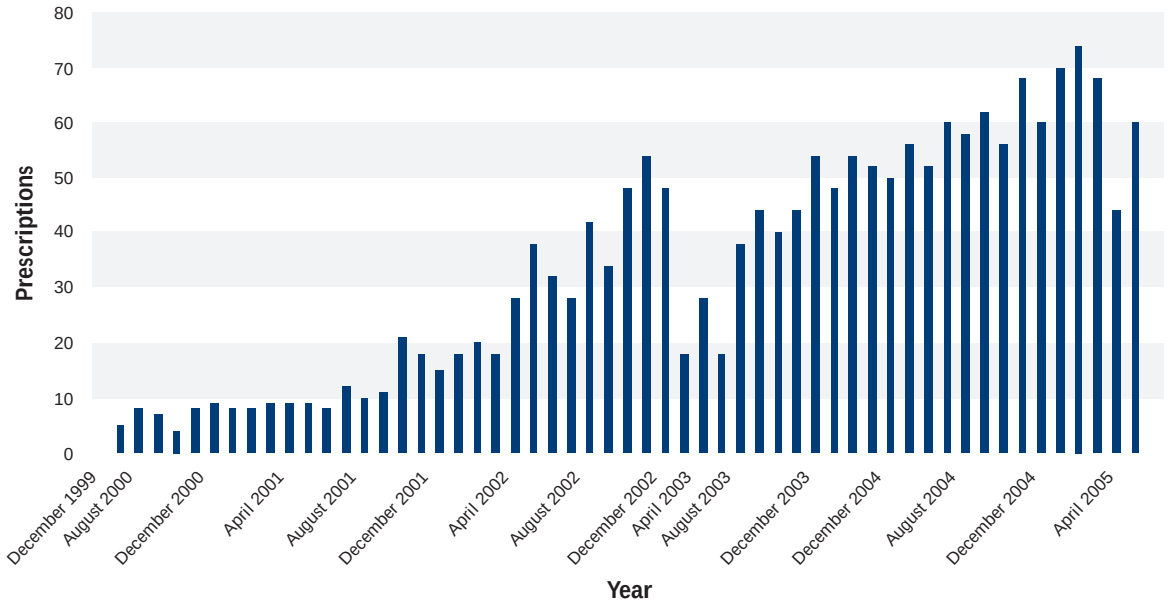
Figure 4: Pharmaceutical opioid base supply (grams) Australia from 1991-2007



Source: Dobbin 2008, Morphine, Unpublished paper provided to the Drugs and Crime Prevention Committee. Data extracted from the National Drug-control System (NDS) domestic transaction data by the Commonwealth Department of Health and Ageing.

Data from Australian Capital Territory (ACT) show the substantial increase in the number of prescriptions of OxyContin from the year of its approval 1999 to 2005 (Figure 5). [59]

Figure 5: OxyContin prescription in the ACT, December 1999 to April 2005



Source: Tedeschi M, Chronic nonmalignant pain - The rational use of opioid medication, *Australian Family Physician* 2006; 35 (7):465-560

OxyContin is available in tablet sizes up to 80mg, compared with maximum 20mg for normal release formulations, for which reason it appears to be more sought after by illicit drug users.

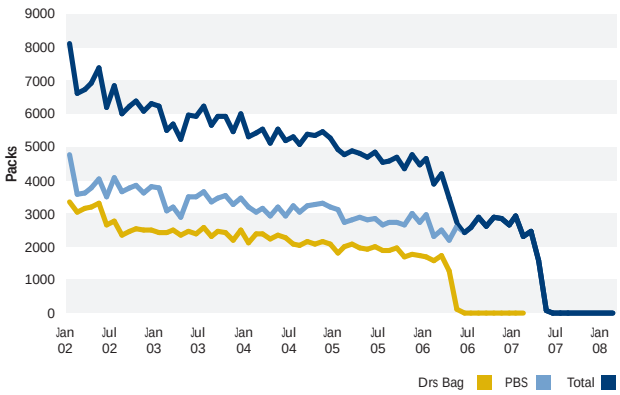
Pethidine

Pethidine is a synthetic opioid provided as a drug for injection. Its use is complicated by multiple drug interactions, and unique, potentially serious side effects. Some of these adverse effects are due to the accumulation of norpethidine, a neurotoxic metabolite of pethidine that causes CNS excitation and seizures. Professional guidelines provided by many different professional organisations have recommended against its use for many years, and as a result, the supply to Australia in 2004 had declined to half that in 1994.

Pethidine injections are regarded as the opioid and the formulation with the greatest potential for dependence and problematic use. Pethidine was supplied without cost to medical practitioners through the PBS Emergency (Doctor's Bag), posing special risks to medical practitioners prone to self-administration of drugs. Pethidine injection use in after hours services creates specific difficulties for locums with little knowledge of the patient's clinical or drug seeking history. A submission forwarded to the Pharmaceutical Benefits Advisory Committee by the Victorian Drug Usage Advisory Committee in 2004 [60] recommended that this drug be deleted from the list of drugs supplied through the PBS Emergency (Doctor's Bag) Supply. The PBAC agreed, and the drug was deleted from this list in April 2006. (See Figure 7)

Pethidine was removed from the list of general pharmaceutical benefits on 1 April 2007.

Figure 6: PBS General and Doctor's bag supply: Pethidine 100mg amps (x5), by month, Australia 2002-2008



Source: Pharmaceutical Benefits Schedule Item Statistics website, Medicare Australia: http://www.medicareaustralia.gov.au/statistics/dyn_pbs/forms/pbs_tab1.shtml(accessed 1 August 2008)

Dextropoxyphene

Dextroproxyphene is a weak analgesic, and dangerous in overdose owing to accumulation of potentially cardiotoxic metabolites. Dextroproxyphene was identified as having no clinical advantages over alternative analgesics and high toxicity in overdose, and its removal from the market was recommended. [61] [62] As this is a non-PBS item, surveillance data in Australia are limited to RPBS scripts, cross sectional studies, and overdose records.

Use of dextropropoxyphene by Australian veterans was shown to decline between 1998 and 2004 [63] coinciding with increased use of Cox-2-selective NSAIDS and tramadol, despite no change in its S4 classification or subsidy status (non-PBS, but RPBS subsidised).

In the United Kingdom a study of national mortality statistics and local non-fatal self poisonings concluded that self poisoning with co-proxamol (tablets combining paracetamol 325mg and dextropropoxyphene 32.5mg) was particularly dangerous and contributed substantially to drug related suicides. It recommended restricting availability of co-proxamol could have an important role in suicide prevention.[64]

Subsequently the Committee on the Safety of Medicines recommended withdrawal of propoxyphene-paracetamol drugs from the UK market because of its disproportionate contribution to overdose deaths. [65]

Over the counter analgesics containing codeine

Codeine containing analgesics are available over the counter (OTC) from pharmacies without a prescription subject to certain constraints, including that the dose of codeine in each tablet is less than 10mg, and the codeine is compounded with a simple analgesic (paracetamol, aspirin or ibuprofen). Codeine is a weak analgesic, but because of the widespread availability from pharmacies without a prescription, these products are subject to non-medical use. Users may begin on the recommended therapeutic dose and escalate the dose when the psychoactive effects of codeine is recognised, leading to escalation of daily dose to multiples of the maximum recommended dose.

Recently a problem has been recognised across Australia of individuals taking high daily doses of products (Nurofen Plus® and Panafen Plus®) containing codeine combined with ibuprofen, a non-steroidal anti-inflammatory (NSAID) drug. The most serious adverse effects of NSAID use include serious and life threatening upper gastrointestinal haemorrhage and perforation, renal failure, and hypocalcaemia. This risk is dose related even within the therapeutic range, but increases substantially when higher supratherapeutic doses are taken.

A paper prepared for the National Drugs and Poisons Schedule Committee (NDPSC) in Australia described 77 cases of individuals who had experienced adverse effects from non-medical use of high doses of these products. [66] The cases had escalated their dose of tablets to an average of 50 tablets a day for an average two and one half years, because of dependence on codeine, and many had experienced secondary life threatening harm from the extraordinarily high doses of ibuprofen in these combination products. There were 39 cases of gastrointestinal haemorrhage or perforation, 7 cases of renal failure, 5 cases of serious hypokalaemia, 15 cases of anaemia, and one death due to perforation of a gastric ulcer. Many (31 cases) commenced pharmacotherapy treatment for opioid dependence, and 7 cases were treated with medicated opioid withdrawal because of dependence on these products.

In 2008 an Emergency Medicine Registrar at an outer Melbourne hospital published an article describing two cases of perforated gastric ulcer resulting from heavy use of Nurofen Plus. [67]

Comparison with use of prescription opioids in the United States of America

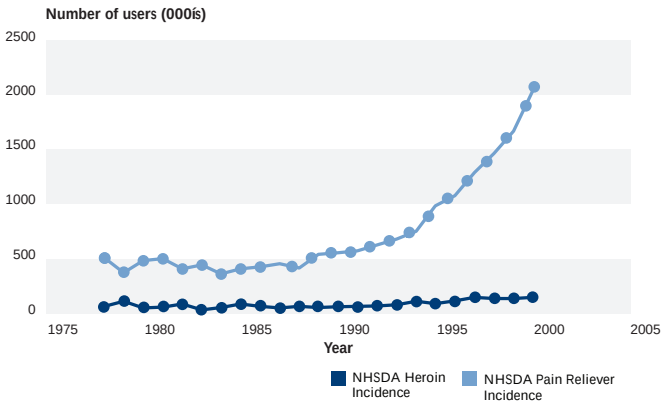
In the US, opioid therapy is mostly prescribed by general practitioners or non-specialists, and 95 per cent of long acting opioids are prescribed for non-cancer pain.

In the US the supply of prescription opioids has increased over the past two decades, with the prescription opioid market currently valued at USD7.7 billion and expected to increase over the next 10 years at a rate of 2.4 per cent. [68] Increasing unsanctioned use of prescription drugs, primarily opioids, has been reported, particularly by young people, and prescription drugs are now reported as the second most commonly abused category of drugs after cannabis, ahead of cocaine, heroin, and methamphetamine.[3]

A recent study showed high rates of use of prescription opioids involving diversion among street drug users in New York. Methadone was used (71.9 per cent) and sold (64.7 per cent) more commonly than OxyContin, Vicodin (hydrocodone with paracetamol), and Percocet (oxycodone with paracetamol), these being used by between 34 per cent and 38 per cent of users and sold by between 28 per cent and 41 per cent of sellers of prescription opioids.[69]

Figure 7 shows The National Household Survey on Drug Abuse (NHSDA) data of rising incidence of use of 'Pain Relievers' in relation to relatively static incidence of heroin use between 1995 and 2000.

Figure 7: National Household Survey on Drug Abuse (NHSDA) Incidence (all ages) US, 2006



In 2008, fentanyl transdermal patches used for the management of CNMP in Canada were related to a number of serious adverse reactions.[70] Over the past 15 years, sales of opioid analgesics, including oxycodone, hydrocodone, methadone and fentanyl, have increased in the US, and deaths from these drugs increased in parallel with these sales. In 1995 the use of opioid analgesics increased at a rate four times that of heroin.[5]

Harms resulting from use of fentanyl transdermal patches highlight the need for careful surveillance, dispensing and safe storage of this product, to reduce unsanctioned use and prevent accidental overdose.

2.2 Adverse clinical events associated with opioid use

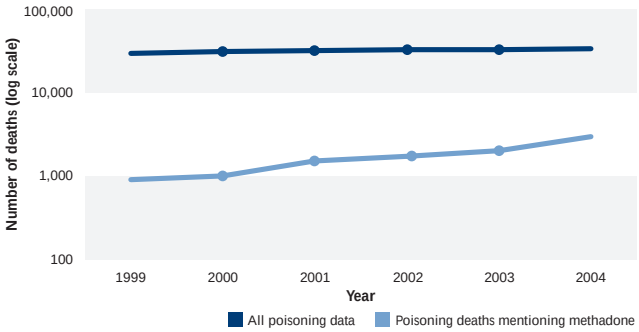
Death associated with opioids

In South Australia during the two years 1993-1994 there was an increase in methadone related overdose deaths due to methadone tablets prescribed for chronic pain rather than methadone syrup. [71] In half of the cases methadone had been illegally diverted to non-patients and the relative risk of death due to methadone tablets versus syrup was 7.3.

In the US between 1998 and 2005, four of the 15 medications most frequently reported to the Food and Drug Administration (FDA) Adverse Event Reporting System as 'suspect' for deaths and serious non-fatal adverse events were opioid analgesics (oxycodone, fentanyl, morphine and methadone). Overall oxycodone was the most common 'suspect' medication of any type in cases of death, with an increase in oxycodone associated deaths from 14 in 1998, to 2414 in 1996, declining to 1007 in 2005.[4 5 6 7] There were also increases in deaths associated with morphine (82 in 1998, 329 in 2005), fentanyl (92 in 1998, 1245 in 2005) and methadone (8 in 1998, 329 in 2005). This may be related to an increase in the amount of these opioids prescribed during this period.[72] Although deciding on causality is difficult - this data reports only reported suspected association - this data highlights the importance of developing an efficient system to manage the risks of prescribed opioid medications.

Some of the increase in deaths was associated with an increase of prescribing of methadone tablets used to treat pain. Methadone tablet prescriptions in the US increased from 437, 030 in 2001 to 2,609,613 in 2004 (See Figure 8). Increased methadone prescription may have been due to concern arising from publicity about the diversion and unsanctioned use of sustained release formulations of morphine and oxycodone, and because of the relatively low cost of methadone tablets compared to the cost of these sustained release analgesics. [73]

Figure 8: Poisoning and methadone – US poisoning deaths: 1999-2004



Source: National Centre for Health Statistics Data from the National Vital Statistics System, 2007. [74]

Methadone has a complicated pharmacology, with an analgesic effect that lasts for four to six hours, and elimination half life that may be as long as 40 hours, leading to a risk of accumulation during initiation of treatment. [75] [76] The pharmacology of methadone is also subject to considerable inter-individual variability, adding an additional consideration to the risk of use of this drug as an analgesic.[77]

Due to the increase in the supply of methadone tablets in the United States for the treatment of pain and the contribution of these tablets to the increase in methadone related deaths, in July 2006, the US FDA issued a Public Health Advisory stating that methadone used for pain control may result in death or life threatening changes in breathing and heart beat. [78]

Number and nature of adverse drug events (ADEs) related to opioids

In Australia it is estimated that 17.5 million people make 95 million visits to their general practitioner annually, [79] and that 10.4 per cent of patients attending general practice (two million people) experienced an adverse drug event in the last six months. [80] Most of these adverse events were moderate or severe and 138,000 people required hospitalisation, a finding consistent with previous estimates. [81] The individual drugs possibly causing the ADEs were not identified, nor were the duration of exposure or dose; however, in another study opioids were listed as the third most common type of drug (4,793 adverse events or 6.9 per cent of total) associated with an adverse event. [82]

Hospitalisations for prescription opioid use

An inquiry in 2006 [20] reported difficulty in identifying the service impacts attributable to prescription opioids. While such data might in theory be available from agencies that keep records (such as the HIC), most reports currently in the public domain have included 'heroin and other opioids' as one category. There is a need for better reporting of service utilisation statistics for pharmaceutical opioids as a distinct category.

Statistics from the DirectLine [83] telephone information and counseling service in Victoria are shown here (see Table 1) as an indirect measure of benzodiazepine and prescription opioid use.

Of the 12,000 drug related ambulance attendances in Victoria in 2000-2001, almost half were associated with benzodiazepines and analgesics, and the majority of patients attended to were female. During this period, women were likely to stay in hospital twice as long as men for benzodiazepine related admissions. [84]

Table 1: Total number of calls to DirectLine where opioids were cited as drugs of concern, Victoria, 1999-2004

Year	Total number of calls to DirectLine	Total calls drug identified	* Other opioids a drug of concern	# per cent of drug identified	per cent of all calls
1999	39,284	21,351	3,690	17	9
2000	39,440	19,746	4,019	20	10
2001	41,159	20,992	3,839	18	9
2002	45,307	24,990	6,214	25	14
2003	48,151	24,861	6,950	28	14
2004	48,776	26,990	7,798	29	16

Source: Department of Human Services (DHS) Victoria 2006, p.81.
* Number of calls in which opioids other than heroin were identified as a drug of concern
# Percentage of all calls identified as drug-related, in which opioids other than heroin were identified as a drug of concern

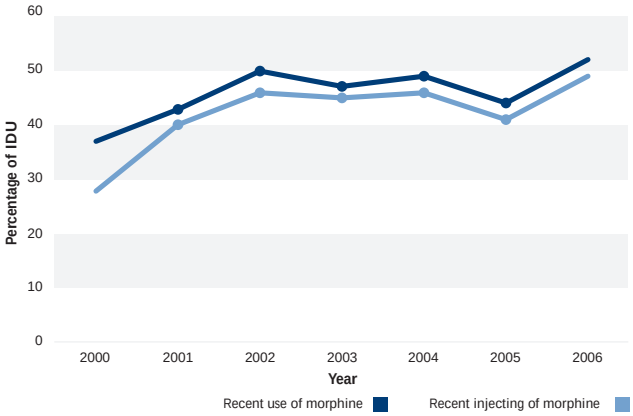
2.3 Unsanctioned use of prescription opioids

Australian data on use of prescription opioids show major differences in unsanctioned use between jurisdictions. This may be at least partly explained by heroin scarcity in parts of Australia.[85] There is evidence of a high demand for OxyContin (oxycodone in a controlled release formulation) in Australia (section 2.1) and that this drug is commonly diverted (see below). It is possible that this trend reflects both scarcity of heroin and unmet demand for OST, for treatment both of illicit drug dependence and of opioid dependence arising out of the treatment of CNMP. In most countries the treatment of drug dependence has limited capacity, poor quality and a narrow range of options. [86] This contributes a demand for black market opioids. This is particularly the case in New Zealand where heroin has been relatively unavailable for several decades, and injection of prescription opioids has long been prevalent. [87] [88] [89]

While there have been substantial benefits from the use of sustained released oral opioids preparations in the management of CNMP, their ready availability has provided an opportunity for them to be used to meet this unmet demand.

In Australia, in 2007, the proportion of injecting drug users reporting morphine as the last drug injected increased from 7 per cent in 2002 to 11 per cent in 2007 and was in third place after heroin. [90] A high proportion, 40-50 per cent, of injecting drug users surveyed by the Illicit Drug Reporting System reported injection of morphine in the last 12 months (see Figure 9).

Figure 9: Recent use and injection, of morphine by injecting drug users: Australia 2000-2007



Illicit Drug Reporting System (IDRS) [9]

Problematic prescription opioid use by a hidden population

While the Illicit Drug Reporting System provides data about the diversion and problematic use of prescription opioids and other psychoactive pharmaceutical drugs, there is little data about problematic use by those not captured by this and other related datasets. There appears to be a recent increase in the number of people without a prior history of illicit drug use who are seeking treatment for opioid dependence.[91] [92] [93]

It is possible that a large, though currently unquantifiable, number of people without a history of injecting drug use have escalated their dose beyond recognised therapeutic doses. They may have developed problematic use, including drug seeking from multiple prescribers and pharmacists, high doses taken by mouth episodically or chronically, behaviours which expose them to the risk of overdose death.

There is sparse information about this 'hidden' population, because their activity is not described by any current dataset, unlike the situation with injecting drug users, where information about unsanctioned use of prescription opioids is well described. [9]

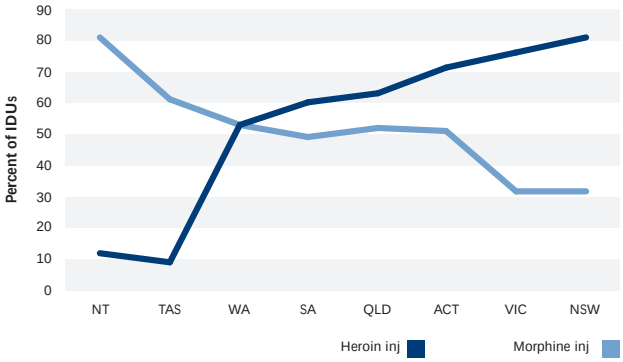
Injecting drug use (IDU) of prescription opioids

The IDRS data, which includes surveys of injecting drug users in each Australian state and territory, indicates that more than one in six of the sample had used pharmaceutical drugs illicitly (i.e. using medications not prescribed for them) over the previous six months. Rates of illicit use of morphine and methadone were higher in the Northern Territory (NT) and Tasmania than in other jurisdictions which may be attributed to the reduced availability of heroin in these two jurisdictions. For the first time, IDRS interviewees in 2005 were specifically asked about the use of oxycodone. Nationally, 3 per cent reported licit oxycodone use and 25 per cent reported illicit use in the previous six months.

In 2006, the proportion of people injecting oxycodone who report recent use of illicitly obtained drugs as opposed to their own prescribed medication was highest in Western Australia (WA) (42 per cent), followed by Tasmania (29 per cent). In 2006, compared with 2005, the use of illicit oxycodone remained stable in some jurisdictions; increasing by less than five per cent in New South Wales, Tasmania, Western Australia and in the Northern Territory, and increasing by five per cent to nine per cent in the Australian Capital Territory, Victoria, South Australia and Queensland. The recent injecting of licit oxycodone was no higher than eight per cent in all jurisdictions, compared with seven per cent in 2005. Of those who reported recent oxycodone use, the majority (80 per cent) reported illicit oxycodone as the form most used, ranging from 64 per cent in the Northern Territory to 93 per cent in Tasmania. [9 20]

Figure 10 demonstrates that the prevalence of morphine injection is inversely proportional to the availability of heroin. That is, where heroin is less available, it appears that injecting drug users surveyed choose to inject morphine, and perhaps other pharmaceutical opioids. [9 20]

Figure 10: Morphine and heroin use in the preceding six months by IDRS respondents in each Australian jurisdiction, 2007



Source: Illicit Drug Reporting System (IDRS) [9]

In 2006, the Medically Supervised Injecting Centre (MSIC) in Sydney (NSW Australia) reported an increase in the number of people injecting pharmaceutical opioids compared with 2004. It was noted that this trend coincided with the withdrawal of temazepam gel caps and a decrease in the use of heroin. From 2005 the proportion of all visits at which other opioids (and excluding temazepam) were injected started to increase more sharply as follows:

- 12 per cent of all visits in the three months prior to Nov 2005;
- 18 per cent in the quarter to Feb 2006;
- 32 per cent in the quarter to May 2006; and,
- 40 per cent of all visits to the end of July 2006.

This more rapid increase appeared to coincide with a further deepening of the heroin shortage in Kings Cross, as heroin represented only 32 per cent of visits compared with 40 per cent to inject other opioids in the last quarter of 2006 and 71 per cent to inject heroin in late 2005. However, the rapid increase also coincided with the removal of the two month rule for sustained release opioids (morphine and oxycodone) in NSW, whereby doctors no longer have to apply for an authority to continue prescription after an initial two month period (see Ch 5, Regulation).

The MSIC has also noted that the rate of other opioid overdose was significantly lower (2.3 per 100 visits) than for heroin (4.7 per 100 visits) in the quarter to May 2006.

Table 2 below illustrates jurisdictional differences in the drug of choice among IDUs. In New South Wales, the Australian Capital Territory, Victoria and South Australia, more than half of the people who inject drugs nominated heroin as their drug of choice and 27 per cent or less in these jurisdictions nominated methamphetamine as their drug of choice. Heroin is not as widely available in the Northern Territory and Tasmania and this may influence the reports of drug of choice. However, the data suggest that the majority of IDUs in most jurisdictions prefer opioids. Cocaine was nominated as the drug of choice by 11 per cent in New South Wales in 2007.

Table 2: Drug use patterns among people who inject drugs (IDU), by jurisdiction, 2007

	National N=909	NSW n=153	ACT n=101	VIC n=150	TAS n=100	SA n=100	WA n=80	NT n=106	QLD n=119
Mean age first injected	19	19.6	18.9	19.2	18.8	19.4	19.3	20.1	19.1
First drug injected (per cent)									
Heroin	41	61	46	47	11	39	43	39	34
Amphetamine	47	33	50	49	58	55	43	45	53
Morphine	6	1	1	1	16	1	10	13	5
Cocaine	2	5	2	1	0	2	0	0	2
Methadone	<1	0	1	0	4	0	0	<1	0
Other drugs	3	0	1	1	11	3	3	2	6
Drug of choice									
Heroin	52	67	55	69	27	55	54	38	42
Methamphetamine	21	17	30	16	30	24	15	13	24
Morphine	10	0	1	3	15	8	10	26	20
Cocaine	3	11	1	0	2	1	1	3	<1
Methadone	3	<1	7	0	13	0	5	2	2
Cannabis	6	2	5	5	6	7	7	13	6
Other drugs	4	2	1	5	7	5	5	6	5

Source: Illicit Drug Reporting System (IDRS) [9]

Adverse impacts and perceived advantages of injecting pharmaceutical opioids

Some of the problems caused by the diversion of opioid analgesic tablets and capsules and their use for injection result from the inclusion of talc, an inorganic material used as an excipient in many commonly used products, and other fillers that can cause embolism. Talc injected intravenously initially lodges in the lungs, causing talc pulmonary granulomatosis, and in the long term this can lead to potentially fatal pulmonary hypertension. Talc particles can also break through into the systemic circulation causing talc particles to lodge in the liver and retina.

Injecting drug users and other people engaged in unsanctioned use of prescription opioids may perceive a number of advantages of using these drugs instead of street and 'homebake' heroin such as:

- They are relatively easy to procure, either directly from a medical practitioner and pharmacist, or on the black market from a patient for whom they have been prescribed, or a dealer;
- There is a predictable and assured dose;
- The drugs are pharmaceutical grade drugs without unknown diluents or contaminants;
- They are perceived as being prepared and packaged in a clean industrial environment;
- They are cheap, particularly if the individual is eligible for concessional rates of co-payment under the Pharmaceutical Benefits Scheme;
- They reduce the need to commit crime to fund purchase of heroin;
- They are easily portable because of the way they are packaged (for instance in foil blister packs);
- Possession of a prescription makes possession of the drugs themselves legal, thus avoiding legal problems of unauthorised possession or possession of illicit drugs;
- There is a high profit margin if the drugs are to be trafficked, particularly if obtained as a concessional pharmaceutical benefit;
- The drug seeker can avoid contact with other drug users, drug traffickers and the criminal scene by obtaining the drugs directly from medical/pharmacy sources; and
- There is ample peer information about how to prepare the opioid tablets and capsules for injection.

Adverse consequences of injecting diverted pharmaceutical drugs are difficult to quantify. While there are some secondary data available on service utilisation as indicators of harm, extraction of these data from publicly available sources is difficult.

Many users of heroin also use benzodiazepines and prescription opioids. Heroin users are about 13 times more likely to die in any one year than their age-mates who do not use heroin, [94] with annual mortality rates of between 1 to 3 per cent. [95] The risk of non-fatal and fatal drug overdose is higher in heroin users who also use benzodiazepines.

Table 3: Presence of other drugs in heroin (morphine) related overdose deaths, Victoria, 2001-2005 (per cent)

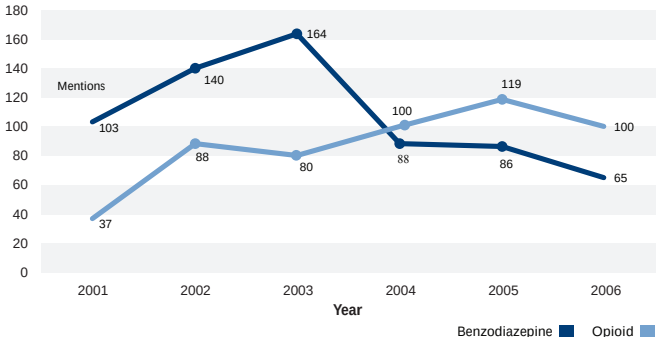
	2001	2002	2003	2004	2005	Overall
Morphine only	16	16	32	18	15	20
Morphine + benzodiazepines	71	67	48	59	54	60
Morphine + alcohol	31	24	31	36	34	31
Morphine + cannabinoid	22	12	9	11	21	15
Morphine + amphetamine	22	14	9	8	14	13
Morphine + other opioid drugs#	4	6	7	8	8	7

Notes: Total percentage equals more than 100 per cent as multiple combinations of other drugs were also present. # i.e. methadone, propoxyphene, oxycodone, etc. Source: Woods [96]

2.4 Prescription fraud and diversion

Each year Australian GPs write more than 15 million prescriptions for medications of the types which may be used problematically, particularly opioid analgesics. [97] In Victoria (Australia), the incidence of prescription related offences increased by 80 per cent in 1998, (669 cases) from 1997 (371 cases). Oxycodone was the most frequently sought drug. [98]

Figure 11: Forged prescription reports: Victoria, 2001-06



Source: Malcolm Dobbin 2008

Figure 11 illustrates the number of forged prescription reports from Victoria from 2001 to 2006. In this period, forged prescriptions for opioids increased from 37 mentions in 2001 to 100 mentions in 2006 and overtook benzodiazepines as the drug of preference. Trends in forged prescriptions are not located centrally and these data are maintained by each jurisdiction.

The economics of diversion

Some people using fraudulent means to get opioid analgesics may have a genuine need for treatment of pain. Others may intend to divert the medications to others.

Even a single prescription for opioids could yield up to AUD800 (from table 4, this could be up to AUD1,600 in some jurisdictions) on the black market. This figure arises from extrapolating the findings from Illicit Drug Reporting System (IDRS) where one tablet of OxyContin may fetch up to AUD30-40 on the black market.

It costs AUD30.70 for 20 tablets of OxyContin from a legal prescription, but one tablet has an average street value of AUD35 (220 per cent profit). Table 4 illustrates the significant monetary incentives that exist for people to divert prescription drugs.

When considering US data it must be remembered that in the US prescription opioids are not subsidised as they are in Australia and New Zealand. Methadone is cheap because it is out of patent, and this low cost might be one reason why doctors prescribe it for their chronic pain patients, especially in the United States. There is limited public subsidy for the cost of drugs in the United States, and prescribers may take cost considerations into account when deciding on choice of analgesic drugs.

By contrast opioids can be provided free of charge or at a cheaper rate on the PBS in Australia, and in New Zealand. If patients feign pain they are more likely to get the drug at a cheaper rate on the PBS. Many people who use opioids problematically hold a concession card entitling them to a lower patient contribution (AUD5 as of 11 August 2008) for PBS subsidised drug prescriptions. It is generally much cheaper for people to get opioids on prescription than on the black market.

Table 4: Cost of selected legally prescribed opioids and their street value, 2006, Australia

Drug brand name (generic name)	Pack size PBS maximum quantity	Cost*	Street value (per tablet or capsule)**	Estimated street value of pack***
MS Contin® 100mg tablet (morphine controlled release)	20	$59.99 $30.70 $4.90	$20-$80	$400-$1600
Kapanol® 100mg capsule (Morphine – containing sustained release pellets)	20	$59.99 $30.70 $4.90	$20-$60	$400-$1200
OxyContin® 80mg tablet (Oxycodone controlled release)	20	$70.43 $30.70 $4.90	$25-$60	$450-$1200
Physeptone® 10mg tablet (methadone)	20	$13.39 $13.39 $4.90	Range $5-$150, most paid $5-$15	$100-$300

* Information about cost (AUD) for legally prescribed drugs is provided for:

- Dispensed price for maximum quantity as listed in the Schedule of Pharmaceutical Benefits, December 2006
- Patient contribution for general patients if no concession is claimed
- Patient contribution for concessional patients holding other cards (Pensioner Concession Card, Commonwealth Seniors Health Card, Healthcare Card etc.)

** Source: O'Brien S, Black E, Degenhardt L et al. Australian Drug Trends 2006. Findings from the Illicit Drug Reporting System (IDRS), NDARC Monograph No. 60, National Drug and Alcohol Research Centre, Sydney NSW, 2007. Additional information also obtained from individual State/Territory IDRS reports.

Street price describes prices reported by IDRS subjects in different Australian States/Territories

*** Estimated by multiplying reported street price per unit by pack size

2.5 People who use other drugs and who obtain opioids legally or illegally

There is no current information available in Australia or New Zealand on the numbers or characteristics of people with other substance use problems, including poly-drug users, who obtain opioids illegally or legally for CNMP. The literature suggests that much of the problematic use of opioid analgesics is by 'recreational' and 'street users' and individuals with co-morbid psychiatric conditions. [99] [100] [101]

A study of young people in Victoria (aged 15-24 years old) who died of heroin related overdoses between 1994 and 1999, using linkage of Medicare and Pharmaceutical Benefits Scheme and Coroner's Court records, found polydrug use was reported in 90 per cent of toxicology reports, with prescription drugs present in 80 per cent of subjects. The study raised the question of supply and source of these drugs by medical providers. Many of the people studied in this report would not be identified as doctor shoppers by HIC criteria or by GPs (See also Ch 6.3.). [102]

In another study of young heroin users, the number of PBS prescription drugs used was strongly associated with overdoses of other opioids, tricyclic antidepressants and benzodiazepines. [103] The authors advocated improved data linkage to PBS records for GPs to facilitate safer prescribing practices. A study of 238 deaths among methadone maintenance treatment (MMT) patients in Australia reported autopsy evidence of high rates of other substance use, including benzodiazepines (in 55 per cent), morphine (which may be a heroin metabolite but could also be prescription morphine, in 34 per cent), other opioids (in 20 per cent) and alcohol (in 16 per cent). [104]

Between 1993 and 2002 a UK study assessing a collection of heroin-related toxicological assessments found ethanol in 50 per cent of cases, followed by diazepam (34 per cent), temazepam (13 per cent) and methadone (10 per cent). [105] More than 75 per cent of heroin fatalities involved one or more of these concomitant substances. Thirty seven per cent of all index cases involved at least one benzodiazepine. This report recommended that strategies to prevent opioid overdoses target alcohol use in people who use opioids.

2.6 Opioid use in prisons

In Australia in 2005, 27 per cent of persons incarcerated by police or in correctional centres tested positive for opiates on urine drug screens. The proportion of opiate positive specimens increased from 10 per cent in 2000, to 18 per cent in 2001 and 23 per cent in 2002. [106] However these data refer to police detainees, rather than longer term prisoners. Further, not all of the inmates' specimens testing positive for opiates are likely to reflect heroin use: codeine-containing compounds, including OTC medicines, and morphine, whether licitly or illicitly obtained, also give positive tests for opiates. As tests for opioids are not routinely performed, standard urine drug testing arrangements will not detect such drugs as oxycodone, methadone, buprenorphine, pethidine and dextropropxyphene.

Data are lacking for the prevalence of illicit opioid use among longer term prisoners. Chronic pain management

among prison inmates is a major issue in clinical services, especially as many inmates have a history of musculoskeletal and head injuries. [107] To minimise diversion of opioids prescribed for pain, inmate patients may be placed on an MMT program.

Conclusions

It is currently not possible accurately to quantify the extent of inappropriate opioid prescribing and problematic opioid use in Australia and New Zealand. Existing monitoring systems cannot identify and track opioid prescriptions and supply down to the individual patient level. There are reasonable data about use by injecting drug users from the sample reporting in the Illicit Drug Reporting System, but it is possible there is a substantial 'hidden' population for whom information about problematic pharmaceutical opioid use is not currently accessible through existing data sources.

There has been a substantial increase in the supply of prescription opioids in Australia and New Zealand in recent years. It is not known how much of this increase is due to unsanctioned use. An unknown number of people who die from drug related causes are patients with CNMP using medications for which they had a legitimate prescription. There is insufficient evidence to determine to what extent drugs diverted onto the black market originate from prescription forgeries or drug seeking behaviour e.g. feigning pain at GP rooms or emergency departments.

In Australia access to prescription shopping program information is limited to PBS prescriptions, requires written consent of the patient, and does not provide real time medication history available to potential prescribers or to pharmacists. Fraudulent presentation for opioid prescription is difficult to identify. In New Zealand, there is currently no national register to track supply of opioid prescription medications.

An additional problem is that there is little systematic coordination of information about pharmaceutical opioid supply to individuals between different Australian jurisdictions. The result of this is that individuals seeking these drugs across State/Territory borders can escape detection by existing jurisdictional level monitoring systems where they exist.

The variety of ways in which opioids may be obtained indicate that prevention of problematic pharmaceutical use will require action at several levels, including engaging national and state statutory bodies, professional boards and organisations, and implementing responses through law enforcement, health and community services.

What needs to be done?

There is a need for improved systems for collection of complete data regarding the prescription and use of prescription opioids, including both sanctioned and unsanctioned use, the incidence and prevalence of adverse health consequences of their use, and on the sources of illegally used prescription opioids.

More information is needed about people with problematic use of pharmaceutical opioids, including any 'hidden' population of these people, in order to develop strategies for prevention, to improve identification of individuals with problematic use and to optimise their treatment. There is an urgent need to know more about areas of high prevalence, demographics factors associated with problematic use, methods of procurement, drugs sought and routes of administration.

Such information will allow analysts to:

- Examine how people manage to divert prescription drugs from the drug distribution system;
- Develop an evidence base for understanding the complex relationships between unintentional poisoning, problematic opioid use and diversion, and the medical use of opioid analgesics; [108] [109]
- Work closely with local and federal organisations charged with measuring the national incidence and prevalence of adverse health consequences from inappropriate prescribing of opioids;
- Support regulatory authorities working to achieve balance at the state level by taking disciplinary action against those few practitioners who divert prescription pain medications; and
- Develop policies to encourage better education of practitioners to take necessary precautions when prescribing opioid analgesics.

There is a need in Australia and New Zealand for access to real time medication history available to potential prescribers at the time of prescribing, and to pharmacists at the time of dispensing. Data collection systems should provide privacy safeguards and establish an audit trail to identify every time the patient's record is accessed.

Prescription of opioids should require robust identification of the patient at the time of medical consultation and at the pharmacy. Measures such as tamper resistant prescription pads and increased electronic prescribing should be considered to reduce fraudulent access to opioids. [110]

3. Chronic non-malignant pain in Australia and New Zealand

1. In Australia and New Zealand there is insufficient epidemiological information on people who have CNMP, and on costs of CNMP to the health system, the workplace and to families and communities.
2. CNMP not only affects children and older people but also is associated with people who are most disadvantaged. Australians and New Zealanders are living longer and becoming more obese, thereby increasing the number of people at risk of developing conditions that cause CNMP.
3. The management of CNMP should include a multidisciplinary approach:
   - To minimise the pain
   - To maximise the patient's level of function
   - To minimise the side effects of medication
4. In Australia and New Zealand there is a need for practical, evidence-based prescribing guidelines for the management of CNMP:
   - To create consistency in opioid prescribing
   - To ensure doctors work together with regulators
   - To motivate the ownership, use and implementation of the guidelines particularly in general practice where the bulk of prescription opioid prescribing is initiated and maintained.

This chapter will discuss the epidemiology of CNMP and outline issues to be considered in its management.

3.1 Epidemiology of CNMP

Studies in Australia, New Zealand and Canada have shown that 5-10 per cent of the population have severe persistent pain. [10 11 111] In 2002, an Australian study [10] reported that up to 20 per cent of the population suffered pain and that pain was strongly associated with markers of social disadvantage. CNMP is associated with elderly populations, retirement and inability to take part in the paid workforce.[112] The reported prevalence of opioid dependence among CNMP patients varies among clinical settings. [12] A review of studies conducted in tertiary care pain clinics in the US found that prevalence ranged from 3 per cent to 19 per cent or more. [13 14]

The prevalence of chronic pain in New Zealand ranged from 8 per cent to 80 per cent, due in part to the differences and inconsistencies in the definitions of chronic pain used. [113]

It is estimated over a six month period that one in six adults in the Australian workforce experience pain every day for three months. In the same workforce study, analgesics (2.5 per cent) were the fourth most common drug reported to have been used in the past 12 months. [114]

In 2007, in Australia, the total cost of chronic pain was estimated at AUD34.3 billion or AUD10, 847 per person with chronic pain. Most of these costs (55 per cent) were carried by individuals with chronic pain mainly due to the burden of disease; 22 per cent of total costs were borne by the Federal Government, due primarily to its share of health system and productivity costs. Employers bear 5 per cent, State Governments 5 per cent, family and friends bear 3 per cent, while the remaining 10 per cent is borne by society.[15]

Productivity costs are the largest component, making up around AUD11.7 billion (34 per cent) and reflecting the relatively high impact on work performance and employment outcomes of chronic pain. [15]

3.2 CNMP in children and young people

Common examples of persistent pain of childhood are chronic disease (e.g. cancer, arthritis and sickle cell disease), neuropathic pain (e.g. complex regional pain syndrome, phantom limb pain), recurrent pain syndromes (e.g. migraine, recurrent abdominal pain) and pain due to somatisation.

There is a lack of data on the prevalence of chronic pain in children (between the ages of 0-14 years). While the experience of experts in the field suggests that chronic pain in children is as prevalent as that experienced by adults, the lack of survey data makes the impact difficult to estimate. [15]

A random survey from the Netherlands of over 6,000 children aged 0-18 indicated an overall prevalence of 25 per cent. [115] The prevalence of chronic pain increased with age, and was significantly higher for girls, particularly girls 12 to 14 years of age. The most common types of pain were limb and abdominal pain and headache. Half of the respondents who had experienced chronic pain reported to have multiple sites of pain and one-third experienced it as frequent and severe. These findings indicate that chronic pain is common in children and young people. Sex differences exist in the pain experiences and pain coping strategies of adolescents with chronic pain. [116] Females use more social supports and positive statements whereas males report engaging in more behavioural distraction.

The first Australian [117] report on chronic pain in childhood suggested chronic pain had disturbing consequences for many children. The incidence of school absenteeism, sleep disruption and inability to play sport was high.

Despite the relatively high prevalence of chronic pain in childhood and its significant physical, psychological, social and economic impact on children and their families, it is often under-recognised by clinicians. The reasons for this are multiple and include a child's dependence on caregivers as advocates, and the reduced economic impetus towards a comprehensive approach for children with chronic pain as children do not generally impose a burden on the insurance and compensation system. [118] Children with chronic pain can often be met with a dismissive attitude from their caregivers, especially if no organic cause of their pain is found.

Given the many physical and psychological variables in children experiencing chronic pain and the different modalities of treatment now available, the assessment of a child with chronic pain needs to be comprehensive. The team approach involves, firstly, an assessment of the physical, psychological and environmental parameters and, secondly, developing pain management strategies including pharmacological and non-pharmacological approaches, and individual and family therapy as required. The long term outcome of these strategies is not known, although it has been suggested there is at least short term benefit.

It is only in recent years that a team approach to chronic pain in children delivered through a few specialised clinics has evolved in Australian and overseas centres. On the basis of US data, strategies for the incorporation of pain management and palliative care principles into the care of children with life threatening and life limiting illness should be a high priority.

The socioeconomic cost of CNMP in children and adolescents is considerable, with implications for the child (education, self esteem, friendships), the parents (time off work caring for the child and attending appointments, cost of medication, hospitalisation and complementary therapies) and the healthcare system (medical care, including serial referrals to multiple specialists, medication and hospitalisation and allied healthcare costs).

3.3 CNMP in older people

There is a lack of data on assessment and management of pain in older people, especially those with cognitive impairment. In Australia and New Zealand, the prevalence of chronic pain is projected to increase as the population ages (in Australia in people who are aged over 65 years from around 3.2 million in 2007 to 5.0 million by 2050). The prevalence of chronic pain is projected to increase in men from 13.9 per cent to 15.4 per cent and in women from 16.5 per cent to 18.4 per cent. [15]

The impact of poorly managed chronic pain on the quality of life of elderly patients and the problems related to its management are widely acknowledged.

Underutilisation of opioids is a major component of poor pain management in this group of patients, despite good evidence for the effectiveness of opioids and published guidelines directing their use. [119]

3.4 Occupational disability due to CNMP

CNMP can affect a person's ability to work. Most population based surveys of back pain report a point prevalence of 15-30 per cent, a one year prevalence of 50 per cent, and a lifetime prevalence of 60-80 per cent. [120] In Australia, back problems are the leading musculoskeletal cause of health system expenditure, with an estimated total cost of AUD700 million in 1993-1994.

Work related injury and illness are costly to the individual, both in pain and suffering and in monetary terms. Work related injury and illness is also costly to the community. It has been estimated that, for the 2000–01 financial year, the total cost to the Australian economy of workplace related injury and illness was AUD34.3 billion or 5 per cent of Gross Domestic Product (GDP). [121]

In Australia, among adults, the attributable burden of work place exposure was nearly 44,000 Disability Adjusted Life Years (DALYs) amounting to 1.7 per cent of the total burden of disease and injury in 1996. Many of these deaths occurred at a younger age, increasing the mortality burden to 2 per cent of the total. In 1998, the labour force participation rate for people with disabilities was 53 per cent, while for all people it was 76 per cent. Back injuries accounted for 25 per cent of claims, making the back the most commonly injured part of the body. People with disabilities are less likely to be in the labour force than those without a disability [27] placing a significant socioeconomic burden on the individual and the community.

In New Zealand, the Accident Compensation Corporation (ACC) manages about 1.6 million injury claims every year at a cost of NZ40million. ACC cover is available when any person suffers accidental personal injury (including occupational disease and medical misadventure) at any time in New Zealand or, in a few cases, overseas. Fault is not a consideration, except for cases of suicide, intentional self-injury or injury suffered during criminal conduct resulting in a prison sentence.

While work related injury is a small proportion of all injury related hospitalisations, it is an important cause of hospitalisation among working age people, particularly young males. The hospitalisation rate per 100,000 workers was more than four times higher for males than females and the hospitalisation rate per million hours worked was more than three times higher for males than females.[122]

In some instances, patients may elect to avoid medication appropriate to treat their CNMP if they are working or seeking employment, as many companies require a medical examination, including drug screening testing, before offering or during employment.

3.5 People receiving opioid substitution treatment (OST) who have CNMP

Limited access to good quality, affordable and attractive Opioid Substitution Treatment (OST) for heroin dependent persons may be contributing significantly to the increasing diversion of opioids by increasing the price of black market prescription opioids. It is important to minimise unmet demand for opioid substitution therapy, by increasing the range of treatment options for heroin and prescription opioid dependent people and providing OST as attractively as possible, by making it easy to access, providing good quality care and providing OST free or charging minimum fees.

The prevalence of CNMP among people who are on OST in Australia and New Zealand is not known, nor how many OST patients receive other opioids for CNMP. It is possible that rates of CNMP in OST may vary among different countries, due to differing access to OST.

Evidence from the US and Israel suggests chronic pain is common and problematic in MMT patients. A study of patients from two MMT programs in the US found that 37 per cent reported chronic severe pain. [123] This study also showed that this group of patients with CNMP was more likely to self medicate with illicit medication for their pain. This may be the result of a lack of suitable treatment centres and the lack of a consensus on management options for people receiving MMT.

In another US study of 248 MMT patients, 61 per cent reported chronic pain. These subjects having significantly more health and psychiatric problems than others, and 44 per cent of them believed that opioids prescribed for pain had led to their addiction. [124] In a study of 170 consecutive MMT patients in Israel, 55 per cent experienced chronic pain, and this group had significantly higher methadone doses than those without chronic pain.[125] Compared to patients without pain, patients who reported significant pain at entry into MMT showed poorer psychosocial functioning one year later. [126]

In a study of patients who were on prescribed opioids prior to enrolling in an MMT program in New York State, 89 per cent had a lifetime history of use of oxycodone. [127] This group of patients was also significantly more likely to have chronic pain and to report pain as a reason for enrolling in the MMT program.

3.6 CNMP and mental illness

Many people with CNMP develop affective, cognitive and behavioural components at some stage. The identification of these components is an important clinical challenge.

Estimates of the proportion of patients with CNMP with mental disorders in the US vary widely from 1.5 to 60 per cent. [128] [129] Presence of major depression, dysthymia, generalised anxiety disorder, or panic disorder were associated with initiation and use of prescribed opioids in a general population survey. [130] A review paper has concluded that risk of death by suicide is at least doubled in chronic pain patients, compared with controls. [131]

CNMP and depression are closely correlated with one-half to two-thirds of people with CNMP being less able or unable to exercise, enjoy normal sleep, perform household chores, attend social activities, drive a car, walk or have sexual relations. Pain may have adverse effects on relationships with family and friends, which may become strained or broken. [132]

Through a comprehensively assessed clinical diagnosis of CNMP and good communication with the patient, problems such as anxiety, depression and problematic use of medications may be minimised or avoided. [133] Reassurance that the diagnosis is not life or ability threatening, and encouragement to resume activities of daily living with the use of analgesics are important aspects of management.

3.7 Management of CNMP

Managing CNMP effectively is a challenge for clinicians. As in many other areas of potentially difficult clinical practice, a good doctor-patient relationship is critical and improves health outcomes. Although pharmacological aspects of CNMP management are usually emphasised, nonpharmacological aspects are also very important.

In Australia and New Zealand, patients with CNMP are managed by a number of medical groups:

General practitioners;

- Specialists of all disciplines, traditionally depending on the site of pain e.g. orthopaedic surgeons for back pain, neurologists for migraine, rheumatologists for joint pain;
- Pain specialists (Fellows of the Faculty of Pain Medicine, ANZCA) as pain medicine has been recognised in Australia as a medical specialty;
- Specialists in addiction medicine (Fellows of the AChAM);
- Accredited multidisciplinary pain clinics. These clinics may be difficult to access due to demand and usually act in an advisory capacity (patient is sent back to a GP or specialist with a plan);
- Drug and alcohol clinics where some patients with CNMP would be on an opioid treatment program. These clinics usually act in an advisory capacity where patients are referred if problematic drug use of prescribed drugs is suspected. They would not usually act as prescribers except in the case of initiating OST; or,
- Hospital emergency departments where patients with CNMP, such as those who suffer from migraines, may present. Emergency departments regularly attend to patients who seek parenteral opioids for CNMP.

Principles underlying the management of CNMP

The overall goal for management of CNMP is to ensure best practice to allow patients to pursue their lives as normally as possible. If CNMP is left untreated, is under-diagnosed or misunderstood, patients are likely to have poorer outcomes. [2] People from a lower socioeconomic background or from families with profound and multiple problems are over-represented in populations of CNMP. People with CNMP often have difficulty accessing medical care, and clinicians are challenged when faced with patients who have mental health problems, or complex medical histories with multiple comorbidities. For some patients, a clear source for their ongoing reports of pain may not have been established and questions regarding prior substance use may not have been asked during their evaluation.

Patients are helped if they can understand that the causes of the pain are complex, that the aims of pain management are to reduce pain to acceptable levels with acceptable side effects of treatment and to improve function as much as possible. This includes the recognition that non-pharmacological aspects have an important role to play alongside pharmacological agents and that medications including analgesics have limitations.

Objectives of a multidisciplinary team approach

There is substantial evidence (and broad consensus by experts in the field) that a multidimensional pain management approach, covered by a range of medical and allied health disciplines, can return individuals to work who would otherwise be unemployed or not participating in the workforce. [15] [134] In a three month uncontrolled trial of patients with CNMP, being treated with opioids at a multidisciplinary, primary care based, management program improved pain, depression and disability scores. [14] To achieve improved outcomes, appropriately trained health professionals are needed to assess and treat the broad range of problems in patients with CNMP.

Multidisciplinary pain management centres typically utilise the services of a range of health professionals to assess the multidimensional aspects of pain and to design appropriate programs of treatment aimed at control of pain and improvements in functional outcomes. Such professionals may include physicians with a background in anaesthesia, medicine, psychiatry or rehabilitation medicine, and clinical psychologists, physiotherapists, occupational therapists, rehabilitation counsellors and social workers.

Role of opioid pharmacotherapy

Although the issue is still contentious, there is a consensus among experts in pain medicine that non-parenteral opioids play an important place in the management of CNMP. This matter is taken up in detail in the next chapter.

Ideally all people who are commenced on opioids for CNMP should have been assessed by a multidisciplinary pain service. [135] [136] [137] [138] [139] Given the logistical difficulties with this there should have been, as a minimum, an assessment by experienced health professionals from an appropriate range of disciplines and an adequate trial of non-drug and non-opioid treatment.

Non-pharmacological options for CNMP management

Non-pharmacological management options for patients with CNMP include:

- Modification of social factors relevant to the patient's situation;
- Attention to lifestyle factors, including diet, exercise and sleep management; [140]
- Psychological techniques, such as such as relaxation, cognitive-behavioural therapy, various forms of counseling (supportive, rehabilitation, financial); and
- Physical techniques such as physiotherapy, exercise programs, hydrotherapy, activity pacing and modification of tasks. [141] [142]

All attempts must be made to ensure that patients fully understand the nature of CNMP, including provision of self help literature for managing their pain. While most people with CNMP may be managed effectively by coordinated services at the community level, a number will need the resources of multidisciplinary pain management centres of services. [143] Currently in New Zealand and Australia there are not enough multidisciplinary services available for people with CNMP. As described in Chapter 2 of this document, there are inequities in the distribution of services as most people who have CNMP live in disadvantaged areas.

Role of GPs

Most people with CNMP are treated primarily by GPs, at least in the first instance.[144] The majority of prescriptions for opioids are written by GPs. [103] In some circumstances the opinion of a pain specialist may be required for the continuation of authority to prescribe an S8 drug. Access to pain clinics is limited, with long waiting times at most major hospitals. [145]

A number of factors can discourage primary care doctors from managing CNMP patients with opioids. Some fear the cognitive, respiratory, and psychomotor side effects of opioids. Others may be concerned about the risk of creating or exacerbating problematic drug use, or contributing to diversion of prescription drugs to the black market. [24 25]

In Australia under Medicare, GPs are currently enabled to coordinate Multidisplinary Care Plans and Team Care Arrangements providing benefits for limited access to physiotherapy, chiropractic, osteopathy services, and dieticians. However these are each limited to maximum five services each per calendar year, and again often there are large out of pocket expenses. Acupuncture services may be provided by accredited GPs but there is no current provision for Medicare subsidy of acupuncture provided by other practitioners.

Access to allied health professionals and role of complementary medicine in management of CNMP

Many people with CNMP turn directly to alternative health practitioners including chiropractors, osteopaths, acupuncturists, herbalists, aroma therapists, hypnotherapists, practitioners of Alexander, Pilates and Feldenkrais techniques. Although specific data is unavailable for the use of these services for treatment of CNMP, there has been a trend to increasing utilisation of such services in Australia. [146 147 148]

For some of these services there is evidence of benefit for treatment of some types of pain, while for others the evidence base is poor or nonexistent. Reasons for the use of these services in preference to medical treatment may include actual or perceived benefit, disappointment with services provided by medical practitioners, reluctance to accept treatment with medications including experience of, or fear of side effects, and difficulty in getting access to conventional treatments.

Some of these services are subsidised by private health insurance funds, although often there are large out of pocket expenses. Access to these services is very limited for those many people with CNMP and low income.

Medical practitioners should be encouraged to:

1. Acknowledge the right and be respectful towards people who choose to use alternative services;
2. Consider the extent to which failure to provide optimal medical treatment may be a factor in the choice of alternatives; and
3. Consider the principles and evidence base for various alternative treatments in order to provide appropriate information and allow patients to make informed choices.

Conclusions

Chronic pain in Australia and New Zealand is prevalent and likely to increase, with substantial personal, social, economic costs including occupational disability.

Gaps in the epidemiology of people with CNMP include the following:

- Prevalence of CNMP in drug dependent populations;
- Numbers of poly-drug users who obtain opioids for CNMP;
- Attitudes of medical practitioners to CNMP, to the use of opioid analgesics in pain control, to the use of guidelines and to regulation; and
- Comorbidity of CNMP with depression and other mental health illnesses.

The prevalence of CNMP in populations on OST programs in Australia and New Zealand is not known, but based on evidence from other countries, may be substantially higher than in the general population.

Most patients with CNMP are managed mainly in a primary care setting. Multidisciplinary models of care, both in primary care and in specialist referral centres, are important to optimise pharmacological and non-pharmacological management of CNMP. There is currently an unmet need in the population with CNMP for services specialising in pain medicine and addiction medicine.

What needs to be done?

It is important to have sufficient multidisciplinary pain management centres to enable timely assessment. These centres should always include an Addiction Medicine Physician and a Pain Physician and make provision for patients with a personal or family history of problematic substance use, or other psychological problems, to be assessed.

Strategies for improving management of CNMP need to recognise the essential role of GPs, and support the provision of multidisciplinary care at the primary care level.

Clear and up to date information should be available to medical practitioners about the evidence base for various alternative treatments for CNMP. This should be provided by an appropriate body with resources to develop evidence based guidelines for practitioners. Consideration should be given in Australia to the need for Medicare subsidy of more than the current limited number of services for allied health services for people with CNMP.

Early assessment and intervention should be encouraged, particularly where CNMP is limiting the ability of people to return to work. This can be facilitated through improved awareness and education of people with chronic pain, and among medical practitioners and employers. In the workplace context, strategies are needed to counter workplace misperceptions and discrimination against people with chronic pain especially if the cause of chronic pain is not obvious, to help induce cultural change among employers and employees and to identify and implement long term solutions.

To increase access to multidisciplinary pain management in both primary care and referral centres, there is a need to increase training positions and increase the availability of qualified practitioners in geographical areas where they are lacking. Research capacity should be developed to overcome gaps in the body of evidence on effective management of people with CNMP and promote best practice.

Given the prevalence of chronic pain in children and the potentially serious physical and psychological consequences, a considerable research effort as well as a review of services for children, is required.

The issue of the use of opioids for CNMP is controversial, with some people questioning whether these drugs are appropriate at all given their propensity to induce tolerance and dependence. In the absence of firm evidence, it is difficult to devise straightforward guidelines on the ethical use of opioids for CNMP. Consequently prescribing patterns vary widely.

Evidence of benefit of opioids for CNMP has been shown only in the short term, [17] [149] but the evidence that opioids in CNMP are associated with severe side effects is weak. Considering the large numbers of people who are prescribed opioids for CNMP, relatively few experience problems (including dependence).[19] However those patients who do experience problems generate many visits to GPs and specialists, costly investigations and substantial conflict between patients, healthcare workers, pharmacists, government health departments and insurers.

Recent evidence of diversion, trafficking, and harm from problematic use adds a new dimension to already difficult risk/benefit decisions, both in individual patients and at a population level. There is a need to exercise stewardship over the supply and use of pharmaceutical opioids to enable optimal management of pain, by creating a situation where medical practitioners can be confident that supply is appropriate, and the risk of diversion is small.

4. Opioid pharmacotherapy in CNMP

The use of opioids in patients with CNMP is controversial and characterised by polarised viewpoints. Clinicians prescribing opioid pharmacotherapy in CNMP need to consider:

- Their duty of care to control pain 'as well as possible';
- That the evidence for benefit from long term opioids is weak and the evidence for harm is unclear;
- The increasing rates of consumption of prescription opioids;
- That problematic opioid use has the potential to be a major health burden;
- Whether comprehensive treatment principles are being followed;
- The concept of universal precautions in pain medicine; and
- The risk of developing opioid dependence ('addiction') in the context of treating CNMP is unknown.

4.1 Ethical considerations in the use of opioids for CNMP

This area of medical discourse is plagued by myth and misinformation. On the one hand has been a pervasive *opiophobia*, characterised by frequent under-treatment of pain, false accusations against patients when uncontrolled pain rather than deliberate drug seeking prompts their behaviour, fear of the risks of 'addiction' and of falling foul of regulatory authorities. On the other hand there is the admonition to attend to the needs of the patient, including relieving suffering.[150] Perhaps influenced by the principle that the treatment of pain should not be different from the treatment of other ailments, there has been an exponential increase in the prescription of opioids in the treatment of cancer pain and CNMP, based on the assumption that adverse effects to the patient and society are minimal.

Clinicians must balance the need to ensure that patients with pain receive appropriate treatment with the need to protect patients and society in general from the consequences of opioid dependence, diversion and trafficking. [151]

Some principles may be articulated:

- The patient with CNMP has a right to be treated in a way that reduces their pain in order for them to enjoy a functional life;
- The clinician has a duty of care to the patient with CNMP to control their pain as well as possible, while respecting the principle of *primum non nocere*;
- This responsibility of the clinician extends to acquiring the knowledge and skills for assessing and managing pain;
- Patients with pain have a right to be informed of the clinician's philosophy of pain management, experience in providing it and knowledge of and adherence to current clinical practice guidelines;
- Informed consent assumes that patients are capable of assessing harm and benefit when presented with adequate and accurate information;
- Patients' privacy concerns in this respect remain paramount; and,
- The prescription of opioids always entails a calculation of benefit and risk, the latter including the problems of increasing dose and diversion.

4.2 Evidence for efficacy and side effects of opioids in CNMP

Double blind studies are very difficult to conduct in patients with CNMP due, among many factors, to the heterogeneity of such a patient population. None of the studies reviewed lasted more than a few weeks. There are no longitudinal

randomised controlled trials on the long term effectiveness and consequences of opioid use in CNMP patients.

Five recent reviews are summarised here.

(i) Opioids in chronic non-cancer pain; systematic review of efficacy and safety. [152]

Eleven studies (1025 patients) compared oral opioids with placebo over periods ranging from four days to eight weeks. Substance misuse was an exclusion criterion in most studies. Comparative studies were not included. Mean decrease in pain in most studies was of the order of 30 per cent. Eighty per cent of patients experienced at least one adverse effect: constipation (41 per cent), nausea (32 per cent) and somnolence (29 per cent).

(ii) Efficacy and safety of opioid agonists in the treatment of neuropathic pain of nonmalignant origin: systematic review and meta-analysis of randomised controlled trials. [153]

Twenty-two articles met the inclusion criteria for this review but only eight were of 'intermediate' term of treatment (range 8-56 days, median 28 days); the other 14 were less than 24 hours of treatment. Meta-analysis of 6 of these 8 found mean post-treatment visual analogue scores of pain to be 14 points lower (95 per cent CI –18 to –10) on a 0-100 scale than after placebo. Common side effects identified were nausea, constipation, drowsiness, vomiting and dizziness.

(iii) Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side-effects.[16]

Data was extracted from 41 'randomised' trials that met inclusion criteria (6019 patients), although randomisation was judged to be adequate in only 17. Eighty per cent of the subjects had 'nociceptive' pain; mean duration of opioid treatment was 8-9 weeks for 'fibromyalgia' and 'mixed' pain, and 4-5 weeks for other nociceptive and neuropathic pain. Patients with 'addiction' were excluded from 25 trials. However 17 of the trials (3433 patients) were with tramadol; only 10 trials (964 patients) used controlled release morphine or oxycodone.

Meta-analysis of 28 placebo-controlled trials found standard mean differences (SMD) for comfort of –0.60 (95 per cent CI –0.69 to –0.50) in favour of opioids and SMD for functional improvement of –0.31 (95 per cent CI –0.41 to –0.22) in favour of opioids. Meta-analysis of 8 comparative trials showed non-significant SMD for pain relief although dissection of this did find that strong opioids were more effective than other drugs. Side effects included constipation (absolute risk difference RD 16 per cent), nausea (RD 15 per cent), dizziness (RD 8 per cent), drowsiness (RD 9 per cent), vomiting (RD 5 per cent) and pruritus (RD 4 per cent).

(iv) Systematic review: opioid treatment for chronic back pain: prevalence, efficacy and association with addiction. [154]

This review found little evidence for the use of opioids such as codeine and oxycodone for chronic back pain. Five of the studies on effectiveness compared an opioid with a placebo or a non-opioid analgesic, and meta-analysis of the most suitable four (all randomised trials) found no significant benefits associated with opioids. Another five studies compared one opioid with another. Meta-analysis of the best five found a non-significant trend towards improvements from baseline in treated individuals.

The following conclusions may be drawn from these studies:

- Opioids were effective in the treatment of CNMP over short periods, being associated with reduced pain and improved functional outcomes compared with placebo;
- Opioids were more effective than placebo for nociceptive and neuropathic pain;
- Strong opioids (oxycodone and morphine) were statistically superior to naproxen and nortriptyline (respectively) for pain relief but not for functional outcomes;
- Weak opioids (propoxyphene, tramadol and codeine) did not significantly outperform NSAIDs or TCAs for either pain relief or functional outcomes; and
- Clinically (10 per cent) and statistically, only constipation and nausea were significantly more common with opioids.

Although recent studies [17] [155] have indicated that endocrinological abnormalities and erectile dysfunction can be experienced by patients taking opioid medication for chronic conditions, most researchers did not ask participants about sexual dysfunction. The few studies that collected such data were relatively short for the observation of any endocrinological abnormalities. The only two studies [156] [157] that reported data on sexual function showed that patients taking opioids actually perceived themselves as doing better in terms of sexual behaviour compared with those in the control groups. Improvement of wellbeing secondary to better pain control may account for this result.

(v) Another approach to this issue was taken in a Danish study in which a random sample of 10,066 individuals was interviewed face to face and completed a self administered questionnaire. [158] Of these, 1906 individuals responded that they had pain lasting six months or more (pain group). Almost one-third of this group used opioid analgesics compared with 4 per cent of the control group; opioids were used regularly or continuously by 12 per cent of the pain group overall or by 20 per cent of those who reported moderate or severe

pain as opposed to 3 per cent of those who reported mild pain. Opioid use in the pain group was associated with reporting of moderate, severe or very severe pain, with poor self rated health, living alone, not being engaged in employment or not being physically active in leisure time. Although no causal relationships can be inferred, it was asserted that the use of opioids in the pain group was not associated with achievement of improvement in pain control, functional status or quality of life.

In summary randomised controlled trials provide evidence that opioids can provide initial benefit in terms of reduction in pain and increase in function in patients with CNMP. However this demonstrated efficacy of opioids over the short term does not necessarily predict long term effectiveness with respect to pain, function or quality of life. Although RCTs are considered to provide 'best evidence', they can play only a limited role in the assessment of the effectiveness and suitability of long term opioid treatment in CNMP, due among many factors to the impracticality and artificiality of conducting them and the lack of generalisability to wider, less homogeneous populations. [159] This suggests that the long term role of opioids in the management of CNMP depends on the outcome of a therapeutic trial in individual patients using agreed outcome measures.

4.3 Evidence for risk of dependence

There is currently no Australian data from which to infer the numbers of people with CNMP who are legally prescribed opioids for the relief of their pain and who subsequently develop dependence on opioids. However, general consensus is that this number is generally small. [19]

Methods for detecting and measuring severity of prescription opioid dependence are weak. The published randomised trials have been of too short duration to allow for the development or detection of atypical drug use, even if appropriate screening tools for addiction or dependence had been used. Some studies excluded patients with 'addiction.' In others adequate criteria for diagnosing 'addiction' were lacking. For example, it is hazardous to equate reported 'drug craving' or 'reported symptoms and signs of addiction' with addiction. In only a minority of comparative trials have investigators even attempted to approach this question. Furthermore, none of the studies were rigorous enough to draw conclusions about opioid prevalence of addiction or use. [16]

A search for evidence on the risk of dependence found a handful of poor quality observational studies reporting that up to 43 per cent of patients receiving opioids for back pain had a current substance use disorder, and between 5 per cent and 24 per cent showed 'aberrant medication taking behaviour'.

A secondary analysis of 15,160 chronic users of opioids (other than methadone) for CNMP in a veteran's population found a 2 per cent rate of new opioid misuse or dependence diagnosis. This was associated with mental health disorders and with non-opioid substance misuse. Higher rates of misuse/dependence were seen in older age and with more prolonged exposure. [160]

Prevalence of opioid addiction (using DSM IV Criteria) in patients with intractable headache receiving daily opioids fell from 31 per cent to 2 per cent when 'pain related behaviour' was excluded. [161]

4.4 Principles of opioid maintenance for CNMP

Pharmacotherapies are the most frequently used treatment for patients with CNMP.[162] The decision to prescribe opioid analgesics is complex, as clinicians often balance several disparate considerations when deciding the best course of action. Influences on prescribing may include information from the evidence based literature, 'detailing' from the pharmaceutical industry, the experience of peers, medical education seminars and prior experience. In opioid prescribing, doctors may also weigh up the potential for problematic use of opioids, addiction, adverse effects, tolerance and medication interactions. Some clinicians are more comfortable prescribing opioids for terminal cancer than for CNMP or for patients with a history of drug or alcohol dependence.[163] There is also evidence that doctors often feel uncertain about the merits of some therapies and believe they lack knowledge in the areas of pain medicine and of addiction medicine.[164]

Patients taking medications for CNMP have been shown to be concerned about addiction, their perceived needs, unfavourable scrutiny by others, adverse effects, tolerance, mistrust on the part of the doctor, and drug withdrawal symptoms. Each of these domains predictably relates to the dose of medication used and the presence of co-existing physical or mental health problems such as depression or disability. [165] Interventions that try to respond to these concerns may influence the use of medication in CNMP and the development of adverse consequences.

The criteria for identifying problematic use of opioids in patients are well documented. Clinicians should take a history of problematic drug and alcohol use in all patients. This includes current and past use of opioids, alcohol and other drugs as well as history of previous treatment for drug and alcohol use and family history. [13] Most people do not have past or current problematic use of alcohol or other drugs. It is also common to see people with major problems who have a history of 'illicit drug use' but present with 'genuine pain at the moment'.

The following principles for prescribing opioid analgesics for CNMP have been extracted from a number of sources.[17 45 166 167 168 169]

1. There should be a comprehensive assessment:
    - Somatic assessment to identify nociceptive or neuropathic contributions to pain and whether those are directly treatable;
    - Psychological assessment, especially regarding beliefs, behaviour and mood;
    - Assessment of social environment; and
    - Assessment of actual and potential substance use in patients and their family.
2. There should be failure of adequate trial of other therapies:
    - Consider the range of treatment options available, including non-pharmacological techniques, non-opioid analgesic drugs and/or adjuvant analgesic drugs; and
    - Note that an assertive approach to rehabilitation may include the use of opioids on a short term basis with the express aim of restoring function.
3. There should be a contractual approach to opioid use:
    - Only one prescriber, or team, to be in charge of prescribing opioids;
    - Particular caution to be taken with patients who are not known to the team or prescriber;
    - Long term opioid therapy is a serious undertaking that requires commitment of physician and patient;
    - Reasonable and measurable goals to be set with discontinuation of opioid therapy if these goals are not met;
    - These goals to include not just pain abatement, but also improvement in function; and
    - Use of written agreement, contract or consent.
4. Practical considerations:
    - Consider opioid therapy as an adjunct, not as a sole modality;
    - Use longer acting/sustained release oral, suppository or transdermal preparations;
    - Avoid the use of 'breakthrough' medication, especially parenterally;
    - Emphasise outcome of improved function not just increased comfort;
    - Initiate therapy as a trial; ensure regular and careful review of both pain and function;
    - Monitor using pharmacy databases, pill counting or urine toxicology; and
    - Maintain good documentation.
5. Response to apparent increase in dose requirements should be assessed:
    - Has there been a change in underlying disease state?
    - Has there been a change in psychological or other stressors?
    - Has there been an improvement in function?
    - Has tolerance developed?

4.5 Universal precautions in pain medicine

A relationship of trust between prescriber and patient will reassure the patient that developing problems can be discussed safely. If problematic drug use is suspected, the prescriber will need to discuss concerns sensitively with the patient. Increasing frequency of clinic visits and prescription of small quantities of drugs may improve adherence to the agreed treatment plan. Clinicians may be asked to provide replacement prescriptions for drugs or prescriptions that have been lost or stolen. If there are concerns at the start of the treatment plan, patients should be advised that lost or stolen drugs or prescriptions should be reported to the police and that documentary evidence of this should be given to the prescriber. Specifying on the prescription the name of the pharmacy at which the patient intends to have it dispensed will avert the situation where the patient has it dispensed at a remote pharmacy but claims to have lost the prescription. If such loss is recurrent it is reasonable to terminate the prescription of opioids. It should be kept in mind that lost medication may pose a risk to children or others who find it, adding to the need to exercise close supervision of supply.

Unusual behaviours that appear during therapy must be comprehensively assessed and documented. This alerts future prescribers to the potential for problems. If the differential diagnosis of dependence is made, the patient can be referred to an addiction specialist for an opinion or continuing management.

One particular formulation of many of the above principles (Section 4.4) has been articulated by Canadian authors with an interest in the nexus of opioid use for pain and addiction under the rubric 'Universal precautions in pain medicine.' [13 170]

The analogy is with universal precautions taken by health professionals to prevent spread of blood borne infections. The key to this idea is that the precautions be universal, in recognition of the ubiquity of risk, and to reduce stigma associated with any targeted use of such precautions.

This approach stresses the following:

- The idea of a continuum between pain and addiction, rather than a dichotomy between them;
- The importance of a comprehensive substance use history and family history to identify people at risk of developing problems;
- The usefulness of urine drug toxicology to assist in identifying at-risk patients;
- A treatment agreement based on informed consent regarding the risks of dependence; and
- Clear boundaries surrounding the use of opioids.

Use of opioids for chronic pain is always on the basis of a trial of their usefulness, subject to ongoing evaluation.

This approach has potential for prevention and early identification of problematic opioid use as well as appropriate 'triage' into levels of specialist care as needed, including pain and addiction specialist care. It may have particular utility for GPs.

4.6 Urine drug testing [171] and therapeutic blood monitoring

Urine is considered to be the best biologic specimen for detecting the presence or absence of certain drugs due to specificity, sensitivity, ease of administration, non-invasiveness, and cost of the assay. There are controversies regarding the clinical value of urine drug testing (UDT), partly because the most current methods are designed for, or adapted from, forensic or occupational deterrent based testing for unsanctioned drug use and are not necessarily optimised for clinical applications in CNMP management. In CNMP management, when used with an appropriate level of understanding, urine drug testing can improve a physician's ability to manage therapeutic prescription drugs with controlled substances by giving an indication of other substance use.

Urine drug testing is often used in monitoring other substance use in OST, and is increasingly used in workplace and other legal or forensic settings (such as probation and parole or medical/nursing board supervision) governed or required by laws, courts orders and/or regulations.

In North America there is increasing use of UDT in pain management.[13] [172] UDT may be most effective where the results are used to improve communication, and in line with the idea of 'universal precautions' outlined above. [173] However there is evidence that many doctors employing UDT in management of pain and in other contexts [174] lack proficiency in the interpretation of tests. It is questionable whether Australian or New Zealand GPs have the necessary expertise and training to deal with ethical issues that arise in interpreting urine toxicology for the workplace. [175]

The 'validity of self-reports of substance use can vary considerably depending on context.' [176] There is evidence that self-report of substance may be effectively supplemented and improved by UDT,[177] especially under certain conditions: 'when patients are in treatment, when urine samples are collected with patients' prior knowledge, when patients are well-known to staff, and when honest self-reporting is encouraged.' [178]

There are differences between various tests and even among the testing laboratories and manufacturers of various rapid drug screen tests, including the number of drugs tested, cross-reactivity patterns, cut-off concentrations, and drug interferences.

In clinical practice, urine drug testing can be used for accurate record keeping, to identify use of undisclosed substances. It has a limited place in determining appropriate intake of prescribed substances, as most screening tests (immunoassays such as cloned enzyme donor immunoassay (CEDIA), and (EMIT) are qualitative or semi-quantitative and cannot distinguish between occasional and regular use of opioids. CEDIA screening has a high sensitivity for morphine and codeine, but not for oxycodone, so may provide a false negative result for detecting oxycodone. Gas chromatography mass spectrometry (GC/MS) tests are more specific and more reliably quantitative but are expensive. GC/MS can also distinguish which particular benzodiazepine has been taken by the patient.

The role of therapeutic blood monitoring in this area is still being developed. Laboratory services for blood monitoring of opioids is variable across Australia and New Zealand. Some of the therapeutic ranges are still being developed, however blood (or urine monitoring) can help establish whether a patient is taking any of their prescribed opioids or not. Therapeutic monitoring is relied on by experts in some specialised areas. One of the difficulties in this area is the inability at present to measure the extent of tolerance or dependence and to take these into account when measuring blood levels. Another disadvantage is that obtaining a blood sample is necessarily invasive.

4.7 Management of CNMP in illicit opioid users

The treatment of opioid dependence (addiction), whether to heroin or prescription opioids, with OST (that is, methadone or buprenorphine) is effective. OST decreases illicit opioid drug use, increases treatment retention, decreases criminal activity, improves individual functioning, and decreases HIV and possibly other blood borne virus transmission.

Addiction brings out neurophysiologic, behavioural, and social responses that increase people's experience of pain and complicate provision of adequate analgesia. These complexities are heightened for patients with opioid dependence who are receiving OST, for whom the neural responses of tolerance or hyperalgesia may increase the pain experience. As a consequence, opioid analgesics are less effective and higher doses administered at shortened intervals are required. Opioid agonist therapy provides little, if any, analgesia for acute pain. Fears that opioid analgesia will cause addiction relapse or respiratory and CNS depression are unfounded. Furthermore, clinicians should not allow concerns about being manipulated to cloud good clinical assessment or judgment about the patient's need for pain medications. Reassurance regarding uninterrupted OST and aggressive pain management will mitigate anxiety and facilitate successful treatment of pain in patients receiving OST. [26]

In Australia and New Zealand, there are currently no guidelines for practitioners for treating CNMP in patients enrolled in OST. Patients on MMT programs may experience a heightened sensitivity to pain and mood disturbances.[179] Patients receiving MMT who have acute pain can additionally receive other opioids, when indicated, in addition to their daily methadone maintenance dose. [26] A possible benefit in managing CNMP with a different opioid than OST is improved titration of analgesic dose. However, the risks of additional oral opioids in unstable patients receiving OST cannot be ignored. These risks include diversion, self injection, and stockpiling for suicide attempts. Another option is to use adjunctive medication such as paracetamol, antidepressants or anticonvulsants.

Other studies have focussed on opioid tolerance in patients on MMT and suggest that group is cross-tolerant to the analgesic effects of morphine. As a result, pain relief, when obtained, does not last as long as expected. This phenomenon, of incomplete cross-tolerance for opioids, may in part explain why patients receiving MMT may require higher and more frequent doses of opioid analgesics to achieve adequate pain control. [180] More recent explanations for opioid-induced hyperalgesia have been re-examined and suggest that analgesic tolerance counteracts the analgesic effects of opioids and complicates pain management. [26]

Methadone for Pain guidelines [181] were developed in Canada in 2004. Methadone was recognised as having a particularly useful role in pain management on the basis of its activity at the N-methyl-D-aspartate (NMDA) receptor. As well, its long half-life may help stabilise patients who experience fluctuations in their opioid drug levels and who are developing withdrawal symptoms between doses (also referred to as 'withdrawal mediated pain'). This was identified as being particularly useful for the relatively small but important subgroup of pain patients who suffer from addictive disorders, as well as CNMP. However it should be kept in mind that the pharmacology of methadone is complex and its use as a stand alone analgesic carries substantial risk of accumulation to delayed toxicity over the first few days of initiation of treatment.

There is also large inter-individual variation in the pharmacokinetics of this drug. [182] The authors of this document recommend extreme caution in use of this analgesic due to the risk of accumulation and opioid toxicity unless the prescriber is experienced in its use. The patient should be reviewed for symptoms and signs of over sedation 4-6 hours after dosing over the first five days of use.

Opioid-induced hyperalgesia has been used to refer to:

(i) a decline in analgesic efficacy during opioid treatment for pain; and

(ii) an increased sensitivity to stimuli in individuals with opioid *addiction*.

It is very difficult to distinguish between 'opioid-induced hyperalgesia' and opioid *tolerance*. That the cellular mechanisms of opioid-induced hyperalgesia have much in common with those of opioid tolerance and of neuropathic pain (the latter traditionally considered to be relatively opioid-nonresponsive) serves only to add to the confusion.

There may be two phenomena:

1. Patients on OST for addiction and who do not have pain may nonetheless develop increased sensitivity to noxious or potentially noxious stimuli. The clinical importance of this phenomenon is not clear.
2. It is not known whether patients with CNMP treated with long term opioids develop such increased sensitivity. Such patients may develop a decline in analgesic efficacy that may be due to opioid tolerance or to other (usually psychosocial) factors but it is not appropriate to label that as opioid-induced hyperalgesia.

In the context of opioid treatment of CNMP, an undue emphasis on the idea of opioid-induced hyperalgesia can detract from considerations of tolerance or other stressors. It is relevant to (i) the unresolved issue of ceiling effect of opioids in this situation and (ii) the practice of the dose of opioid being increased in response to an apparent decline in analgesic efficacy when the opposite should be done because of opioid non-responsiveness or the development of dysphoric withdrawal phenomena.

4.8 Existing guidelines for the use of opioids in management of CNMP

There are a number of guidelines currently available to assist practitioners in managing chronic pain and opioid use. Appendix 5 assesses available guidelines on opioid use in relation to CNMP using NHMRC principles (shown in Table 6), discusses their relevance and utility to the Australian practitioner and makes recommendations for their use.

Until further evidence is available any evidence based guidelines will be hampered by the lack of studies of the long term use (16 weeks) of opioids in CNMP: few strong studies have been completed in this area.

Clinical practice guidelines may assist practitioners and patients to make better decisions about appropriate healthcare for specific clinical circumstances [183] and can bring about change and improve health outcomes. Little information is available about adherence to the existing guidelines for opioid use in CNMP by Australian and New Zealand medical practitioners. One reason for this may be the number and variety of these guidelines, none of which is universally accepted or used. However there is substantial evidence that practitioners generally do not consistently use available clinical guidelines in other areas of medical practice.[184]

Conclusions

In Australia and New Zealand there are a number and variety of guidelines for opioid use in CNMP. Unfortunately there is little information in relation to adherence to existing guidelines by Australian and New Zealand medical practitioners. There is a need for clear guidelines for management of people with CNMP who use illicit opioids. Many medical practitioners lack skills in the interpretation of urine toxicology.

Guidelines on managing patients with CNMP, including the prescription of opioids, need to be broadly consistent across Australia and New Zealand, widely agreed upon, especially by GPs, and compliance with guidelines needs to be better monitored.

The approach 'Universal precautions in pain medicine' has potential for prevention and early identification of problematic opioid use as well as appropriate 'triage' into levels of specialist care as needed, including pain and addiction specialist care.

What needs to be done?

There is a need for academic pain medicine to develop consumer satisfaction instruments, guidelines that are more practical to GP settings, ownership of these issues by GP professional bodies, better dissemination and implementation of guidelines, and better evaluation and surveillance.

GPs require greater support to take the lead in the development and implementation of guidelines as most patients with CNMP are managed mainly in a primary care setting.

Provision should be made for compliance with guidelines to be monitored, and for effective and reasonable sanctions on medical professionals who repeatedly and consistently breach guidelines for prescribing opioids for CNMP.

Information on the interpretation of urine toxicology should be provided in accessible form for all doctors, especially for GPs. Consistent guidelines should also be developed for management of CNMP in illicit opioid users and poly-drug users.

There is a need to improve medical practitioners' skills in identifying patients at risk of developing opioid dependence or likely to be involved in diversion of opioids, and being aware of indicative unusual behaviours that may appear during therapy. There may be benefit in introducing electronic prescribing software that (i) identifies patients who turn up early for repeat doses; (ii) flags certain medications; (iii) calculates the number of pills used/day.

Research efforts should be directed at the following unresolved questions:

- Is opioid therapy beneficial in the long term?
- If so, what factors predict benefit and how can benefit be maximised?
- Should there be a maximum dose of prescription opioids?
- Does the dose of prescription opioids have differential effects on efficacy and safety?
- What is the realistic probability of dependence (addiction)?
- How can the risk assessment of problematic opioid use be improved?

5. Regulation of opioid prescribing

This chapter will highlight the range and differences in jurisdictions across Australia and New Zealand. The rationale for the regulation of opioid prescribing is to achieve an optimal balance between making these drugs as available as possible in order to maximise their benefits while coordinating their supply to individuals, and controlling their use to minimise the harms from unsanctioned use.

5.1 Effects of regulation

A general principle in drug scheduling is that drugs considered to be more dangerous are more restricted and the availability of drugs considered to have minimal risks when used in excess are less restricted.

Clinicians who prescribe Schedule 8 (S8) drugs for controlling CNMP know that they will be more carefully scrutinised than if they prescribe drugs from medications from lower schedules. Therefore, one of the effects the current scheduling system has on clinicians is to move them from prescribing S8 drugs to prescribing lower schedule drugs. S8 are also a way of classifying drugs that require surveillance and monitoring and accordingly a balance is required to ensure patients receive adequate and appropriate pain control. Chapter 2 presents some of the consequences the current system has on opioid prescribing and regulation from a clinician and patient perspective.

It is half a century since the Commonwealth of Australia prohibited the production of heroin. This prohibition was opposed at the time by the RACP.[185] In 2008 it was 103 years since the first Commonwealth legislation concerned with controlling psychotropic drugs, the *Opium Proclamation* of 1905. The Queensland and South Australian Parliament passed legislation, *Aboriginals Protection and Restriction of the Sale of Opium Act 1897* to prevent farmers paying their Aboriginal workers in opium. [186] In Australia and New Zealand the main focus of early policy was on preventing the smuggling of opium and pursuing and prosecuting Chinese opium smokers. In contrast, non-Chinese suffering from the illness of addiction were treated medically.

Australia and New Zealand's response followed that of the United Kingdom and was in contrast to the United States where users and/or those dependent on opiates, cocaine and marijuana were stigmatised as morally degenerate or as criminals.[187] Once regulations were introduced, there was an opportunity for profiteers to enter the market along with an increase in related problems such as the stigma attached to opioids which has affected the use of opioids for relieving pain.

5.2 Under and over prescribing of opioids: differences in opinion and practice

As discussed in Chapter 4, some physicians may be reluctant to prescribe opioid medications owing to fear of cognitive, respiratory, or psychomotor side effects, iatrogenic drug addiction, prescription drug diversion or regulatory issues. [24] Fears of cognitive, respiratory, and psychomotor side effects and of worsening drug addiction are generally unwarranted in using opioids for treatment of pain in the context of OST.

Difference of opinion and practice are such that regulation of prescribing is very difficult. What one 'expert' might define as 'inappropriate' prescribing or 'problematic' use might be quite acceptable to another. The powers of a surveillance authority to identify 'rogue prescribers' are weak. Responses to identification of inappropriate prescribing include:

1. Counselling the doctor and seeking clarification as to the rationale for the prescribing that is occurring. Any evidence of 'doctor shopping', needs to be brought to the attention of the prescriber(s);
2. Denying the S8 application (if one has been lodged). This may be subject to appeal by the prescriber; and
3. Reporting the matter to the State Medical Registration Board. This is unusual due to the lack of consensus mentioned above, and would most commonly happen in instances where the doctor was him/herself suspected of problematic drug use.

5.3 Regulation in Australia and New Zealand

In Australian and New Zealand government jurisdictions, legislation and controls govern the prescription, supply and control of problematic drug use. Controls are placed upon drugs and poisons to protect the public from harm.

Australia

Within Australia the scheduling of drugs and poisons is determined by the National Drugs and Poisons Schedule Committee (NDPSC). This committee was established under section 52B of the *Therapeutic Goods Act 1989* and consists of State and Territory members and other persons appointed by the Health Minister, such as technical experts and representatives of various sectional interests. The Schedules are detailed within the Standard for the Universal Scheduling of Drugs and Poisons (SUSDP). Individual Australian jurisdictions (the States and Territories) usually adopt these schedules in full, although there have been some differences in their adoption between jurisdictions.

In Australia, the use of opioid drugs is mainly controlled by S8 legislation and several other schedules and laws in each jurisdiction. These vary but are similar in that prescribers providing chronic opioid treatment for individual patients, or seeking to prescribe opioids to a person recognised to be drug dependent need to seek approval from the relevant government departments, such as the Pharmaceutical Service Branch (PSB) in New South Wales. Approvals may need to be renewed periodically. In this way, State and Territory branches of pharmaceutical services attempt to monitor use of opioids, coordinate supply to individuals, and identify drug seeking behaviour where a patient seeks opioids from more than one source.

Many practitioners do not comply with requirements to apply for approval to prescribe Schedule 8 drugs, and there is variation between jurisdictions. The reliability of data acquired in this way is questionable. 'Treaties and Monitoring', and other Federal bodies are able to monitor total amounts of opioid imports, production and distribution down to the individual pharmacy level and other sites of supply, but this data is far removed from the coalface and of little day to day use by regulatory authorities.

Schedule 4 of the SUSDP (restricted drugs) contains drugs which are only available on prescription. These include the benzodiazepine class of drugs (with the exception of flunitrazepam which is Schedule 8) and some opioid analgesics.

Schedule 8 (these require a prescription and they are also controlled drugs) includes drugs such as morphine, methadone, oxycodone and pethidine. These are drugs which are determined to need greater controls because of their capacity for dependence. The additional controls placed upon these drugs include monitoring of the wholesale movements of these drugs, additional controls on storage (these have to be stored within a locked drug safe), and additional controls on their use by practitioners above those for Schedule 4 drugs.

The regulations surrounding the prescription, supply and custody of drugs of dependence differ between the States and Territories (See table 5). In general, controlled (S8) drugs can be prescribed for up to two months to patients for treatment of medical conditions unless the patient uses drugs problematically. Prior authority is required to prescribe drugs of addiction for any period to patients who are drug dependent. [188]

In Victoria, the Australian Capital Territory, Tasmania, Western Australia or South Australia a permit (written authority) must be obtained after eight weeks continuous therapy. In Queensland the prescriber needs to advise that they are intending to prescribe on an ongoing basis.

An exception is NSW, where changes in regulations in January 2006 removed the requirement for an authority after 2 months for prescription of sustained release opioids, including oxycodone and morphine formulations (eg OxyContin, MS-Contin). The requirement for an authority after 2 months of treatment remains in place for all other S8 opioids. The steep increase, from the end of 2005, in the number of people injecting pharmaceutical opioids at the Medically Supervised Injecting Centre in Sydney is described in Section 2.3. The impact of the removal of the 'two month rule' for these medications has not yet been formally evaluated. [189]

Prior authority is required to prescribe these drugs for people who are dependent on opioids, and certain other drugs (generally including amphetamines and cocaine but not including alcohol) in all jurisdictions. The reasons for this are:

- to prevent problematic use in patients for whom greater control is necessary (for instance a formal opioid treatment program with an OST);
- to provide controls to prevent escalation of dose (such as a limit on the daily dose and/or frequency of the collection of the medication); and
- to prevent the patient from obtaining the medication from multiple sources.

There are usually additional controls on the prescription and/or dispensing of controlled drugs in particular jurisdictions, such as the need to write the amount prescribed in both words and figures on the prescription and allowing no restricted drugs to be written on a controlled drug prescription. Both of these are designed to make alteration of the prescription more difficult. Other controls imposed by individual jurisdictions included the requirement to write a date of birth on a prescription, or for the pharmacist to seek identification prior to dispensing a prescription. There are usually additional requirements on pharmacists to record details of controlled drugs dispensed, and most jurisdictions the prescriptions of these drugs to individual patients are monitored by the jurisdictional government (with the exception of New South Wales and Victoria).

As some of these controls differ significantly between jurisdictions, it is important for practitioners to obtain specific information on the prescription and use of controlled drugs within their jurisdiction from their State or Territory health department.

The Australian Government through Medicare Australia administers the Pharmaceutical Benefits Scheme (PBS). This subsidises many prescription medications, including both Schedule 4 restricted drugs and Schedule 8 controlled drugs. For a patient to obtain some of this medication at the subsidised rate, and/or in increased quantities, it is necessary in some instances for the treating medical practitioner to advise the PBS that they have complied with the relevant jurisdiction legislation such as obtaining a permit from the relevant heath department. In certain instances, the practitioner must affirm that the pain is severe, chronic and not responding to 'non-narcotic analgesics'.

New Zealand

The New Zealand Misuse of Drugs Act is a national drug control law that classifies drugs into three classes, or Schedules, based on their risk of harm as follows:

- Class A, or First Schedule: Very high risk of harm;
- Class B, or Second Schedule: High risk of harm; and
- Class C, or Third Schedule: Moderate risk of harm.

The Fourth Schedule relates to the precursor substances. The Expert Advisory Committee on Drugs (EACD) makes scheduling decisions, based on scientific and medical evidence and/or international treaty obligations. [190]

In New Zealand regulation of opioids makes a major distinction between the prescription of opioids for management of pain (of any sort) and addiction. There are no restrictions on prescribing for pain management and any registered doctor may prescribe any amount of any opioid for an unlimited period of time. Prescribing of opioids for the treatment of opioid dependence is tightly controlled and only doctors working for a formally gazetted addiction treatment service or the very few doctors individually gazetted may initiate prescription for the treatment of dependence. Once treatment is initiated, other doctors may be authorised by a gazetted doctor to continue the prescription; this authorisation is required on an individual patient basis. Authorisation usually defines maximum dose and the conditions of dispensing, and must be renewed three monthly. There is however, no registration of individuals receiving treatment with any central authority.

There is an obvious incentive for people with opioid dependence to present as requiring treatment for chronic pain rather than addiction, given the tight controls on dispensing in New Zealand OST programs and the almost complete absence of controls when opioids are prescribed for pain.

5.4 Direct to consumer advertising

New Zealand is one of only two industrialised countries that permit direct to consumer advertising (DTCA) for pharmaceuticals, the other being the USA. DTCA is supported by some consumer groups on the basis that it shifts the balance of control in a consultation by alerting patients to all the possible risks and potential treatment choices that they might otherwise not get from the doctor.[191] European consumer groups contended that allowing DTCA would 'lead to a US style spiral of unsustainable health care spending'. [192] In the US spending on DCTA has increased rapidly since 1996, with one survey showing 86 per cent of consumers in 2001-02 exposed to DCTA.[193] [194] Opioids have not been among the products most heavily promoted by DTCA in the USA,[195] although OxyContin has been aggressively promoted there by other means, with the manufacturers agreeing in 2007 to pay more than $700 million 'to resolve criminal charges and civil liabilities' in relation to the promotion and marketing of this product.[196] The impact of DTCA has not been reported for New Zealand. [194]

Conclusions

Patterns of opioid prescribing for CNMP vary between some prescribers who rarely or almost never use these drugs for this purpose, and other clinicians who are more likely to prescribe opioids and are also not averse to using higher doses. In the absence of consensus on this issue, neither approach could be judged to be right or wrong.

Regulation of opioid prescribing varies among different jurisdictions and the impact of this differing regulation is not clear, owing largely to incomplete capture of data for opioid use.

What needs to be done?

Different jurisdictional legislation may impede development of guidelines and implementation of strategies to deal with the problem; these should be examined to identify the most appropriate system and develop uniform legislation. The impact of regulatory differences and changes (eg DTCA on pharmaceutical opioid sales in New Zealand, and the removal of the '2 month rule' for ongoing prescription opioid supply in NSW) should be monitored.

There is a need in Australia and New Zealand to improve the current system of opioid prescribing and monitoring. Modern technology enables electronic data management of prescribing and dispensing, provides for encryption and secure electronic data transmission, and provides this in real time. Electronic prescribing for example has the potential to substantially reduce diversion and forgery. Computerisation and standardisation will both facilitate and improve monitoring and surveillance, and enable coordination of essential data about drug seeking individuals between jurisdictions. Reducing supply may shift the problem to

some extent and not resolve the real issues unless strategies include a demand control approach and harm minimisation.

Pharmacists, like doctors, have among their professional responsibilities an important role in monitoring and questioning the use of prescription opioids, and advising patients on the most effective and safe way to take their medications. [197] There should be an emphasis on increasing pharmacists' ownership of issues related to opioid control, and improving pharmacists' screening of prescriptions and patients. [198] Pharmacists should be recognised as key stakeholders in a multidisciplinary group to implement and evaluate policy.

PBS subsidisation of controlled drugs may have a role in improvement of management of CNMP and minimising diversion.

Prior to the introduction of a dedicated online real time prescription monitoring system, the PBS could be directed to arrange for data about all opioid prescribing (both PBS and private nonsubsidised prescriptions) to be provided to the PBS, and arrangements made for the prescribers and pharmacists to be able to view this online in real time.

Alternative interim suggestions have included requiring patients who receive S8 drugs for more than 60 days to 'sign (a) contracts to limit their source of S8 drugs to one designated medical and pharmacy provider and (b) privacy release forms for access to drug history data held by the Health Insurance Commission (HIC) and state health departments to the designated medical and pharmacy provider before prescribing and dispensing respectively.' [197]

Considering all options, there is a strong argument that opioids should not be dispensed as 'private' prescriptions which bypass surveillance and monitoring mechanisms. Another option in Australia would be to limit opioid supply to PBS monitored prescriptions. Close examination would be needed of costs and benefits of such a change, especially in view of the complex flow on effects between illicit opioid and prescription opioid use discussed in the Introduction. Among questions which need to be considered are:

- How many people might be refused medications because they do not have a current Medicare card, because they have lost it or it is out of date?
- What arrangements will be made for people who are not permanent residents and not eligible for Medicare, such as refugees, other people of undetermined immigration status, tourists, overseas students?
- Should a (non universal) health insurance scheme be used as tool of enforcement, as mechanism for determining access to medications? What would be the reaction if access to insulin, or antibiotics, were made dependent on card carrying status in an insurance scheme?
- How many people, with what resulting harms, will turn to use of illicit substances or other harmful substances (such as alcohol) if access to prescription opioids is limited to Medicare card holders? To what extent will new black market mechanisms, involving third parties with Medicare cards, develop to circumvent this restriction, and with what harms?

Adoption of such a scheme would require thorough consideration of, and mechanisms for monitoring, the totality of outcomes to determine whether there is a net benefit. Potential costs and benefits of such measures have been discussed in some detail in the *Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria*. [20]

Table 5: Jurisdictional differences (Accessed 19.12.2007)*

Jurisdiction	Regulation for prescribing opioids
All Australia	http://www.tga.gov.au/ndpsc/stdpu.htm#act
New South Wales	Poisons and Therapeutic Goods Act 1966 No 31 http://www.legislation.nsw.gov.au/viewtop/inforce/act+31+1966+FIRST+0+N/
Victoria	The Drugs, Poisons and Controlled Substances Act 1981 (the Act) and the Drugs, Poisons and Controlled Substances Regulations 2006 (the Regulations). http://www.health.vic.gov.au/dpu/
South Australia	http://www.legislation.sa.gov.au/LZ/C/A/CONTROLLED per cent20SUBSTANCES per cent20ACT per cent201984/CURRENT/1984.52.UN.PDF
Western Australia	Poisons Act 1964 Poisons Regulations 1965 http://www.slp.wa.gov.au/pco/prod/filestore.nsf/Documents/MRDocument:5610P/$FILE/PoisonsRegs1965_08-c0-00.pdf?OpenElement
Northern Territory	Poisons and Dangerous Drugs Amendment Act 2006 (No 37 Of 2006) - Sect 6 Schedule 8 and Restricted Schedule 4 Substances http://www.austlii.edu.au/au/legis/nt/num_act/paddaa200637o2006422/s6.html
Queensland	Health (Drugs and Poisons) Regulation 1996. http://www.legislation.qld.gov.au/LEGISLTN/CURRENT/H/HealDrAPoR96.pdf
Australian Capital Territory	ACT Drugs of Dependence Act 1989 http://www.legislation.act.gov.au/a/alt_a1989-11co/current/pdf/alt_a1989-11co.pdf
Tasmania	Alcohol and Drug Dependence Act 1968 http://www.thelaw.tas.gov.au/tocview/index.w3p;cond=;doc_id=61 per cent2B per cent2B1968 per cent2BAT per cent40EN per cent2B20071122140000;histon=;prompt=;rec=;term=
New Zealand	Misuse of Drugs Amendment Act 2005, http://www.stanz.org.nz/images/ASSENT81.PDF

* Readers are reminded that the contents of these State & Territories and New Zealand regulations frequently change: make sure you are consulting the most recent version.

6. Prevention of inappropriate prescribing of opioids and its consequences

6.1 Prevention of CNMP

There is very little data on prevention or the identification of risk factors that are required to develop strategies to prevent CNMP. CNMP is discussed here in light of the following factors: the pathophysiology of CNMP, common causes, and strategies identified that may prevent CNMP becoming even more debilitating.

Work place injuries

The strategies identified relevant to primary prevention (reducing risks entirely proactively) and secondary prevention (reducing risks in response to evidence indicating injury precursor states or early symptoms of injury) are risk assessment methods. These must to some degree be adapted, as many hazard identification checklists have already been, more directly to match the kind of work and work environments where they are intended to be applied. [199]

Early assessment and intervention should be encouraged where reports of pain are limiting return to work. This could help avoid unnecessary suffering, disability, and associated legal and other costs. [200]

Prevention of injuries such as sports injuries and injuries on the road

The Australian National Injury Prevention and Safety Promotion Plan [201] encompasses the concepts of safety promotion and injury prevention. It examines unintentional injury, self harm and harm to others. Australia has achieved some significant gains in the prevention of a number of different types of road injuries mainly due to improvements in road safety over the past twenty-five years. The road toll in Australia has fallen from 3,578 (25.2 per 100,000 population) in 1977 to 1,715 (8.7 per 100,000 population) in 2002. [202] The reduction in road deaths occurred despite significant growth in population, vehicle numbers and kilometres travelled. Initiatives such as random breath testing, compulsory seat belts, speed blitzes, car design and safety features (e.g. air bags), better roads, ongoing community education regarding road safety, and improved life saving medical procedures and trauma care have all contributed to the decline in the number of vehicle related fatalities.

Overweight, obesity and physical activity

In Australia, 62 per cent of men and 45 per cent of women are overweight or obese.[203] This is a concern for the cost burden of obesity related illness on individuals, the community and the health system. Among 45-55 year olds, when osteoarthritis first becomes a significant health problem, the population attributable risk (PAR) for osteoarthritis associated with obesity was estimated to be 25 per cent for men and 22 per cent for women, using a relative risk (RR) of 2.4, and obesity estimates of 23.3 per cent for men and 20.1 per cent for women. In terms of major health sequelae of the obesity epidemic, this is second to obesity related type 2 diabetes. [204]

Rates of overweight and obesity in Australia and New Zealand are increasing mainly due to poor diet and sedentary lifestyles. There is evidence that people who have a sedentary lifestyle are more likely to complain of pain. A person who is obese with a body mass index (BMI) over 30 is 76 per cent more likely to feel pain. Disability is related to increasing weight status, with increased BMI associated with more days per week with both reduced activity and complete disability. Weight has been associated with co-morbid disability, depression, and reduced quality of life for physical function in CNMP. Calculation of the BMI should become a routine part of the screening evaluation with patients who have CNMP, with additional screening for disability and psychologic distress in patients with elevated BMIs. [205]

Few studies have investigated the effects of exercise (particularly long term, extended periods of exercise) on chronic pain. Some clinical studies suggest that exercise reduces chronic pain in syndromes such as fibromyalgia, chronic low back pain, osteoporosis pain, myofascial pain, cancer treatment-related pain, and neck pain. [206] [207] [208] [209] [210] [211] [212] Others report that exercise increases the pain associated with fibromyalgia [213] and chronic fatigue syndrome. [214]

6.2 Improved management of CNMP to prevent inappropriate prescribing of opioids and opioid dependence

Important principles for the use of opioids in chronic pain are described in sections 3.5, 4.5 and 4.6, and these will not be repeated here.

Dependence on opioids may develop slowly and insidiously and in some cases dominates the clinical picture of CNMP. Therefore the problem of dependence is best avoided from the start by always trying to ensure that the lowest doses are used consistent with the overall goal of allowing patients to pursue their lives as normally as possible.

Patients should be gently confronted with the issue of potential or actual opioid dependence in such a way that their worth is not devalued and their perception of pain is not trivialised, so that they can appreciate the complexities of the issues and the importance of managing any emotional and substance dependence problems. While this course may be difficult the alternative can be even more difficult in the long run. The treating team and the patient must have shared goals if the problem is going to be adequately managed. The role of interventional technologies is poorly supported by evidence yet these techniques can have substantial adverse complications. Medication treatment goals are an important part of planning with this group of patients. [215] [216]

Universal Precautions in Pain Medicine is a simple conceptual framework unifying the perspectives of pain and addiction medicine which may be used by GPs and specialists alike. It has potential to reduce problematic prescribing of opioids and prevent dependence from developing and allowing early identification of people at risk.

6.3 Prevention of problematic use of opioids

Healthcare professionals have a responsibility to prescribe controlled substances appropriately, guarding against problematic use while ensuring that patients have required medication available when they need it. They have a personal responsibility to protect their practice/service from becoming a source of drug diversion.

A few prescribers prescribe too generously, most prescribe cautiously and a few prescribe too stringently. Peer pressure may be a major factor influencing this, and good information and guidelines are essential to improving medical practice.

Providing good information and guidelines

Although studies specific for opioid prescription are lacking, numerous studies have been performed into the effectiveness of professional behaviour change interventions for prescribing practice for various medications, both in Australia and New Zealand and internationally. These range from 'passive' approaches, such as mailing information and conferences, to more complex and/or multifaceted interventions such as outreach visits, workshops, audit and feedback, and medication reviews.

Systematic reviews suggest passive interventions are generally of low effectiveness compared with more active interventions, although there is a great deal of variability among studies, both in type of intervention and results achieved. [217] [218] [219] [220]

In Australia, such interventions have given mixed results, with positive impact of interventions to reduce prescription of benzodiazepine [221] and antibiotics, and pethidine prescribing in emergency departments, [222] [223] but little or no effect in other cases. [224] [225] [226]

There is evidence of some effect of PBS subsidy on prescribing patterns for benzodiazepines [227] [228] [229] although such effects are limited, and in the case of prescription of testosterone supplements, were only temporary. [230]

With modest published evidence of effectiveness of medication review interventions, [231] domiciliary medication reviews have been incorporated as Medicare subsidised services for GPs and pharmacists in Australia.

In Australia the National Prescribing Service is a quality use of medicines service primarily aimed at GPs, established to promote implementation of national medicines policy, using multifaceted interventions, including newsletters, prescriber audit and feedback, and educational visits, in collaboration with the Divisions of General Practice. There is evidence of substantial savings to the PBS from changes in prescribing practices resulting from the NPS. [232] [233]

As discussed in section 2.1, prescribing of dextropropxyphene declined between 1998 and 2004 in Australia, despite no change in its S4 classification or subsidy status, possibly reflecting greater awareness of its toxicity in overdose and limited benefit compared with other analgesics.

Monitoring opioid use

Systematic monitoring of opioid prescription may have the following benefits:

1. Providing feedback to doctors about their practice compared with other doctors (the NPS does this for GPs in Australia);
2. Identifying doctors whose practice may be aberrant for counseling, education or other interventions; and
3. Enabling doctors to identify patients whose behaviour is problematic (e.g. doctor shoppers).

Some limitations of the Medicare Australia (formerly Australian Health Insurance Commission (HIC)) and The National Prescribing Service (NPS) data sets for audit and monitoring of use of opioids have been described in Chapter

2. Both data sets are based on prescriptions provided within the PBS and do not provide data for private or Veterans Affairs prescriptions. There is also considerable delay in provision of prescriptions to Medicare Australia, and data processing and analysis.

In February 2008, a prescription shopper was defined by *Medicare Australia (Functions of CEO) Direction 2003* (reissued 2005) – under *Medicare Australia Act 1973* as 'a person, who within any 3 month period:

a. has had supplied to him or her pharmaceutical benefits prescribed by six or more different prescribers (excluding specialists and dentists); or

b. has had supplied to him or her a total of 25 or more target pharmaceutical benefits (currently only central nervous system drugs NO2-NO7) ; or,

c. has had supplied to him or her a total of 50 or more pharmaceutical benefits (of any type).'

Doctors can find out whether a given patient has been identified as a prescription shopper according to these criteria, provided they have the Medicare number of the patient. As discussed in section 2.5 some people at risk may not meet HIC doctor shopper criteria, and improved GP data linkage to PBS records has been recommended. [234]

Experienced 'doctor shoppers' may be aware that having a prescription dispensed as a private (non-PBS) prescription avoids surveillance by the Prescription Shopping Project dataset accessible to medical practitioners.

S8 prescriptions are subject to audit at the level of individual pharmacies by the relevant state authority, but are not centrally collected in NSW or Victoria, nor aggregated nationally.

In the US, prescription monitoring programs (PMPs) have been developed to prevent diversion and misuse of prescription controlled substances, at the same time ensuring their availability for legitimate medical use. Twenty-seven states in the US have adopted PMPs to monitor the prescribing of certain controlled substances and detect inappropriate prescribing and dispensing. Typically, PMPs collect prescribing and dispensing data from pharmacies, conduct review and analysis of the data, and make it available under certain circumstances to regulatory and law enforcement agencies, as well as practitioners. [235] Limitations of these monitoring systems include that they provide retrospective information about supply, are not readily accessible to prescribers and pharmacists, and are in many cases collected and analysed by regulatory authorities with a prosecutory frame of reference. There are also limitations in establishing the identity of individuals, creating the potential for identity fraud.

An online 'real time' monitoring database called PharmaNet was introduced in Canada (British Columbia) in 1995. This was in response to perceived problems associated with adverse drug reactions, inappropriate prescribing of opioids, diversion, 'doctor shopping', and prescription fraud. [236] PharmaNet is a secure computer network that links all British Columbia community pharmacies to a central database. In addition to saving lives, the PharmaNet database has reduced prescription fraud and problematic use. People who go to numerous doctors to get the same prescription filled at numerous pharmacies can be identified when the pharmacist checks their records on the database. Pharmacare, the Canadian government's prescription drug program that often subsidises prescriptions, estimated a savings of CAND10 million to CAND35 million a year by identifying and preventing drug fraud. [237]

Although prescriptions for all drugs, not only narcotics, are entered into PharmaNet, the system makes special provision for the monitoring of opioid analgesics. Each time a prescription for an opioid analgesic is entered, an automatic entry is also made in the electronic log kept by the CPSBC (College of Physicians and Surgeons of British Columbia). If a physician receives a supply of an opioid drug for practice use (or office use, as it is called), the supply will be entered into PharmaNet. [20]

In the US, Purdue Pharma has implemented the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) system to obtain information concerning the prevalence of problematic use and diversion of prescription drugs. Specifically, this system is meant to monitor drugs containing morphine, hydrocodone, oxycodone, buprenorphine and fentanyl. [238]

In Australia and New Zealand, with the uptake of electronic prescribing in hospitals and in general practice, there is the potential to decrease the risk for diversion of opioids. Electronic prescribing also provides the opportunity to develop systems to audit and monitor prescriptions which provide data for professional profiling, for guidelines compliance and feedback to clinicians.

It is important for monitoring initiatives to maintain a balance between providing optimal efficacy and treatment of legitimate pain and the reduction of inappropriate prescribing of opioids. Adverse effects of monitoring pharmaceuticals on those who genuinely require them need to be kept to a minimum. (See also Conclusions in Chapter 5)

Improving management of dependence on illicit and prescription opioids

As discussed in Chapter 1, improved access to well resourced opioid treatment programs including OST for illicit opioid dependence is an important component of any strategy to minimise diversion of prescription opioids.

There are currently approximately 39,000 people receiving OST in Australia, with evidence that difficulty in finding an OST prescriber and cost issues are currently factors limiting OST access for some people. [239] [240] Another consideration

is that many individuals with CNMP and prescription opioid dependence are not necessarily attracted to, or suited to, existing OST or drug dependence services, which have historically targeted illicit drug users and alcohol dependent people.

In the US, 'office based opioid treatment' has been expanded in recent years. This concept involves specialists in primary care receiving fairly rudimentary training in addiction medicine and then treating a limited number of drug dependent patients who may have a history of street drug use, prescription drug problems and/or chronic pain.[241] The number of patients that these doctors are allowed to manage at any time has recently been increased.

In Australia, the uptake of 'office based opioid treatment' using combination buprenorphine/naloxone has so far been limited, owing to limited takeaway doses in some states, and in NSW where up to a month's supply may be dispensed at a time under existing regulations, probably other factors including restrictions on prescribing and supply, and the conservatism of OST prescribers. It remains to be seen whether 'office based opioid treatment' will make a substantial difference to access to OST in Australia.

6.4 Public health and early intervention measures

Data for the effectiveness of public education/awareness programs for prescription opioid use is lacking. Consumer information and community awareness campaigns may have contributed to reduced prescribing of benzodiazepines and antibiotics in Australia. [242]

Restriction of pack size of paracetamol in the UK apparently led to reduced total sales and fewer cases of severe paracetamol poisoning, however benefit of overall benefit, considering shift to other analgesics, is lacking.[243] [244] Data is lacking about the possible effects of smaller pack size when dispensing opioids, whether over the counter (OTC) or prescribed.

Early intervention

A recent follow up of two randomised controlled prevention trials of an 'early intervention' delivered in the teens in public schools in the United States suggest some benefit in reducing later problematic drug use for 17–21 year-olds. [245] [246] There is a great need for more research in this potentially important area.

6.5 Reducing harm from unsanctioned use of prescription opioids

Most of the measures advocated in this report are aimed at reducing inappropriate demand for and supply of prescription opioids. However, some level of unsanctioned use of these medications is likely to continue. Among measures for reducing harms associated with injecting of prescription opioids:

1. *Needle and syringe program (NSPs)* may have similar benefits as for illicit drugs through the provision of clean sterile injecting apparatus, an important step for the prevention of HIV and HCV injection. Although NSPs are widely located throughout Australia and New Zealand, problems in access remain, especially after hours.

2. *Filters for injection* (such as Minisart® Syringe Filters) are available with differing pore size. Sterile filtration with pore sizes < 0.2 µm is for removal of small microorganisms and particles; clarification with pore sizes > 0.45 µm is for removal of larger particles (such as talc) and larger microorganisms (such as yeasts and moulds), and may be performed before sterile filtration. Access to filters, for example, through needle and syringe programs is variable, depending on local policy, availability and funding arrangements.

3. *Safe injecting facilities* operate only in Australia, (Kings Cross, Sydney). In 2008 there were about 65 medically supervised injecting centres in 8 countries including a centre in Sydney which opened in 2001. These centres are located adjacent to major illicit drug markets. Evaluation consistently using very conservative assumptions demonstrates that these facilities have a number of important benefits including a reduction in fatal and non-fatal overdoses, increased referral to treatment and primary health care and improvement in neighbourhood amenity without any major unintended negative consequences.

   There is some evidence that these centres are also cost effective. Data from the Sydney MSIC [247] annual surveys by the National Centre in HIV Epidemiology and Clinical Research (NCHECR) of injecting drug users attending needle syringe programs in Australia,[248] and the Illicit Drug Reporting System (IDRS) show that the injection of diverted [9] prescription opioids is of increasing importance in Australia and sometimes is as prevalent as the injection of street heroin. In 2007, diverted prescription opioids were reported to be the most recently injected drug by 14 per cent of respondents in a survey of injecting drug users attending needle syringe programs in Australia. MSICs may also help to modify dangerous injecting practices as experienced health care workers in these centres advise clients about the importance of using pill filters and other harm reduction measures. This advice probably then diffuses to other injecting drug users and changes community norms and expectations.

4. *Novel pharmaceutical products* - the addition of naloxone (a short acting opioid antagonist with a high affinity for the mu-opioid receptor) may attenuate the effects of injected opioids or produce an aversive

response by precipitating opioid withdrawal. [249]
There is some evidence that addition of naloxone to buprenorphine (the combination product 'Suboxone') may be associated with reduced injection of and reduced demand for buprenorphine.[250] Combination formulations of methadone/naloxone were developed in the 1970s but never extensively trialed or used in clinical practice. Emerging products such as morphine-naltrexone or oxycodone-naltrexone combinations, and future combination products of other opioids with naloxone have potential to reduce both demand for and injecting of these opioids, subject to demonstration of their efficacy, safety and evidence of cost effectiveness. Safety concerns include delayed emergence of overdose symptoms owing to the short half-life of naloxone compared with opioid agonists, and the possibility of severe withdrawal reactions if naloxone is injected by a person with current opioid tolerance (these are not a major concern for current users of buprenorphine, due to its higher affinity for the opioid receptor and lower risk of respiratory depression than other opioids).

Conclusions

Primary and secondary prevention measures in relation to work place injuries, sports injuries and injuries on the road, and reduction of overweight, obesity are important in reducing the burden of CNMP. More effective treatment of CNMP involves attention to both pharmacological and non-pharmacological aspects of care. The Quality Use of Medicine (QUM) framework is an appropriate way of improving management and achieving better clinical and population health outcomes.

Prescription monitoring programs have the following potential benefits:

1. Providing feedback to doctors about their practice compared with other doctors (the NPS does this for GPs in Australia);
2. Identifying doctors whose practice may be aberrant, for counseling, education or other interventions; and
3. Enabling doctors to identify patients whose behaviour is problematic (doctor shoppers).

Providing good information and guidelines within multifaceted professional behaviour change interventions is an appropriate way to improve professional medical practice. There is little evidence about the effectiveness of public education and early intervention measures to reduce problematic use of opioid medications.

Limited access to good quality and affordable OST may contribute to the demand for diversion of opioids. 'Office based opioid treatment' is one possible strategy to improve access to OST.

NSPs, including the provision of filters, remain a cornerstone of harm reduction for injecting drug use. Novel pharmaceutical products may in the future have a role in discouraging the injection of prescription opioids.

What needs to be done?

As discussed in Chapter 2, there is a need in Australia and New Zealand for access to real time medication history available to potential prescribers at the time of prescribing, and to pharmacists at the time of dispensing with robust identification of individuals and privacy safeguards. Introduction of prescription monitoring programs or limiting opioid prescriptions to the PBS in Australia should be considered.

It is important to minimise unmet demand for opioid substitution therapy, by increasing the range of treatment options for heroin and prescription opioid dependent people and providing OST as attractively as possible, by making it easy to access, providing good quality care and charging a minimum cost.

The provision of clean sterile injecting equipment should remain a public health priority, with efforts to reduce remaining obstacles to access. Injecting drug users should be encouraged to use filters, especially where pharmaceutical opioids containing particulate matter are injected. This may require educational outreach through users' representative groups and NSPs.

Novel pharmaceutical products which may discourage the injection of prescription opioids should be evaluated like any other new medications for efficacy and safety, with emphasis on their safety in the setting of unsanctioned use.

Increased collaboration of AChAM, FPMANZCA and RACGP is needed in clinical training and with the NPS with respect to feedback, audit and other professional behaviour change interventions, informed by clear treatment guidelines. Research is also needed into effective public education and early intervention measures to reduce problematic use of opioid medications.

The practice of medicine is based on research seeking evidence for interventions that are effective, safe and cost effective. This is a very difficult and complex area of medicine in which measurement and research pose ethical challenges. To ensure that patients receive evidence-based care for the treatment and management of CNMP, there must be a long term commitment to research, particularly by health professionals who are committed to this area of medicine. In other chronic complex conditions such as diabetes, sustained research over a long period of time has brought significant benefits. CNMP requires a research agenda as rigorous and as well supported as that for other chronic conditions.

7. Education and Training

This document has outlined the size and complex nature of the clinical problem of managing patients with CNMP. The implications for the community and its health professionals are profound. There is an urgent need to attend to the provision of improved services for pain management and drug dependence and to the development and provision of educational and training opportunities.

Since 2004, the International Association for the Study of Pain and the World Health Organization have sponsored an annual 'Global Day Against Pain'. [251] This public awareness campaign focuses on educating society regarding pain and to advocate for adequate provision, resourcing and expansion of acute and chronic pain management services in healthcare facilities and the community.

In specialist medical school curricula in Australia and New Zealand, the disciplines of Pain Medicine and Addiction Medicine have a low profile. Education and training in these areas in the early postgraduate years has received some attention and, at the specialist training level, pain as a problem in its own right is being addressed through the Australian and New Zealand College of Anaesthetists and its Faculty of Pain Medicine.

In New Zealand, the range of health professionals required to work in areas associated with the provision of opioid substitution treatment includes physicians, pharmacists, nurses, case workers and general practitioners. [21] The OST centres are subjected to regular monitoring and review including appropriate levels of training, not only in clinical aspects, but also cultural appropriateness. [252]

As identified in this document, CNMP needs to be part of the basic and advanced training curriculum of all Colleges, to ensure that patients in the future receive good quality care. This includes special education for physicians who prescribe opioid analgesics.

It is commendable that currently addiction medicine trainees spend time in pain clinics, and trainees in pain medicine spend time in addiction clinics. However, as most of the management and treatment of CNMP occurs in general practice, opportunities for a closer association between general practitioners and specialists in pain medicine and addiction medicine need to be explored. As discussed in Chapter 6, increased collaboration of AChAM, ANZCA and RACGP is needed in developing, in collaboration with the NPS, feedback and audit and other professional behaviour change interventions informed by clear treatment guidelines.

What needs to be done?

The topics CNMP and problematic opioid use should be part of both the basic and advanced curricula of physician, psychiatrist, general practitioner and anaesthetist training. The closely connected relationships between pain and drug dependence must be clearly articulated. In Australia GPs have identified five areas of pain management that require consideration within the curriculum: [144]

1. Communication skills and the patient-doctor relationship;
2. Applied professional knowledge and skills;
3. Population health and the context of general practice;
4. Professional and ethical role; and
5. Organisational and legal dimensions.

The AChAM, ANZCA and RACGP should jointly develop a module on CNMP and problematic opioid use, to be used in primary and continuing professional education. Learning Objectives developed by the RACGP should be the basis for such a module.

Appendix

Appendix one: Definitions used in this policy paper for patients with CNMP

WHO 1992,1998 APA – DSM IV 1994	AAPM, APS, ASAM 2001
Tolerance	**Tolerance**
Need for markedly increased amounts of substance to achieve desired effect OR Markedly diminished effect with continued use of same amount of substance	Decrease in effect of substance over time so that increased amount required to achieve same effect
Physical dependence	**Dependence**
Development of withdrawal or abstinence syndrome with abrupt dose reduction or administration of an antagonist	Physiological adaptation to substance whereby abrupt reduction in dose leads to withdrawal (abstinence) syndrome
Substance dependence	**Addiction**
Pattern of maladaptive behaviours, including loss of control over use, craving and preoccupation with non-therapeutic use, and continued use despite harm resulting from use (with or without physical dependence or tolerance)	Psychosocial disorder or disease characterised by compulsive use of a substance and preoccupation with obtaining it, despite evidence that continued use results in physical, emotional, social or economic harm
Substance dependence criteria	
Three or more of: 1. Tolerance (as defined above) 2. Withdrawal 3. Use of substance in larger amounts or over longer periods than intended 4. Persistent desire or unsuccessful efforts to control substance use 5. Much time spent in obtaining, using or recovering from the substance 6. Interference with social, occupational or recreational activities 7. Continued use of the substance despite knowledge of problems associated with it	
Therapeutic dependence	
Drug seeking behaviour in presence of adequate pain relief (arising out of fear of re-emergence of pain or perhaps of emergence of withdrawal symptoms)	
Drug seeking behaviour	**Pseudo-addiction**
Directed or concerted effort by patient to obtain opioid medication or to ensure an adequate medication supply (an appropriate response to inadequately treated pain)	A set of behavioural changes similar to opioid dependence or addiction but which are secondary to inadequate pain control
Pseudo-opioid resistance	
Report of persistent pain when pain relief adequate (to prevent reduction in current dose)	

A list of parallel terminologies is presented below. One of the recommendations from the working group is to achieve standardisation of terminologies and definitions. Inconsistencies in addiction terminology have greatly hampered efforts to define and quantify opioid addiction arising as a direct result of treatment for opioid treatment for CNMP.

PARALLEL TERMINOLOGIES

Ex-DSM IV 1994	Based on AAPM/APS/ASAM consensus 2001 [17]
ILLICIT DRUG USE CONTEXT	**PRESCRIPTION DRUG USE CONTEXT**
(Individual initiated and maintained)	(Physician initiated and maintained)
SUBSTANCE ABUSE (SPORADIC)	**PROBLEMATIC OPIOID USE (OPIOID MISUSE)**
no tolerance or withdrawal Maladaptive pattern of substance use with consequences (role fulfilment, danger, legal, social, interpersonal) but NOT fulfilling criteria for substance dependence	tolerance or withdrawal may occur 1. Overwhelming focus on opioid issues during clinic visits that impedes progress withother issues 2. Pattern of early refills or escalating drug use 3. Multiple calls/visits for more drug 4. Pattern of lost, spilt, stolen medications 5. Supplemental sources of opioids
SUBSTANCE DEPENDENCE (= 'ADDICTION')	**DRUG ADDICTION OPIOID ADDICTION IATROGENIC OPIOID ADDICTION**
(continuous) may include tolerance or withdrawal progression more or less certain	meet DSM IV criteria progression uncertain

Possible explanations for problematic opioid use are; [17]

1. They may result from psychological or physical dependence;
2. They may result from a chaotic lifestyle;
3. They may indicate a search for sympathy, understanding, meaning or a social context; or they may indicate a preoccupation with being unwell;
4. They may be produced by inadequate treatment of pain (Pseudo addiction); [253]
5. They may reflect a need for opioids to relieve a comorbid condition such as depression or anxiety. [254]

Appendix two: Glossary of acronyms

AAPM	American Academy of Pain Medicine
ACC	Accident Compensation Commission (New Zealand)
AChAM	Australasian Chapter of Addiction Medicine
APA	American Psychiatric Association (Associated with DSM)
APS	American Pain Society
ASAM	American Society of Addiction Medicine
AUD	Australian Dollar
BNZ	Benzodiazepines
CBT	Cognitive behaviour therapy
CI	Confidence interval
CME	Continuing medical education
CNMP	Chronic non-malignant pain
CNS	Central nervous system
CPSBC	College of Physicians and Surgeons of British Columbia
CPD	Continuing professional development
DALYs	Disability adjusted life years
DSM	Diagnostic and Statistical Manual of Mental Disorders
DUMA	Drug Use Monitoring in Australia
EDDP	2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine
FDA	Food and Drug Administration
FPMANZCA	Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists
GC/MS	Gas Chromatography (GC) and Mass Spectrometry (MS)
GP	General Practitioner
HCV	Hepatitis C virus
HBV	Hepatitis B virus
HIC	Health Insurance Commission
HIV	Human Immunodeficiency Virus
HPLC	High Performance Liquid Chromatography
IDRS	Illicit Drug Reporting System
IDU	Injecting drug use
JFICM	The Joint Faculty of Intensive Care Medicine
MSIC	Medically Supervised Injecting Centre
MMT	Methadone maintenance treatment
NDPSC	National Drugs and Poisons Schedule Committee
NPS	National Prescribing Service
NSAIDs	Non-steroidal anti-inflammatory drugs
NSW	New South Wales
NSW TAG	The NSW Therapeutic Assessment Group
OST	Opioid substitution therapy
PBS	Pharmacetical Benefits Scheme
PMPs	Prescription Monitoring Programs
PSB	Pharmaceutical Service Branch
QUM	Quality Use of Medicines
RACGP	The Royal Australian College of General Practitioners
RADARS	Researched Abuse, Diversion and Addiction-Related Surveillance
RANZCP	The Royal Australian and New Zealand College of Psychiatrists
RD	Absolute risk differences
RR	Relative Risk
S4	Schedule 4
S8	Schedule 8
SMD	Standardised mean differences
SROO (S)	Slow release oral opioids
SUSDP	Standard for the uniform scheduling of drugs and poisons
TCAs	Tricyclic antidepressants
UK	United Kingdom
US	United States of America
WHO	World Health Organization

Appendix three: Opioid comparative information[255]

Drug	Suggested dose equivalent to 10 mg IM/SC morphine[1]	Approximate duration of action (hours)[2]	Comments
Agonists			
Codeine[3] (analgesic only)	200 mg oral	3–4	Mild to moderate pain; do not exceed 60 mg single dose
Dextropropoxyphene[3]	unknown	4–6	Mild to moderate pain; avoid long term use
fentanyl	100–150 mcg IV/SC	0.5–1	Moderate to severe acute or chronic pain; preferred in renal impairment
Hydromorphone[3]	1.5–2 mg SC/IM; 6–7.5 mg oral	2–4	Moderate to severe acute or chronic pain
methadone (analgesic only)	10 mg SC/IM; 20 mg oral[4]	8–24 (chronic dosing)	Severe chronic pain
morphine[3]	30 mg oral	2–3; 12–24 (controlled release)	Moderate to severe acute or chronic pain
oxycodone	15–20 mg oral	3–4; 12–24 (controlled release)	Moderate to severe acute or chronic pain
pethidine[3]	75–100 mg IM	2–3	Not recommended
tramadol[3]	100–120 mg IM/IV; 150 mg oral	3–6	Moderate to severe pain
Partial agonists			
buprenorphine (analgesic only)	0.4 mg IM; 0.8 mg sublingual	6–8	Not first line for analgesia

[1] doses given are a guide only
[2] duration of action depends on dose and route of administration active metabolite;
[3] based on single dose studies

Appendix four: Approximate Opioid Equianalgesic Doses

Different authorities quote somewhat different equianalgesic doses. The equianalgesic dose in any transfer will be affected by a number of factors. It may be worthwhile reducing the dose of the new opioid by about 25 per cent to allow a safety margin.

Approximate conversions for oral dose:

a. morphine : oxycodone 1.5 : 1
b. morphine : methadone 3 : 1, for morphine<100mg/d (see table below)
c. oxycodone : methadone 2 : 1 (see also table below)
d. morphine : hydromorphone 7.5 : 1
e. morphine : tramadol 1 : 5
f. morphine : codeine 1 : 6

Approximate oral/transdermal conversions

g. morphine oral: fentanyl transdermal 100:1
fentanyl transdermal 12 mcg/hr ~ oral morphine 45mg daily
fentanyl transdermal 25 mcg/hr ~ oral morphine 90mg daily

h. morphine oral: buprenorphine transdermal 75:1
Buprenorphine transdermal 5 mcg/hr ~ oral morphine 9mg daily (~10mg/day)
Buprenorphine transdermal 10 mcg/hr ~ oral morphine 18mg daily (~20mg/day)
Buprenorphine transdermal 20 mcg/hr ~ oral morphine 36mg daily (~40mg/day)

Methadone conversions

Daily oral Morphine	Approx mor: met
<100mg	3:1
100-300mg	5:1
300-600mg	10:1
600-800mg	12:1
800-1000mg	15:1
1000mg	20:1

References

Source: Ayonrinde OT, Bridge DT. *Med J Aust* 2000; 173:536-540.
Anderson R et al. *J Pain Sympt Manage* 2001; 21:397-406.
Pereira J et al. *J Pain Sympt Manage* 2001; 22:672-687.
Australian Medicines Handbook 2004.
(Available at http://www.amh.net.au)

Appendix five: Guidelines for CNMP

There is little scientific evidence to support the long term use (16 weeks) of opioids in CNMP.[256] The guidelines below are useful to assist practitioners. However, until further evidence is available, any evidence based guidelines will be hampered by this fact. All the guidelines discussed above are useful; however none fully addresses the nine principles set out by the NHMRC.

Clinical practice guidelines are 'systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances'. Over the past decade there has been a move towards developing such statements to assist clinicians in the management of specific conditions.

The procedures used to develop the statements are increasingly based on a thorough evaluation of the evidence, including meta-analysis of published research studies on the outcomes of various treatment options, rather than the consensus of expert panels. The statements are intended to be 'a distillation of current evidence and opinion on best practice'.[257]

While guidelines do not have binding legal force, they clarify standards of practice for those regulated by an agency. This section will discuss guidelines on opioid use in relation to CNMP. Guidelines must be specific to opioid management as guidelines are not generalisable from one setting to another.[258] Clinical practice guidelines are increasingly proposed to improve the quality of patient care in all areas of medicine.[259] [260]

The WHO stated that better pain management could be achieved throughout the world if governments used evaluation guidelines to identify and overcome regulatory barriers to the availability and appropriate medical use of opioid analgesics.

It would appear that the current management of chronic pain with opioids in Australia varies greatly. Many practitioners feel that they do not have the necessary skills or support to manage this problem adequately. There are a number of guidelines available to assist practitioners in managing chronic pain and opioid use. This section will discuss the currently available guidelines on opioid dependence in relation to chronic non malignant pain and their relevance and usefulness to the Australian practitioner and make recommendations for use.

While clinical practice guidelines may assist practitioners and patients to make better decisions about appropriate healthcare for specific clinical circumstances and can be effective in bringing about change and improving health outcomes, there is substantial evidence that practitioners are not using currently available guidelines.

This chapter uses the NHMRC principles to assess the guidelines. The following guidelines are currently available:

1. The Pain Society, Recommendations for the appropriate use of opioids for persistent non-cancer pain. A consensus statement prepared on behalf of the Pain Society, the Royal College of Anaesthetists, the Royal College of General Practitioners and the Royal College of Psychiatrists March 2004 ISBN: 0-9546703-1-0

These British guidelines published in 2004 focus on outcomes, with the goal of treatment being *'pain relief, which is likely to be partial with a secondary gain of improvement in physical and social functioning'*. They acknowledge the lack of good quality research regarding the risks and benefits of opioids in the management of CNMP but do not clearly state the level of evidence for recommendations given.

A multidisciplinary review with consumer representatives, it explicitly states the target audience and discusses the problems of underuse and overuse and briefly describes special cases for inclusion and exclusion. It then refers the reader to the BNF (British National Formulary, similar to MIMS) for further advice about use in specific clinical situations. There is some good discussion of issues around benefits, adverse reactions, problematic use and patient selection. A short section provides some guidance on practical aspects of prescribing. It has an excellent executive summary.

There is little discussion of resource constraints, though the cost of treatment is briefly discussed.

There is no discussion of assessing impact, implementation, dissemination or revision, however the guidelines underwent three months consultation with healthcare professionals involved in the management of chronic pain and other professional bodies and groups prior to publication.

The guidelines encourage the development of local protocols. The different healthcare delivery systems in the UK may limit the use of these guidelines in the Australian context without revision.

2. Jovey RD et al. Use of opioid analgesics for the treatment of chronic non cancer pain; A consensus statement and guidelines from the Canadian Pain Society, 2002. *Pain Res Manage* Vol 8 Suppl A Spring 2003

These Canadian guidelines from 2002 offer overarching principles for the use of opioids in CNMP. They offer a consensus statement from professionals working in the field of chronic pain and offer some practical suggestions for the clinical management of opioids in CNMP.

While the guidelines are outcome focused there is little discussion about whether the suggested guidelines produce a change in health, the document states *'patients have the right to the best possible pain relief possible… health professionals need to understand pain management strategies, including non-pharmacological techniques and the appropriate use of opioids'*. The guidelines are focused on whether practitioners adhere to recommended practices. It would appear that there is currently not enough scientific evidence to be able to assess whether suggested management will affect clinically significant outcomes.

The document does not give levels of evidence for any recommendation. It does not discuss quality, relevance or strength of evidence. However the guidelines appear to be practical and sensible despite the lack of evidence.

The document is not multidisciplinary and there are no consumer representatives. It does not discuss resource constraints, dissemination, impact or implementation. The document states that it will be updated but gives no timetable for this.

The document acknowledges other guidelines, and contains some good practical clinical suggestions for the use of opioids.

3. Lingford et al. Evidence based guidelines for the pharmacological management of substance misuse, addiction and comorbidity: recommendations from the British Association of Psychopharmacology, *Journal of Psychopharmacology*, 2004; 18: (3): 293-335.

These British evidence-based guidelines discuss the pharmacological management of problematic substance use, addiction and comorbidity. They do not discuss the management of CNMP and opioids so are not discussed here.

4. Guideline for opioid use in persistent pain: Hunter New England Area Health Service www.hunter.health.nsw.gov.au/docs/HIPS_GuidelineForOpioidUseInPersistentPain.pdf

These guidelines were produced by Hunter Health. Last updated in 2006, they are a very good brief guideline. Five pages in length with a summary page, flow chart and references, they contain a good summary of the issues related to opioids and chronic non malignant pain. They have local contact numbers and protocols that are locally based, so would need alterations to be used in other settings. They do not describe the patient population well and while they suggest excluding some patients, the rationale for this is not well described. Patient preferences are not discussed. The current evidence is referred to in general terms but level of evidence is not explicitly described. The techniques used and strength of professional consensus are not described. Health benefits/risks are not described and while other sets of guidelines are identified there is no discussion of potential conflict. There is no information on which to assess whether the guidelines were independently reviewed or pretested.

The language is concise and clear, the document well set out, with clear headings and summaries. There is no mention of scheduled review and the panel used to develop guidelines is not included. As a result it is difficult to know who wrote these guidelines and whether various interested groups were involved in their development.

1. TAG. NSW Therapeutic Assessment Group. Rational use of Opioids in Chronic or Recurrent Non-Malignant Pain. General Principles. Dec 2002 http://www.health.nsw.gov.au/public-health/psb/pubs.html

2. TAG. NSW Therapeutic Assessment Group. Rational use of Opioids in Chronic or Recurrent Non-Malignant Pain. Migraine. 2002 http://www.health.nsw.gov.au/public-health/psb/pubs.html

3. TAG. NSW Therapeutic Assessment Group. Rational use of Opioids in Chronic or Recurrent Non-Malignant Pain. Lower back pain. 2002 http://www.health.nsw.gov.au/public-health/psb/pubs.html

All three guidelines follow a similar format and were produced by the same body, a multidisciplinary group comprising specialists, representatives from specialist services, government bodies, academic general practitioners and a consumer representative. The guidelines are written for primary care and cover the rational use of opioids in acute and ongoing management or migraine, lower back pain and chronic or recurrent nonmalignant pain. The evidence is synthesised into clinically useful recommendations. The lack of a place for pethidine in the management of CNMP is particularly highlighted. Local conditions are taken into account; however there is no discussion of constraints due to costs.

The guidelines do not discuss the role of patients in the decision making process. They are outcome focused and clearly state the level of evidence for each management option. They are short, easy to read and important points are highlighted in boxes. They do not have a great deal of background information and their usefulness is limited by this. However they are in an excellent form to assist the busy practitioner.

The concise six page guidelines, while useful for the busy clinician, cannot fully develop the issues associated with use of opioids in CNMP. It is a pity that they are not accompanied by a more in-depth document for practitioners interested in understanding the issues more fully.

It is unclear how they are to be disseminated and implemented. It is also unclear how many practitioners are aware of them. There is no information on plans for revision.

5. Therapeutic Guidelines. Analgesics, Version 4, 2002 (available on http://www.tg.com.au/)

These excellent guidelines are part of a series of guidelines covering many aspects of clinical practice, the most well

known are the antibiotic guidelines. The analgesic guidelines fulfil most categories of the NHMRC guideline principles. However, they do not discuss resource constraints and there is no note of how implementation and the impact of the guidelines are to be evaluated. The guidelines are regularly revised and it would appear that there is a high degree of awareness of the existence of therapeutic guidelines series among practitioners.

The guidelines contain good definitions of acute and chronic pain and other modalities for treatment. They also discuss doses and general issues of pain management with opioids. However, they only cover the issue of opioids and CNMP very briefly; *'the role of opioids in this situation is controversial and guidelines for their use have been established (Graziotti PJ, Goucke CR. The use of oral opioids in patients with chronic non-cancer pain. Management strategies. Med J Aust 1997; 167(1): 30-4).'* The Graziotti paper is listed below in useful papers but does not fulfil the NHMRC definition of guidelines.

6. NSW Health Pharmaceutical Services Branch Guidelines for the management of patients with chronic non-cancer pain June 2006

This two page document from the NSW Pharmaceutical Services Branch (PSB) lists some general principles for the management of CNMP. It was written in response to concerns about the increasing applications from practitioners to prescribe pethidine. It refers readers to the TAG documents, analgesic guidelines (discussed above) and the NHMRC guidelines for the management of acute pain.

It does not discuss level of evidence or best method for synthesising this evidence. It was not written using a multidisciplinary process. It does not discuss the need to adapt to varying local conditions, resource constraints, dissemination, implementation, impact, implementation, or revision.

7. College of Physicians and Surgeons of Ontario. Evidence-Based Recommendations for Medical Management of Chronic Non-Malignant Pain. Nov 2000 and Reference Guide for Clinicians for Medical Management of Chronic Non Malignant Pain. 2002

This 120 page Canadian document is accompanied by a 32 page reference guide. Outcomes focused, the document covers many of the modalities currently available for the treatment of CNMP. Chapter 9 begins the discussion of the use of opioids for the management of CNMP. These 6 pages discuss the evidence and level of evidence. The document concludes that *'Opioid therapy should therefore be part of a comprehensive treatment program that includes a graduated exercise program and psychological and behavioural approaches to pain management. Such an approach, however, depends on underlying medical condition and clinical judgment is required.'* Chapter 11 devotes eight pages to specific recommendations for opioids use in CNMP and clearly states the level of evidence for these recommendations. The guidelines have a number of helpful appendices including sample pain scales, a treatment contract, and information for patients.

It reviews existing guidelines and surveys the members of the College of Physicians and Surgeons of Ontario to find out their concerns, interests and what they considered might be helpful. The document is not multidisciplinary and there are no consumers representatives.

It discusses the review process, both the issues of peer review prior to publication and the issue of regular updating. It states that this will take place one year after the original guidelines. However it would appear that this has not taken place as the guidelines were published in 2000. Patient preferences, cost, local protocol development, dissemination and implementation are discussed.

It has some good practical advice under the heading *'Dos and Don'ts for prescribing narcotics for CNMP'*. These guidelines are excellent, covering many modalities for treatment, but would need revision for use in the Australian context.

8. The Federation of State Medical boards of the United States, Inc. Model Guidelines for the use of Controlled Substances for the Treatment of Pain. May 1998. www.medsch.wisc.edu/painpolicy/domestic/model.htm

This four page document does not fulfil the NHMRC principles; however it gives a clear statement of the professional body's consensus on the place of narcotics in the management of pain. It has few references and does not assess level of evidence. *'The appropriate application of up-to-date knowledge and treatment modalities can serve to improve the quality of life for those patients who suffer from pain as well as to reduce the morbidity and costs associated with untreated or problematically treated pain. The Board encourages physicians to view effective pain management as a part of quality medical practice for all patients with pain, acute or chronic, and it is especially important for patients who experience pain as a result of terminal illness. All physicians should become knowledgeable about effective methods of pain treatment as well as statutory requirements for prescribing controlled substances.'*

It goes on to give some brief practical points to assist the practitioners with the management of opioids for CNMP.

9. Opioid prescription in chronic pain conditions: Guidelines for South

Australian general practitioners. The Australian Pain Society, The Faculty of Pain Medicine, Australia and New Zealand College of Anaesthetists, Drug and Alcohol Services South Australia, South Australian Divisions of General Practice. 2005 (available at http://www.dassa.sa.gov.au/

webdata/resources/files/Opioid_prescription_chronic_pain_guidelines_for_SA_GPs.pdf)

These South Australian guidelines were modelled on US guidelines; however they have been adapted and expanded. One shortcoming of the use of these excellent guidelines is the failure to discuss CNMP separately from malignant pain.

They are outcome focused and the cost of the untreated or poorly treated condition is covered.

While each section is referenced, there is no documentation of level of evidence. The guidelines are set out clearly and the evidence is used effectively to create meaningful clinical recommendations. The guidelines were written by a multidisciplinary team but this did not include a consumer representative.

The document does not discuss dissemination, implementation or how the authors plan to assess and evaluate the impact and implementation of the guidelines. The timetable for revision is not covered.

The guidelines have some useful appendices including a pain management screening tool and a patient contract. There are good sections on side effects and how to manage these and detailed information on the different available forms of opioids and routes of administration. The guidelines also discuss patients' rights and what they can expect from their doctor. There is also a short section on opioids and driving and serum opioid assays.

Out of the above guidelines these are the most detailed and most adequately address the NHMRC principles. They could be easily adapted for use in other jurisdictions ideally including greater information regarding resource constraints, dissemination, implementation and evaluation of impact and revision of document.

10. Trescot AM, Helm S, Hansen H, Benyamin R, Glasier SE, Adlake R et al Opioids in the management of chronic non-cancer pain: An update of American Society of the interventional pain physicians' (ASIPP) guidelines. *Pain Phys* 2008; 11:S5-S62.

Following an extensive review and analysis of the literature, the evidence for the effectiveness of long term opioids in reducing pain and improving functional status for 6 months or longer is variable. Opioids were commonly prescribed for chronic non-cancer pain and reported to be effective for short term pain relief. However, long term effectiveness of 6 months or longer was variable. These guidelines were based on the best available evidence and do not constitute inflexible treatment recommendations.

Table 6: Assessment of currently available guidelines

Guideline number	Outcome focused	Best Available Evidence	Best Method	Multi-Disciplinary Process	Flexible adaptable	Resource Constraints	Dissemination Implementation	Impact Implementation Evaluated	Revision
1	✓✓	✓✓	☐	✓✓✓	✓	☐	☐	☐	✓
2	✓✓	✓✓	☐	no	✓	☐	☐	☐	✓
3					N/A				
4	✓✓	✓	☐	☐	✓✓✓	☐	☐	☐	☐
NSW TAG	✓✓✓	✓✓✓	✓✓✓	✓✓✓	☐	☐	☐	☐	✓✓
NSW TAG	✓✓✓	✓✓✓	✓✓✓	✓✓✓	☐	☐	☐	☐	✓✓
NSW TAG	✓✓✓	✓✓✓	✓✓✓	✓✓✓	☐	☐	☐	☐	✓✓
5					N/A				
6	✓	☐	☐	☐	☐	☐	☐	☐	☐
7	✓✓✓	✓✓✓	✓✓✓	no	✓✓✓	✓✓✓	✓✓	✓✓	? see text
8	✓✓✓	✓	✓	☐	✓	☐	✓	☐	☐
9	✓✓✓	✓	✓✓	✓✓	✓✓	✓	☐	☐	☐
10	✓✓✓	✓✓✓	✓✓✓	no	✓	✓	✓✓✓	✓✓✓	✓✓✓

☐ No information

The number of ✓ indicates the level in each criterion, the more ✓ given the better the information

Summary

There is little scientific evidence to support the long term use (16 weeks) of opioids in CNMP. Few strong studies have been completed in this area. While the above guidelines are useful to assist practitioners, until further evidence is available any evidence based guidelines will be hampered by this fact. All the guidelines discussed above are useful; however none fully addresses the nine principles set out by the NHMRC.

Appendix six: Further reading

Further readings on non-pharmacological interventions are:

- Critchley DJ, Ratcliffe J, Noonan S, Jones RH, Hurley MV. Effectiveness and cost effectiveness of three types of physiotherapy used to reduce chronic low back pain disability: a pragmatic randomized trial with economic evaluation *Spine,* 2007*;* 32(14):1474-81.
- Svenson JE, Meyer TD. Effectiveness of non-narcotic protocol for the treatment of acute exacerbations of chronic non-malignant pain *Am J Emerg Med,* 2007; 25(4):445-9.
- Jensen M, Paterson DR. Hypnotic treatment of chronic pain *J Behav Med*, 2006; 9(1):95-124.
- Kroeling P, Gross AR, Goldsmith CH. Cervical Overview Group a Cochrane review of electrotherapy for mechanical neck disorders *Spine* 2005; 30(21):E641-8.
- Morley S, Eccleston C, Williams A. Systematic review and meta-analysis of randomized controlled trials of cognitive behaviour therapy and behaviour therapy for chronic pain in adults, excluding headache *Pain* 1999;80(1-2):1-13.

The papers below may be useful for the practitioner considering prescribing opioids.

1. Tedeschi M Chronic non malignant pain: The rational use of opioid medication Australian Family Physician 2006; 35 :(7) 509-512.
2. Molloy AR The role of opioids in chronic non malignant pain. *Medicine Today Pain Management Supplement* August 2003.
3. Furlan AD et al Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects. *CMAJ* May 23 2006; 174(11).
4. Blyth FM et al Chronic pain-related disability and use of analgesia and health services in a Sydney community *Med J Aust* 2003; 179.
5. Goucke CR The management of persistent pain *Med J Aust* 2003; 178.
6. Portenoy RK Opioid Therapy for Chronic Non malignant Pain: A Review of the *Critical Issues Journal of pain and Symptom Management* 1996; 11: (4).
7. Kalso E et al Recommendations for using opioids in chronic non-cancer pain *European Journal of Pain* 2003; 7: (5):381-386.
8. Graziotti PJ Goucke CR The use of oral opioids in patients with chronic non-cancer pain: management strategies *Med J Aust* 1997; 167: 30-34.
9. Martell BA et al Systematic review: Opioid treatment for chronic back pain: Prevalence, efficacy and association with addiction. *Ann Intern Med* 2007; 146:116-127.
10. Trescot AM, Helm S, Hansen H, Benyamin R, Glasier SE, Adlake R et al Opioids in the management of chronic non-cancer pain: An update of American Society of the interventional pain physicians' (ASIPP) guidelines. *Pain Phys* 2008; 11:S5-S62.

References

1 The Government of The Commonwealth of Australia and the Governments of the States of Victoria, Queensland, Western Australia and Tasmania, Australian Royal Commission of Inquiry into Drugs, References to pharmaceutical drug misuse/abuse *Australian Government Printing Service* Canberra 1980.

2 Cohen M, Jasser S, Herron PD, Margolis CG. Ethical perspectives: Opioid treatment of chronic pain in the context of addiction, *Clin J Pain* 2002; 18: (4): S100-S107.

3 2006 *Synthetic Drug Control Strategy* (available at http://www.whitehousedrugpolicy.gov/ publications/synthetic_drg_control_strat/synth_strat.pdf). (Accessed 20.08.2007)

4 *The National Survey on Drug Use and health NSDUH report* (available at http://www.oas.samhsa.gov/2k6/pain/pain.pdf). The report extracted data from the 2004 US National Survey on Drug Use and Health.

5 Paulozzi LJ, Budnitz DS, Yongli X. Increasing deaths from opioid analgesics in the United States, *Pharmacoepidemiology and drug safety* 2006; 15: 618–627.

6 Paulozzi LJ, Ryan GW. Opioid analgesics and rates of fatal drug poisoning in the United States. *Am J Prev Med* 2006; 31(6):506-11.

7 Paulozzi LJ. Opioid analgesic involvement in drug abuse deaths in American Metropolitan Areas. *Am J Pub Health* 2006; 96:1755-7.

8 Degenhardt L, Black E, Breen C, Bruno R, Kinner S, Roxburgh A, et al. Trends in morphine prescriptions, illicit morphine use and associated harms among regular IDU in Australia . *Drug Alc Rev* 2006; 25:403-12.

9 Black E, Roxburgh A, Degenhardt L, Bruno R, Campbell G, de Graff et. al. Australian drug trends 2007: Findings from the Illicit Drug Reporting System (IDRS), Australian drug trends Series No. 1, National Drug and Alcohol Research Centre (NDARC), University of New South Wales, Sydney 2008.

10 Blyth FM, March LM, Brnabic AJ M, Jorm LR, Williamson M, Cousins MJ. Chronic pain in Australia: a prevalence study *Pain* 2001; 89: 127-134.

11 James FR, Large RG, Bushnell JA, Wells JE. Epidemiology of pain in New Zealand *Pain* 1991; 44:279–83.

12 Fishbain DA, Rosomoff HL, Rosomoff RS. Drug abuse, dependence, and addiction in chronic pain patients *Clin J Pain* 1992; 8:77-85.

13 Kahan M, Srivastava A, Wilson L, Gourlay D, Midmer D. Misuse of and dependence on opioids Study of chronic pain patients *Can Fam Physician* 2006; 52:1081-1087.

14 Chelminski PR, Ives TJ, Felix KM, Prakken SD, Miller TM, Perhak JS, et al. A primary care, multi-disciplinary disease management program for opioid-treated patients with chronic non-cancer pain and a high burden of psychiatric comorbidity *BMC Health Serv Res* 2005; 5(1):3.

15 Access Economics Pty Limited, *The high price of pain: the economic impact of persistent pain in Australia,* Canberra, MBF Foundation in collaboration with University of Sydney Pain Management Research Institute November 2007.

16 Furlan AD, Sandoval JA, Mailis-Gagnon A, Tunks E. Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects *CMAJ* 2006; 174(11):1589-94.

17 Ballantyne JC, LaForge KS. Opioid dependence and addiction during opioid treatment of chronic pain, *Pain* 2007; 129: 235–255.

18 Rashidian A Russell I, Towards better prescribing - a model for implementing clinical guidelines in primary care organisations in the NHS *Clinical Governance* 2003; 8(1): 26-32

19 Fleming MF, Balousek SL, Klessig CL, Mundt MP, Brown DD. Substance Use Disorders in a Primary Care Sample Receiving Daily Opioid Therapy, *J Pain* 2007; 8(7):573-582.

20 Drugs and Crime Prevention Committee, DCPC *Inquiry into the Misuse/Abuse of Benzodiazepines and Other Forms of Pharmaceutical Drugs in Victoria — Interim Report*, Parliament of Victoria

ISBN: 0-9579188-9-5 August 2006. Available at http://www.parliament.vic.gov.au/dcpc/Current_Inquiries/pharmaceuticalmisuse/DCPC-Report_Benzo_2006-08-24.pdf

21 *Opioid Substitution Treatment New Zealand Practice Guidelines* Available at http://www.moh.govt.nz/moh.nsf/49ba80c00757b8804c256673001d47d0/43c7fe2ae5863e39cc256cf30002b8ad?OpenDocument (Accessed 21.04.2008)

22 Stafford J, Degenhardt L, Black E, Bruno R, Buckingham K, Fetherston J et.al. *Australian drug trends 2005: Findings from the Illicit Drug Reporting System (IDRS)*, Monograph no. 59, Sydney National Drug and Alcohol Research Centre (NDARC), University of New South Wales 2006.

23 Grol R. Successes and failures in the implementation of evidence-based guidelines for clinical practice. *Med Care* 2001; 39 (suppl 2)**:** 46-54.

24 Lander J. Fallacies and phobias about addiction and pain. *Br J Addict*. 1990; 85:803-9.

25 Savage SR**.** Opioid use in the management of chronic pain. *Med Clin North Am.* 1999; 83:761-86.

26 Alford DP, Compton P, Samet JH. Acute pain management for patients receiving maintenance methadone or buprenorphine therapy *Ann Intern Med.* 2006; 144:127-134.

27 Australian Institute of Health and Welfare (AIHW) *2004 National drug strategy household survey: Detailed findings*, cat. No. PHE 66 (Drug Statistics Series No. 16), Canberra: AIHW. 2005.

28 National Consensus Development Panel on Effective Medical Treatment of Opiate Addiction, Effective medical treatment of opiate addiction. National Consensus Development Panel on Effective Medical Treatment of Opiate Addiction. *JAMA*. 1998; 280:1936-43.

29 O'Connor PG, Fiellin DA. Pharmacologic treatment of heroin-dependent patients. *Ann Intern Med.* 2000; 133:40-54.

30 The National Drug Strategy, Australia's Integrated Framework 2004–2009.

31 Drug Policy Modelling Program (DPMP) available at http://www.dpmp.unsw.edu.au/ 2008

32 The global epidemiology of methamphetamine injection: A review of the evidence on use and associations with HIV and other harm. Available at http://www.idurefgroup.unsw.edu.au/idurgweb.nsf/page/Publications (Accessed 28.07.2008)

33 Donovan DM, Assessment of addictive behaviors: Implications of an emerging biopsychosocial model. In D. M. Donovan & G. A. Marlatt (Eds.), *Assessment of addictive behaviors* (pp. 3-48.) New York: Guilford. 1988.

34 Buchanan D, Cohen M, Katz J, Quintner J Williamson O, Beyond biopsychosocial: a new framework for pain medicine? Presented at Australian and New Zealand College of Anaesthetists Annual Scientific Meeting 2007.

35 Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol Bull.* 2007; 133(4):581-624.

36 World Health Organization (WHO), *Effective drug regulation: A multicountry study*, Report prepared for the World Health Organization by Sauwakon Ratanawijitrasin and Eshetu ondemagegnehu, Geneva: WHO, 2002.

37 World Health Organization (WHO), *Lexicon of alcohol and drug terms,* Geneva: WHO 1994.

38 Khantzian EJ. The self-medication hypothesis of addictive disorders: focus on heroin and cocaine dependence. *Am J Psychiatry* 1985; 142:1259-64.

39 Khantzian EJ. The self-medication hypothesis o substance use disorders: a reconsideration and recent applications. *Harvard Rev Psychiatry* 1997; 4:231-44.

40 Loxley W, Toumbourou JW, Stockwell T. Summary. The prevention of substance use, risk and harm in Australia: a review of the evidence, Edited by Angela Kirsner. *The National Drug Research Institute and the Centre for Adolescent Health*, Ministerial Council on Drug Strategy, Canberra, Commonwealth of Australia 2004.

41 Adhikari P, Summerill A. *National Drug Strategy Household Survey: Detailed findings*. Canberra: AIHW (Drug Statistics Series No.6) AIHW cat.no. PHE 27 2000.

42 Cormier RA, Dell CA, Poole N. Women and substance abuse problems. *BMC Women's Health* 2004, 4(Suppl 1):S8 2004.

43 *Classification of chronic pain: description of chronic pain syndromes and definitions of pain terms.* Eds. Merskey H, Bogduk N. Seattle: IASP Press, 1994.

44 World Health Organization (WHO) Expert Committee on Drug Dependence, *WHO Expert Committee on Drug Dependence: thirty-third report*. Geneva, Switzerland 2002.

45 The Pain Society, Recommendations for the appropriate use of opioids for persistent Non-cancer pain: A consensus statement prepared on behalf of the Pain Society, the Royal College of Anaesthetists, the Royal College of General Practitioners and the Royal College of Psychiatrists March 2004. London. Access on 21.04.2008) http://www.britishpainsociety.org/pdf/opioids_doc_2004.pdf

46 Comptom P, Darakjian J, Miotto K. Screening for addiction in patients with chronic pain and 'problematic' substance use: evaluation of a pilot assessment tool, *J Pain Symptom Manage* 1998; 16: 355-66.

47 McAvoy BR, Addiction and addiction medicine: exploring opportunities for the general practitioner, *Med J Aust* 2008; 189:115-117.

48 McCormick R, Treating drug addiction in general practice, *NZ Fam Physician* 2000; 27(4):27-29.

49 Scott I, Alcohol and other drug problems in primary care, *NZ Fam Physician* 2007; 34(2):82-84.

50 Wilkins C, Casswell S, Bhatta K, Pledger M, Drug use in New Zealand: national surveys comparison 1998 and 2001. Auckland: University of Auckland Public Health Research Unit, 2002.

51 http://www.shore.ac.nz/projects/idms_study.htm Available at http://www.shore.ac.nz/projects/idms_study.htm (Access on 18.07.2008)

52 (This is as yet unpublished data from Deering, Sellman et al).

53 Tedeschi M. Chronic nonmalignant pain: The rational use of opioid medication *Aust Fam Phy* 2006; 35(7) 509-512.

54 Australian Bureau of Criminal Intelligence, *Australian Illicit Drug Report 2002* Canberra Commonwealth of Australia ISSN 1327-9068, 2003.

55 Bruni R, Mclean S. Tasmanian Drug Trends 2003: *Findings from the Illicit Drug Reporting System (IDRS) Technical Report No 178 2004.*

56 O'Reilly B. *Northern Territory Drug Trends Findings of the Illicit Drug Reporting System (IDRS)* NDARC 2002.

57 Pharmaceutical Benefits Scheme. *Highest Volume PBS Drugs by Generic Name, Year Ending June 2006, Expenditure and prescriptions twelve months to 30 June 2006.* (Available at) *http://www.health.gov.au/internet/wcms/Publishing.nsf/Content/A58720844CBFCB47CA257218000D91C7/$File/complete.pdf*

58 Bell JR. Australian trends in opioid prescribing for chronic noncancer pain. *Med J Aus* 1997; 167:26–9.

59 Tedeschi M. Chronic nonmalignant pain: The rational use of opioid medication *Aust Fam Phy* 2006; 35(7) 509-512.

60 Dobbin M. *PBS Emergency Drug (Doctor's Bag) Supply: the case for discontinuation of pethidine injection*. Victoria, Department of Human Services, June 2004.

61 Buckley NA, Whyte IM, Dawson AH, McManus PR, Ferguson NW. Correlations between prescriptions and drugs taken in self-poisoning. Implications for prescribers and drug regulation. *Med J Aust.* 1995 Feb 20; 162(4):194-7.

62 Dore GM. The dangers of dextropropoxyphene. *Aust N Z J Psychiatry.* 1996 Dec; 30(6):864-6.

63 Pearson SA, Ringland C, Kelman C, Mant A, Lowinger J, Stark H, Nichol G, Day R, Henry D. Patterns of analgesic and anti-inflammatory medicine use by Australian veterans. *Intern Med J.* 2007 Dec; 37(12):798-805.

64 Hawton K Simkin S, Deeks J. Co-proxamol and suicide: a study of national mortality statistics and local non-fatal self poisonings. *BMJ* 2003 May 10; 326(7397): 1006–1008.

65 Committee on the Safety of Medicines of the UK. Overdose risk prompts UK withdrawal of propoxyphene combination. *J Pain Palliate* Care Pharmacother 2006; 20(4):49-50.

66 Dobbin M, Tobin C. Over-the counter (OTC) ibuprofen/ codeine analgesics: misuse and harm. Paper prepared for the National Drugs and Poisons Schedule Committee. 22 May 2008.

67 Dutch, M. Nurofen Plus misuse: an emerging cause of perforated gastric ulcer, *Med J Aus* 2008; 188:56-7.

68 DataMonitor, Commercial and pipeline insight: Opioids – Short acting and anti-abuse technologies set to fragment and grow the market. *DataMonitor* March 2008, available at www.datamonitor.com/healthcare.

69 Davis WR, Johnson BD. Prescription opioid use, misuse, and diversion among street drug users in New York City. *Drug Alcohol Depend.* 2008 Jan 1; 92(1-3):267-76. Epub 2007 Oct 29.

70 Fentanyl transdermal patch and fatal adverse reactions, (Accessed on 02.09.2008) Available at http://www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/carn-bcei_v18n3-eng.php

71 Williamson PA, Foreman KJ, White JM, Anderson G. Methadone-related overdose deaths in South Australia, 1984-1994. How safe is methadone prescribing? *Med J Aust*. 1997 Mar 17; 166(6):302-5.

72 Cicero TJ, Surratt H, Inciardi JA, Munoz A. Relationship between therapeutic use and abuse of opioid analgesics in rural, suburban, and urban locations in the United States. *Pharmacoepidemiol Drug Saf* 2007; 16(8):827–40.

73 Dart RC, *Woody GE, Kleber HD.* Prescribing methadone as an analgesic. *Ann Intern Med* 2005; 143:620.

74 Fingerhut LA. *Increases in Methadone-Related Deaths: 1999-2004* Office of Analysis and Epidemiology http://www.cdc.gov/nchs/products/pubs/pubd/hestats/methadone1999-04/methadone1999-04.htm (Accessed 26.11.2007).

75 Leavitt SB, Methadone dosing & safety in the treatment of opioid addiction, *Addiction Treatment Forum* 2003; 1-8 (Available at http://www.atforum.com/pdf/DosingandSafetyWP.pdf#search='methadone dosing and safety') Accessed on 20.08.2008.

76 Goodman F, Jones WN, Glassman P, Methadone dosing recommendations for treatment of chronic pain, *J Forens Sci* 2007;52(6):1389-1395

77 Food and Drug Administration (FDA) Information for Healthcare professionals, Methadone Hydrochloride (available at http://www.fda.gov/cder/drug/InfoSheets/HCP/methadoneHCP.htm) Accessed on 20.08.2008.

78 Methadone Use for Pain Control May Result in Death and Life-Threatening Changes in Breathing and Heart Beat (Available at http://www.fda.gov/CDER/drug/advisory/methadone.htm, Accessed 5 February 2008.

79 Medicare Australia. *Medicare Benefits Schedule (MBS) item statistics reports.* Australian Government, Medicare Australia. Available at: http://www.medicareaustralia.gov.au/statistics/dyn_mbs/forms/mbs_tab4.shtml (accessed October 2007).

80 Miller GC, Britt HC, Valenti L. Adverse drug events in general practice patients in Australia. *Med J Aust* 2006; 184: 321-324.

81 Safety and Quality Council. *Second national report on patient safety: improving medication safety.* Canberra: Australian Council for Safety and Quality in Healthcare, 2002. Available at: http://www.safetyandquality.org/med_saf_rept.pdf (accessed Feb 2006).

82 Runciman WB, Roughead ER, Semple SS, Adam RJ. Adverse drug events and medication errors in Australia *IntJ for Qual in Healthcare* 2003; Vol 15, Suppl: i49–i59.

83 DirectLine provides a 24-hour telephone counseling, information and referral service for Victorians wishing to discuss drug-related issues. The service receives calls from individual drug users, relatives and friends of drug users, people seeking drug information generally and professionals in related services fields.

84 *Victorian Drug Statistics Handbook.* Patterns of drug use and related harm in Victoria, Department of Human Services. 2002 www.health.vic.gov.au/drugservices/pubs/drugstats.htm

85 O'Brien S, Black E, Degenhardt L, Roxburgh A, Campbell G, de Graaff B, et al. Australian Drug Trends 2006 Findings from the Illicit Drug Reporting System (IDRS) National Drug and Alcohol Research Centre (NDARC) Monograph No. 60 ISBN 978 0 7334 2483 0 NDARC 2007.

86 Csete J, Pearshouse R Dependent on Rights: Assessing Treatment of Drug Dependence from a Human Rights Perspective. Toronto: *Canadian HIV/AIDS Legal Network*. 2007.

87 Sellman JD, Robinson GM. Death as a result of consuming opioid drugs: A New Zealand Perspective National Centre for Treatment Development GM, Capital Coast Health. Available at http://www.med.unsw.edu.au/NDARCWeb.nsf/resources/Mono_1/$file/Mono.35.pdf(Accessed 02.02.2008)

88 Bedford KR, Nolan SL, Onrust R, Siegers JD. The illicit preparation of morphine and heroin from pharmaceutical products containing codeine: 'homebake' laboratories in New Zealand. *Forensic Sci In.* 1987; 34:197–204.

89 Reith D, Fountain JM, Tilyard M. Opioid poisoning deaths in New Zealand (2001–2002) *NZMed J* 2005; 118: 1209: 1-8.

90 National Centre in HIV Epidemiology and Clinical Research. *Australian NSP Survey National Data Report 2002-2006.* Sydney, NSW. National Centre in HIV Epidemiology and Clinical Research, the University of New South Wales, 2007.

91 Rosenblum A, Parrino M, Schnoll SH et al. Prescription opioid abuse among enrollees into methadone maintenance treatment. *Drug Alcohol Depend* 2007; 90:64-71.

92 Sigmon SC. Characterizing the emerging population of prescription opioid abusers. *Am J Addict* 2006; 15; 208-12.

93 Dore GM, Hargreaves G, Niven BE. Dependent opioid users assessed for methadone treatment in Otago: patterns of drug use. *NZMed J* 1997; 110:162-5.

94 English DR, Holman CD, Milne E, Winter MH, Hulse GK, Codde, et. al. The quantification of drug caused morbidity and mortality in Australia, Canberra: Commonwealth Department of Human Services and Health, 1995.

95 Darke S, Zador D. Fatal heroin 'overdose': A review, *Addiction,* 1996; (91):1765–1772.

96 Woods J, Gerostamoulos, D, Drummer OH, Cordner S. *Heroin deaths in Victoria, report no. 9*, Melbourne: Victorian Institute of Forensic Medicine & Department of Forensic Medicine, Monash University, 2006.

97 Australian Institute of Health and Welfare (AIHW) Australian GP Statistics and Classification Centre. SAND abstract 82 from the BEACH program 2005–06: Prevalence and management of chronic pain. Sydney: AGPSCC University of Sydney, 2006

98 Lloyd A. Forged Prescriptions Study Report to Pharmaceutical Society of Australia (Victorian Branch) Ltd. 2000.

99 Cicero TJ, Inciardi JA, Munoz A. Trends in abuse of OxyContin and other opioid analgesics in the United States: 2002–2004. *J Pain* 2005; 6(10): 662–672.

100 Hays LR. A profile of OxyContin addiction. *J Addict Dis* 2004; 23(4): 1–9.

101 Kurtz SP, Inciardi JA, Surratt HL, Cottler L. Prescription drug abuse among ecstasy users in Miami. *J Addict Dis* 2005; 24(4): 1–16.

102 Martyres RF, Clode D, Burns JM. Seeking drugs or seeking help? Escalating 'doctor shopping' by young heroin users before fatal overdose, *Med J Aust* 2004; 180: 211-214.

103 Kamien M, 'Doctor shoppers': at risk by any other name *Med J Aust* 2004; 180(1):204 -5

104 Zador D, Sunjic S. Deaths in methadone maintenance treatment in New South Wales, Australia 1990-1995. *Addiction* 2000; 95(1):77-84.

105 Oliver P Forrest R Keen J. Study to determine the relationship between blood-heroin/methadone and concomitant drug levels in fatal opioid poisonings, Sheffield: The National Treatment Abuse Centre, University of Sheffield, April 2007.

106 Smith L, Mouzos J. Drug use among police detainees The Picture in 2005, Alcohol and Other Drugs Council of Australia *ADCA News* 2006; 33: 1-2.

107 Butler T, Milner L. The 2001 New South Wales Inmate Health Survey. Sydney, NSW: Corrections Health Service. 2003.

108 Joranson DE, Gilson AM. Wanted: a public health approach to prescription opioid abuse and diversion *Pharmacoepidemiology and Drug Safety* 2006; 15: 632–634.

109 Cited by Reuter M. SAMHSA Update. Presented at National Association of State Controlled Substances Authorities (NASCA) Conference, 2007. Division of Pharmacologic Therapy, Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration, 2007. http://www.nascsa.org/Folder2/confer2007.htm (Accessed 5 February 2008).

110 The Law & Controlled Substances Prescribing Issue 2 PharmaCom Group, Inc. Available at http://www.tafp.org/cme/monocme/LCSP/lcsp2.pdf

111 Van Den Kerkhof EG, Hopman WM, Towheed TE, et. al. The impact of sampling and measurement on the prevalence of self-reported pain in Canada. *Pain Res Manag* 2003; 8:157–63.

112 Collett B-J. Chronic opioid therapy for non-cancer pain, *Brit J Anaesth* 2001; 87(1): 133-43.

113 International Association for the Study of Pain (IASP), Subcommittee on Taxonomy. Classification of chronic pain. Descriptions of chronic pain syndromes and definitions of pain terms. *Pain* 1986;Suppl 3:S1–S226, 1986

114 Bywood P, Pidd K, Roche A. Illicit drugs in the Australian Workforce: Prevalence and patterns of use. National Centre for education and training on Addiction (+NCETA), Flinders University, 2006.

115 Perquin CW, Hazebroek-Kampschreur AAJM, Hunfeld JAM, Bohnen AM, Lisette WA, et. al. Pain in children and adolescents: a common experience. *Pain* 2000; 87: 51-58.

116 Keogh E, Eccleston C. Sex differences in adolescent chronic pain and pain-related coping. *Pain* 2006; 123: 275-284.

117 Chalkiadis GA. Management of chronic pain in children. *Med J Aust* 2001; 175 (9):453-4.

118 McGrath PJ, Unruh AM, Branson SM. Chronic nonmalignant pain with disability. In: Advances in Pain Research and Therapy (Volume 15), Eds. Tyler DC, Krane EJ, New York: Raven Press, 1988.

119 Auret K, Schug SA. Underutilisation of opioids in elderly patients with chronic pain: approaches to correcting the problem. *Drugs Aging.* 2005; 22(8):641-54.

120 Buchbinder R, Jolley D Wyatt M. Breaking the back of back pain *Med J Aust* 2001; 175: 456-457.

121 National Occupational Health and Safety Commission, The Cost of Work-related Injury and Illness for Australian Employers, Workers and the Community. Canberra NOHSC 2004.

122 Directions in Injury Prevention Report 2: Injury Prevention Interventions—good buys for the next decade. A report from the National Injury Prevention Advisory Council Commonwealth of Australia 1999.

123 Rosenblum A, Joseph H, Fong C, Kipnis S, Cleland C, Portenoy R. Prevalence and characteristics of pain among chemically dependent patients in methadone maintenance and resident treatment facilities, *JAMA* 2003;289(18): 2370-2378.

124 Jamison RN, Kauffman J, Katz NP. Characteristics of methadone maintenance patients with chronic pain. *J Pain Symptom Manage.* 2000 Jan; 19(1):53-62.

125 Peles E, Schreiber S, Gordon J, Adelson M. Significantly higher methadone dose for methadone maintenance treatment (MMT) patients with chronic pain. *Pain* 2005 Feb; 113(3):340-6.

126 Ilgen MA, Trafton JA, Humphreys K. Response to methadone maintenance treatment of opiate dependent patients with and without significant pain. *Drug Alcohol Depend.* 2006 May 20; 82(3):187-93.

127 Rosenblum A, Parrino M, Schnoll SH, Fong C, Maxwell C, Cleland CM, et. al. Prescription opioid abuse among enrollees into methadone maintenance treatment *Drug and Alcohol Dependence* 2007; 90: 64–71.

128 Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain comorbidity: a literature review. *Arch Int Med* 2003; 163:2433–45.

129 Polatin PB, Kinney RK, Gatchel RJ, Lillo E, Mayer TG. Psychiatric illness and chronic low back pain. The mind and the spine – which goes first? *Spine* 1993; 18:66–71.

130 Sullivan MD, Edlund MJ, Zhang L, Unützer J, Wells KB. Association between mental health disorders, problem drug use, and regular prescription opioid use. *Arch Intern Med*. 2006; 166(19):2087-93.

131 Tang NK, Crane C. Suicidality in chronic pain: a review of the prevalence, risk factors and psychological links. *Psychol Med*. 2006; 36(5):575-86.

132 McPherson ML, Chronic pain management, a disease based approach, Pharmacotherapy self assessment program, http://www.accp.com/p5b8sample01.pdf (Accessed 11.02.2008)

133 Turk DC, Okifuji A. What factors affect physicians' decisions to prescribe opioids for chronic noncancer pain patients Clinical *Pain* 1997; 13(4):330-6.

134 Critchley DJ, Ratcliffe J, Noonan S, Jones RH, Hurley MV. Effectiveness and cost effectiveness of three types of physiotherapy used to reduce chronic low back pain disability: a pragmatic randomized trial with economic evaluation *Spine* 2007; 32(14):1474-81.

135 Coluzzi F, Pappagallo M. Opioid therapy for chronic noncancer pain: practice guidelines for initiation and maintenance of therapy. *Minerva Anestesiologica* 2005; 71: 425-33.

136 Hansen GR. Management of Chronic Pain in the Acute Care Setting. *Emerg Med Clin N Am* 2005; 3: 307-338.

137 Jage J. Opioid tolerance and dependence- do they matter? *European Journal of Pain* 2005; 9:157-162.

138 Antoin H, Beasley RD. Opioids for chronic noncancer pain. *Postgraduate Medicine* 2004; 116(3): 37-44.

139 National Centre for Education and Training on Addiction (NCETA) Consortium. Alcohol & other Drugs: A handbook for health professionals. Canberra: Australian Government Department of Health and Ageing. 2004.

140 Government of South Australia, Pharmaceutical Services, Department of Human Services, Adelaide Environmental Health Branch.

141 Niemisto L, Rissanen P, Sarna S, Lahtinen-Suopanki T, Lindgren KA, Hurri H. Cost effectiveness of combined manipulation, stabilizing exercises, and physician consultation compared to physician consultation alone for chronic low back pain: a prospective randomized trial with 2-year follow-up *Spine* 2005;30(10):1109-15.

142 Haas M, Sharma R, Stano M. Cost effectiveness of medical and chiropractic care for acute and chronic low back pain *Journal of Manipulative and Physiological Therapeutics*, 2005; 28(8):555-563.

143 Bashir K, King M, Ashworth M Controlled evaluation of brief intervention by general practitioners to reduce chronic use of benzodiazepines. *Brit J Gen Pract* 1994; 44: 408–412.

144 RACGP The RACGP Curriculum for Australian general Practice, Available at http://www.racgp.org.au/curriculum#downloadcurriculum, (accessed 20.11.2008)

145 Nicholas MK, When to refer to a pain clinic, *Best Practice & Research Clinical Rheumatology* 2004; 18(4): 613–629, 2004.

146 Easthope G, Justin J Beilby JJ, Gerard F Gill GF, Tranter BK Acupuncture in Australian general practice: practitioner characteristics *Med J Aust* 1998; 169: 197-200.

147 Paramore LC. Use of alternative therapies: estimates from the 1994 Robert Wood Johnson Foundation National Access to Care Survey. *J Pain Symptom Management* 1997; 13:83–9.

148 Britt H, Miller GC, Henderson J, Bayram C, Patient-based substudies from BEACH: abstracts and research tools 1999–2006. General practice series no. 20. AIHW cat. no. GEP 20. Canberra: Australian Institute of Health and Welfare 2007.

149 Moore RA, McQuay HJ, Prevalence of opioid adverse events in chronic non-malignant pain: systematic review of randomised trials of oral opioids *Arthritis Res Ther*. 2005; 7(5):R1046-51.

150 Melzack R. The tragedy of needless pain. *Sci Amer* 1990; 262:27-33.

151 Rich BA. Ethics of Opioid Analgesia for Chronic Noncancer Pain, *Pain Clinical Updates* 2007 XV (9).

152 Kalso E Edwards JE, Moore RA, McQuay HJ et. al, Opioids in chronic non-cancer pain; systematic review of efficacy and safety. *Pain* 2004; 112:372-380.

153 Eisenberg E, McNicol ED, Carr DB. Efficacy and safety of opioid agonists in the treatment of neuropathic pain of nonmalignant origin: systematic review and meta-analysis of randomized controlled trials. *JAMA* 2005; 293:3043-52.

154 Martell BA, O'Connor PG, Kerns RD, Becker WC, Morales KH, Kosten TR. Systematic Review: Opioid Treatment for Chronic Back Pain: Prevalence, Efficacy, and Association with Addiction *Ann Intern Med* 2007; 146:116-27.

155 Daniell HW. Hypogonadism in men consuming sustained-action oral opioids. *J Pain* 2002; 3:377-84.

156 Watson CP, Moulin D, Watt-Watson J, Gordon A, Eisenhoffer J. Controlled-release oxycodone relieves neuropathic pain: a randomized controlled trial in painful diabetic neuropathy. *Pain* 2003; 105:71-8.

157 Arkinstall W, Sandler A, Goughnour B, Babul N , Harsanyi Z, Darke AC. Efficacy of controlled-release codeine in chronic non-malignant pain: a randomized, placebo-controlled clinical trial. *Pain* 1995; 62:169-78.

158 Eriksen J, Sjogren P, Bruera E, Ekholm O, Rasmussen NK. Critical issues on opioids in chronic non-cancer pain: An epidemiological study. *Pain* 2006; 125:172–9.

159 Ballantyne JC, Shin NS. Efficacy of opioids for pain: A review of the evidence. *Clin J Pain* 2008; 24:469-478.

160 Edlund MJ, Steffick D, Hudson T, Harris M, Sullivan M. Risk factors for clinically recognised opioid abuse and dependence among veterans using opioids for chronic non-cancer pain. *Pain* 2007; 129:355-362.

161 Saper JR, Lake AE 3rd, Hamel RL, Lutz TE, Branca B, Sims DB, Kroll MM. Daily scheduled opioids for intractable head pain: long term observations of a treatment program. *Neurology* 2004; 62(10):1687-94.

162 Paice JA, Toy C, Shott S, Barriers to cancer pain relief: fear of tolerance and addiction. *Pain Symptom Manage* 1998; 16:1-19.

163 Bhamb B, Brown D, Hariharan J, Anderson J, Balousek S, Fleming F. Survey of select practice behaviors by primary care physicians on the use of opioids for chronic pain, *Curr Med Res Opin* 2006;22(9):1859-1865.

164 Bendtsen P, Hensing G, Ebeling C, Schedin A. What are the qualities of dilemmas experienced when prescribing opioids in general practice, *Pain* 1999; 82: 89-96.

165 McCracken LM, Hoskins J, Eccleston J. Concerns about medication and medication use in chronic pain. *Pain* 2006; 7: 726-34.

166 Graziotti PJ, Goucke CR. The use of oral opioids in chronic non-malignant pain. Management strategies. *Med J Aust* 1997; 176:30-34.

167 Maddox JD, Joranson D, Angarola RT. The use of opioids for the treatment of chronic pain (position statement). *Clin J Pain* 1997; 13:6-8.

168 Workplace Safety & Insurance Board of Ontario. *Statistical supplement to the annual report 2000*. Technical report. Workplace Safety & Insurance Board of Ontario, Toronto, Ontario, 2001.

169 Kalso E, Allan L, Dellemijn PLI, Faura CC, Ilias WK, Jensen TS, et al, Recommendations for using opioids in chronic non-cancer pain. *Eur J Pain* 2003; 7: 381-386.

170 Gourlay DL, Heit HA, Almahrezi A. Universal precautions in pain medicine: a rational approach to the treatment of chronic pain. *Pain Med.* 2005 Mar-Apr; 6(2):107-12.

171 Opioid guidelines in the management of chronic non-cancer , Available at: pain.http://www.guideline.gov/summary/summary.aspx?ss=15&doc_id=8806&nbr=4853#s21

172 Reisfield GM, Bertholf R, Barkin RL, Webb F, Wilson G. Urine drug test interpretation: what do physicians know? *J Opioid Manag.* 2007 Mar-Apr; 3(2):80-6.

173 Heit HA, Gourlay DL. Urine drug testing in pain medicine. *J Pain Symptom Manage.* 2004; 27(3):260-7.

174 Jaffee WB, Trucco E, Teter C, Levy S, Weiss RD. Focus on alcohol & drug abuse: ensuring validity in urine drug testing. *Psychiatr Serv.* 2008 Feb; 59(2):140-2.

175 Evans A, Thornett A. Do we have the training? The ethics of workplace drug testing and the GP. *Aust Fam Physician*. 2003 Aug; 32(8):645-7.

176 Babor TF, Brown J, DelBoca FK: Validity of self-reports in applied research on addictive behaviors: fact or fiction? *Behav Assess* 1990; 12:5–31.

177 Zanis DA, McLellan AT, Randall M. Can you trust patient self-reports of drug use during treatment? *Drug Alcohol Depend.* 1994 Apr; 35(2):127-32.

178 Weiss RD, Najavits LM, Greenfield SF, Soto JA, Shaw SR, Wyner D. Validity of substance use self-reports in dually diagnosed outpatients. *Am J Psychiatry.* 1998 Jan; 155(1):127-8.

179 Dyer KR, White JM. Patterns of symptom complaints in methadone maintenance patients, *Addiction* 1997; 92:1445–1455.

180 Doverty M, Somogyi AA, White JM, Bochner F, Beare CH, Menelaou A, et. al. Methadone maintenance patients are cross-tolerant to the antinociceptive effects of morphine. *Pain* 2001; 93:155-63.

181 College of Physicians and Surgeons Canada Methadone for Pain Guidelines 2004. Canada Ontario: *College of Physicians and Surgeons* 2004.

182 Fainsinger R, Schoeller T, Bruera E. Methadone in the management of cancer pain: a review. *Pain* 1993;51:137-47

183 Field MJ, Lohr KL. Guidelines for clinical practice, from development to use. *Institute of Medicine. National Academy Press* 1992.

184 Grimshaw JM, Russell IT. Effect of clinical guidelines on medical practice: a systematic review of rigorous evaluations *Lancet* 1993; 342: 1317-22.

185 Manderson D. *Mr Sin to Mr Big.* 1993. P.128. Oxford University Press Australia. ISBN: 0 19 553531 6.

186 The Parliament of the Commonwealth of Australia and Indigenous Peoples 1901-1967 available at http://www.aph.gov.au/library/Pubs/rp/2000-01/01RP10.htm (accessed 08.02.2008)

187 Wartell J, La Vigne NG, Problem-Oriented Guides for Police Problem-Specific Guides Series Guide No. 24 Prescription Fraud U.S. Department of Justice, Office of Community Oriented Policing Services, May 2004.

188 Hilmer S, Seale P. Alternatives to injectable opioids for acute analgesia, *Med Today* 2005; 6(2): 39-47.

189 (Personal Communication, B. Battye, NSW PSB)

190 Pharmaceutical Schedule, PHARMAC 2008 Available at http://www.pharmac.govt.nz/2008/07/01/Schedule.pdf (Accessed 03.07.2008)

191 Rosenthal MB, Berndt ER, Donohue JM, Frank RG, Epstein AM. Promotion of prescription drugs to consumers. *N Engl J Med* 2002; 346:498505.

192 Health Action International and the European Public Health Alliance (HAI/EPHA). 2002. Joint Statement on the Proposed Relaxation of the EU Ban on Direct-to-Consumer Advertising of Prescription Medicines. February 4. Available online at http://haiweb.org/campaign/DTCA/jointstatement.html (accessed December 2004).

193 Liu Y, Doucette WR, Does Direct-to-Consumer Advertising Affect Patients' Choice of Pain Medications? *Current Pain and Headache Reports* 2008; 12:89–93.

194 Weissman JS, Blumenthal D, Silk AJ, Zapert K, Newman M, Leitman R. Consumers' reports on the health effects of direct-to-consumer drug advertising, *Health Aff (Millwood)* 2003 Jan-Jun;Suppl Web Exclusives:W3-82-95.

195 Donohue JM, Cevasco M, Rosenthal MB A Decade of Direct-to-Consumer Advertising of Prescription Drugs N Engl J Med 2007; 357:673-81

196 FDA Announces Results Of Investigation Into Illegal Promotion Of OxyContin By The Purdue Frederick Company, Inc http://www.medicalnewstoday.com/articles/70690.php (Accessed 05.11.2008)

197 Berbatis C, Sunderland VB, S8s - amber lights flashing for pharmacy. *Aus Pharm* 2003; 22: 500.

198 National Association of State Controlled Substances Authorities and Alliance of States with Prescription Monitoring Programs (2002). *Prescription Monitoring Program Model Act.* www.nascsa.org/resolutions/ res0201.pdf.

199 Macdonald W, Evans O. Research on the Prevention of Work-Related Musculoskeletal Disorders Stage 1 - Literature Review 2006, Department of Employment and Workplace Relations OHS Expert Research Panel 2006.

200 Molloy AR, Blyth FM, Nicholas MK. Disability and work-related injury: time for a change? *Med J Aust* 1999; 170:150-51.

201 National Public Health Partnership (NPHP), The National Injury Prevention and Safety Promotion Plan: 2004-2014. Canberra: NPHP 2005

202 Australian Transport Safety Bureau (ATSB) 2003. Road crash data and rates. Australian states and territories 1925 to 2002. Canberra: ATSB.

203 Australian Bureau of Statistics, National Health Survey: summary of results *2004-05*. Canberra: ABS, 2006.

204 Allman-Farinelli MA, Aitken, RJ, King LA, Bauman AE. Obesity and Osteoarthritis— the forgotten obesity-related epidemic with worse to come, Letter *Med J Aust* 2008; 188(5): 317.

205 Marcus DA. Obesity and the impact of chronic pain *Clin J Pain*. 2004;20(3):186-91.

206 Chatzitheodorou D, Kabitsis C, Malliou P, Mougios V. A pilot study of the effects of high-intensity aerobic exercise versus passive interventions on pain, disability, psychological strain, and serum cortisol concentrations in people with chronic low back pain. *Phys Ther* 2007; 87:304-312.

207 Ferrell BA, Josephson KR, Pollan AM, Loy S, Ferrell BR. A randomized trial of walking versus physical methods for chronic pain management. *Aging (Milano)* 1997; 9:99-105.

208 Gowans SE, Dehueck A, Voss S, Silaj A, Abbey SE. Six month and one-year follow up of 23 weeks of aerobic exercise for individuals with fibromyalgia. *Arthritis Rheum* 2004; 51: 890-898.

209 Hayden JA, van Tulder MW, Malmivaara AV, Koes BW. Meta-analysis: Exercise therapy for non-specific low back pain. *Ann Intern Med* 2005; 142:765-775.

210 Malmros B, Mortensen L, Jensen MB, Charles P. Positive effects of physiotherapy on chronic pain and performance in osteoporosis. *Osteoporos Int* 1998; 8:215-221.

211 McCain GA, Bell DA, Mai FM, Halliday PD. A controlled study of the effects of a supervised cardiovascular fitness training program on the manifestations of primary fibromyalgia. *Arthritis Rheum* 1988; 31:1135-1141.

212 Robb KA, Williams JE, Duvivier V, Newham DJ. A pain management program for chronic cancer-treatment-related pain: A preliminary study. *J Pain* 2006; 7:82-90.

213 Vierck CJ Jr, Staud R, Price DD, Cannon RL, Mauderli AP, Martin AD. The effect of maximal exercise on temporal summation of second pain (windup) in patients with fibromyalgia syndrome. *Pain* 2001; 2:334-344.

214 Whiteside A, Hansen S, Chaudhuri A. Exercise lowers pain threshold in chronic fatigue syndrome. *Pain* 2004; 109:497- 499.

215 National Centre for Education and Training on Addiction (NCETA) Consortium. Alcohol & Other Drugs: A Handbook for Health Professionals. Canberra: Australian Government Department of Health and Ageing 2004.

216 Miotto, Compton P, Ling W, Conolly M. Diagnosing Addictive Disease in Chronic Pain Patients. *Psychosomatics* 1996; 37: 223-235.

217 Grimshaw JM, Shirran L, Thomas R, Mowatt G, Fraser C, Bero L, Grilli R, Harvey E, Oxman A, O'Brien MA. Changing provider behavior: an overview of systematic reviews of interventions. *Med Care.* 2001; 39:II2–45.

218 Oxman AD, Thomson MA, Davis DA, Haynes RB. No magic bullets: a systematic review of 102 trials of interventions to improve professional practice. *CMAJ.* 1995 Nov 15; 153(10):1423-31.

219 Freemantle N, Harvey EL, Wolf F, Grimshaw JM, Grilli R, Bero LA. Printed educational materials: effects on professional practice and health care outcomes. Cochrane Database Syst

Rev. 2000; (2):CD000172. Links Update in: *Cochrane Database Syst Rev*. 1997; (2):CD000172.

220 Jamtvedt G, Young JM, Kristoffersen DT, Thomson O'Brien MA, Oxman AD. Audit and feedback: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev.* 2003:CD000259.

221 Dollman WB, Leblanc VT, Stevens L, O'Connor PJ, Roughead EE, Gilbert AL. Achieving a sustained reduction in benzodiazepine use through implementation of an area-wide multi-strategic approach. *J Clin Pharm Ther.* 2005; 30(5):425-32.

222 Kaye KI, Welch SA, Graudins LV, Graudins A, Rotem T, Davis SR, Day RO. Pethidine in emergency departments: promoting evidence-based prescribing. *Med J Aust.* 2006; 184(1):44.

223 Taylor SE, Braitberg G, Lugt J. Multifaceted education initiative minimizes pethidine prescribing in the emergency department. *Emerg Med Australas.* 2007; 19(1):25-30.

224 Zwar NA, Wolk J, Gordon JJ, Sanson-Fisher RW. Benzodiazepine prescribing by GP registrars. A trial of educational outreach. *Aust Fam Physician.* 2000; 29(11):1104-7.

225 O'Connell DL, Henry D, Tomlins R. Randomised controlled trial of effect of feedback on general practitioners' prescribing in Australia. *BMJ* 1999; 318(7182):507-11.

226 Pit SW, Byles JE, Henry DA, Holt L, Hansen V, Bowman DA. A Quality Use of Medicines program for general practitioners and older people: a cluster randomised controlled trial. *Med J Aust.* 2007; 187(1):23-30.

227 Mant A, Whicker SD, McManus P, Birkett DJ, Edmonds D, Dumbrell D. Benzodiazepine utilisation in Australia: report from a new pharmacoepidemiological database. *Aust J Public Health.* 1993; 17(4):345-9.

228 King MA, Roberts MS. The influence of the Pharmaceutical Benefits Scheme (PBS) on inappropriate prescribing in Australian nursing homes. *Pharm World Sci* 2007; 29(1):39-42.

229 Breen CL, Degenhardt LJ, Bruno RB, Roxburgh AD, Jenkinson R. The effects of restricting publicly subsidised temazepam capsules on benzodiazepine use among injecting drug users in Australia. *Med J Aust*. 2004 Sep 20; 181(6):300-4.

230 Handelsman DJ. Trends and regional differences in testosterone prescribing in Australia, 1991-2001. *Med J Aust*. 2004 Oct 18; 181(8):419-22.

231 Sorensen L, Stokes JA, Purdie DM, Woodward M, Elliott R, Roberts MS. Medication reviews in the community: results of a randomized, controlled effectiveness trial. *Br J Clin Pharmacol*. 2004; 58(6):648-64.

232 Weekes LM, Mackson JM, Fitzgerald M, Phillips SR. National Prescribing Service: creating an implementation arm for national medicines policy. *Br J Clin Pharmacol.* 2005; 59(1):112-6.

233 Beilby J, Wutzke SE, Bowman J, Mackson JM, Weekes LM. Evaluation of a national quality use of medicines service in Australia: an evolving model. *J Eval Clin Pract.* 2006; 12(2):202-17.

234 Burns JM, Martyres RF, Clode D, Boldero JM. Overdose in young people using heroin: associations with mental health, prescription drug use and personal circumstances. *Med J Aust.* 2004; 181(7 Suppl):S25-8.

235 World Health Organization. Achieving Balance in National Opioids Control Policy: Guidelines for Assessment. Geneva, Switzerland: World Health Organization; 2000. (Available at http://www.medsch.wisc.edu/painpolicy/publicat/00whoabi/00whoabi.htm). (Accessed 18.09.2006)

236 Health Canada. Towards an evaluation framework for electronic health records: An inventory of electronic health records initiatives across Canada. 2004. Available from http://www.hc-sc.gc.ca/hcssss/pubs/kdec/nf_eval/nf_eval3_e.html

237 Chee E, Schneberger S. *British Columbia's PharmaNet project*, London, Ontario: University of Western Ontario, 2003.

238 Purdue Pharma. Purdue Pharma implements national surveillance system to track diversion and abuse of controlled pain medications 2002. Available from http://www.pharma.com/pressroom/news/oxyContinnews/20020627.htm

239 Australian Institute of Health and Welfare, Alcohol and other drug treatment services in Australia 2005–06: report on the National Minimum Data Set. Drug Treatment Series no.7. Cat. No. HSE 53. Canberra: *AIHW* 2007.

240 Australian Institute of Health and Welfare (AIHW) National Opioid Pharmacotherapy Statistics Annual Data collection: 2007 report. Bulletin no. 62. Cat. no. AUS 104. Canberra: AIHW 2008

241 Clark HW. Office-based practice and opioid-use disorders. *N Engl J Med*. 2003; 349:928-30.

242 Dollman WB, LeBlanc VT, Stevens L, O'Connor PJ, Turnidge JD. A community-based intervention to reduce antibiotic use for upper respiratory tract infections in regional South Australia. *Med J Aust.* 2005 Jun 20; 182(12):617-20.

243 Sheen CL, Dillon JF, Bateman N, Simpson KJ, MacDonald TM. Paracetamol pack size restriction: the impact on paracetamol poisoning and the over-the-counter supply of paracetamol, aspirin and ibuprofen *Pharmacoepidemiology and Drug Safety* 2002; **11(4): 329-331.**

244 Hawkins LC, Edwards JN, Dargan PI. Impact of restricting paracetamol pack sizes on paracetamol poisoning in the United Kingdom: a review of the literature. *Drug Saf.* 2007; 30(6):465-79.

245 Spoth R, Trudeau L, Shin C, Redmond C. Long-term effects of universal preventive interventions on prescription drug misuse. *Addiction.* 2008 Jul; 103(7):1160-8.

246 Bond L, Butler H, Thomas L, Carlin JB, Glover S, Bowes G, Patton G. Social and school connectedness in early secondary school as predictors of late teenage substance use, mental health and academic outcomes. *J Adoles Health* 2007; 40 (4): 357e9-357e18.

247 NCHECR, 2007. Sydney Medically Supervised Injecting Centre Evaluation Report No. 4: Evaluation of service operation and overdose-related events. National Centre in HIV Epidemiology and Clinical Research, University of New South Wales, Sydney, NSW.

248 The National Centre in HIV Epidemiology and Clinical Research, Australian Needle and Syringe Survey National Data Report 2003-2007 The National Centre in HIV Epidemiology and Clinical Research The University of New South Wales, Sydney NSW 2008.

249 Nutt D, Lingford-Hughes A, Addiction: the clinical interface *Brit J Pharmacol* 2008; 154: 397–405.

250 Bell J, Byron G, Gibson A, Morris A, A pilot study of buprenorphine naloxone combination tablet (Suboxone) in treatment of opioid dependence, *Drug and Alcohol Review,* 2004; 23(3): 311-7.

251 International Association for the study of pain, *World Health Organization supports global effort to relieve chronic pain* http://www.who.int/mediacentre/news/releases/2004/pr70/en/

252 New Zealand Ministry of Health. 2007. *Service Audit and Review Tool: Opioid Substitution Treatment in New Zealand.* Wellington: Ministry of Health.

253 Weissman D, Haddox J. Opioid pseudoaddiction – an iatrogenic syndrome. *Pain* 1989; 36:363–6.

254 Webster L, Webster R. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. *Pain Med* 2005; 6:432–42.

255 AMH Pty Ltd. *Australian Medicines Handbook*, Last modified by Australian Medicines Handbook: July, 2007.

256 Trescot AM, Helm S, Hansen H, Benyamin R, Glasier SE, Adlake R et al Opioids in the management of chronic non-cancer pain: An update of American Society of the interventional pain physicians' (ASIPP) guidelines. *Pain Phys* 2008; 11:S5-S62.

257 Clover K. et. al. Project 5: the development of consensus guidelines, Hunter Access to Surgery Research Project, Hunter Area Health Service, May 1995.

258 Fervers B, Burgers JS, Haugh MC, Latreille J, Mlika-Cabanne N, Paquet L, Coulombe M, Poirier M, Burnand B. Adaptation of clinical guidelines: literature review and proposition for a framework and procedure *Int J for Quality in Healthcare* 2006; 18(3): 167–176.

259 Smith TJ, Hillner BE. Ensuring quality cancer care by the use of clinical practice guidelines and critical pathways. *J of Clinical Oncology* 2001; 19: 2886–2897.

260 Woolf SH. Practice guidelines: a new reality in medicine. I. Recent developments. *Archives of Intern Med* 1990; 150: 1811–1818.

Notes

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145 Macquarie Street
Sydney NSW 2000, AUSTRALIA
Tel: +61 2 9256 5444 Fax: +61 2 9252 3310
Email: racp@racp.edu.au

www.racp.edu.au

5th Floor, 99 The Terrace (PO Box 10601)
Wellington 6036, NEW ZEALAND
Tel: +64 4 472 6713 Fax: +64 4 472 6718
Email: racp@racp.org.nz

www.racp.org.nz

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