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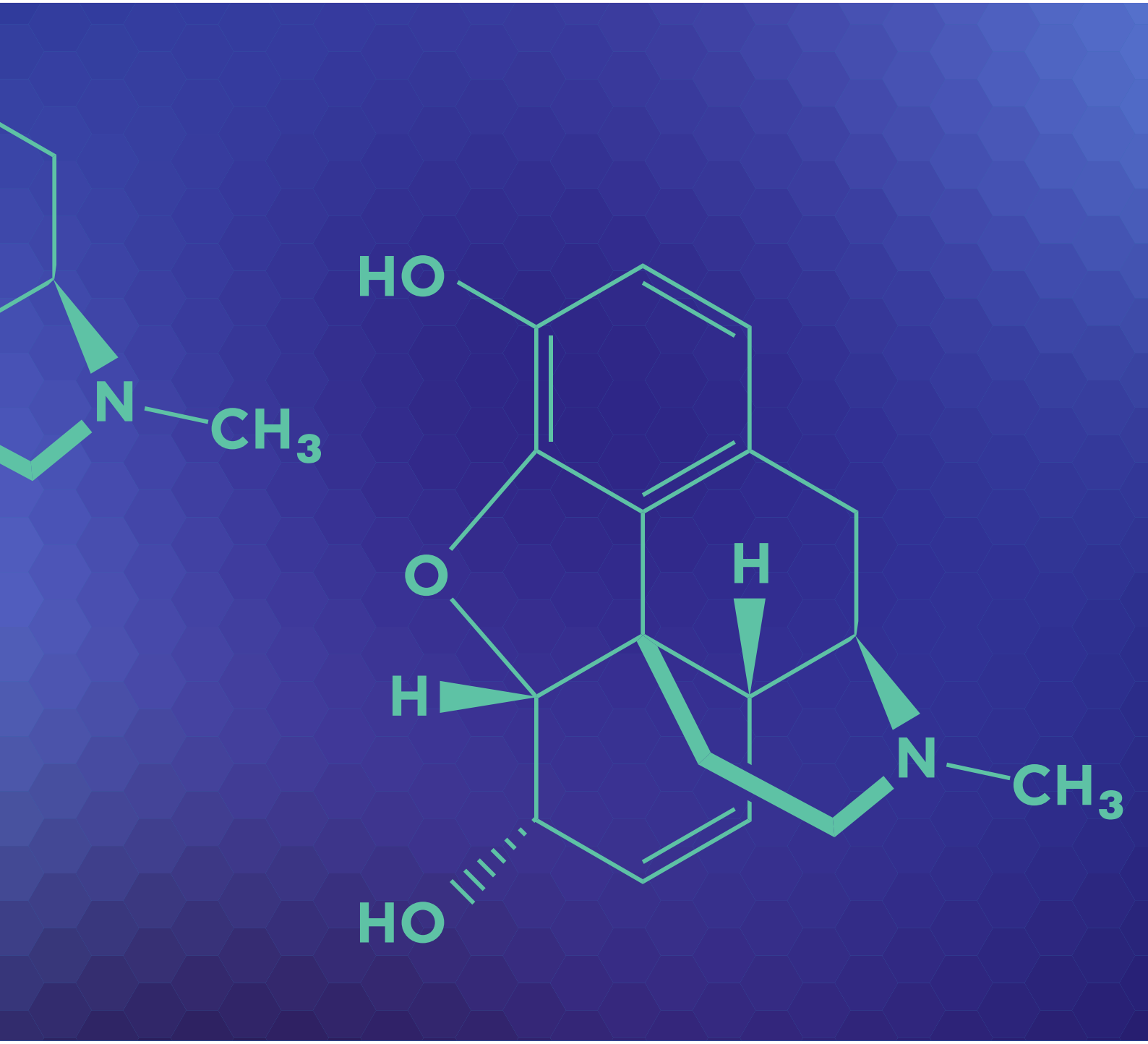
Royal Australian College *of* General Practitioners

# *Prescribing drugs of dependence in general practice, Part C2*

## The role of opioids in pain management



**Prescribing drugs of dependence in general practice, Part C2: The role of opioids in pain management**

### Disclaimer



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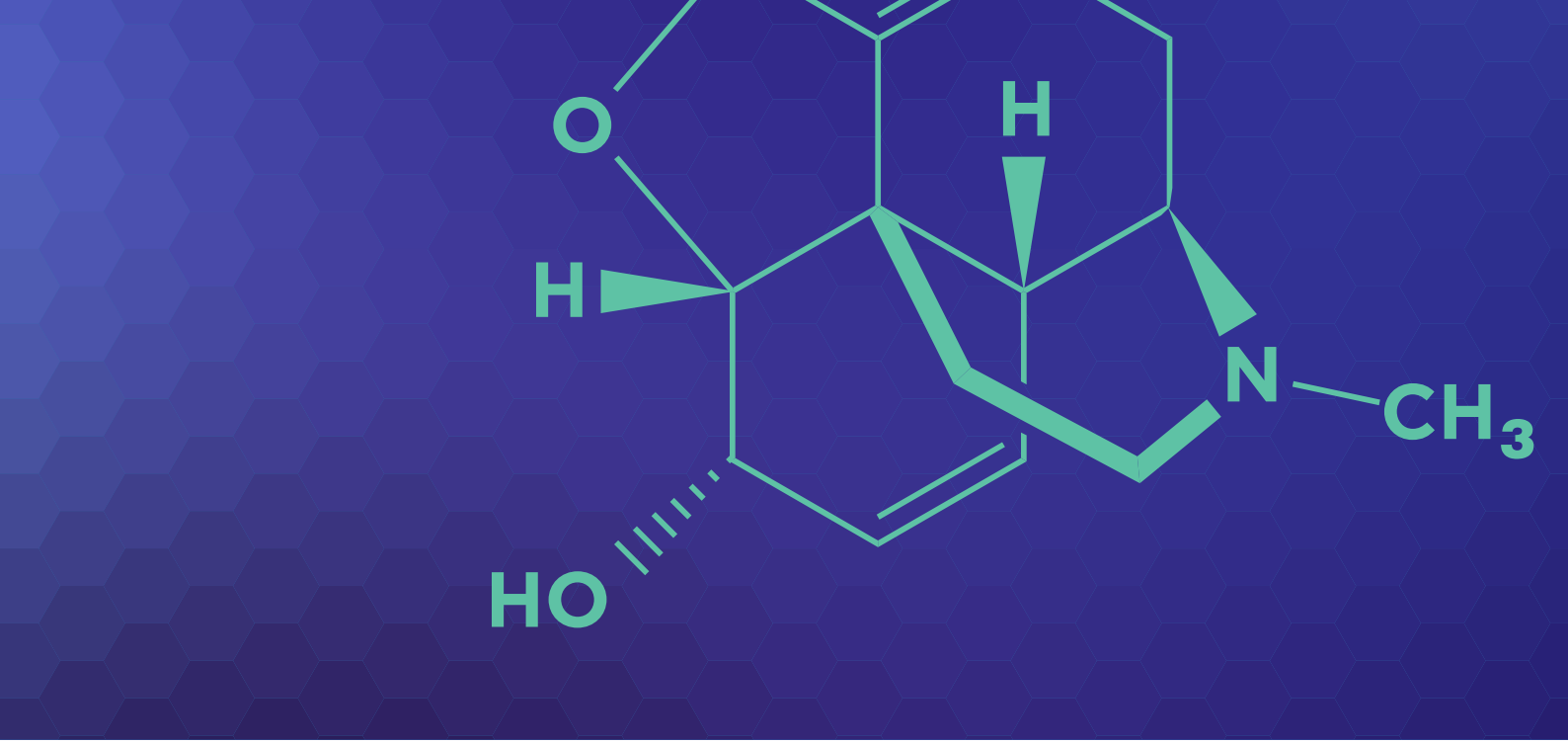
*We acknowledge the Traditional Custodians of the lands and seas on which we work and live, and pay our respects to Elders, past, present and future.*

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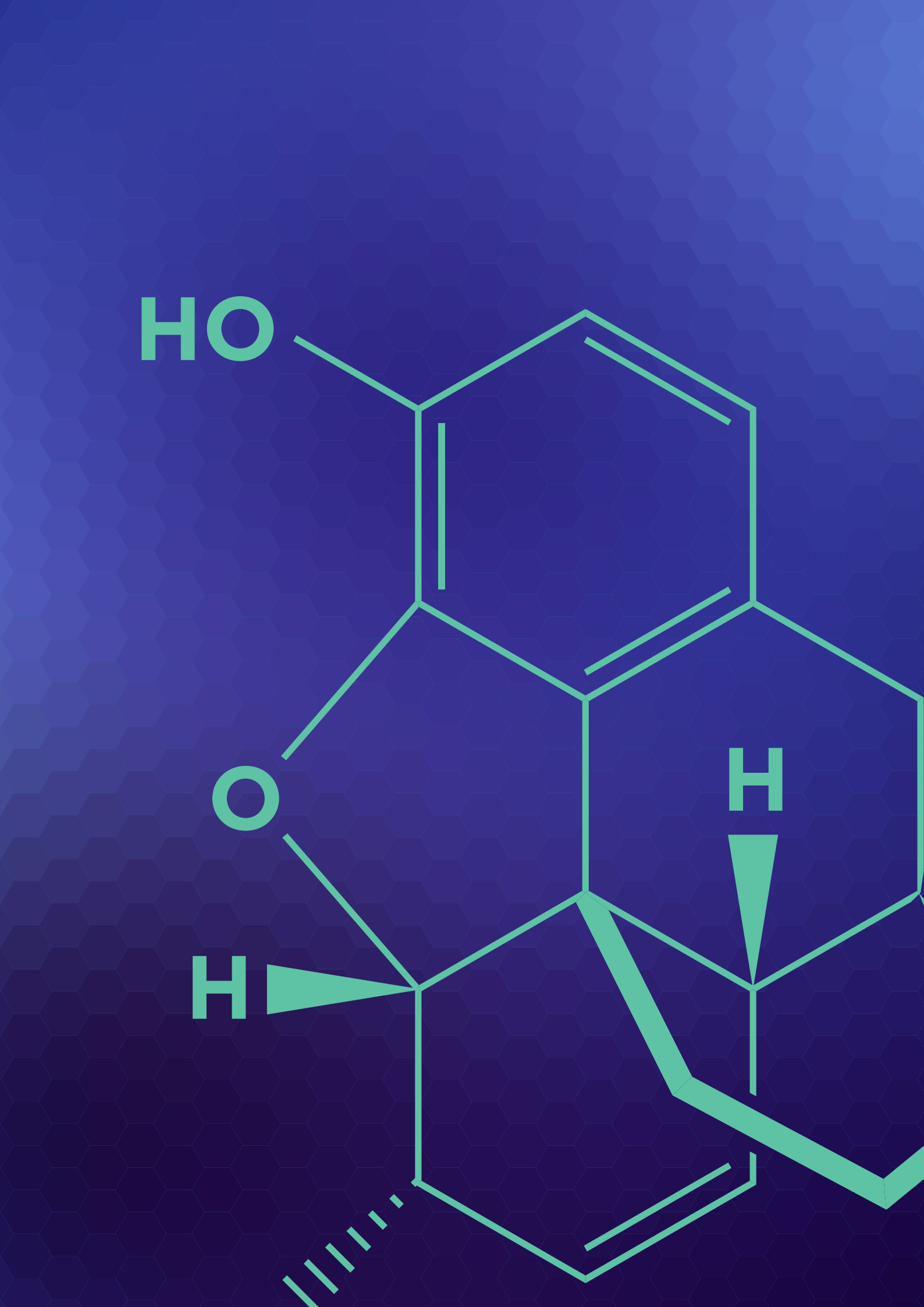
## The role of opioids in pain management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# *Foreword*

Pain management is a core general practitioner (GP) skill. But the complex (and sometimes controversial) nature of pain, particularly the management of chronic pain, can push the limits of this skill.

Pain is described as an unpleasant sensory and emotional experience – not a disease.[1] In accepting this, we need to understand the nature of patient experience, and realise that there will be no one simple pain treatment for all patients.

Good pain management has significant benefits. For many people, it can transform their quality of life, allowing them to work, be active, and participate in the community rather than being functionally disabled by pain. GPs should take care not to stigmatise patients due to their painful condition or their therapeutic regimes.

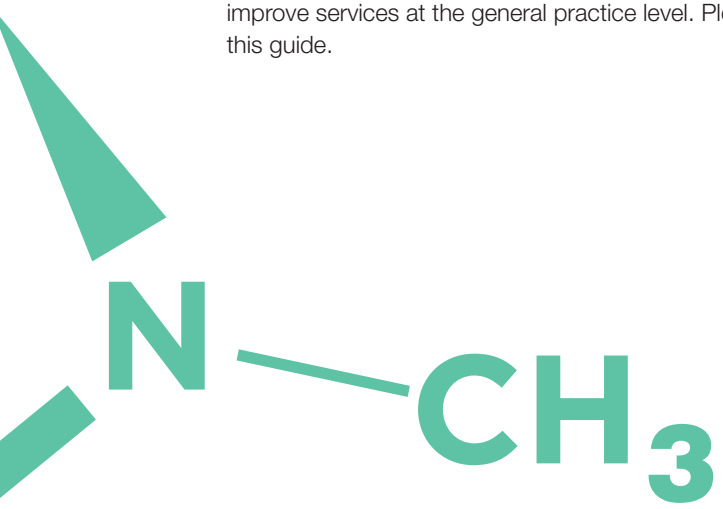
In a typical week, 20–40% of adult consultations in Australian general practice involve a chronic pain complaint.[2,3] GPs need to feel comfortable managing these patients.[2,4] Nowhere is it more important for GPs to have a biopsychosocial approach, in order to provide continuous longitudinal care in a supportive environment. Drug therapies will only ever have a partial role in managing complex biopsychosocial issues that characterise pain management. In the modern health environment, we must explore and use non-drug therapies, and redefine the place for existing medications. It is also important to be able to communicate with patients about the risks and benefits of different pain therapies.

Key to effective pain management is understanding the significant difference between acute and chronic pain with regard to definition, aetiology and complexity. The clinical dilemma remains in that no analgesic drug works well in all patients with chronic pain. Most analgesics work well only in a small proportion of patients. The analgesic adjuvants are also variable in their effectiveness in pain management, and may also have problematic use issues. Despite the risks, opioids remain a necessary therapeutic option in managing some chronic pain presentations.

This guide, in conjunction with *Part C1: Opioids*, represents a synthesis of the best available evidence for opioids and adjuvants in the primary care setting. In particular, it provides recommendations for GPs who are prescribing opioids for acute and chronic pain outside of active cancer treatment, palliative care, and end-of-life care. This guide addresses when to initiate, continue and discontinue opioids for chronic pain; which opioids to select (with information about dosage, duration, follow-up and discontinuation); and how to assess risk and address harms of opioid use.

In completing this guide, we acknowledge the work of the key advisers and reviewers, and the many people who have provided constructive feedback.

The Royal Australian College of General Practitioners (RACGP) welcomes feedback on this guide to continually improve services at the general practice level. Please use the feedback section on our website to help co-create this guide.



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The publication has been produced in accordance with the rules and processes outlined in the *RACGP Conflict of Interest Policy*. The Policy is available at www.racgp.org.au/support/policies/organisational

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# *Acronyms*

| | |
|---|---|
| **ACSQH** | Australian Commission for Safety and Quality in Health Care |
| **ADEC** | Australian Drug Evaluation Committee |
| **AIHW** | Australian Institute of Health and Welfare |
| **ANZCA** | Australian and New Zealand College of Anaesthetists |
| **CBT** | cognitive behavioural therapy |
| **CDCP** | Centers for Disease Control and Prevention |
| **CI** | confidence interval |
| **CIPN** | chemotherapy-induced peripheral neuropathy |
| **CNCP** | chronic non-cancer pain |
| **CPSP** | chronic post-surgical pain |
| **CR** | controlled release |
| **CRPS** | complex regional pain syndrome |
| **DDD** | defined daily dose |
| **DVA** | Department of Veterans' Affairs |
| **DSM-5** | *Diagnostic and statistical manual of mental disorders* (5th edition) |
| **ED** | emergency department |
| **FDA** | Food and Drug Administration |
| **GRADE** | Grading of Recommendations Assessment, Development and Evaluation |
| **GP** | general practitioner |
| **HIV** | human immunodeficiency virus |
| **IASP** | International Association for the Study of Pain |
| **IM** | intramuscular |
| **IV** | intravenous |
| **MBS** | Medicare Benefits Schedule |
| **MOH** | medication-overuse headache |
| **NHS** | National Health Service |
| **NNT** | number needed to treat |
| **NPS** | National Prescribing Service |
| **NSAID** | non-steroidal anti-inflammatory drug |
| **OIH** | opioid-induced hyperalgesia |
| **OME** | oral morphine equivalent |

| | |
|---|---|
| **OMEDD** | oral morphine equivalent daily dose |
| **ÖMPQ** | Örebro musculoskeletal pain questionnaire |
| **ORT** | opioid replacement therapy |
| **OSA** | obstructive sleep apnoea |
| **OTC** | over-the-counter |
| **PBS** | Pharmaceutical Benefits Scheme |
| **PDMP** | prescription drug monitoring program |
| **PEG** | Pain, Enjoyment, General activity (tool) |
| **PHN** | Primary Health Network |
| **PRN** | *pro re nata* (as needed) |
| **PSIS** | Prescription Shopping Information Service |
| **PSP** | Prescription Shopping Programme |
| **RCT** | randomised controlled trial |
| **RPBS** | Repatriation Pharmaceutical Benefits Scheme |
| **RTPM** | real-time prescription monitoring |
| **S4** | Schedule 4 |
| **S8** | Schedule 8 |
| **S100** | Section 100 (highly specialised drugs) |
| **SC** | subcutaneous |
| **SDM** | shared decision making |
| **SNRI** | serotonin noradrenaline reuptake inhibitor |
| **SSRI** | selective serotonin reuptake inhibitor |
| **SUD** | substance use disorder |
| **TCAs** | tricyclic antidepressants |
| **TdP** | Torsades de Pointes |
| **TGA** | Therapeutic Goods Administration |
| **UDS** | urine drug screen |
| **UDT** | urine drug test |

# *Key principles for appropriate opioid prescribing in general practice*

The RACGP series Prescribing drugs of dependence in general practice recognises that drugs of dependence have important therapeutic uses, but that prescription of these medicines must always be clinically appropriate and supported by national and state law.

During the development of *Prescribing drugs of dependence in general practice, Part C1: Opioids*, it became apparent that pain management needed its own focus. Hence, we have *Part C1: Opioids* and *Part C2: The role of opioids in pain management*. These two together provide evidence and strategies to support accountable prescribing of opioids.

## Key principles

- As with any treatment, prescription of opioids should be based on a comprehensive biopsychosocial-based assessment; a diagnosis; thoughtful consideration of the likely benefits and risks of any medication, as well as of non-drug alternative interventions; and a management plan derived through shared decision making (SDM) and continual clinical monitoring.
- General practitioners (GPs) should be aware of the common concerns associated with opioids, such as potential dependence, withdrawal, problematic drug use (including diversion and misuse) and known harmful effects, including falls, potential cognitive effects and motor vehicle accidents. These risks should be discussed with patients.
- Opioid treatment seeks to maximise outcomes for health and social functioning of the patient while minimising risks. To minimise risks, opioids should be prescribed at the lowest effective dose for the shortest clinical timeframe.
- Avoid prescribing opioids to patients with comorbid alcohol or substance use disorders or polydrug use. GPs should consider seeking specialist opinion in the management of these patients. Patients who use two or more psychoactive drugs in combination (particularly benzodiazepines and opioids) and those with a history of substance misuse may be more vulnerable to major harms.
- Opioids are generally regarded by clinical practice guidelines as a short-term therapeutic option. Long-term use should be uncommon, made with caution and based on consideration of the likely risks and benefits of opioids.
- If alternatives to opioid treatment fail, have limited benefit or are inappropriate, supervised opioid treatment may remain an acceptable long-term therapeutic option.
- Long-term opioid prescriptions should be at the lowest effective dose, and regular attempts at reduction should be scheduled. Continued professional monitoring of health outcomes is required.
- Opioids should be prescribed from one practice and preferably one GP and dispensed from one pharmacy.
- GPs may wish to use the diagnosis of substance use disorder (SUD) rather than dependence, addiction or abuse; this is based on the sedative, hypnotic or anxiolytic use disorder criteria in the *Diagnostic and statistical manual of mental disorders* (5th edition) (DSM-5). This is a more neutral term that may reduce stigmatisation of patients with problematic use of opioids, benzodiazepines and other drugs or alcohol.
- GPs should have communication strategies and safety processes in place to manage inappropriate requests for opioids by patients.
- All patients, including those who use opioids and other drugs or alcohol problematically, have the right to best practice care that is respectful and promotes their dignity, privacy and safety.

# *A summary of opioid use for acute pain in general practice*

Acute pain is an unpleasant sensory and emotional experience usually related to surgery, injury or disease. It is associated with actual or potential tissue damage to non-neural tissue and is experienced due to activation of nociceptors. This is also known as nociceptive pain.

Acute pain includes inflammatory pain; that is, pain that occurs in response to tissue injury and the subsequent inflammatory response. Typically, inflammatory pain disappears after resolution of the initial tissue injury. However, in chronic disorders (eg rheumatoid arthritis) the pain may persist for as long as inflammation is active.

Effective management of acute pain requires:

- tailoring treatment to the individual patient
- awareness of the science behind contextual and placebo effects
- competence with multimodal analgesia (ie the concurrent use of different classes of analgesics)
- providing patient reassurance
- providing education, including expected duration of pain episode and warning signs that would require immediate medical attention.

For accountable prescribing in managing acute pain, GPs should

- undertake a complete biopsychosocial assessment of the patient with pain
- be familiar with the evidence for selected acute pain presentations in general practice where opioids are not routinely recommended
- prescribe opioid medications only for the treatment of acute nociceptive pain when non-opioid pain medications and therapies have failed or are likely to fail
- undertake a patient selection/exclusion process before commencing opioids.

If opioids are commenced for the pain of acute nociception, there is a need to give clear direction about the anticipated duration of therapy. Typically, opioids should be weaned and ceased as the acute injury heals. Usually three days or less of opioid therapy will be sufficient for non-traumatic pain not related to major surgery. Even in complex postoperative cases, this should be within 90 days.[5]

GPs need to be familiar with the complexities of care in patients on long-term opioid therapy who present with an acute exacerbation or new acute pain.

# *A summary of opioid use in chronic non-cancer pain in general practice*

Chronic pain has historically been defined as continuous or recurrent pain that persists for an extended period (generally more than three months). However, the biological mechanisms for chronic pain are quite different from those of acute nociception, and should not be considered as 'unhealed' acute pain. Chronic non-cancer pain (CNCP) is a collection of clinical conditions with involvement of single or multiple pathophysiological mechanisms leading to persistent pain. It is also an individual, multifactorial experience influenced by culture, previous pain events, beliefs, expectations, mood and resilience.

Due to methodological weaknesses of chronic pain studies, interpretation and translation of evidence into practice is difficult. There is limited evidence to determine long-term benefits of opioids (outside of end-of-life care); however, there is evidence of risk of harm that increases with dose. While guidelines suggest opioids in the management of some chronic pain conditions, they are not recommended for routine or first-line use.

For accountable prescribing in managing CNCP, GPs should:

- undertake a complete biopsychosocial assessment of the patient with pain
- optimise non-drug therapies, and optimise non-opioid therapies as the primary interventions of care.

Opioids for CNCP should be reserved for selected patients with moderate or severe pain that has not responded to other therapies and that significantly affects function or quality of life. If primary interventions fail or are suboptimal, opioid therapies may be considered. GPs should share the decision-making process with the patient, and if opioid therapy is considered, there should be:

- a patient selection/exclusion process before a therapeutic opioid trial
- formal care planning based on specific goals and risks
- an opioid trial, which is undertaken to determine a patient's response to opioid therapy. This trial includes the selection of an appropriate opioid, formal measures of analgesia and functionality, a trial of dose reduction, and a drug cessation plan if the trial fails
- an ongoing assessment and evaluation by the accountable prescriber if the trial shows opioid benefit
- opioid tapering and cessation if suboptimal results or aberrant behaviour occurs.

Long-term use should be uncommon, undertaken with caution and based on consideration of the likely risks and benefits of opioids. Intermittent use is preferable.

GPs should also be aware of chronic pain conditions where there are known clinical complexities involving opioids. These complex clinical areas include the exacerbation of pain or new acute pain in patients on long-term opioid therapy, managing opioids after a non-fatal overdose, and managing the inherited patient.

Some patients on long-term treatment with opioids for CNCP may represent de facto maintenance treatment for iatrogenic opioid dependence. GPs should aim to taper patients taking >100 mg oral morphine equivalent (OME) per day.

# *Introduction*

Pain is a common general practice presentation and pain management is a fundamental general practitioner (GP) role. An estimated 20–40% of patient presentations involve chronic pain, which makes it the most prevalent condition managed in general practice.[2,3] Almost 10% of this pain is measured at Grade IV (the highest level of severity using Von Korff's pain scale). This level of pain is highly disabling and severely limiting.[3]

Bettering the Evaluation and Care of Health (BEACH) data revealed that most of the chronic pain seen in general practice is musculoskeletal (of that, 48% is osteoarthritis and 28% low back pain).[3] However, one in five chronic pain presentations is neurological (of that, 20% is peripheral neuropathy).[3]

Opioids are important in the management of pain and are highly beneficial to some individuals. However, there are increasing community concerns regarding their use and safety. GPs need to be aware of the broad issues around opioid use in society, as well as specific problems at a patient level, and how to address these issues with evidence-based interventions.

## Aims

This guide is a resource designed to assist with the appropriate and accountable prescribing of analgesic medications in the general practice context. Used in combination with *Prescribing drugs of dependence in general practice, Part C1: Opioids,* it is designed to discourage inappropriate use and reduce harms of opioids. It provides GPs with evidence-based guidance and practical advice regarding pain and pain management. In particular, this guide provides recommendations for GPs who are prescribing opioids for acute and chronic pain outside of active cancer treatment, palliative care, and end-of-life care.

## Scope

The guide specifically relates to general practice patients (18 years and older) who have acute pain and CNCP. It covers:

- pain – the experience, classifications and assessment
- pain management – non-drug and drug therapies
- the place of opioids (and other interventions) in pain management in general practice
- the evidence-based recommendations for opioid prescribing in general practice, particularly regarding CNCP, including
  - when to initiate, continue and discontinue opioids for chronic pain
  - which opioids to select (with dosage, duration, follow-up and discontinuation)
  - how to assess risk and address harms of opioid use
- the options for opioid tapering and withdrawal in general practice.

Implementing principles from this guide should facilitate improved patient care and reduce the risk that GPs will be involved in an adverse event associated with prescribing opioids.

This document does not examine opioid use in cancer-related pain, palliative care or end-of-life care, nor does it address use of opioids in the management of opioid dependence.

# How to use this guide

## Wording of key principles and recommendations

Within the key principles and recommendations, the term 'should' refers to a recommended action, 'must' refers to an obligation, 'must not' to a prohibition, and 'may' refers to a discretionary action.

This guide is a reference for opioid prescribing and forms part of the RACGP's series of guidance on drugs of dependence. Freely available on the RACGP website, the series includes:

- *Prescribing drugs of dependence in general practice, Part A: Clinical governance framework*

This document provides general practices with a framework to ensure accountable prescribing for drugs of dependence in general practice. It provides information on national and state laws and a range of strategies (with templates) for use at the practice level. Part A is available at www.racgp.org.au/your-practice/guidelines/drugs-of-dependence-a

- *Prescribing drugs of dependence in general practice, Part B: Benzodiazepines*
  Part B is available at www.racgp.org.au/your-practice/guidelines/drugs-of-dependence-b
- *Prescribing drugs of dependence in general practice, Part C1: Opioids* Part C1 is a companion to Part C2. Part C1 is available at www.racgp.org.au/download/Documents/Guidelines/Addictive-drugs/Addictive-drugs-guide-C2.pdf

# How was this guide developed?

Systematic searches on PubMed and Cochrane databases were conducted to identify relevant recommendations and evidence levels to guide GP prescribing of opioids in acute pain and CNCP.

The literature search was divided into two sections. Stage I of the literature search was performed to identify guidelines, health assessments and systematic reviews in order to facilitate guidance on opioid prescribing in acute conditions and CNCP. Further literature analysis (Stage II) was performed to identify the overall management of acute conditions and CNCP. Several publications on guideline comparisons were used.

Other selected publications and references were also considered with respect to individual conditions or drugs under consideration.

To ensure consistency with other Australian guidelines, state health-based publications, Hunter Regional Health, and publications from the Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists (ANZCA) were also included. External sources of recommendations include the management of pain in acute patient settings, for aged care facilities, GP after-hours services and within general practices.

The pharmacology of opioids, common concerns involving side effects and adverse reactions, and the principles of prescribing were collated from reputable national and international texts.

The RACGP has made a decision to transition to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.[6] This method specifies the systematic review of scientific evidence and offers a transparent approach to grading quality of evidence and strength of recommendations. The method grades the overall quality of each body of evidence as high, moderate, low, or very low.

High-quality publications using the GRADE approach were selected for consideration. Due to the recency and robustness of development, the Centers for Disease Control and Prevention (CDC) publication on opioids formed the basis for many of the final recommendations on the management of CNCP with opioids.

However, where supported by the evidence, Australian context-generated recommendations are asserted in these guidelines.

All conflicts of interest were managed according to RACGP policy.

The Expert Group members wish to disclose they have no financial conflicts of interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters.

Two consultation periods involved broad stakeholder (including consumer organisations) input to the guidelines. A list of all consultation bodies is found in the introductory pages.

The guideline is freely available on the RACGP website. It contains infrastructure for feedback, and a section for detailing/logging updates and corrections.

# 1. Evidence-based guidance for opioids in acute and chronic pain

## 1.1 Accountable prescribing of opioids in general practice

As with any treatment, prescription of opioids should be based on:

- a comprehensive medical assessment
- a diagnosis
- consideration of the likely risks and benefits of any medication, as well as alternative interventions
- a management plan derived through shared decision making (SDM) and continual clinical monitoring.

Opioid treatment seeks to maximise outcomes for the health and social functioning of the patient while minimising risks. To minimise risks, opioids should be prescribed at the lowest effective dose for the shortest clinical timeframe.

Accountable prescribing also involves an assessment of patient risk stratification, provision of adequate therapeutic monitoring, dose limitations and compliance with national and state law.

As a general precaution, GPs should avoid prescribing opioids to patients with comorbid alcohol or substance use disorders (SUDs) or polydrug use. Patients who use two or more psychoactive drugs in combination (polydrug use) and those with a history of substance misuse may be more vulnerable to major harms. GPs should consider seeking specialist opinion in the management of these patients.

## 1.2 Opioids for management of acute pain in general practice

### Key points

- Most acute pain conditions presenting in general practice can be treated with non-opioid analgesia.
- GPs should be familiar with common acute pain presentations where opioids are not recommended.
- Patients with an acute pain in the context of existing chronic pain should be assessed with caution and usually by, or in conjunction with, their usual doctor or healthcare team.
- GPs should prioritise non-opioid therapies for initial pain management.
- Opioid medications should only be used for the treatment of acute pain when non-opioid pain medications and therapies have failed or are likely to fail to provide adequate pain relief.
- When opioid medications are prescribed for treatment of acute pain, they are often prescribed in addition to paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs).

| Evidence statements | Grade |
|---|---|
| The efficacy of opioid therapy in acute pain is supported by strong evidence from randomised controlled trials (RCTs)[7] | |
| Long-term opioid use often begins with mistreatment of acute pain[8]<br>When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids[8] | Strong recommendation, very low quality of evidence |
| Less than three days of opioid analgesia will often be sufficient for acute pain; more than seven days will rarely be needed[8] | Strong recommendation, very low quality of evidence |

## 1.2.1 Evidence into practice – Acute pain

### Background to managing acute pain in general practice

Acute pain is an unpleasant sensory and emotional experience usually related to surgery, injury or disease. It is associated with actual or potential tissue damage to non-neural tissue and is experienced due to activation of nociceptors. This is also known as nociceptive pain.

Acute pain includes inflammatory pain; that is, pain that occurs in response to tissue injury and the subsequent inflammatory response. Typically, inflammatory pain disappears after resolution of the initial tissue injury. However, in chronic disorders (eg rheumatoid arthritis) the pain may persist for as long as inflammation is active.

Effective management of acute pain requires tailoring treatment to the individual patient; awareness of the science behind contextual and placebo effects; competence with multimodal analgesia (ie the concurrent use of different classes of analgesics); and providing patient reassurance and education, including expected duration of pain episode and warning signs that would require immediate medical attention.

In managing acute pain, GPs should:

- undertake a complete biopsychosocial assessment of the patient with pain
- be familiar with the evidence for selected acute pain presentations in general practice and conditions where opioids are not routinely recommended
- prescribe opioid medications only for the treatment of acute nociceptive pain when non-opioid pain medications and therapies have failed or are likely to fail
- undertake a patient selection/exclusion process before commencing opioids.

If opioids are commenced for the pain of acute nociception, there is a need to give clear direction about the anticipated duration of therapy. Usually three days or less of opioid therapy will be sufficient for non-traumatic pain not related to major surgery. Typically, opioids should be weaned and ceased as the acute injury heals. Even in complex post-surgical cases this should be within 90 days.[5]

For a review of all acute pain issues, GPs are advised to review the evidence collated by ANZCA's Faculty of Pain Medicine, available at http://fpm.anzca.edu.au/documents/apmse4_2015_final

### Minor analgesic for pain

GPs should prioritise non-opioid therapies for initial pain management or for the patient being assessed and managed in a general practice. GPs should be familiar with the evidence for selected acute pain presentations in general practice and conditions where opioids are not routinely recommended (Table 1).

In managing acute pain presentations:

- paracetamol by itself is no longer first-line treatment for most mild to moderate acute pain because of lack of clinical effect[9–11] and possible superiority of non-steroidal anti-inflammatory drugs (NSAIDs)[12]
- ibuprofen and naproxen are appropriate first-line NSAIDs for mild to moderate acute pain (based on effectiveness,[11] adverse effect profile,[13] cost and over-the-counter [OTC] availability)
- non-selective NSAIDs given in addition to paracetamol improve analgesia compared with either medicine given alone, in particular ibuprofen combined with paracetamol[14,15]
- paracetamol or NSAIDs combined with codeine (at a dose above 60 mg) provide clinically important pain relief in the immediate term[16]
- cyclooxygenase-2 (COX-2) selective NSAIDs are second-line medications for mild to moderate pain based on their similar effectiveness to non-selective NSAIDs.[17]

**Table 1. Acute pain conditions where opioid medications are not recommended[18,19]**

- Uncomplicated back and neck pain
- Uncomplicated musculoskeletal pain (eg shoulder pain)
- Uncomplicated headache or migraine
- Renal colic
- Non-traumatic dental pain
- Self-limited illness (eg sore throat)
- Trigeminal neuralgia
- Primary dysmenorrhea
- Irritable bowel syndrome
- Any functional or mental disorder of which pain is a leading manifestation
- Acute exacerbation of chronic non-cancer pain (CNCP)

## Patient selection/exclusion process for opioid therapy

Opioid medications should only be used for the treatment of acute pain when non-opioid pain medications and therapies have failed or are likely to fail to provide adequate pain relief, or other contraindications exist.

There are several patient groups in which caution is advised before commencing opioid therapy (refer to Table 2). GPs are advised to be familiar with prescribing precautions in these groups. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids.[8] The number of doses dispensed should be no more than the number needed (and should not be *pro re nata* [PRN]). This should be based on the expected duration of pain severe enough to justify prescribing opioids for that condition.

Usually three days or less of opioid therapy will be sufficient for non-traumatic pain not related to major surgery. Continuing requirements for opioid therapy after this time should prompt review. Long-term and problematic opioid use, including sharing with others, often has its origins in the acute pain setting. Clinical discipline is needed to restrict opioid use to time periods and conditions for which it is beneficial.

**Table 2. Patient groups that require caution when considering opioid therapy[20]**

- Pregnant and breastfeeding women
- Older patients
- Aboriginal and Torres Strait Islander peoples
- Māori people and other ethnic groups and non-English speaking people
- Patients with obstructive sleep apnoea (OSA) or respiratory insufficiency
- Patients with concurrent liver or renal disease
- Patients who are opioid tolerant
- Patients undergoing opiate withdrawal
- Patients with a substance use disorder
- Patients with cognitive behavioural and/or sensory impairments
- Patients with significant mental health conditions

## 1.2.2 Evidence for selected acute pain presentations in general practice

### Pain in patients with an existing chronic pain condition

Patients with existing chronic pain sometimes present with acute pain, which is a specific area of pain management. Before initiating care, GPs are strongly advised to be familiar with issues involving:

- acute exacerbations of existing chronic pain
- opioid withdrawal presenting as acute pain
- new painful presentation or diagnosis unrelated to chronic pain.

### Acute musculoskeletal pain

For acute back pain, targeted reassurance can result in improved changes in psychological factors such as fear, worry, anxiety, catastrophising and healthcare utilisation.[21] Given that most patients with acute or sub-acute low back pain improve over time regardless of treatment, clinicians and patients should select non-pharmacologic treatment with superficial heat (moderate-quality evidence), or massage (low-quality evidence).[22]

For acute pain resulting from strains, sprains or sports injuries (eg ankle sprain), oral and topical NSAIDs are effective analgesics.[23–27]

### Renal colic

Renal colic is a common presentation in general practice. Similar analgesia may be achieved with intravenous (IV) paracetamol,[28] non-selective NSAIDs and opioids.[29] Hence IV paracetamol and NSAIDs should be considered as first-line treatments before opioid medication is considered.[29–32]

Compared to standard therapy, ureteral calculus expulsive therapy using alpha-blockers (eg tamsulosin) reduces the number of pain episodes, the need for analgesic medication and even hospitalisation.[33]

### Biliary colic

Guidelines recommend relief of biliary colic pain may be achieved with NSAIDs.[7] These have been found to be better than placebo or spasmolytics and equivalent to opioids.[34] NSAIDs may also lower the rate of complications, in particular preventing progression to cholecystitis.[34] Opioids are an alternative for patients who cannot take or fail to respond to NSAIDs.[35,36]

## Dental pain

Guidelines recommend dental pain can be appropriately managed with non-opioid medications, or non-opioid combination analgesics.[7,19] The combination of paracetamol and NSAIDs is more effective than paracetamol or NSAIDs alone.[14] This combination may be a more effective analgesic, with fewer untoward effects, than many of the currently available opioid-containing formulations.[37] This is particularly well documented for the combination of paracetamol and ibuprofen in the setting of wisdom tooth removal.[15]

## Primary dysmenorrhoea

Simple analgesics such as paracetamol, aspirin and NSAIDs are effective in most women. These options interrupt the activity of cyclo-oxygenase pathways, thereby inhibiting prostaglandin production. Nonselective NSAIDs are more effective analgesics in dysmenorrhoea than placebo; however, they are associated with an increased rate of adverse effects.[38] There appears to be no difference between NSAIDs and paracetamol with regard to efficacy and safety.[38] Oral contraceptives are an option for women who wish to avoid pregnancy.

## Herpes zoster–associated pain

Herpes zoster–associated pain may be severe; early and effective treatment is essential. Analgesia options during herpes zoster include:

- antiviral agents (particularly famciclovir or valaciclovir) given within 72 hours of rash onset[39]
- paracetamol in addition to an opioid such as oxycodone[39–41] or tramadol
- gabapentin – a single dose of 900 mg has been shown to reduce acute pain intensity by 66% (33% for placebo) and also reduced the area and severity of allodynia for up to six hours.[42] This was also found with pregabalin (150 mg)[43]
- topical lignocaine patches (5%) applied for 12 hours twice daily (on intact skin).[44]

For prevention of post-herpetic neuralgia, the early administration of antiviral therapy has not been shown to be effective.[45] Early intervention with corticosteroids[46] or antidepressants[47] was also not effective.

## Tension-type headache

Tension-type headache (TTH) is a common cause of acute pain. Psychological, physical and environmental factors are important in TTH and should be addressed during assessment and treatment. Oral paracetamol (1000 mg), ibuprofen (400 mg) and ketoprofen (25 mg) have similar efficacy.[48] However, a combination of paracetamol/aspirin and caffeine appears to be superior to paracetamol alone. There is limited low-quality evidence for physiotherapy or other manual interventions.[49,50]

## Medication-overuse headache and rebound headaches

Medication-overuse headache (MOH) is one of the most common chronic headache disorders and a public health problem with a worldwide prevalence of 1–2%. It is a condition characterised by chronic headache and overuse of different headache medications. Withdrawal of the overused medication is recognised as the treatment of choice.

Rebound headaches can occur after taking an opioid and during the withdrawal stage. They are common with short-acting opioids (eg codeine).

In both MOH and rebound headaches, aim to use non-opioid and non-pharmacological treatments to wean and cease opioid usage, and manage persistent symptoms with the described strategies. Most patients experience withdrawal symptoms lasting 2–10 days after detoxification. The most common symptom is an initial worsening of the headache, accompanied by various degrees of nausea, vomiting, hypotension, tachycardia, sleep disturbances, restlessness, anxiety and nervousness.

### Migraine

Patients who experience mild migraine-related headache and disability may be effectively treated with simple analgesics, either alone or in combination with an antiemetic. Paracetamol,[51] aspirin,[52] ibuprofen[53] and diclofenac[54] have all shown benefit. Appropriate antiemetics include (parenteral) metoclopramide[55] and prochlorperazine.[56,57]

Triptans or IV ketorolac[58] may be particularly effective in the presence of severe pain and disability where simple analgesia has failed to provide adequate relief in the past.[59]

Opioids are of limited benefit in the treatment of migraine and are not recommended.[60] Opioid use for migraine is associated with more severe headache-related disability, symptomology, comorbidities (depression, anxiety and cardiovascular disease and events), and greater healthcare utilisation.[61] However, opioids may be considered as a last resort when other migraine treatments are contraindicated.[62]

### Cluster headaches

Cluster headache is a rare primary headache disorder, presenting predominantly in males,[63–65] with recurrent acute episodes of brief severe unilateral periorbital pain. Guidelines for the treatment of cluster headache attacks propose first-line treatments to be high-flow oxygen (eg 100% oxygen at 6–12 L/min)[66–69] and tryptans (eg sumatriptan 6 mg subcutaneously, zolmitriptan 5 mg and 10 mg intranasally).[70,71]

### Temporomandibular dysfunction

Headache or facial pain attributed to the temporomandibular joint is often associated with tension headache[72] and cervical spine dysfunction.[73] Teeth grinding (bruxism) is a common contributor. The most effective therapies include interocclusal appliance therapy.[74] There is limited evidence for the successful pharmacological management of temporomandibular dysfunction (TMD) pain.[75] If a medication is going to be used, the best evidence exists for naproxen (1000 mg/day), which is more effective than celecoxib (200 mg/day) and placebo.[76]

## 1.3 Opioids in management of chronic non-cancer pain

**Key points**

- Chronic non-cancer pain (CNCP) is a collection of clinical conditions that may have involvement of single or multiple pathophysiological mechanisms leading to persistent pain.
- Outside of end-of-life care, the research on long-term opioid therapy for chronic pain remains limited and insufficient to determine long-term benefits. Available evidence suggests dose-dependent risk of serious harms.
- Guidelines identify only a selective place for opioids in the management of some chronic pain conditions; opioid use is not routine and is not first-line or second-line therapy. Opioids for CNCP should be reserved for selected patients with moderate or severe pain that significantly affects function or quality of life and that has not responded to other therapies.

### 1.3.1 Evidence into practice – Chronic pain

Chronic pain has been historically defined as continuous or recurrent pain that persists for an extended period (generally more than three months). However, the biological mechanisms for chronic pain are quite different from those of acute nociception, and should not be considered as ‘unhealed’ acute pain. CNCP is a collection of clinical conditions with involvement of single or multiple pathophysiological mechanisms leading to persistent pain. It is also an individual, multifactorial experience influenced by culture, previous pain events, beliefs, expectations, mood and resilience.

Due to methodological weaknesses of chronic pain studies, interpretation and translation of evidence into practice is difficult. There is limited evidence to determine long-term benefits (outside of end-of-life care); however, there is evidence of risk of harm that increases with dose. While guidelines suggest opioids in the management of some chronic pain conditions, they are not recommended for routine or first-line use.

In managing CNCP, GPs should:

- undertake a complete biopsychosocial assessment of the patient with pain
- optimise non-drug therapies, and optimise non-opioid therapies as the primary interventions of care.

Opioids for CNCP should be reserved for selected patients with moderate or severe pain that significantly affects function or quality of life and which has not responded to other therapies. If primary interventions fail or are suboptimal, opioid therapies may be considered. GPs should share the decision-making process with the patient, and if opioid therapy is considered, there should be:

- a patient selection/exclusion process before a therapeutic opioid trial
- formal care planning based on specific goals and risks
- an opioid trial, which is undertaken to determine a patient's response to opioid therapy. This trial includes the selection of an appropriate opioid, formal measures of analgesia and functionality, a trial of dose reduction, and a drug cessation plan if the trial fails
- an ongoing assessment and evaluation by the accountable prescriber if the trial shows opioid benefit
- opioid tapering and cessation if suboptimal results or aberrant behaviour occurs.

Long-term use should be uncommon, undertaken with caution and based on consideration of the likely risks and benefits of opioids. Intermittent use is preferable.

GPs should also be aware of chronic pain conditions where there are known clinical complexities involving opioids. These complex clinical areas include the exacerbation or new acute pain in patients on long-term opioid therapy, managing opioids after a non-fatal overdose, and managing the inherited patient.

Some patients on long-term treatment with opioids in CNCP may represent de facto maintenance treatment for iatrogenic opioid dependence. GPs should aim to taper patients taking >100 mg oral morphine equivalent (OME) per day.

## Assessment of patients with chronic non-cancer pain

### Key point

Management of CNCP should be based on a comprehensive biopsychosocial assessment, a diagnosis, and thoughtful consideration of the likely risks and benefits of any intervention or medication.

The foundation of care for CNCP is a comprehensive biopsychosocial assessment, and a complete documentation of the patient's pain condition, general medical condition and psychosocial history, psychiatric status, and substance use history.[77,78] A biopsychosocial assessment completes a more complex understanding of the patient's pain perspective. Factors do not always neatly fit into one category; for example, depression may have physical and social aspects as well as being a psychological factor influencing pain.

A comprehensive pain assessment includes a:

- general assessment and pain specific history (that explores the pain type, severity, functional impact, context, and the patient's meaning of pain, expectations and fears)
- physical examination (assessing for signs of tissue damage or disease that might indicate nociceptive and/or neuropathic mechanisms of pain)

- psychological assessment (the pain experience is affected by mood, stress, coping skills, fear avoidance, and catastrophising).

This will inform the selection of treatment options most likely to be effective. The assessment may need to be repeated reasonably frequently, particularly while establishing a diagnosis and appropriate pain management.

## Non-drug therapies for chronic pain

### Key point

The basis for good pain management is a strong continuous therapeutic relationship.

| Evidence statements | Grade |
|---|---|
| Non-drug therapy and non-opioid pharmacologic therapy are preferred for chronic pain[8] | Strong recommendation, low quality of evidence |

Before any therapies are undertaken, GPs are advised to consider the science and evidence of contextual and placebo effects in pain management. The manner in which a clinician explains and delivers therapy has an impact on outcome.[79] Practitioners who master not only the disease and treatment, but also cultivate a therapeutic relationship may be more effective at pain management.[80]

The basis for pain management is a strong continuous therapeutic doctor–patient relationship.

Management should optimise general health, including addressing comorbid physical and mental health conditions. GPs should provide adequate patient education about the causes of chronic pain. Further information regarding neuroscience education can be found here.

GPs should engage in a frank discussion and negotiation about different pain strategies and the goals of treatment. These goals should go beyond pain relief alone (eg improvement in physical, social, emotional and mental functioning, including an increase in activity) and there should be an agreement that if the goals are not met, then the treatment will be discontinued.

Non-drug and non-opioid pharmacological therapies are preferred options for management of CNCP.[8] Multimodal interventions are effective.[81] Exercise,[82–86] selective psychological interventions,[87,88] social interventions, and non-opioid therapies are all advocated.

Most patients with chronic pain are physically deconditioned from inactivity.[89] Movement and exercise therapies, regardless of their form, are recommended in the management of patients with chronic pain.[86] Physiotherapists and exercise physiologists with an interest in chronic pain are advocated. Further information on the effectiveness of movement and exercise interventions can be found here.

Psychological approaches aim to increase self-management, behavioural change, and cognitive change rather than directly eliminate the locus of pain. Psychologist intervention is advocated for assessment and management of selected presentations. Further information on the effectiveness of psychological interventions can be found here.

### Box 1. Handbook of non-drug interventions

The RACGP's *Handbook of non-drug interventions* (HANDI) provides multiple non-drug therapies for various pain conditions such as osteoarthritis, back pain and foot pain, and is available at www.racgp.org.au/handi

For an explanation of exercise and reconditioning, refer to 'Graded exercise therapy for chronic fatigue syndrome', available at www.racgp.org.au/your-practice/guidelines/handi/interventions/other/graded-exercise-therapy-for-chronic-fatigue-syndrome

## Non-opioid medication for chronic pain

Effective management requires knowledge of the frameworks for pain, different treatment approaches, and an individualised multifaceted intervention plan for the patient[5,78,86,89–93] depending on specific contributors of pain.

Where analgesics are considered appropriate, the optimal approach to manage chronic pain is without opioids, prioritising use of minor analgesics and analgesic adjuvants (eg antidepressants, anticonvulsants) instead.[5,8] 'Adjuvants' refers to medications that are co-administered with analgesics to enhance pain relief via other pathways. The evidence for effectiveness of adjuvants varies for pains with different nociceptive, neuropathic and nociplastic origins. A brief overview of the evidence can be found here.

In countries where they are available, cannabinoids may have a place in relieving chronic neuropathic pain.[94,95] However, the evidence for effectiveness is considered weak and their role is being debated in Australia.[96,97]

GPs should prescribe one analgesic/adjuvant drug at a time and monitor individual responses. While it is accepted practice to run a clinical trial over several weeks, many of the agents will elicit an analgesic response within the first two weeks of treatment (if achieved, the response tends to last).[98–100] If functionally meaningful benefit does not ensue, stop the drug and try an alternative. Because of individual variation in pain, patients may respond to one drug within a class, but not to others (eg a patient may respond to naproxen, but not ibuprofen). Therapy failure due to inadequate relief or side effects should not stop doctors from trialling alternative medications from the same class (eg NSAIDs, anti-epileptics). Combination adjuvants (anticonvulsants and antidepressants) are common but inadequately studied.

For patients who achieve clinically meaningful analgesia, use the lowest individualised effective dose to minimise adverse effects. Reassess regularly (eg every two weeks), and trial medication withdrawal to determine that the response is due to the drug and not natural history. It is recognised that patients treated with a placebo can also improve over time.[100]

## Patient selection/exclusion process before an opioid trial

### Key point

Long-term opioid therapy is dependent on an appropriate patient selection process, considered care planning, and an 'opioid trial' to determine responsiveness to opioid treatment.

| Evidence statements | Grade |
|---|---|
| GPs should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose | Strong recommendation, very low quality of evidence |
| Before starting opioid therapy, GPs should evaluate risk factors for opioid-related harms[8] | Strong recommendation, very low quality of evidence |

If alternatives to opioid treatment fail, have limited benefit or are inappropriate, a supervised opioid trial may be initiated. Opioids for CNCP should be reserved for select patients with moderate or severe pain that significantly affects function or quality of life and that has not responded to other therapies.

Prescription of opioids, as with any treatment, should be based on a comprehensive medical assessment; a diagnosis; thoughtful consideration of the likely risks and benefits of any medication, as well as alternative interventions; and a management plan derived through SDM and continual clinical monitoring.

In selecting or excluding patients before starting opioid therapy, GPs should:

- be aware of the limitations of opioids in managing some pain syndromes (eg functional visceral pain, such as irritable bowel syndrome and bladder pain syndrome, is not sensitive to opioids)

- be aware of patient groups or contexts requiring additional caution or exclusion. Additional advice needs to be considered when patient selection for opioid therapy involves pregnancy, workers' compensation injuries, patients who drive, patients with sleep apnoea and disordered breathing, patients aged 65 or older, patients with renal disease, patients with hepatic disease, culturally and linguistically diverse patients, and patients with mental health conditions
- evaluate risk factors for opioid-related harms in individual patients, including review of the patient's history of controlled substance prescriptions using the Prescription Shopping Programme (PSP) or state PDMP data to determine whether the patient is receiving opioid dosages or dangerous combinations (especially benzodiazepines[101]) that put him or her at high risk for overdose
- avoid prescribing opioids to patients with polydrug use, comorbid alcohol or substance use disorders. GPs should consider tapering benzodiazepines and seeking specialist opinion or a specialised pain management facility[90] in the management of these patients.

## Care planning for an opioid trial

### Key points

- Long-term opioid therapy is dependent on an appropriate patient selection process, considered care planning, and an 'opioid trial' to determine responsiveness to opioid treatment.
- A treatment plan is discussed including a plan to discontinue opioids if there is no objective functional improvement.

| Evidence statements | Grade |
|---|---|
| GPs should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient[8] | Strong recommendation, low quality of evidence |
| Before starting opioid therapy, GPs should discuss with patients known risks and realistic benefits of opioid therapy, and patient and clinician responsibilities for managing therapy[8] | Strong recommendation, very low quality of evidence |
| Before starting opioid therapy for chronic pain, GPs should establish treatment goals with all patients, including realistic goals for pain and function, and consider how opioid therapy will be discontinued if benefits do not outweigh risks | Strong recommendation, very low quality of evidence |
| When prescribing opioids for chronic pain, GPs should consider using a urine drug test (UDT) before starting opioid therapy to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs[8] | Strong recommendation, low quality of evidence |
| GPs should incorporate into the management plan strategies to mitigate risk, including consideration of offering naloxone, when factors that increase risk for opioid overdose (such as history of overdose, history of substance use disorder, higher opioid dosages [50 mg OME] or concurrent benzodiazepine use) are present | Strong recommendation, very low quality of evidence |

The aim of an opioid trial is to discover the individual's responsiveness to opioid therapy in terms of decreased pain, increased function and improved quality of life. Before starting opioid therapy for chronic pain, GPs should:

- ensure patients are aware of known risks and realistic benefits of opioid therapy, and of their responsibilities for managing therapy (including risks to other individuals if opioids are intentionally or unintentionally shared)
- establish treatment goals with all patients, including realistic goals for pain and function, and consider how opioid therapy will be discontinued if goals are not met or benefits do not outweigh risks[8,92]
- consider a UDT to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

Care plans should incorporate strategies to mitigate risk including having only one prescriber for ongoing analgesics;[5,91] offering naloxone when factors that increase risk for opioid overdose are present (eg history of overdose or substance use disorder, higher opioid dosages or concurrent benzodiazepine use); and sharing care for high-risk patients with clinical specialists.[8]

While screening for opioid risk, treatment agreements[89] and urine testing[5,78,92,93,102] are often advocated, they have not been shown to reduce overall rates of opioid prescribing, misuse, or overdose.[5,103] Patient treatment agreements do serve an administrative role, clarify expectations and behaviour standards, and have educational purposes.[104,105] GPs should use their discretion when considering candidates for a urine drug screen (UDS) and treatment agreements.

It is important to have an 'exit strategy' if the trial fails to achieve agreed outcomes. The strategy should preserve the therapeutic relationship while also managing possible misuse of opioids.

## Box 2. Naloxone

Discussion about take-home naloxone (THN) as part of an overdose response plan is an effective brief intervention. The use of naloxone fits within both harm reduction strategies and patient-centred care. Naloxone is safe, effective, inexpensive, and relatively easy to administer via intramuscular (IM) injection.[106–108]

Naloxone injection is dual listed as a Schedule 4 medicine subsided by the Pharmaceutical Benefits Scheme (PBS), and as a Schedule 3 medicine available from a pharmacist. It is beneficial for GPs or pharmacists to provide patients with brief instructions on how to prevent, recognise and respond to overdose including how to store, carry and administer naloxone. It may be appropriate to involve the patient's family and/or other potential overdose witnesses relevant to the patient, as these are the people most likely to be responding to an overdose. GPs should also advise patients that naloxone can be obtained over-the-counter (OTC) from local pharmacies by a third party to protect co-residents (eg children) of the patient from intentional or unintentional overdose.

Prescribers are encouraged to provide a prescription for THN for patients at high-risk of overdose (eg high opioid dose, complex care, or recently released from a controlled environment).

For further resources on naloxone therapy, refer to www.copeaustralia.com.au

## Box 3. Care planning tool

All patients prescribed longer-term opioids for CNCP should have a care plan, and one principal prescribing doctor nominated. The patient should be managed primarily by the one GP. When the principal GP is absent, another GP should be designated to manage the patient in accordance with the care plan.

A simple tool for care planning in chronic pain is available at the NSW Pain Management Network website at www.aci.health.nsw.gov.au/chronic-pain/health-professionals/quick-steps-to-manage-chronic-pain-in-primary-care?utm_campaign=Get%20Involved&utm_medium=Email&utm_source=Pain

**Care planning for high-risk patients**

For GPs with a specific interest in this area, guidance for planning and use of care plans in high-risk patients has been developed by the NSW Department of Health for both opioid dependent patients and patients with severe comorbidity, available at www.health.nsw.gov.au/mhdao/Documents/pj-kit2.pdf

## Undertaking an opioid trial

### Key point

An opioid trial is undertaken to discover the individual's responsiveness to opioid therapy in terms of decreased pain, increased function and improved quality of life.

| Evidence statements | Grade |
|---|---|
| If opioids are used, they should be combined with non-pharmacologic therapy and non-opioid pharmacologic therapy, as appropriate[8] | Strong recommendation, low quality of evidence |
| GPs should use caution when prescribing opioids at any dosage. Carefully reassess evidence of individual benefits and risks when increasing dosage to 50 mg OME or more per day. Avoid increasing dosage to 100 mg or more OME per day, or carefully justify a decision to titrate dosage to 100 mg or more OME per day[5,8] | Strong recommendation, low quality of evidence |

Opioids for CNCP should be reserved for select patients with moderate or severe pain that significantly affects function or quality of life and that has not responded to other therapies. An opioid trial should occur in conjunction with formal measures of analgesia and functionality. Validated brief assessment tools that measure pain and function (eg Pain, Enjoyment, General activity [PEG][109] in Appendix E) or other validated assessment tools may be helpful and time effective.

When trialling opioids for chronic pain, opioid selection should be based on evidence of safety and benefit for the pain type and patient factors. The opioid should be in addition to appropriate non-drug therapy and non-opioid drug therapies.

Unless clinically contraindicated, consider selecting an effective opioid with less potential for harm such as oral tapentadol, transdermal buprenorphine or oral tramadol.[8,78] Start opioids at a low dosage, increase gradually (refer to individual opioids) and monitor opioid effectiveness using the 5As of chronic pain management and the PEG tool until optimal dose is attained.[8,78,101]

Patients likely to benefit from opioids in the long term will demonstrate a favourable response within 2–4 weeks of initiating therapy. It is accepted practice to run a clinical trial over 8–12 weeks to allow for normal variations of life. An important part of any trial is to reduce opioid doses to establish minimal needs.

Patients who do not experience clinically meaningful pain relief early in treatment (ie within three months) are unlikely to experience pain relief with longer-term use.[110] Suboptimal therapeutic response may be due to failure to recognise psychosocial aspects of the patient's pain.

If the initial choice of opioid is ineffective, or if adverse effects are unacceptable, opioid rotation may be tried. In clinical practice, opioid rotation must be performed with consideration of individual patient characteristics, comorbidities (eg concurrent psychiatric, pulmonary, renal, or hepatic illness), and concurrent medications.[111] Reduce the starting dose of the new opioid by 50% of the calculated equianalgesic dose of the first opioid. This reduction in dose may result in improved tolerability while incomplete cross-tolerance may result in equivalent efficacy.

To minimise risks, opioids should be prescribed at the lowest effective dose for the shortest clinical timeframe. Caution should be used when increasing dose from low to moderate (ie above 40–50 mg per day OME).[8] While there is no international consensus on a maximum (ceiling) dose,[5,112] a ceiling of 100 mg per day OME is recommended for Australian GP prescribing.[5,8,92] Above this dose, specialist review is advocated.[92]

## Ongoing therapy, assessment and monitoring

### Key points

- Long-term opioid therapy requires ongoing structured monitoring and review of benefits and harms.
- GPs should taper and discontinue opioids in the absence of functional improvement, when planned care fails, or aberrant behaviours become apparent.

| Evidence statements | Grade |
|---|---|
| GPs should evaluate benefits and harms with patients within 1–4 weeks of starting opioid therapy for chronic pain or of dose escalation[8] | Strong recommendation, very low quality of evidence |
| GPs should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety[8] | Strong recommendation, very low quality of evidence |
| Periodically during opioid therapy, GPs should discuss with patients known risks and realistic benefits of opioid therapy, and patient and clinician responsibilities for managing therapy[8] | strong recommendation, very low quality of evidence |
| GPs should evaluate benefits and harms of continued therapy with patients at least every three months[8] | Strong recommendation, very low quality of evidence |
| GPs should consider a UDT at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs[8] | Strong recommendation, low quality of evidence |
| If benefits do not outweigh harms of continued opioid therapy, GPs should optimise non-opioid therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids[8] | Strong recommendation, very low quality of evidence |

Long-term opioid use should be uncommon, undertaken with caution and based on thoughtful consideration of the likely risks and benefits of opioids. If opioids provide benefit (pain relief and improved functioning), opioid analgesia can be an acceptable long-term therapeutic option.

GPs should continually evaluate treatment efficacy and harms, and monitor for known comorbidities. Patients should be re-evaluated at least every three months, and within four weeks of any dose escalation.[8]

Although the evidence for use of instruments to assess patient-reported safety, efficacy, or misuse of current opioid therapy for chronic pain is lacking,[113] it is advised that patients are evaluated using the 5As of chronic pain management.[8,114] Only continue opioid therapy if there is documented clinically meaningful improvement in pain and function that outweighs risks to patient safety.[5,8,78,101]

**Table 3. The 5As of chronic pain management[114]**

| |
|---|
| **Activity**<br>**How have the patient's activities of daily living (work, play and socialisation) been positively or negatively impacted by pain or analgesic regimen?**<br>• What progress has been made in your functional goals?<br>– Sitting tolerance<br>– Standing tolerance<br>– Walking ability<br>– Ability to perform activities of daily living |
| **Analgesia**<br>**Is the patient experiencing a reduction in pain?**<br>• On a scale from 0–10 where 0 = no pain and 10 = worst possible pain, how do you rate the following over the last 24 hours/week?<br>– Your average pain?<br>– Your worst pain?<br>• How much relief have pain medications provided? (eg 10%, 20%, 30%) |
| **Affect**<br>**Have there been any positive or negative changes to the way the patient has been feeling or sleeping?**<br>• Have you felt depressed or anxious?<br>• Are you sleeping more or less, and what is the quality of your sleep? |
| **Adverse effects**<br>**Have there been any significant adverse effects?**<br>• Have you experienced any adverse effects from medication? (eg constipation, nausea, dizziness, drowsiness) |
| **Aberrant behaviours**<br>**Is there evidence of aberrant substance-related behaviours?**<br>• Has the patient been taking medication/s as prescribed?<br>• Has the patient exhibited any signs of problematic behaviours or medication abuse/misuse? (eg signs of drug and alcohol use, unsanctioned dose escalations)<br>• Has the patient reported lost prescriptions or requested early repeats? |

While baseline UDTs are recommended,[5,78,92,93,102] prescribers can use discretion for ongoing testing according to patient risk. Consider UDTs at initiation and then at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.[8,92] When using UDTs be aware of benefits and limitations, appropriate test ordering and interpretation, and have a plan to use results.[92]

In all states except NSW, GPs should also seek state regulatory authorisation for any patient who has been prescribed Schedule 8 (S8) opioids for two months or longer.[115] In NSW, only certain oral opioids (buprenorphine, hydromorphone and methadone) require an authority.

Pharmaceutical Benefits Scheme (PBS) regulations dictate an independent opioid prescribing review at 12 months of therapy. The RACGP recommends a structured review using a checklist for this purpose.

Long-term opioid prescriptions should be at the lowest effective dose, and regular attempts at reduction should be scheduled.[103] Intermittent use has also been advocated.[103] Proper management of opioids in well-selected patients with no history of SUD can lead to long-term (≥26 weeks) pain relief for about 25% of patients.[116,117] Continued professional monitoring of health outcomes is required.

Where continued opioid therapy is inappropriate due to failure of benefits to outweigh harms, or if there is evidence of problematic use (eg rapid dose escalation), work with patients to taper and discontinue opioids.[8,90,101]

This involves preserving the therapeutic relationship, optimising non-opioid therapies, and working with patients

to taper opioids to lower dosages or to discontinue opioids.[5,90] Patients have the right to respectful care that promotes their dignity, privacy and safety; abruptly discontinuing opioid treatment without offering a feasible plan for tapering treatment could be considered a failure of duty of care.

GPs should regularly assess whether the patient satisfies individual state health legal definitions of drug dependence and seek advice from the state regulatory authorities if issues arise. All states and territories run drug and alcohol advisory services, which offer information, advice, referral, intake, assessment and support 24 hours a day. They offer services for individuals, their family and friends, GPs, and other health professionals.

# 1.4 Specific chronic pain conditions

## 1.4.1 Chronic post-surgical pain

### Key points

- The prevention of the progression of acute to chronic pain should be the aim of all practitioners whenever they treat an acutely painful condition.
- Both surgical and patient factors influence the development of chronic post-surgical pain (CPSP).
- CPSP may have biomedical components – GPs need to understand the role of different analgesics and adjuvants in different pain processes.

### Management of chronic post-surgical pain

CPSP is defined as pain developing and persisting beyond the time expected for the normal healing process (ie persisting for at least two months). CPSP can affect 15–60% of all surgical patients.[118] The incidence of CPSP varies with the type of operation and it is more common where nerve trauma is inevitable (eg amputation) or where the surgical field is richly innervated (eg chest wall).[119–121] For example, following:

- inguinal hernia repair or caesarean section, 10% of patients report ongoing pain and disabilities six months after surgery
- mastectomy or lumpectomy, 20–30% of women report chronic pain
- amputation, thoracotomy or coronary bypass surgery, 30–50% of patients report persistent pain.[122]

Depending on the type of surgery, CPSP is often neuropathic pain (on average one-third of cases; range from 6% to 54%). Pain involving such a neuropathic component is usually more severe than nociceptive pain and often affects the quality of life more adversely.[123]

Nociceptive and neuropathic processes in the periphery (including nerve injury) and neuroplastic processes (leading to peripheral and central sensitisation) are all implicated in the transition from acute to chronic pain. The relative degree of ongoing inflammation or intraoperative nerve injury resulting in peripheral and central sensitisation may explain the variation in risk and, to an extent, the characteristics of CPSP for different operations.

In addition to the type of surgery, the development of CPSP is influenced by patient factors including:

- psychological factors such as anxiety, depression, stress, fear of surgery, hypervigilance and pain catastrophising[124,125]
- demographic factors, such as younger age for adults and female gender
- genetic and epigenetic factors, which influence both the sensitivity of individuals to analgesics and their risk of CPSP.[126,127]

All practitioners should aim to prevent the progression of acute to chronic pain. Treatments that address

nociceptive and neuropathic pain should be considered, including opioids where appropriate.

Pregabalin and gabapentin may have a role in preventing CPSP due to their effect on neuropathic pain. However, considerable uncertainty exists regarding efficacy with limited and contradictory evidence.[7]

## 1.4.2 Chronic visceral pain

Visceral pain refers to pain in the trunk and abdominal areas of the body that includes the heart, lungs, abdominal and pelvic organs. Examples of chronic visceral pain include chronic chest pain, chronic pancreatitis, and chronic pelvic pain.

Visceral pain is diffused and can be difficult to localise.[128] It may be accompanied by nausea, vomiting and changes in vital signs. Treatment goals are both causal and symptomatic and involve holistic strategies including patient education.[129]

## 1.4.3 Fibromyalgia

Fibromyalgia is a common and potentially disabling condition affecting 2% of the population in developed countries, predominantly young to middle-aged women.[130] Fibromyalgia has a varied and fluctuating clinical spectrum. Cardinal features include widespread musculoskeletal pain and tenderness; poor quality, unrefreshing sleep; significant levels of fatigue; cognitive disturbances, particularly problems with concentration and memory; and high distress levels.[131]

Fibromyalgia pain is considered to be due to central sensitisation.[132] Exercise remains the strongest therapeutic recommendation.[133] Specific guideline recommendations should be consulted prior to therapies.[134–137]

## 1.4.4 Complex regional pain syndromes

Complex regional pain syndrome (CRPS) is a debilitating, painful condition in a limb associated with sensory, motor, autonomic, skin and bone abnormalities. Pain is typically the leading symptom, but it is often associated with limb dysfunction and psychological distress.[138] There is usually a history of precipitating event or injury; however, the severity of the clinical pain presentation is often disproportionate to the severity of the inciting event.

Exact mechanisms for the pathogenesis of CRPS are not understood.[139–143] A combination of elements including inflammation, dysfunction within sympathetic and somatosensory nervous system, and cortical (not psychological) factors are thought to contribute to the generation and perpetuation of symptoms.[138] There is no evidence that paracetamol assists in CRPS, and insufficient evidence regarding the efficacy of NSAIDs and opioids. Although there is no evidence supporting the long-term effectiveness of anticonvulsants for CRPS, these agents may be useful in providing pain relief in the earlier stage of the disease.[144]

GPs should seek specialist advice with presentations with CRPS.

# 1.5 Other chronic pain management situations involving opioids

**Key point**

GPs should use caution in patients presenting with acute exacerbations of chronic pain.

## 1.5.1 Acute exacerbation of existing chronic pain

If patients experience an acute exacerbation of CNCP, the aetiology of the pain must be identified rather than just treating it as an acute nociceptive event. The aetiology may be multifactorial, and it is advised that the patient's mental health status and social situation should be formally assessed to determine if additional resources may be appropriate. It may also be appropriate to check the PDMP and patient-controlled electronic medical record (if present) for history of opioid prescriptions.

The treatment for the chronic pain patient may be significantly different from the acute episode. Exacerbations of pain should be managed with non-opioid therapy: physical therapies and NSAIDs should be used for periodic flare-ups of mild to moderate inflammatory or non-neuropathic pain.[19,89] Because of potential risks and adverse effects, clinicians are encouraged to avoid prescribing increased dosage or additional opioids.[19]

## 1.5.2 New painful condition in a patient with chronic pain

As with acute exacerbation of chronic pain, in any new pain presentation it is important to identify the source of pain rather than just treating for an acute nociceptive event, avoid prescribing increased dosage or additional opioids,[19] use non-opioid therapy as appropriate,[89] and assess the patient's mental health status and social situation to determine if additional resources are required.

If a new presentation does dictate opioid treatment, consider monitoring in an appropriate care setting. Dosing opioids for acute pain in a patient already taking opioids is problematic. The patient may require a higher dose to achieve the same analgesic effect. The higher dose puts the patient at greater risk for an adverse event. Note that patients already taking opioids do not require a longer than normal course of treatment for acute pain. Once the acute event has passed, reduce opioids to maintenance levels.

## 1.5.3 Opioid withdrawal presenting as acute pain

Consider opioid withdrawal when evaluating opioid-tolerant patients who present with acute pain complaints or gastrointestinal symptoms. Opioid withdrawal can occur when patients have stopped, lost or overused their medications. Patients are often reluctant to share this information with their clinician.

Opioid withdrawal generally presents with anxiety 12 hours after the last dose, and becomes physically detectable within 24 hours after the last use of short-acting opioids and 48 hours after last use of long-acting opioids.

Unless the patient is otherwise medically unstable, withdrawal is not life threatening. However, it may be very distressing and necessitate reassurance and comfort measures. All states and territories run an alcohol and drug information service, which offers information, advice, referral, intake, assessment and support 24 hours a day.

## 1.5.4 Managing opioid therapy after non-fatal overdose

Patients who have had a presentation or admission for opioid accidental or non-accidental overdose are at significant risk for another overdose and further harms.[145]

At two years, the cumulative incidence of repeated overdose was:[145]

- 17% (95% confidence interval [CI]: 14%, 20%) for patients receiving high dosages of opioids after the index overdose
- 15% (CI: 10%, 21%) for those receiving moderate dosages
- 9% (CI: 6%, 14%) for those receiving low dosages
- 8% (CI: 6%, 11%) for those receiving no opioids.

Opioid discontinuation after overdose is associated with lower risk for repeated overdose.[145]

Non-fatal opioid overdose is an opportunity to identify and treat substance use disorders, pain and mental health issues.

All patients admitted or presenting to hospital emergency departments (EDs) with non-fatal opioid overdose must have a full pain and psychiatric evaluation prior to discharge, and consideration of opioid cessation or provision of naloxone for peer or family member administration. A clear plan for opioid safety after discharge and communication with usual treating practitioners in the community is essential.

Naloxone distribution programs are firmly rooted in the principles of harm reduction. Naloxone is safe, effective, inexpensive, and relatively easy to administer via intramuscular (IM) injection.[106]

## 1.5.5 The inherited patient – Continuation of long-term opioid management plans initiated by other healthcare providers

### Key points

- Patients with chronic pain and/or SUDs have the same entitlement to respectful and appropriate care as other patients.
- Referral according to clinical handover standards should be arranged by the original authorised prescriber.
- Clinical handover in primary care takes time. Adequate prescriptions from the original prescriber should cover this handover period.
- All new patients 'inherited' by the practice should receive a comprehensive re-evaluation and renewed care planning.
- Patient care strategies must be defensible, rational, and compassionate. Doctors should prescribe opioids according to their best clinical judgement, with individual risk benefit analysis for each patient.
- Before opioid prescriptions are written, relevant state authority must be obtained.
- In the event of an SUD being detected, the management plan should also include remedial programs or referral to appropriate drug misuse agencies.
- Patients who satisfy practice appropriateness criteria and are accepted should be prescribed ongoing medication under the continued care of a single doctor.

## Overview

Patients often arrive from other practices or institutions requesting continuation of their long-term opioid management programs. These situations can produce a therapeutic dilemma for the new practitioner. Patients' histories and management regimes may be quite complex, and some practices and institutions have prescribing practices that are variable or may not be evidence based or safe.

Patient requests for ongoing pain management may be quite legitimate, but, unfortunately, this type of presentation is also common for drug-seeking behaviour for opioids. In both situations, the patient may be physically dependent on opioids. When these patients are deprived of opioid medication, they may experience acute withdrawal.

In the inherited-patient situation, caution is advised while acknowledging the patient's right to respectful care that promotes their dignity, privacy and safety. Patients with legitimate clinical indications for long-term opioid therapy have expressed concern regarding stigmatisation and lack of access to ongoing care. It is important GPs independently make a thorough clinical assessment of each patient's opioid use, and develop an individual management treatment plan consistent with clinical guidelines while safeguarding against abuse and diversion. Treatment should seek to maximise health outcomes across a range of domains (eg patient pain acceptance, functionality, risk).

In the event of an SUD being detected, this plan should also include remedial programs or referral to appropriate drug misuse agencies. Practice policies should be in place to assist the management of the inherited patient using drugs of dependence.

## Comprehensive clinical assessment of the inherited patient

The assessment of an inherited patient with an existing long-term opioid treatment plan includes:

- a review of the patient's general health conditions, including any SUD (eg alcohol, benzodiazepines, opioids)
- a full social and psychological assessment
- confirmation of the pain diagnosis, which may require a formal in-depth review of the pain diagnosis including radiology, response to therapeutic interventions, and current functionality
- establishing the medical necessity and the appropriateness of prescribing regimen
  - assess the risk–benefit ratio – some existing plans may have evidence-based multimodal therapy; others may have quite high-risk or inappropriate regimes with mixed and multiple opioids, multiple psychoactive drugs or drugs that are contraindicated or not consistent with regulations
  - confirm that opioid drugs and doses are correct (ie calculate the patient's daily morphine equivalent dose for all opioids prescribed to determine whether these dosages are safe or at increased risk)
  - determine pain and function with this level of opioids and other medications and ask 'Is this patient at risk if I maintain the same prescription?'
- deciding whether the regimen represents rational accountable prescribing, is outside the scope of practice or the doctor, or needs optimisation
- assessing aberrant behaviours using the 5As approach
  - tolerance and physical dependence are normal consequences of sustained use of opioid analgesics and are not the same as addiction
  - patients treated for 'legitimate' pain may become physically dependent on the supervised therapy of opioid medications, but this does not constitute a substance use disorder.
- contacting prescription shopping services or real-time prescription monitoring services.

Prescribers should verify patient-reported treatment plans and any identified concerns about misuse or dependency with the previous prescriber and pharmacist directly.

### Box 4. Triaging the inherited patient

An assessment of an inherited patient will triage patients into one of three groups:

- Patients who have reasonable function and are being managed on a course of therapy that is both reasonable and appropriate for the diagnosis
- Patients who have been managed in a fashion that is not totally consistent with the new clinician's experience and resources, and may reflect a clinical picture that can be optimised
- Patients whose course of therapy is (for a variety of reasons), not evidence based, or presents significant risk to the patient and others, and so is not something the new clinician feels able to support

## Assessment of risk with the inherited patient

Even when a case for ongoing care is established, the general risk category of the patient should be considered and GPs are not obliged to take full responsibility for care of all patients. For each patient, the risk category is dependent on patient factors, practitioner factors and resources.

### Box 5. Risk categories

Patients may be placed into one of three risk categories:

- Group I (low risk) includes patients who the clinician feels able to confidently manage on their own
- Group II (medium risk) includes patients who the clinician feels able to co-manage with speciality support
- Group III (high risk) includes patients who the clinician feels are best referred to speciality clinics

Higher-risk situations also include those where:

- staff safety may be impacted
- care is outside the expertise of the practitioner
- long-term health prospects of patients are being compromised by lack of access to state or territory facilities
- patients have serious mental illness or are taking antipsychotic medication
- patients have past family or personal history of substance misuse
- polydrug use is present
- patients have been recently discharged from a correctional services facility.

For more information about deciding when to seek advice or consider referral to a psychiatrist or pain/addiction specialist refer to *Prescribing drugs of dependence in general practice, Part A.*

## Care planning for the inherited patient

Patients who satisfy practice appropriateness criteria and are accepted should be prescribed ongoing medication under the continued care of a single doctor. This doctor needs to:

- communicate empathically but honestly with patients about opioid use (including realistic expectations about the likely or potential outcomes of their treatment)

- develop a defensible, rational, and compassionate patient care strategy
- obtain relevant permits to prescribe opioids from the state or territory authorities.

Patients need to be informed about the purpose, importance, benefits and risks of their medicines. This enables them to engage in SDM, which has been shown to build trust, prevent harm and reduce surprise and distress if complications or adverse events occur.

Not all SDM will result in agreement. It is challenging when there is pharmacologic or other therapeutic disagreement with a patient. But there is a difference between patient-centred care and patient-controlled care. Acknowledging patient beliefs, expectations and preferences does not involve crossing professional boundaries, ignoring laws or continuing therapy that is considered detrimental to the patient's health.

In this situation, it is necessary to maintain professional discipline and clinical honesty. If a patient refuses the advice of a GP, they should be advised about the implications of deciding not to receive the healthcare offered. The patient should be given sufficient time to consider and clarify any information in order to make an informed decision, taking into account the context of the clinical situation.[146]

Where GPs suspect an opioid use disorder, they should be honest with the patient while reassuring them that effective treatments are available. Scripting sentences and techniques for GPs are available to assist in politely refusing to provide opioid prescriptions. Appropriate management includes the initiation of remedial programs or referral to appropriate drug misuse centres. In some states such as Victoria, South Australia (and possibly New South Wales in 2018) GPs are permitted to prescribe opioid replacement therapy (ORT). Advice from state-based drug and alcohol services is available at all times.

GPs should not evict patients from their practice because of manipulative behaviour or therapy refusal.

## Using legislation to assist with challenging patients

Clinicians should not see legislation covering the prescription of controlled substances as a barrier to appropriate prescribing. Instead, legislation acts as protection for prescribers as well as for patients.

When patients make demands for opioids, practitioners can strongly state their duty to act within state, territory and national legislative frameworks, and to manage their prescribing practices within the laws and clinical and professional standards.

Practitioners should determine who is the patient's authorised prescriber. If the prescriber is not in the state or territory where the consultation is being made, new authorisation will need to be obtained. Time for the necessary processes will need to allowed.

## Using opioid rotation and rationalisation

When opioids are less effective than expected or a new patient presents with 'irrational pharmacotherapy', then opioid rotation, consolidation (eg using one type, longer acting) or taper (in some cases, to the point of discontinuation) should be considered.

Opioid rotation may help to:

- improve analgesia
- lower the dose of the prescribed medication
- manage loss of analgesic efficacy or the presence of toxicity.[147]

Note that clinically, patients often show incomplete cross-tolerance when rotated from one analgesic to another.

### Use urine drug testing

A baseline UDT should be performed at the initial visit, with a request to include detection of oxycodone and other drugs not usually recognised by immunoassay.

Further testing is used as clinically indicated. Unexpected results from such tests should be interpreted within their limitations: fentanyl, buprenorphine, synthetic drugs, anabolic steroids, and usually oxycodone are not routinely detected and must be requested as additional tests (at extra cost to the patient).

Note that drug misusers may adopt a variety of methods, such as switching urine samples, to influence results.[148]

## 1.6 Getting help with clinically complex patients on opioid therapy

All state and territory health authorities have 24-hour telephone access to assist with drug and alcohol queries.

GPs can get urgent advice and support for patients on opioid therapy, and seek information on referral options or advice on issues on care coordination between multiple providers.

## 1.7 Discontinuing opioids in general practice

### Key points

- Long-term treatment with opioids in CNCP may represent de facto maintenance treatment for iatrogenic opioid dependence.
- GPs should follow an 'exit strategy' for dealing with failure to achieve agreed outcomes of opioid treatment.
- GPs can effectively wean their patients from opioids if there is no benefit, or if risks outweigh benefits.
- Lack of improvement, intolerable side effects and abnormal behaviour are signs of opioid trial failure and indicate the need to taper and/or discontinue opioids.
- GPs should be familiar with opioid reduction and withdrawal processes.

| Evidence statements | Grade |
|---|---|
| If benefits do not outweigh harms of continued opioid therapy, GPs should optimise other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids[8] | Strong recommendation, very low quality of evidence |
| Where there is evidence of SUD doctors should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioural therapies) for patients with opioid use disorder[8]<br>Referral to clinics experienced in substance use disorder is advised | Strong recommendation, low quality of evidence |
| For patients with CNCP who are currently using >100 mg OME of opioids per day or more, we suggest tapering opioids to the lowest effective dose, potentially including discontinuation, rather than making no change in opioid therapy[149] | Weak recommendation, very low quality evidence |

### 1.7.1 Background to opioid tapering

It is not unusual for opioid medication to become ineffective over time, or for adverse effects to develop. Where opioid trials fail to achieve agreed outcomes or harms outweigh benefits, GPs should follow their 'exit strategy' to taper and/or cease opioids while preserving the therapeutic relationship.

In other cases, long-term treatment with opioids in CNCP may represent de facto maintenance treatment for iatrogenic opioid dependence. Tapering should be attempted for all patients who have been on long-term opioid therapy of greater than 100 mg OME per day. Reduction in opioid dose may reduce adverse effects including cognitive impairment and the likelihood of non-fatal or fatal unintentional overdose.

In all cases, patients have the right to respectful care that promotes their dignity, privacy and safety. Ending a relationship with a patient or abruptly discontinuing opioid treatment without offering a feasible plan for tapering or addiction treatment could be considered an abrogation of the accountable prescriber's duty. Such approaches rarely solve the problem.

Patients can experience significant improvement in pain severity, functioning, and mood when their opioid therapy is tapered to a lower, safer dose, or ceased. At present there is very little research available on comparative effectiveness of interventions for opioid withdrawal in CNCP.[150]

GPs should regularly assess whether the patient satisfies the legal definition of drug dependence. If the patient has an opioid use disorder, opioid therapy for pain should be discontinued and the addiction professionally, sympathetically and appropriately treated. Seek authority from the state regulatory authorities when treating these patients.

### Box 6. Educational videos about opioid cessation

Brainman pain management resources, developed by the Hunter Integrated Pain Service at John Hunter Hospital and Hunter Medicare Local, available at www.aci.health.nsw.gov.au/ie/projects/brainman

'Understanding pain: Brainman stops his opioids', available on YouTube at www.youtube.com/watch?v=MI1myFQPdCE

## 1.7.2 Managing opioid tapering or discontinuation

Before attempting opioid discontinuation, GPs should be familiar with opioid reduction and withdrawal processes and patient experiences.[5,90] Some patients will experience stable or improved pain after an opioid taper.[151–153] However, short-term withdrawal can lead to transitory increased pain and hyperalgesia.[154–156]

For patients with long-term opioid treatment for CNCP:

- there is no published comparison of speed of tapers[157]
- there is no evidence to support switching to buprenorphine or methadone for tapering[157]
- key predictors of opioid tapering dropout or relapse are depression, high pain scores and high opioid doses[157] (there is not yet any research to support addressing these factors through pharmacologic and psychological interventions). These patients are also those at higher risk of opioid-related adverse events and tapering of the dose should be strongly considered
- the use of α2-adrenergic agonists (eg clonidine) can reduce symptoms of withdrawal via sympathetic activity.

### Where there is no evidence of substance use disorder

If weaning is required after a shorter period of opioid therapy, such as after failure to achieve the goals of an opioid trial, or after a negotiated treatment phase for acute pain, then a faster rate of weaning is generally appropriate. One option is a stepwise reduction of the daily opioid dose each week by 10–25% of the starting dose.[5]

If weaning is required in response to significant adverse effects or opioid misuse, then daily stepwise reduction may be more appropriate. Alternatively, immediate opioid cessation and pharmacological treatment of withdrawal symptoms can be considered.

Otherwise, a decrease of 10% of the original dose every 5–7 days until 30% of the original dose is reached, followed by a weekly decrease by 10% of the remaining dose, rarely precipitates withdrawal symptoms and facilitates adherence.[157]

### Where there are complex patient comorbidities

Discontinuing opioid therapy is often hindered by patients' psychiatric comorbidities and poor coping skills, as well as the lack of formal guidelines for the prescribers.

If a previous attempt at opioid weaning has proven unsuccessful, then the rate of tapering can be slowed. This can be achieved by reducing the size of the dose reduction each month and/or by increasing the time spent at each dose level (eg two or three months between reductions).

### Where there is evidence of substance use disorder

Importantly, the legislative requirements for prescribing S8 drugs vary depending on the person's dependence, but all are consistent for patients with respect to SUD: S8 medications (most opioids, alprazolam and flunitrazepam) cannot be prescribed without a permit or an appropriate approval from the relevant state or territory health department's pharmaceutical services unit.

In some cases, it may become apparent during weaning that the primary problem is opioid dependency rather than pain. For patients with opioid use disorder, GPs should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine-naloxone or methadone in combination with behavioural therapies). Referral to an addiction specialist is advised.[5,8]

## 1.7.3 Monitoring the taper

The goal of tapering is to improve or maintain patient wellbeing while opioids are being withdrawn. Schedule frequent visits and ask about and emphasise the benefits of taper (eg improved pain, mood, alertness) at each appointment. Referral for counselling or other support during the taper is recommended, especially if there are significant behavioural issues. If a patient is not successfully reducing their dose, or there is an escalation in dose beyond prescription, involve other practitioners.

## 1.7.4 Managing withdrawal symptoms

Symptoms of withdrawal, such as nausea, diarrhoea, muscle pain and myoclonus can be managed with clonidine 0.1–0.2 mg orally every six hours, or simple supportive therapy. Symptoms of mild opioid withdrawal may persist for six months after opioids have been discontinued. However, do not treat withdrawal symptoms with opioids or benzodiazepines after discontinuing opioids.

Rapid recurrence of tolerance can occur from months to years after prior chronic use.

# 2. Pain – The basic concepts

## 2.1 The pain experience

The International Association for the Study of Pain (IASP) defines pain as 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage'.[158]

Acute pain is experienced from actual or threatened damage to tissue and is due to activation of nociceptors. Chronic pain describes persistent or recurrent pain (typically three months or more) and includes multiple pain conditions including CNCP (eg fibromyalgia, non-specific back pain, osteoarthritis, headache), chronic cancer pain and CPSP.[123,159]

The understanding of pain has broadened from a simple stimulus–response model (biomedical) to encompass the whole person. Each individual's pain experience is affected by a complex combination of biomedical, psychological and social factors. The social and psychological factors are commonly the main determinants, especially of CNCP. To reflect this, Australian authorities have formally moved to a biopsychosocial framework. Note that the term 'biopsychosocial' is used in this guide without implying an order of importance.

The degree of pain and disability experienced in relation to similar physical injury varies. Similarly, there is individual variation in response to methods used to alleviate pain. Communication of the pain experience can be difficult. Patients are often frustrated and distressed by the limitations of language in expressing their pain experience.

When planning management and interventions for pain, these factors need to be considered. Additional insights and effectiveness of treatment can be gained by exploring and integrating patients' wishes and their past experiences.

## 2.2 Classifications of pain

In clinical practice, we have traditionally classified pain based on time: acute or chronic. This has limitations, one of which is that it perpetuates the misconception that chronic pain is just 'unhealed' acute pain.[160–162] Instead of classifying pain in terms of time, it is far more important to understand the underlying pathophysiology of pain.

The classification of pain based on pathophysiology is dynamic.[123] A change to the definition of neuropathic pain occurred in 2011, and a third descriptor for pain is currently being debated.[163]

### 2.2.1 Nociceptive pain

Nociceptive pain arises from actual or threatened damage to non-neural tissue and is predominantly due to activation of nociceptors.[158,164] Nociceptive pain guards against tissue injury (eg warns of potentially damaging stimuli such as heat) and supports healing and repair (eg increases pain to normally innocuous stimuli to aid protection/immobilisation of injured tissue). It requires a normally functioning somatosensory nervous system.[163,165]

Nociceptive pain can be further classified depending on the location of nociceptors. 'Visceral' pain results from stimulation (due to stretch, inflammation or ischaemia) of nociceptors within the viscera. Pain experienced by stimulation of nociceptors in the musculoskeletal system is sometimes referred to as 'somatic' pain.

Typically, nociceptive pain only lasts in the presence of continual noxious stimuli and disappears after resolution of the tissue injury. However, certain diseases may generate recurrent or ongoing noxious stimuli to produce chronic nociceptive pain (eg rheumatoid arthritis).[163,165]

## 2.2.2 Neuropathic pain

Neuropathic pain is caused by a lesion or disease of the somatosensory nervous system. It is not a diagnosis but a clinical description of the pain resulting from an injury or damage to either the peripheral or central nervous system by mechanical trauma, metabolic diseases, neurotoxic chemicals, infection, or tumour invasion.[163,165]

To satisfy the diagnostic criteria of neuropathic pain, the lesion or disease must be demonstrable through:

- an appropriate history (eg episode of shingles within the past six months, limb amputation)
- the presence of signs of neurological deficit
- diagnostic interventions (eg imaging, neurophysiology)
- confirmation of underlying cause (eg stroke, type 2 diabetes, multiple sclerosis).

Chronic neuropathic pain is not a single entity, but refers to a heterogeneous group of pain conditions. Nociceptive pain and neuropathic pain may occur together. For example, a study of patients with prolonged low back pain found that about 37% had a predominant neuropathic pain component.[166]

Unfortunately, current treatment of neuropathic pain is less than ideal, with fewer than 50% of patients experiencing satisfactory pain relief and tolerable side effects.[167]

## 2.2.3 Nociplastic pain

Patients initially experiencing nociceptive pain, such as osteoarthritis, may develop alterations in nociceptive processing manifested as altered descending pain inhibition[168,169] accompanied by spread of hypersensitivity.[170–172] Clinicians working in the field of pain have recognised the need for a word to describe pain that arises from altered nociception despite no clear evidence of:

- actual or threatened tissue damage causing the activation of peripheral nociceptors (nociceptive pain)
- disease or lesion of the somatosensory system causing the pain (neuropathic pain).

Nociplastic pain is described as pain caused by altered function of nociceptive pathways in the peripheral or central nervous system. These terms reflect the underlying pathophysiological change (sensitisation) in the nervous system.[163]

This classification describes the pain of conditions including fibromyalgia, CRPS, ‘non-specific’ chronic low back pain, and functional visceral pain disorders (eg irritable bowel syndrome, bladder pain syndrome, chronic abdominal pain, and chronic pelvic pain).

# 2.3 Assessment of pain

The assessment of pain using a biopsychosocial (or sociopsychobiomedical) framework takes into account the multiple factors (social, psychological, biological) that influence the pain experience. It completes a more complex understanding of the patient’s pain perspective as well as identifying other targets for management. Factors do not always neatly fit into one category; for example, depression may have physical and social aspects as well as being a psychological factor influencing pain.

A comprehensive pain assessment includes a:

- general assessment and pain-specific history (which explores the pain type, severity, functional impact, context, and the patient’s meaning of pain, expectations and fears)
- physical examination (assessing for signs of tissue damage or disease that might indicate nociceptive and/or neuropathic and/or nociplastic mechanisms of pain)
- psychological assessment (the pain experience is affected by mood, stress, coping skills, fear avoidance, and catastrophising).

This will inform the selection of treatment options most likely to be effective. The assessment may need to be repeated reasonably frequently, particularly while establishing a diagnosis and appropriate pain management.

The following descriptions provide more detail on the pain assessment including links to useful assessment templates and questionnaires.

## 2.3.1 General assessment and pain history

The standard medical assessment is as important in pain as it is in any other medical or psychological condition. Particularly with pain, history taking will explore multiple aspects such as any injury, details about the pain experience and impact, and attempted treatments (Table 1). The purpose of the assessment is to establish a possible physical mechanism of pain (whether it is nociceptive, neuropathic, nociplastic or a combination of aetiologies) and if there are underlying conditions or psychosocial issues.

When appropriate, a pain screening questionnaire may assist in the understanding of the patient's pain experience. These include the Brief pain inventory, McGill pain questionnaire, DN4 neuropathic pain questionnaire and the Örebro musculoskeletal pain screening questionnaire.

### Social assessment

Social assessment identifies factors in the patient's environment that influence the pain experience. These include family and other relationships, work, life events, housing, sleep, activity and nutrition. Pain may be influenced by culture (eg seen as a way to strengthen the body, purify the soul or deepen the spirit with the idea of 'no pain no gain').

Pain influences interactions with others, occupational performance and self-care. Pain can be socially isolating, which can contribute to the pain–depression cycle. The patient should be questioned about the impact of pain on function (social and physical) and overall quality of life (Table 2). Specific questions might include the following:[173]

- Social and recreational functioning
  - How often do you participate in pleasurable activities, such as hobbies, going out to movies or concerts, socialising with friends, and travel?
  - Over the past week, how often has pain interfered with these activities?
- Mood, affect, and anxiety (for more information, refer to 2.3.3 Psychological assessment)
  - Has pain interfered with your energy, mood, or personality?
  - Are you readily tearful?
- Relationships
  - Has pain affected relationships with family members, significant others, friends or colleagues?
- Occupation
  - Has the pain required that you modify your work responsibilities and/or hours?
  - When was the last time you worked, and (if applicable) why have you stopped working?
- Sleep
  - Does pain interfere with your sleep? How often over the past week?
- Exercise
  - How often do you do some sort of exercise?
  - Over the past week, how often has pain interfered with your ability to exercise?

To assess the true impact of pain on the patient's life, it helps to have familiarity with the patient and/or obtain input from their family, friends and support systems.

Occasionally, pain is used to gain sympathy, protection, benefits or medico-legal compensation.

## 2.3.2 Physical examination

A physical examination, including a thorough musculoskeletal examination, is particularly important in most of the chronic pain conditions and a relevant neurological examination is particularly important for neuropathic pain. A physical examination might include:

- assessing for signs of tissue damage/injury or disease that might indicate nociceptive and/or neuropathic mechanisms of pain (eg tissue deformity and cardinal signs of inflammation, or signs of neural disease or damage)
- careful evaluation for sources of referred pain (including viscera)
- looking for evidence of hypervigilance or guarding with particular movements. Compensatory postures and movements are important to analyse, as they might be placing extra load on sensitive tissues and addressing these early can avoid development of secondary issues
- looking for evidence of allodynia, hypoalgesia and hyperalgesia.

At the end of the examination, the GP should aim to establish a provisional diagnosis for the pain and the biomedical mechanism involved, as well as analysis regarding the disability level of the patient.

**Table 4. Fundamentals of a pain history[7]**

| | |
|---|---|
| **Site of pain** | • primary location: description +/- body map<br>• radiation |
| **Circumstances associated with pain onset** | • include details of trauma or surgical procedures |
| **Character of pain** | • sensory descriptors (eg sharp, throbbing, aching)<br>• neuropathic pain characteristics |
| **Intensity of pain** | • at rest<br>• on movement<br>• temporal factors<br>– duration<br>– current pain, during last week, highest level<br>– continuous or intermittent<br>• aggravating and relieving factors |
| **Associated symptoms** | • eg nausea |
| **Effect of pain** | • on activities<br>• on sleep<br>• on social life<br>• on work life<br>• capacity to do family duties |
| **Treatment** | • current and previous medications (dose, frequency of use, efficacy, adverse effects)<br>• other treatments (eg transcutaneous electrical nerve stimulation)<br>• health professionals consulted |

| Table 4. Fundamentals of a pain history[7] | |
|---|---|
| **Relevant medical history** | • prior or co-existing pain conditions and treatment outcomes<br>• prior or co-existing medical conditions |
| **Factors influencing the patient's symptomatic treatment** | • belief concerning the causes of pain<br>• knowledge, expectations and preferences for pain management<br>• expectations of outcome of pain treatment<br>• reduction in pain required for patient satisfaction or to resume 'reasonable activities'<br>• typical coping response for stress or pain, including presence of anxiety or psychiatric disorders (eg depression, psychosis)<br>• family expectations and beliefs about pain, stress and postoperative course |

Reproduced from Schug S, Palmer G, Scott D, et al. Acute pain management: Scientific evidence. 4th edn. Melbourne: ANZCA, 2015. Available at http://fpm.anzca.edu.au/Documents/APMSE4_2015_Final [Accessed 29 July 2017].

## 2.3.3 Psychological assessment

Psychological assessment explores the patient's mood state, beliefs, thinking styles, coping skills, behaviours and responses that may contribute to the experience of pain, obstacles to recovery and treatment outcome.[174] Psychological factors that contribute to the experience and impact of pain can be amenable to change[175] and thus influence outcomes for the individual.[176] There are screening tools for many of these factors.

Experience of both acute and chronic pain is commonly accompanied and influenced by mood and anxiety disorders.[174] For example, anxiety is one of the most significant predictive factors for the severity of postoperative pain[177] and there is a consistent association between CPSP and depression.[125]

Relevant beliefs include understanding of diagnosis and prognosis, and expectations about treatment, including willingness to be an active participant. Many people have a fear of pain, which contributes to the development of avoidance responses and can ultimately lead to disability. Thinking styles that are overly negative, ruminative and helpless (eg catastrophic thinking) are associated with more severe acute pain as well as persistent pain.[178]

| Table 5. Components of a psychosocial assessment |
|---|
| • Clinical history<br>• Personality traits and psychological comorbidity<br>• Current level of somatic concern, depression, anger<br>• Report of pain and functional limitation<br>• Preliminary behaviour and analysis<br>• Coping strategies/avoidance<br>• Belief about injury, pain and treatment<br>• Family, social, economic, occupational influence/environment<br>• Individual model of explaining pain/meaning of pain<br>• Attitude to health professionals |
| It may also be beneficial to:<br>• obtain and review all supporting documentation – a conversation with previously treating practitioner(s) may be useful<br>• consolidate and integrate the opinions and expertise of other disciplines such as a psychologist, physiotherapist, exercise therapist or medical specialist<br>• become aware of, and utilise, those practitioners who are accessible and who have other expertise in the management of patients with chronic pain<br>• contact the national Medicare Australia Prescription Shopping Programme<br>• obtain information from the drugs of dependence unit (or equivalent) in each state – remember that most patients seeking opioids are not doctor shoppers |

## 2.3.4 Measurement of pain and functional impact

There are several pain scoring systems. Verbal numerical rating scales are often preferred because they are simpler to administer and give consistent results.[179]

The PEG scale may be useful in the general practice setting, particularly when assessing chronic musculoskeletal pain.[109] Scores (out of 30) give a reference point for the patient's overall wellbeing and can be used to compare the same patient seen at different times or by different practitioners.[109]

As so many factors influence the experience (and communication) of pain, it is not surprising that pain scores do not provide information about which patients are likely to respond to opioids.[180]

### Box 7. Pain diary

NPS MedicineWise has a pain diary that patients can access and download at www.guild.org.au/__data/assets/pdf_file/0023/5945/patient-resource-my-pain-diary-nps-medicinewise.pdf

## 2.3.5 Risk assessment

Opioids are often useful analgesics, but care needs to be taken when prescribing these drugs to limit the risks, including inappropriate use and diversion. Clinically, problematic opioid usage is more likely when used in:

- younger patients – substance use issues generally commence before 35 years of age
- patients without a definite patho-anatomic diagnosis
- patients with active substance use problems or who are in contact with patients with such problems
- patients with active psychiatric problems
- patients who use benzodiazepines – concomitant use of opioids substantially increases the risks of side effects, particularly cognitive impairment, sedation and respiratory depression.[181]

Comprehensive assessment addresses the risk of opioid misuse.[182,183] While screening for opioid risk has been recommended, at this point evidence of effectiveness is lacking. Additionally, treatment agreements and urine testing are also recommended but have not been shown to reduce overall rates of opioid prescribing, misuse, or overdose.[5,103]

Patients with a history of SUD are at higher risk of harms. A check of state-based prescription monitoring systems is advocated. Those patients with a history of SUD should probably not be offered opioids in a general practice setting, but, rather, if pain control cannot be gained by other means, should be offered referral to specialist services.

A UDS may reveal evidence of substances of which the practitioner is not aware. Not all substances are routinely tested for (eg oxycodone testing needs to be specifically requested). If such drugs are found, whether illicit or legal, the patient should be referred for specialist assessment and management. Contacting your local pathology provider may be necessary.

# 3. Approach to pain management

## 3.1 Patient focus

Good pain management has significant benefits. For many people, it can transform their quality of life, allowing them to work, go to school and participate in the community rather than being functionally disabled by pain.

Management of pain has tended to rely heavily on medication. People are often aware of the downsides of pain medication, but accept it (or sometimes resent it) as a necessary evil to allow them to get on with their lives. In contrast, they are largely unaware of, or are sceptical about, non-drug pain management techniques. The general impression is that alternative pain management techniques are less likely to work the more severe the pain.

So while prescription of pain medication in Australia has increased markedly over the past 30 years, non-drug therapies have had a much slower uptake (both clinically and in the research context). As understanding of pain improves and evidence of benefit for alternative and comprehensive pain management interventions grows, patients have more options to meet their needs and expectations.

This may have particular benefit for the many patients with pain who have chronic health conditions, which can complicate their pain management with medications.

### 3.1.1 Understanding the contextual and placebo effect in chronic pain management

The manner in which a clinician explains and delivers therapy has an impact on outcome.[79] Practitioners who master not only the disease and treatment, but also cultivate a therapeutic relationship may be more effective at pain management.[80]

Doctor–patient relationships have been acknowledged as having an important therapeutic effect, irrespective of any prescribed drug or treatment.[184,185] Despite limitations, separate systematic reviews consistently report positive clinical findings with positive doctor–patient relationships.[184] A relatively consistent finding is that doctors who adopt a warm, friendly, and reassuring manner are more effective than those who keep consultations formal and do not offer reassurance.[80]

'Context' extends beyond the one-on-one interaction between patient and doctor. A practice environment and culture that nurtures mutual trust, empathy, respect, genuineness, acceptance and warmth can improve the experience of patients, and have a beneficial effect on medical outcomes.[80]

#### Placebo effects

A placebo is a substance or procedure that does not have an inherent ability to produce an expected or desired effect. However, placebos have been shown to have dose-response, time-effect and side-effect profiles similar to non-placebos.[185]

There is some confusion between the terms 'placebo response' and 'placebo effect':

- a placebo response is exactly that – a therapeutic response to the administration of a known placebo[186]
- a placebo effect is the part of the therapeutic response (a genuine or psychological effect) that is not attributable to the properties of active ingredients.[185–187]

Placebo effects are a result of the sociocultural context of treatment. These effects are integral to routine pain management practice.[79,188,189] Outcomes are influenced by multiple contextual determinants including the doctor–patient relationship, expectancy, classical conditioning, and social and observational learning.[7,79,188] There is significant variability in the degree and the duration of these contextual or placebo effects.[190–194]

**Table 6. Clinical use of placebo effects[79]**

| To enhance expectations | To enhance learning components |
|---|---|
| • Emphasise positive effects of medicines<br>• Avoid stressing adverse effects<br>• Explain effects and mechanisms of action of medicines<br>• Interact personally with the patient and in a non-judgemental manner<br>• Do not rely only on written handouts<br>• Avoid unrealistic expectations | • Administer analgesics in an open manner<br>• Connect the administration to positive internal states and external conditions<br>• Combine analgesics with other pain-relieving approaches, preferably with time-contingent administration of analgesics<br>• Reinforce positive and minimise negative experiences |

Source: Klinger R, Colloca L, Bingel U, Flor H. Placebo analgesia: Clinical applications. Pain 2014;155(6):1055–58.

There may be multiple pathways for the placebo effects. Some studies indicate that the magnitude of placebo analgesia is higher when the placebo analgesic effect is induced via suggestion combined with conditioning,[195] rather than via suggestion or conditioning alone. Other studies show that placebo effects in pain can be mediated by endogenous opioids,[196,197] cholecystokinin,[197] endogenous cannabinoid systems,[198] and dopamine release.[199]

As the understanding of placebo effects has progressed, the ethical debate for their use has changed. While it is still widely accepted that placebos should not be administered in a deceptive manner, using the placebo effect to augment routine 'active' treatments has become less contentious.[188,200]

More research in clinical settings is needed to determine the practical value of the use of placebos. However, practitioners should consider the way they deliver information – it may significantly alter expectations, harness placebo effects and potentially optimise treatment outcomes.

## 3.1.2 Understanding the patient experience

It is necessary to have a thorough appreciation of patients' beliefs, needs and expectations about pain and treatment to achieve good pain management.[201]

Even with similar physical injuries, different patients will experience highly variable degrees of pain and disability. As the pain experience is influenced by complex biomedical, psychological and social factors, so too does pain interfere with many and possibly all aspects of the patient's life – restricting daily living, leisure activities and sleep.[202,203]

Patients who experience greater pain severity report lower quality of life. Many patients regard pain reduction as the most beneficial component of their treatment.[204,205] A fundamental part of pain management is building a collaborative partnership between the patient and GP. This involves empathetically showing the patient:

- their experience is valid
- their pain is understood and believed
- you are interested in them as a person (who is experiencing profound changes in their life) and not just in their symptoms
- their opinions about management matter
- you are positive and optimistic about improving their situation.[206–208]

While many patients have a specific diagnosis, they often have not been given an explanation for their pain. Discussing the cause and meaning of the pain is essential because it results in higher motivation to engage in a treatment plan.[203]

The management of chronic pain often involves several medical practitioners and allied health professionals, which may cause some patients to feel confused and overwhelmed. Therefore, it is important to have one person who serves as the primary care doctor – someone who is familiar with the person's medical history and can coordinate the patient's overall medical care. The GP is ideally placed to take on this role.

## 3.1.3 Shared decision making

Management of pain, in particular chronic pain, requires many of the generic skills of GPs. While the evaluation of pain mechanisms is important to determine therapeutic options, pain is fundamentally a patient experience, so addressing patient experiences and thoughts has high priority. SDM is a process of bringing evidence into the consultation and incorporating it into a discussion about the patient's values, expectations and preferences: it is the integration of communication and evidence skills.[209–211]

Very few clinical situations involve just one option and almost no treatments are 100% effective or 100% free of side effects. When considering pain management options, often the evidence does not strongly support a single clinically superior option.[209,210,212] Hence, pain management typically involves a preference-sensitive decision that is likely to be strongly influenced by patients' beliefs and values.[212–214] As most patients overestimate the benefits of medical interventions and underestimate the risks, it is important to know what expectations patients have, help correct any misperceptions and be honest about uncertainty (to do with their pain condition and with treatments).

Integrating the patient perspective has the potential to increase the patient's satisfaction with the consultation, as well as result in better decisions and in improved management of the illness and health outcomes.[215]

## 3.1.4 Communicating likely response to treatment

### Defining success

Patients and doctors need a common understanding of what success means in pain management.

Successful pain relief does not always mean complete resolution of pain. In the research setting, a 50% reduction tends to be considered a successful outcome. However, across a range of pain conditions (acute and chronic), patients rate a 30% reduction in pain intensity as clinically meaningful.[216–220] Before experiencing pain reduction, it may be hard for a patient to judge what amount of resolution would mean success for them. Here, realistic goal setting is needed.

When assessing success of treatment, in addition to pain reduction, it may be useful to look at effect on other factors affected by pain. These include sleep, depression, fatigue, quality of life, function and ability to work.[221]

Success or failure can typically be determined within 2–4 weeks of starting drug therapy; when success is achieved it tends to be long lasting.[221]

### Setting expectations

Not all treatments will achieve clinically meaningful pain reduction and no single drug will successfully treat more than a minority of patients with a painful condition.[221] Many patients will be unaware of this.

Many medications will fail or have unacceptable side effects, however; experience, (and some evidence) suggests that failure with one drug does not necessarily mean failure with others, even within a class. Because success rates are low, a wide range of drugs and non-drug therapies (ie multimodal) may be needed, especially in complex chronic conditions.[81,221] The best order in which to use drugs, in terms of efficacy, harm, or cost, is not always clear.[221]

The principles of treatment should be to measure pain, expect and recognise analgesic failure, and to react to it, pursuing analgesic success rather than blindly accepting failure.[221]

### Box 8. Helping patients make informed decisions

The RACGP's *gplearning* platform has developed an online activity to help GPs communicate information about risk and benefits to patients. The activity provides a framework for assisting patients to share in decisions about their treatment. For more information visit www.racgp.org.au/education/courses/activitylist/activity/?id=54643&q=keywords%3dbenefits%26triennium%3d17-19

## 3.2 Multidisciplinary approach

Multidisciplinary care – when GPs work in collaboration with psychologists, physiotherapists and exercise physiologists to provide non-drug pain therapies – is frequently recommended in chronic pain management.

Multidisciplinary treatments have been reported as effective for various types of chronic pain in adults, but the reports are inconsistent. Inconsistencies in the reported results may be due to the differences in the definition of multidisciplinary treatment, the treatment combinations, treatment intensity, and the setting and heterogeneity of the study populations and control groups. Multidisciplinary biopsychosocial rehabilitation interventions are seen to be more effective than usual care and physical treatments in decreasing pain and disability in people with chronic low back pain.[222]

It is important that all treating team members have a shared understanding of the patient experience, how the team members will work together and what each team member will contribute. This aspect of collaboration is often overlooked.

### 3.2.1 Pain clinics

Referral to a pain clinic should be considered for patients with complex chronic pain, but care should be exercised to determine the philosophy of the clinic. Multidisciplinary pain clinics in Australia tend to have differing philosophies of management; for example, some clinics focus on interventional pain techniques while others focus on multidisciplinary care.

International research reveals that pain facilities use a wide range of pain interventions and employ a variety of healthcare professionals, without evidence to support ideal composition of multidisciplinary services. A comparable situation appears to exist in Australia.

# 4. Brief overview of non-drug therapies for pain

## 4.1 Psychological interventions

Psychological assessment and treatments are designed to manage pain, distress and disability. They can be provided by the primary physician or in collaboration with a clinical psychologist through a care plan.

Although psychological interventions are being used with increasing frequency, efficacy is variable and still emerging. For example, for chronic neuropathic pain there is currently insufficient evidence of the efficacy and safety to recommend psychological interventions.[223]

### Box 9. HANDI for pain

The RACGP's *Handbook for non-drug interventions* (HANDI) provides multiple non-drug therapies for various pain conditions, and is available at www.racgp.org.au/handi

### 4.1.1 Cognitive behavioural therapy

Cognitive behavioural therapy (CBT) helps patients modify situational factors and cognitive processes that exacerbate pain and trains patients in behavioural techniques to manage pain. CBT has shown small positive effects on disability, mood and catastrophic thinking, with some benefits lasting more than six months post treatment.[87] There is a lack of evidence on the efficacy and safety of CBT for people with neuropathic pain.[88]

### 4.1.2 Mindfulness in chronic pain

Mindfulness has become an increasingly popular self-management technique for many long-term conditions, including chronic pain.[224] Mindfulness originates from a Buddhist contemplative tradition, and involves focusing attention on immediate experience (ie 'on the moment') and approaching it with curiosity, openness and acceptance.[224]

There is good evidence for effectiveness (for pain and/or depressive symptoms) of mindfulness-based interventions for patients with chronic pain with heterogeneous pathophysiology[225] but limited evidence of benefit in chronic low back pain. Mindfulness-based interventions may have a positive impact on perceived pain control with a moderate effect size,[226] but there was no evidence of a benefit in terms of clinical outcomes such as pain intensity.[224] There may be benefit in fibromyalgia.[223] More high-quality studies are needed.[86]

### Box 10. Find a psychologist

To find a psychologist working in pain management, visit the Australian Psychological Society's Find a Psychologist website and select 'Pain management' under general health in the 'All issues' section. There is a further option to select 'Mindfulness-based cognitive therapy' in the therapeutic approaches section under 'Refine results'.

## 4.2 Activity and exercise interventions

Movement, exercise and exercise therapies, regardless of their form, are recommended in the management of patients with chronic pain.

Most patients with chronic pain are physically deconditioned from inactivity.[89] There is strong evidence that normalisation of activity, as far as possible, is associated with reduction in the level of pain and improvement in function and wellbeing of patients with CNCP,[22,89,227] including low back pain,[82,228] osteoarthritis of the knee[83] and hip,[84] and fibromyalgia.[85] With low back pain, staying active is associated with less pain intensity,[229] improved function[230] and reduced disability in the long term.[86] Pilates has low-quality and inconsistent evidence of effectiveness in improving chronic low back pain.[231,232]

The Royal Australian College of Physicians (RACP),[233] the RACGP and other bodies recommend that returning to work (where possible and appropriate) has substantial benefits in improving patient morbidity and wellbeing.[233,234]

Australian physiotherapists play a critical role in assisting the management of chronic pain. They are familiar with the biopsychosocial approach to pain and work across all age groups in primary care settings. Physiotherapists provide a range of evidence-based care, designed with the aim of diminishing pain and improving quality of life, to rehabilitate and improve movement.

The effectiveness of physiotherapy will be dependent on the nature and range of physical intervention strategies used and what conditions are treated.[50,230,231,235–241] For example, there is no high-quality evidence to support the use of ultrasound for improving pain or quality of life in patients with non-specific chronic low back pain.[242] There is low to moderate effectiveness of exercise, psychological therapies, multidisciplinary rehabilitation, and massage for chronic low back pain.[230,231,235]

### Box 11. Find a physiotherapist

The Australian Physiotherapy Association website has a Find a Physio facility to assist access to physiotherapists who have enhanced training in pain management.

## 4.3 Neuroscience education in chronic pain

Providing education and training to patients about the nature of pain and its effects can help self-management.[21,230,243,244] When combined with other treatments that are also consistent with a biopsychosocial framework, education appears to offer clinically important improvements in pain and disability.[245–248]

Neuroscience education or pain neurophysiology education (PNE) is a range of educational interventions that present biological information about pain. There is evidence that increasing knowledge of pain-related biology:

- helps patients understand a biopsychosocial approach to rehabilitation
- decreases catastrophising[227,249]
- results in short-term reductions in pain and disability.[228,229,243,245,246]

There is moderate-quality to high-quality evidence that patient education in primary care can provide long-term reassurance for patients with acute or sub-acute low back pain.[21] It also shows promise for patients with fibromyalgia.[250]

Effective teaching strategies (ie those that increase patient knowledge, decrease anxiety and improve patient satisfaction) include those using computer technology, audio and videotapes, written materials and demonstrations.[251]

### Box 12. Patient education resources

- A short Brainman video about the causes and management of CNCP – 'Understanding pain in less than five minutes' www.youtube.com/watch?v=5KrUL8tOaQs
- A video by Dr Mike Evans (founder of the Health Design Lab at the Li Ka Shing Knowledge Institute, Associate Professor of Family Medicine and Public Health at the University of Toronto, and staff physician at St Michael's Hospital [Toronto]) – 'Low back pain' www.youtube.com/watch?v=BOjTegn9RuY
- A fact sheet by Painaustralia – 'The nature and science of pain' www.aci.health.nsw.gov.au/__data/assets/pdf_file/0018/212850/Understanding_Pain_PA.pdf

# 5. Brief overview of analgesic adjuvants

In this guide, 'adjuvants' refers to medications that are co-administered with analgesics to either enhance pain relief or manage adverse effects of the pain medication.

Respecting the caveats of placebo effects in pain, and the known problems of pain trials, the following is a review of the available evidence of pharmacological analgesic adjuvants.

## 5.1 Caffeine

Caffeine has been added to common analgesics such as paracetamol, ibuprofen and aspirin in the belief that it enhances analgesic efficacy.[252] A small but statistically significant benefit has been shown when 100–130 mg dose of caffeine (equivalent to a mug of coffee) is added to these common analgesics. The effect appears to be independent to the pain condition or type of analgesic.[252] With no serious adverse events reported, it is unlikely that adding caffeine to an analgesic will be harmful if the recommended dose is not exceeded.[252]

## 5.2 Antidepressants

There is considerable variation in the comparative types and effectiveness of antidepressants on specific conditions. These variations are detailed under specific conditions.

All classes of antidepressants are associated with withdrawal syndromes[253–256] and should be tapered slowly if the drug is discontinued. Antidepressant abuse and misuse have also been reported, but are rare. Most reported cases of antidepressant abuse occur in individuals with comorbid substance use and mood disorders.

### 5.2.1 Tricyclic antidepressants

#### Musculoskeletal pain

There is no significant difference between tricyclic antidepressants (TCAs) and placebo in pain relief for patients with chronic low back pain.[257,258]

#### Neuropathic pain

While TCAs are considered first-line and second-line therapies in neuropathic pain treatment,[96,167,259–262] guideline recommendations differ and supportive data are of varied quality. Older analyses and guidelines, and those before the definition of neuropathic pain changed in 2011, appear more supportive.

More recent analyses report very modest efficacy compared to other antidepressants and anticonvulsants[263] and suggest that the evidence base for TCAs in neuropathic pain is weak, due to the small magnitude of clinically meaningful effects and the high risk of bias in the RCTs.[100,247,248,264,265] Large placebo responses, inadequate diagnostic criteria and poor phenotypic profiling probably account for modest trial outcomes.[96]

Neuropathic pain associated with cancer or human immunodeficiency virus (HIV) appears refractory to TCAs.

There is also support for some analgesic combinations in selected neuropathic pain conditions.[94]

### Fibromyalgia

In fibromyalgia, the most effective TCA appears to be amitriptyline (number needed to treat [NNT] 4.9).[249,266]

### In practice

Amitriptyline probably provides very good pain relief to some patients with neuropathic pain or fibromyalgia, but in a minority; amitriptyline will not work for most people. When initiating a therapeutic trial, start at the lowest recommended dose (eg amitriptyline 5–10 mg at night) and assess the patient for benefit and harm at one week.[100] If needed, increase the dose slowly to minimise adverse effects; the maximum dose is approximately 75–100 mg at night.

In older patients, TCAs should be used with caution. Medications with anticholinergic activity increases risk of cognitive impairment, risk of falls and even mortality.[267,268]

## 5.2.2 Serotonin noradrenaline reuptake inhibitors

### Musculoskeletal pain

Duloxetine is a recommended treatment in updated guidelines for osteoarthritis.[269] It is as effective as other first-line treatments (eg NSAIDs) for pain and disability of osteoarthritis.[270,271] Duloxetine appears to be well tolerated in older patients with osteoarthritis pain (of the knee).[270]

### Neuropathic pain

There is evidence that some antidepressants, in particular duloxetine and venlafaxine, may be effective first-line treatments for neuropathic pain, including diabetic polyneuropathy.[96,255,256,263] Duloxetine has been shown to be effective and safe for the treatment of painful diabetic peripheral neuropathy in older patients.[272]

Chemotherapy-induced peripheral neuropathy (CIPN) is poorly understood and is resistant to treatment. However, duloxetine (30 mg titrated to 60 mg/day over five weeks) has resulted in a modest reduction in pain severity relative to placebo.[273] Additional benefits included reduced numbness and tingling of the feet, and improved quality of life.[273]

### Fibromyalgia

The serotonin noradrenaline reuptake inhibitor (SNRI) duloxetine is effective in reducing pain and improving quality of life in fibromyalgia.[249,274] The NNT is approximately six.[256,275] However, it is not effective at improving sleep or fatigue.[274]

### In practice

SNRIs are regarded as a first-line therapy for managing neuropathic pain.[96] The NNT is approximately seven for 50% pain relief.[96] When initiating a therapeutic trial, start at the lowest recommended dose (eg duloxetine 30 mg) and assess the patient for benefit and harm at one week. If insufficient but partial pain relief is achieved, increase the dose and reassess within one week; this may be repeated. Modest reduction in pain severity may be achieved with duloxetine dose titrated to 60 mg/day over five weeks. Duloxetine 60–120 mg/day provides analgesia for diabetic neuropathy, with lower efficacy for fibromyalgia.

Use the lowest individualised effective dose to minimise adverse effects, the most common of which is intolerable drowsiness. If the benefit–harm ratio is unacceptable, consider stopping the drug.

### 5.2.3 Selective serotonin reuptake inhibitors

There is only limited evidence for the effectiveness of selective serotonin reuptake inhibitors (SSRIs) in neuropathic pain.[262]

## 5.3 Anticonvulsants

### 5.3.1 Alpha-2-delta ligands (gabapentin and pregabalin)

Gabapentin and pregabalin are commonly used in pain management. Initially classified as membrane stabilisers, recent evidence indicates they are more correctly classified as anticonvulsants.

#### Neuropathic pain

Gabapentin and pregabalin are recommended for use in neuropathic pain and are proposed as first-line treatments.[96] In general practice settings, evidence to support the use of gabapentinoids in treatment of neuropathic pain is varied.

Some analyses found significant benefit with use of gabapentin and pregabalin in chronic neuropathic pain (eg diabetic polyneuropathy, post-herpetic neuralgia, central neuropathic pain)[276–279] and neuropathic pain caused by traumatic or post-surgical nerve injury.[280] However, other analyses suggest that only a minority of people achieved acceptably good pain relief with either drug, benefits of treatment came with a high risk of adverse events,[276] and that the evidence base is weak due to the small magnitude of clinically meaningful effects and the high risk of bias in the RCTs.

#### Fibromyalgia

Gabapentin and pregabalin have shown effectiveness in relieving fibromyalgia pain.[276,281]

#### In practice

Anticonvulsant agents are regarded as one of the main first-line approaches toward management of chronic neuropathic pain. The NNT ranges from four to 10 for the important outcome of reduction of pain intensity by 50% or more.[96,276] Some studies suggest the NNT is greater than 10.[100]

When initiating a therapeutic trial, start at the lowest recommended dose (eg pregabalin 25 mg at night or twice daily) and assess the patient for benefit and harm at one week.[100] If insufficient but partial pain relief is achieved, increase the dose (eg pregabalin can be increased by 25–75 mg per day on a weekly basis) and reassess within one week.[100] Success is either achieved or not within the first two weeks or so of treatment; it tends to last when achieved.[98,99,221] If functionally meaningful benefit is absent during reassessment, stop the drug and try alternative approaches.[100] The most common side effect is intolerable drowsiness.

The dependence, abuse and misuse potential for gabapentinoids is increasingly being reported,[282] but appears to be limited to susceptible populations (eg recreational drug users).[283] Physicians considering prescribing gabapentinoids for pain should carefully evaluate for a possible previous history of SUDs, while being able to promptly identify signs of problematic use of pregabalin or gabapentin and provide possible assistance in tapering off the medication.[284]

## 5.3.2 Other anticonvulsants

Carbamazepine is the first-line agent for trigeminal neuralgia as it is supported by good evidence; however, the evidence for other chronic neuropathic pain is less strong.[268] Valproate may reduce pain in diabetic polyneuropathy based on very small RCTs of poor quality[285] but otherwise lacks evidence support.

Lamotrigine has shown no analgesic benefit in neuropathic pain in large, high-quality, long-duration RCTs.[276]

**Table 7. Adjuvant dosing suggestions for neuropathic pain management[94]**

| Agent | Starting dose and titration | Usual maintenance dose | Comments |
|---|---|---|---|
| **Tricyclic antidepressants** | | | |
| Amitriptyline, nortriptyline, desipramine | 10–25 mg/day; increase weekly by 10 mg/day | 10–100 mg/day | Amitriptyline more likely to produce drowsiness and anticholinergic side effects; contraindicated in patients with glaucoma, symptomatic prostatism and significant cardiovascular disease |
| **Serotonin noradrenaline reuptake inhibitors** | | | |
| Duloxetine | 30 mg/day; increase weekly by 30 mg/day | 60–120 mg/day | Contraindicated in patients with glaucoma |
| Venlafaxine | 37.5 mg/day; increase weekly by 37.5 mg/day | 150–225 mg/day | Dosage adjustments required in renal failure |
| **Anticonvulsants** | | | |
| Pregabalin | 25–50 mg/day; increase weekly by 25–50 mg/day | 150–300 mg twice daily | Similar adjustments in renal failure |
| Gabapentin | 100–300 mg/day; increase weekly by 100–300 mg/day | 300–1200 mg three times daily | Dosage adjustments required in renal failure and in elderly patients |

Source: Moulin D, Boulanger A, Clark AJ, et al. Pharmacological management of chronic neuropathic pain: Revised consensus statement from the Canadian Pain Society. Pain Res Manag 2014;19(6):328–35.

# 6. Overview of opioid analgesics

## 6.1 The challenge of putting evidence into practice

There are significant difficulties translating evidence from clinical pain trials into pain management in practice. This is not only because of issues around the number, quality, bias, duration and construction of studies,[90,96,286] but also because pain is a subjective experience influenced by a complex range of factors.

Additionally, labels such as CNCP do not just describe one condition, but a variety of conditions with diverse aetiologies, for which the evidence for therapeutic impact varies. Patients with the same condition will have unique pain experiences and respond differently to therapeutic interventions.

No analgesic drug works well in all patients. Most analgesics work well in a small proportion of patients. There is often a strong placebo (contextual) effect. Pain relief from therapeutic interventions is not normally distributed but is usually bimodal, being either very good (above 50%) or poor (below 15%).[287–289] Hence, using averages is unhelpful and misleading because few (if any) patients experience 'average' pain relief and it tells us nothing about how many patients will experience clinically useful analgesia.[221]

Clinical trials designed for regulatory purposes consider single interventions and fixed dose regimens, which may exacerbate adverse events and withdrawals, resulting in higher failure rates.[221] For example:

- failure rates for NSAIDs are ≥70% in osteoarthritis, ≥80% in chronic low back pain and 58–72% in ankylosing spondylitis[221]
- for neuropathic conditions, antidepressants and anticonvulsants have failure rates of ≥70% in painful diabetic neuropathy and post-herpetic neuralgia, and ≥87% in fibromyalgia.[221]

This does not reflect the clinical reality of choosing options and individualising doses. For example, about half of osteoarthritis patients with moderate or severe pain on treatment had a significant (30%) reduction in pain intensity when switched to another NSAID.[290]

On review of pain trial studies, it was noted that patient response distributions are U-shaped, not Gaussian, making average values inappropriate. In fact, the 'average pain score' data may mislead. Since 2011, the editors of the Cochrane Pain, Palliative and Supportive Care Systematic Review Group have established new criteria for examining evidence in pain.[291] It is now standard to measure 'responder' analyses; reporting the proportion of patients achieving outcomes that patients consider worthwhile[221] (that is, the proportion of patients who experience at least 30–50% pain reduction).

A minority of patients achieve very large reductions in pain (responders) whereas the majority achieve little relief (non-responders).[292] Individual patient analyses for chronic pain interventions have shown that people who respond also experience improvements in fatigue, depression, and sleep interference.[53,293]

It is standard for patients to delegate 'at least 50% pain reduction' as a successful outcome. It is the minimum outcome that patients want,[293] and may be associated with restoration of function, work, and quality of life lost with chronic pain.[29] Clinically, this has major implications for practice. Use of responder analysis changes judgement of benefit and risk and suggests that classical trials in pain using 'averages' may underestimate efficacy.[221]

Responder analysis also supports clinical practice focus on individual responses to therapy. It enables trialling numerous treatment options to achieve pain relief for the individual.[221] Similarly, non-responders should stop treatment that does not work.

The evidence of failure for paracetamol[295] and NSAIDs[296,297] in musculoskeletal pain and the poor efficacy for opioids, anticonvulsants (gabapentin, pregabalin) and antidepressants for neuropathic pains[100] need to be reconsidered in the light of responders and non-responders. Evidence about a single intervention needs to be considered with individual patient circumstances, tempered with wisdom and experience to be used sensibly in clinical setting.[286]

It is with these caveats in mind that evidence of effect of pain medications in chronic pain should be considered.

# 6.2 Summary of evidence for use of opioids for chronic non-cancer pain

The efficacy of opioid therapy in acute pain is supported by strong evidence from RCTs[5,7] and by systematic reviews in cancer pain,[298,299] palliative care[300] and opioid dependence.[301]

CNCP is very different. It is not a diagnosis, but a group of entities with various aetiologies. The pathophysiologic descriptors of these aetiologies are still changing. Studies examining chronic pain often have methodological weaknesses that make interpretation difficult, and transfer into clinical practice requires care.

The evidence on long-term opioid therapy for chronic pain outside of end-of-life care remains limited; however, this does not mean there is no evidence to guide care.

## 6.2.1 Evidence in different chronic pain conditions

### Musculoskeletal pain

Musculoskeletal conditions account for a large proportion of general practice opioid prescriptions.[302] In trials with at least 12 weeks' duration of opioids for managing osteoarthritis, there is:

- fair evidence for tramadol[303]
- limited evidence for transdermal buprenorphine[303] – it has been shown to be effective and well tolerated (with analgesic effects similar to tramadol)[304]
- limited evidence for tapentadol for arthritic pain.[303,305]

Reviews of opioid therapy in chronic low back pain provide some support for short-term use, but evidence beyond three months is lacking.[306,307] In trials with at least 12 weeks' duration of opioids for managing chronic low back pain, there is some evidence for transdermal buprenorphine,[308] tapentadol[305] and tramadol/paracetamol combinations.[309–311]

Caution should be used in extrapolating evidence from short-term trials into longer-term care. Analysis of open-label extension trials provides some support for sustained opioid effect, but in only 25% of patients originally enrolled.[312] The harms (abuse of prescribed opioids, mortality) of long-term opioid therapy in clinical practice are underestimated by long-term extension studies, probably because patients with major medical diseases and mental disorders were excluded.[312]

### Neuropathic pain

Several guidelines support opioid use in neuropathic pain, but not as a first-line treatment. When first-line medications fail or provide inadequate pain relief, tramadol or a conventional opioid analgesic may be useful as a second-line or third-line treatment.[94,96]

For management of neuropathic pain:

- tramadol has weak GRADE recommendations for its use; generally it is considered a second-line treatment because of safety and tolerability.[96] The tramadol NNT for 50% pain reduction is approximately five[96]
- strong opioids, particularly oxycodone and morphine, have weak GRADE recommendations for use and are recommended as third-line treatments mainly because of safety concerns.[96] The oxycodone NNT for 50% pain reduction is approximately four.[96] Other reviews are less favourable for oxycodone and report a moderate benefit (at least 30% pain relief) NNT at 5.7.[313]

The NNT for benefit in opioids appears similar to other drugs (eg antidepressants, anticonvulsants) used in painful neuropathies such as diabetic neuropathy, post-herpetic neuralgia, peripheral nerve injury, HIV neuropathy, central pain, trigeminal neuralgia and mixed neuropathic pain. The NNT for these non-opioid medications range from around four to eight. Continual critical appraisal of all classes of medication used in long-term pain management is warranted.

Combination therapies are common though few are studied. One meta-analysis demonstrated modest superiority of gabapentin plus opioid versus gabapentin alone, although the combination produced significantly more dropouts due to accentuated side effects related to combination treatments.[314]

## Summary

There is limited evidence for opioids for management of CNCP and insufficient evidence to determine long-term benefits. For well-selected patients with no history of SUDs, proper management with opioids can contribute to long-term pain relief.[116] However, long-term opioid treatment (≥26 weeks) benefits only about 25% of patients.[117] Continuation of opioid therapy is indicated if documentation clearly supports that the opioid results in improvement of existing limitations of pain and functionality,[101] balanced against the adverse effects of the opioid therapy.

**Table 8. Example dosing suggestions for neuropathic pain management[94]**

| Agent (controlled-release [CR] opioid analgesics) | Starting dose and dose interval | Usual maintenance/ maximal dose | Comments |
|---|---|---|---|
| Morphine | 10 mg every 12 hours | 30–50 mg every 12 hours | Constipation requires concurrent bowel regimen; monitor for addiction |
| Oxycodone | 10 mg every 8–12 hours | 10–40 mg every 12 hours | Constipation requires concurrent bowel regimen; monitor for addiction |
| Tramadol | 50 mg/day; increase weekly by 50 mg/day | 100–400 mg daily (CR) | May lower seizure threshold; use with caution in patients with epilepsy. Be aware of the (low) risk of serotonin syndrome when co-prescribed with antidepressants |

Source: Moulin D, Boulanger A, Clark AJ, et al. Pharmacological management of chronic neuropathic pain: Revised consensus statement from the Canadian Pain Society. Pain Res Manag 2014;19(6):328–35.

# 6.3 Specific opioids

Presented in alphabetical order.

**Table 9. Therapeutic Goods Administration approved indications**

| Drug | Indication |
|---|---|
| Buprenorphine | Moderate to severe pain<br>Opioid replacement therapy (ORT) |
| Codeine | Mild to moderate pain |
| Fentanyl | Moderate to severe acute or chronic pain |
| Hydromorphone | Moderate to severe pain |
| Methadone | ORT<br>Severe pain requiring opioids |
| Morphine | Moderate to severe pain |
| Oxycodone | Moderate to severe pain |
| Tapentadol | Moderate to severe chronic pain |
| Tramadol | Moderate to severe pain |

Adapted from the Pharmaceutical Benefits Scheme (PBS) Drug Utilisation Sub-committee (DUSC). Opioid analgesics: Overview. Canberra: Commonwealth of Australia, 2014.

## 6.3.1 Buprenorphine

Buprenorphine is a partial agonist at mu opioid receptors and an antagonist at delta and kappa receptors. It is typically used for analgesia (in low-dose patch formulation) and in ORT, where sublingual formulations are usually used.

### Musculoskeletal pain

There is limited evidence regarding buprenorphine for CNCP due to a lack of high-quality RCTs.[303] However, transdermal buprenorphine for osteoarthritis has been shown to be effective and well tolerated, with analgesic effects similar to tramadol.[304]

### Neuropathic pain

Case reports suggest that buprenorphine is effective in peripheral[315,316] and central neuropathic pain in the clinical setting.[317] However, large trials are lacking and currently there is not enough evidence to support or dispute efficacy of buprenorphine in any neuropathic pain condition.[318]

### Addiction medicine

Buprenorphine is listed for use in ORT (as Section100 [S100]).

### In practice

Buprenorphine is PBS listed for chronic severe pain and ORT.

Transdermal patches (used for pain, not ORT) generally provide a week of analgesia. Occasionally, patients complain that there is release of the drug from the transdermal patch for only six, or rarely five, days. In these instances, the patches may need to be changed more frequently than weekly.

Buprenorphine can be safely used in patients with renal impairment and has less immunosuppressive effect than pure mu-opioid agonists.[319]

As long as sedative medication is not given concurrently, the risk of respiratory depression with buprenorphine is low compared to morphine, methadone, hydromorphone and fentanyl.[320] There is a ceiling effect for respiratory depression but not for analgesia.[321] If buprenorphine-induced respiratory depression occurs it may be completely reversed with naloxone,[319] although higher than usual doses and a longer duration infusion of naloxone are required.[322]

Withdrawal symptoms may occur if buprenorphine is ceased after long-term treatment; however, these symptoms are milder and more delayed in onset (≥72 hours) compared with other opioids.[320]

Buprenorphine binds strongly to the mu receptor site, but does not fully activate it.[323] Therefore, if buprenorphine is combined with pure mu agonists (eg morphine, fentanyl), interactions may occur. For example, if a pure mu agonist is given to a person on maintenance buprenorphine it may be less effective. Conversely, buprenorphine could theoretically cause a withdrawal reaction if given to a patient taking longer-term opioid (mu) therapy.[323]

Antagonism of response to pure mu agonists (precipitated withdrawal) can occur with buprenorphine but it has only been demonstrated at buprenorphine doses exceeding the ranges used for analgesia (eg at dosages for ORT). In practice, these drug interactions are unlikely.

## 6.3.2 Codeine

Codeine is a weak mu receptor agonist (200-fold weaker affinity than morphine) and its analgesic action depends on the metabolism of about 10% of the dose to morphine, via CYP2D6.[324,325] Ultrarapid metabolisers have significantly higher levels of morphine and morphine metabolites after the same dose of codeine.[326] Poor metabolisers do not produce any morphine or gain any analgesic effect.

Codeine is subject to misuse and dependence, and is the commonest prescription opioid associated with fatal overdoses in Victoria.[327] Rates of misuse average between 21% and 29%, and dependence average between 8% and 12%.[327]

### Musculoskeletal pain

Codeine is commonly used in combination with other minor analgesics (eg paracetamol, ibuprofen). There is high-quality evidence that combination codeine medicines provide clinically important pain relief in the immediate term, but this is mostly in acute pain.[16]

### In practice

Codeine is classified as a weak opioid. It is listed by the PBS for mild to moderate pain. There is no role for codeine in chronic pain.

A single 60 mg dose provides good analgesia to few adults: 12 patients need to be treated for one to achieve a 50% reduction in postoperative pain.[328] OTC preparations containing low doses of 8–15 mg codeine phosphate are considered sub-therapeutic.

Combining codeine with non-opioid analgesics provides limited additional analgesic benefit: seven patients need to be treated with ibuprofen 400 mg/codeine 25.6–60 mg for one to obtain at least a 50% reduction in postoperative pain when compared to treatment with ibuprofen 400 mg alone.[328,329]

Given the variability in response and risk of harm, use of codeine should be closely monitored.

## 6.3.3 Dextropropoxyphene

In November 2011, the TGA decided to remove the registration of dextropropoxyphene in Australia.[330] It was withdrawn from the Food and Drug Administration (FDA) in the US due to risks of QT-interval prolongation and possibility of Torsades de Pointes (TdP) and cardiogenic death.

Oral dextropropoxyphene alone is a poorly effective analgesic.[331] In combination with paracetamol, it also provides little benefit above paracetamol alone.[332]

### In practice

Dextropropoxyphene has now been limited to authorised users for previous users only. To prescribe this medication, GPs need to:

- be aware that the medicine is only approved for use in patients not able to be adequately treated with other mild pain killers
- have considered the contraindications for the medicine outlined in the product information and have explained them to the patient at the time of prescribing
- have considered any recent changes to the patient's clinical presentation or biochemical status
- have warned the patient at the time of prescribing about appropriate use of the medicine
- be satisfied at the time of prescribing that the patient's history does not indicate that the patient is at risk of accidental or intentional self-harm.

The conditions also require that a signed Prescriber Confirmation form is presented to the pharmacist dispensing these medicines before supplying them to the patient every time a patient presents for a prescription.

## 6.3.4 Fentanyl

Fentanyl is a highly potent opioid, which is active at the mu receptor. It is metabolised almost exclusively in the liver to minimally active metabolites. This makes it particularly useful in renal failure: <10% of unmetabolised fentanyl is renally excreted.[333]

It is available as transdermal patches, oral transmucosal lozenges or lollipops and injectable preparations. The transdermal system offers an excellent option for long-term treatment of cancer pain, **but the RACGP believes it is not suitable for CNCP**. A 25 ug/hour fentanyl patch is equivalent to approximately 90 mg of oral morphine per day. Oral transmucosal fentanyl rapidly achieves high plasma concentrations and is indicated to treat breakthrough pain in cancer patients who are not opioid naïve.[333]

Fentanyl-related mortality is currently relatively low in Australia compared to the US and parts of Europe. However, fentanyl misuse is on the rise in Australia with a large proportion of these deaths occurring among at-risk groups who inject drugs.[334] Because of the misuse potential, this drug should be used only as indicated. It has known diversional potential, extremely high street value and risk of misuse.

### In practice

Fentanyl is PBS listed for severe disabling pain and is usually used in cancer care or in acute hospital settings.

In the opioid-naïve patient, there is a significant risk of toxicity and overdose. Fentanyl patches are not suitable to be used as the initial agent in the management of pain for opioid-naïve patients due to high morphine-equivalent doses. Fentanyl should only be used in the case of cancer pain when all other options have been exhausted.

Be aware that local heat (eg hydrotherapy pool) may increase absorption from the patch.

## 6.3.5 Hydromorphone

Hydromorphone is an effective strong opioid acting as a mu receptor agonist. It is approximately five times as potent as morphine and provides slightly better clinical analgesia than morphine, but has similar adverse effects.[335,336] The main metabolite of hydromorphone is hydromorphone-3-glucuronide (H3G), which is dependent on the kidneys for excretion, has no analgesic action and can lead to dose-dependent neurotoxic effects.[337]

It is available as solution for injection, oral liquid and tablets. It also has extremely high potential for misuse and high street value for those who divert this drug.

### In practice

Hydromorphone is PBS listed for severe disabling pain, but in practice is usually restricted to malignant pain, or patients undergoing dialysis. It is not suitable to be used as the initial agent in the management of pain for opioid-naïve patients.

## 6.3.6 Methadone

Methadone is a synthetic opioid acting as an agonist at the mu receptor with additional ketamine-like antagonism at the N-methyl-D-aspartate receptor. It is commonly used for the maintenance treatment of patients with an addiction to opioids and in patients with chronic pain.

It has good oral bioavailability (70–80%), high potency, a long duration of action and no active metabolites.[338] But it also has a long and unpredictable half-life (mean of 22 hours; range 4–190 hours), which increases the risk of accumulation.[339]

Concurrent administration of other drugs that are metabolised by the P450 enzyme system may have significant effects. P450 inducers (eg carbamazepine, rifampicin, phenytoin, St John's wort (*Hypericum perforatum*), some

antiretroviral agents) may increase methadone metabolism, which lowers methadone blood levels and leads to potential reduced efficacy or even withdrawal.[340] Use of P450 inhibitors (eg other antiretroviral agents, some SSRIs, grapefruit juice, antifungal agents) may lead to raised methadone levels, which increases risk of adverse effects or overdose.[340] Checking for drug interactions with methadone can be done online at www.opioiddruginteractions.com

### In practice

Methadone is PBS listed for severe disabling pain and for ORT (as S100). Two formulations are available in Australia. Methadone liquid is used once daily for maintenance in opioid dependent patients. Methadone tablets may be used two to four times daily to manage persistent pain.[341]

Methadone use is usually confined to specialist pain medicine areas[342] as it has complicated and unpredictable pharmacokinetics. Extreme caution must be taken when inducting a person onto an appropriate dose of methadone, with a slow titration regimen and close monitoring required. It may take up to two weeks to reach steady state levels, and drug accumulation may cause excessive sedation and high risk of overdose and death if the dose is increased rapidly.[341]

## 6.3.7 Morphine

Morphine has been the most widely used opioid in acute, persistent and cancer pain, and remains the standard against which other opioids are compared.

The main metabolites of morphine (primarily formed by hepatic glucuronidation) are morphine-6-glucuronide (M6G) and morphine-3-glucuronide (M3G). M6G is a mu opioid receptor agonist and is the main mediator of analgesia.[343] M3G has very low affinity for opioid receptors and no analgesic activity, but may be responsible for the neurotoxic symptoms such as hyperalgesia, allodynia and myoclonus, sometimes associated with high doses of morphine.[325] Both metabolites are renally eliminated.

Higher doses, older age, impaired renal function and the oral administration (due to first-pass metabolism) are associated with higher M3G and M6G concentrations and therefore with the potential risk of severe long-lasting sedation and respiratory depression.[344,345]

While the clinical significance is uncertain, morphine is the most immunosuppressive of the currently available opioids.[346,347]

There has been a decrease in morphine prescribing in Australia.[334] Prescriptions are most prevalent among older Australians.

### Musculoskeletal pain

The evidence for morphine in managing CNCP, including low back pain, is poor.[303]

### Neuropathic pain

Strong opioids including morphine have weak GRADE recommendations for use and are recommended as third line mainly because of safety concerns.[96]

### In practice

Morphine formulations are indicated by the PBS for severe disabling pain (cancer, palliative care) and chronic severe pain. Commencement doses vary according to patient selection and age.

## 6.3.8 Oxycodone

Oxycodone action appears to be mediated primarily by mu receptor agonism. Oxycodone contributes the majority of drug effect, as its metabolites, noroxycodone and oxymorphone (via CYP3A4), are only weakly active. However, oxycodone concentration may be dependent on CYP2D6 activity, resulting in ultrarapid metabolisers experiencing better analgesic effects than poor metabolisers, but also higher toxicity.[348,349]

Paradoxically, in acute postoperative pain, the *CYP2D6* genotype does not appear to influence oxycodone requirements.[350] There is an increasing use of oxycodone in the acute, hospital and perioperative settings as it has a faster onset of action than morphine, better oral bioavailability, longer duration of action, fewer concerns about metabolites and lower rate of adverse effects based on these pharmacological properties.[350–352]

Oxycodone-related deaths are currently relatively low in Australia; they are not comparable to numbers reported in the US.[334]

### Musculoskeletal pain

The evidence for oxycodone in the management of CNCP is poor.[303]

### Neuropathic pain

Strong opioids including oxycodone have weak GRADE recommendations for use and are recommended as third line mainly because of safety concerns.[96]

### In practice

Oxycodone is PBS listed for severe disabling pain and chronic severe pain. It is particularly popular in hospital and acute pain settings. Care should be used in rehabilitation settings to minimise chronic use.

Care should also be taken by GPs continuing to prescribe oxycodone in the community post discharge from the hospital setting. All patients should have plans to be weaned off their opioid analgesics post discharge.

The use of oxycodone is increasing rapidly and addiction specialists report that it is often a drug of choice for misuse. A combination of oxycodone with naloxone has recently been released in Australia. This combination substantially reduces the chance of constipation,[353] but the risks of misuse and diversion still exist.

Note that St John's wort (*H. perforatum*) induces metabolism of oxycodone, significantly reducing its plasma concentrations and efficacy.[354]

## 6.3.9 Pethidine

Pethidine is a synthetic opioid active at the mu receptor. IM pethidine has been widely used in Australia for a range of pain problems. Its use is decreasing because of multiple disadvantages compared to other opioids. Repeated dosing or renal failure leads to accumulation of its active metabolite (norpethidine), which is associated with neuroexcitatory effects that range from nervousness to tremors, twitches, multifocal myoclonus and seizures.[355]

When used parenterally, pethidine does not provide better analgesia than morphine, but does induce more nausea and vomiting than morphine.[356]

### In practice

Use of pethidine is discouraged in favour of other opioids.[357,358]

It has high addiction potential and is not recommended for the treatment of persistent pain.

Pethidine is no longer indicated for the treatment of migraines.

## 6.3.10 Tapentadol

Tapentadol is a combined weak mu agonist and noradrenaline reuptake inhibitor (acting on descending pain inhibition pathways) with no active metabolites.[359–361] In a number of chronic pain conditions, tapentadol shows efficacy that is comparable or better than conventional opioids but with reduced rates of gastrointestinal adverse effects (eg nausea, vomiting, constipation), which results in less treatment discontinuation.[362]

At doses up to the maximum recommended 500 mg/day, tapentadol has no effect on heart rate or blood pressure due to noradrenaline reuptake inhibition, even in patients with hypertension and/or on antihypertensives.[363] However, as it is metabolised by the liver, impaired hepatic function may require dose adjustment.[364]

Despite widespread use over several years in the US and Europe, there are only two reported cases of an overdose death.[365] Although it is a controlled medicine in all countries, tapentadol shows a lower rate of misuse and diversion than oxycodone and hydrocodone and a rate comparable to tramadol.[366,367]

There are limited data to support a role for tapentadol in cancer pain.[368]

### Musculoskeletal pain

Currently, relatively few RCTs have studied tapentadol. There is evidence of benefit in osteoarthritis, low back pain and postoperative pain.[305,369–371] Three randomised trials studying tapentadol for managing chronic pain of osteoarthritis and low back found that 32% of patients received greater than 50% pain relief.[303]

### Neuropathic pain

Due to effect of noradrenaline uptake inhibition on descending pathways of pain, tapentadol modulates increased conditioned pain seen with neuropathic pain.[372] This effect has been confirmed in diabetic neuropathy.[360]

### In practice

Tapentadol is PBS listed for chronic severe pain.

Start at low dose 50 mg and titrate the dose according to response increase: every three days, increase the dose by 50 mg for each twice-daily dose until adequate analgesia or the 50 mg OME dose of 125 mg/day is reached.

## 6.3.11 Tramadol

Tramadol acts as both a weak opioid agonist and as a serotonin and noradrenaline reuptake inhibitor. Due to the combined effects, it is commonly referred to as an atypical centrally acting analgesic.[361,373]

Tramadol is metabolised by CYP2D6 to an active metabolite, O-desmethyltramadol (M1), which is a more potent mu opioid receptor agonist than the parent drug.[374] Hence, patients who are poor metabolisers receive less analgesic effect from tramadol.[375]

The adverse-effect profile of tramadol is different from other opioids. The most common side effects are nausea and vomiting, which occur at rates similar to morphine.[376,377] However, tramadol has less effect on gastrointestinal motor function than morphine.[377,378] It causes less respiratory depression than other opioids at equianalgesic doses.[379,380] Tramadol does not increase the incidence of seizures compared with other analgesic agents,[381,382] although there is a risk of inducing serotonin toxicity when tramadol is combined with other serotonergic medicines, in particular SSRIs.[383]

Tramadol has a lower potential for misuse than conventional opioids.[384]

### Musculoskeletal pain

There is fair evidence for tramadol in managing osteoarthritis.[303]

### Neuropathic pain

Tramadol has a weak GRADE recommendation for use in neuropathic pain,[96] and is regarded as generally second line because due to tolerability and safety.[96,385]

### In practice

Tramadol is listed on the PBS for acute or chronic pain not responding to aspirin and/or paracetamol; short-term treatment of acute pain.

Side effects often limit use, but tramadol can be useful if tolerated.

# 6.4 Opioid formulations and doses

## 6.4.1 Formulations

The practical usefulness of opioids is related to the available formulations (Table 10).

**Table 10. Opioid formulation[386]**

| Drug | Oral | | | Injection | Other |
|---|---|---|---|---|---|
| | Conventional | Controlled release | Sublingual or oromucosal | | |
| **Buprenorphine** | | | Tablet | IV, IM | Patch |
| **Codeine** | Tablet, liquid | | | | |
| **Dextropropoxyphene** | Capsule | | | | |
| **Fentanyl** | | | Lozenge | IV, SC, epidural, intrathecal | Intranasal solution, patch |
| **Hydromorphone** | Tablet, liquid | Tablet | | IV, SC, IM | |
| **Methadone** | Tablet, liquid | | | SC, IM | |
| **Morphine** | Tablet, liquid | Tablet, capsule, liquid | | IV, SC, IM, epidural, intrathecal | |
| **Oxycodone** | Tablet, capsule, liquid | Tablet | | IV, SC | Suppository |
| **Pethidine** | | | | IV, SC, IM, epidural | |
| **Tapentadol** | | Tablet | | | |
| **Tramadol** | Capsule, liquid | Tablet | | IV, IM | |

Reproduced from the *Australian medicines handbook* 2015. Adelaide: Australian Medicines Handbook Pty Ltd, 2015.

## 6.4.2 Approximate equivalence doses

Oral morphine is the standard that other opioids are measured against. Full opioid agonists given in equianalgesic doses produce the same analgesic effect.[387] However, accurate determination of equianalgesic doses is difficult due to individual variability in pharmacokinetics and dynamics.[147]

There are several published tables providing approximate equianalgesic doses. These are typically based on single-dose studies in opioid-naïve subjects and may not be as relevant when conversions are made after repeated doses of an opioid.[337] They also do not take into account incomplete cross-tolerance and patient-specific factors.[342]

Converting to methadone requires special caution. Regardless of how much other opioid the patient is being prescribed, commence methadone at low doses in accordance with the *National guidelines for medication-assisted treatment for opioid dependence* (available at www.nationaldrugstrategy.gov.au/internet/drugstrategy/Publishing.nsf/content/ng-mat-op-dep) or in consultation with pain or addiction specialists.

### Box 13. Useful tools for calculating equivalent doses

- ANZCA's Faculty of Pain Medicine has created a free opioid calculator smartphone app available at http://fpm.anzca.edu.au/front-page-news/free-opioid-calculator-app
- The Centre for Palliative Care Research and Education has developed the GP Pain Help app and website available at www.gppainhelp.com/Title.html

## 6.4.3 Commencing and increasing dosage

Starting doses are a guide only and may vary according to the clinical situation, condition of the patient and previous analgesic requirements. For example, older patients generally require lower opioid doses.[388]

At each review, assess pain intensity, cardiorespiratory status, level of sedation and other adverse effects. Titrate dose according to response, sedation score (an early indicator of respiratory depression) and respiratory rate. Use small dose increments as the dose required may vary more than 10-fold between patients of similar age, irrespective of weight.[388]

Adjust the dose of controlled-release (CR) opioids, not the frequency of administration. However, if increasing the dose fails, it may occasionally be appropriate to administer doses more frequently for patients with pain that regularly occurs shortly before the next dose is due.[388]

## 6.4.4 Opioid ceiling doses

Use caution when prescribing opioids at any dosage. Many harms are dose related, so aim for the lowest effective dose then carefully reassess for evidence of individual benefits and risks, especially when increasing dosage to 50 mg OME or more per day. GPs must be able to justify a decision to titrate dosage to 100 mg or more OME per day and should avoid increasing dosage to 100 mg or more OME per day without specialist involvement.[8] Higher opioid doses may be acceptable in cancer-related pain.

**Table 11. Opioid doses[5,8,92]**

| | |
|---|---|
| Low dose | ≤50 mg OME |
| Moderate dose | 51–100 mg OME |
| High dose | ≥101 mg OME |

# 6.5 Tolerance and opioid-induced hyperalgesia

Tolerance is a predictable state of adaption in which exposure to a drug induces changes that result in diminution of one or more of the drug's effects over time.[389] The patient become 'desensitised' to the drug and increased doses are then needed to get the same effect.

The decrease in the effectiveness of opioid analgesia has traditionally been attributed to opioid tolerance (a desensitisation of anti-nociceptive pathways to opioids). However, it is now known that administration of opioids can also result in opioid-induced hyperalgesia (OIH), which is a sensitisation of pro-nociceptive pathways leading to pain hypersensitivity. Both tolerance and OIH can significantly reduce the analgesic effect of opioids.[390,391]

The predictable and physiological decrease in the effect of a drug over time may be referred to as 'pharmacological tolerance'. 'Apparent tolerance' occurs when both tolerance and OIH contribute to a decrease in the effectiveness of opioids.[392,393]

There is some evidence that administration of 'commonly used' dosages of oral opioids does not result in abnormal pain sensitivity.[394]

In an individual patient displaying decreased effectiveness of opioid therapy, it can be impossible to determine whether tolerance or OIH is causing a reduction in pain control, creating a management dilemma: inadequate pain relief due to tolerance may improve with opioid dose escalation, while improvements in analgesia in the presence of OIH may follow a reduction in opioid dose.[392] The only reasonable action in these circumstances is to reduce opioid doses.

Tolerance also occurs to some of the adverse effects of opioids. Rapid tolerance may develop to sedation, cognitive effects, nausea and respiratory depression. However, there is little, if any, change in miosis or constipation.[392]

## 6.6 Dependence and withdrawal

'Dependence' has historically been defined in pharmacological terms: a time-limited state that develops during chronic drug treatment in which cessation elicits an abstinence reaction (withdrawal) and is reversed by renewed administration of the drug.[157]

Opioid withdrawal syndrome is characterised by signs and symptoms of sympathetic stimulation due to decreased sympathetic antagonism by opioids (Table 12).[157] Symptoms start two to three half-lives after the last dose of opioid. For example, oxycodone has a half-life of 3–4 hours: symptoms would start after 6–12 hours, peak at approximately 48–72 hours, and resolve within 7–14 days.[157] Timelines and symptoms vary depending on the duration of action,[19] specific dose, speed of taper, and duration of use.[157]

Withdrawal can be minimised by gradual reduction of opioid use. Where it does occur, unless a patient has significant comorbidity or is otherwise medically unstable, withdrawal is not life threatening, although it may be very distressing.[19,157] Acute withdrawal (when opioids are stopped suddenly, or an antagonist such as naloxone or naltrexone is administered) should be treated by reintroducing opioids or by IV fluids, glucose, and adrenergic-blocking drugs. Clonidine is useful in this situation.[157] Reassurance and comfort measures may also be required.[157]

**Table 12. Opioid withdrawal syndrome signs and symptoms[157]**

| | |
|---|---|
| Anxiety (which can also enhance other symptoms) | Anorexia |
| Hypertension | Dizziness |
| Tachycardia | Dysphoria |
| Restlessness | Hot flashes |
| Mydriasis | Shivering |
| Diaphoresis | Myalgias or arthralgias |
| Tremor | Rhinorrhoea, sneezing |
| Piloerection | Lacrimation |
| Nausea, abdominal cramps and diarrhoea | Insomnia |
| | Yawning |

A secondary abstinence syndrome, including general malaise, fatigue, decreased wellbeing, poor tolerance to stress and craving for opioids, has been described in patients with SUD for up to six months,[157] but is uncommon in other patients.[388]

Adapted from Berna C, Kulich RJ, Rathmell JP. Tapering long-term opioid therapy in chronic noncancer pain: Evidence and recommendations for everyday practice. Mayo Clin Proc 2015;90(6):828–42.

# 6.7 Harms associated with opioids

## 6.7.1 Adverse effects

Common opioid-related adverse effects are sedation, pruritus, nausea, vomiting, slowing of gastrointestinal function and urinary retention.[395–397] Uncommonly, opioids (methadone, oxycodone) are associated with prolonged QT-interval with a risk of TdP and cardiac arrest.[398,399] These effects are dose related.

**Table 13. Adverse effects of opioids**

| Side effect | Notes |
|---|---|
| **Common** | |
| Nausea and vomiting | Commonly occur in the first few days and may subside with continued use |
| Drowsiness | Commonly occur in the first few days and may subside with continued use. This is very dependent on dose, context and other drugs. |
| Itching | Can become intolerable and force discontinuation of the medication. Once it occurs, it tends to occur with all opioids |
| Urinary retention | Generally caused by either obstruction or reduced detrusor muscle function. May be painful and distressing to the patient. Management includes catheterisation |
| Constipation | Should be managed with aperients and diet. A combined formulation of CR oxycodone and naloxone has been studied in patients with CNCP, producing similar analgesic efficacy but less bowel dysfunction[400] |
| Cognitive impairment | During periods of dosage increase there will be cognitive impairment. Patients should not drive during periods of dose escalation or when they feel cognitively impaired. This generally occurs for a few days after each dose increase. Where polypharmacy occurs (such as in older patients), there is a greater risk of cognitive impairment which can be sustained |
| Dentition | There is an increased risk of dental caries in those taking opioids, at least partly due to reduced excretion of saliva. Patients on long-term opioids should be warned to be meticulous in their dental care |
| **Less common** | |
| Weight gain | |
| Weight loss | |
| Respiratory depression | This is generally only a problem with too-rapid dose increase, when taking other drugs that can have a depressant effect, and in patients with existing respiratory compromise. Be particularly careful with rapid dose increases of methadone and in the morbidly obese. Patients with sleep apnoea and respiratory compromise may be at higher risk and should be carefully monitored. When possible opioid-sparing analgesia should be used |
| Hormonal/endocrine effects | These are well recognised and include reduced adrenal function, reduced sexual function and infertility. They only seem to occur in about 50% of those taking long-term potent opioids. Practitioners need to warn patients about these possibilities and seek specialist assistance if any issues arise |
| Falls | Newly prescribed opioids (alone or in combination with other medications) may trigger injurious falls (especially first two weeks). The effect lowers with duration of use and is less pronounced with increasing age (ie most common in young adults). The risk is also higher for fall from height[401] |

**Table 13. Adverse effects of opioids**

| Side effect | Notes |
|---|---|
| Fracture risk | There is an increased risk of fractures in patients taking long-term opioids. The causes are complex and include opioid-induced hypogonadism and increased risk of falls. As older persons are at increased risk of developing osteoporosis and pain, the opioids used to treat pain in this population may increase the risk of subsequent fractures. Risk is highest in the week after initial prescription and decreases over time[402–405] |
| Pregnancy | While opioids are not precluded by pregnancy, this is a specialist area and opioid prescribing for women who are, or may become pregnant, is better left to specialist services |
| Immunological effects | There are a range of immunological effects but their clinical significance, if any is unclear |
| Hyperhidrosis (excessive sweating) | |
| Xerostomia (dry mouth) | |

# 7. Patient selection for opioid therapy

GPs should be aware that certain patient groups have increased risks of harm in association with opioid use. As part of a patient selection and risk stratification approach, the following patient group attributes should be considered.

## 7.1 Opioid use in pregnancy and breastfeeding

Most drugs that are used for pain management cross the placenta. The Australian Drug Evaluation Committee (ADEC) classifies drugs according to fetal risk and notes that there are particular times of concern during pregnancy: weeks 4–10 (organogenesis), and just before delivery. Opioid analgesics taken just before delivery may cause respiratory depression in the newborn, and withdrawal effects may occur in neonates of dependent mothers.

It is always better to avoid drugs during pregnancy. If medication for constant pain relief is required during pregnancy, consultation should occur with a specialist obstetrician or pain physician.

### In practice

Prescribers should avoid initiating opioid therapy in pregnant women whenever possible. It is accepted that prescription of ORT for pregnant women with opioid related substance misuse is a harm minimisation strategy.

For pregnant women already on opioids, opioid therapy should be tapered to the lowest effective dose slowly enough to avoid withdrawal symptoms and then discontinued if possible.[78] GPs should access appropriate expertise if considering tapering opioids because of possible risk to the woman and to the fetus if withdrawal occurs.[8]

During breastfeeding, occasional doses of opioids are considered safe, but codeine should be avoided. Use repeated doses with caution, especially if the infant is premature or under four weeks of age. The infant should be monitored for sedation and other adverse effects.[157]

## 7.2 Opioid use in workers' compensation injury

Patients on workers' compensation are at risk of being prescribed high-dose opioids, because of higher levels of psychological distress, poorer surgical outcomes and protracted involvement in legal proceedings.[406]

It is well recognised that patients who are psychologically distressed after a work injury have poorer outcomes.[234,407] Therefore, as soon as distress is recognised (even at the first consultation), the patient should be referred to an appropriate health professional (commonly a psychologist) and therapeutic steps undertaken to minimise opioid use.

Evidence also shows that, where possible and appropriate, returning to work has substantial benefits in improving patient morbidity and decreasing mortality.[408] When assessing the capacity of the patient to return to work, patient self-assessment of ability is usually reliable, if it matches clinician impression. Activity is not limited to work but includes the usual activities that the patient undertakes in sport, recreation and at home.

For low back pain, patients are most at risk of developing chronic pain syndrome in the period between 8–12 weeks following the date of pain onset.[409,410] However, recovery rates are not improved by commencing a new activity program in the first 4–6 weeks after injury.[82,411]

### In practice

Clinicians and patients should be aware of the risks involved with workers' compensation patients, and focus rehabilitation on increasing function, non-pharmacological approaches and keeping opioid analgesia to a minimum.

The most important treatment modality for musculoskeletal injuries is returning to as much of the patient's usual activity as soon as possible. For cases of increased complexity multidisciplinary involvement is beneficial, including teamwork with specialists and a physiotherapist with pain management experience.

## 7.3 Prescribing opioids to patients who drive

Opioids can interfere with a complex task such as driving due to sedation; diminished reaction times, reflexes and coordination; reduced peripheral vision due to the persistent miotic effects;[412] and decreased ability to concentrate.[413]

There is little direct evidence that opioid analgesics (eg hydromorphone, morphine or oxycodone) have direct adverse effects on driving behaviour.[414] The risk of accidents appears at increased risk in the first weeks of starting opioid therapy or after increasing the dose.[413,415] This may be dose dependent.[416]

There does not appear to be evidence that any one opioid has less impact than another.[417] However, stable doses of sustained-release opioids do not appear to impair driving activity.[415,418,419]

According to Austroads, a person is not fit to hold an unconditional licence if they have an alcohol disorder or other SUD (eg substance dependence, heavy frequent alcohol or other substance use) that is likely to impair safe driving.[414,420]

The state or territory driver licensing authority may consider a conditional licence. This is subject to periodic review, taking into account the nature of the driving task and information provided by the treating doctor as to whether the following criteria are met:[420]

- The person is involved in a treatment program and has been in remission for at least three months.
- There is an absence of cognitive impairments relevant to driving.
- There is absence of end-organ effects that impact on driving.

### In practice

Each patient should be considered individually and it is ultimately the prescriber's judgement that determines opioid prescription.[421–424] Where there are concerns about a patient's ability to drive (eg high doses of opioids or opioids plus other sedative medication), a formal driving assessment may be considered.

When starting opioid therapy, patients should be advised that they are likely to be impaired and should not drive until a stable regime has been obtained for at least two weeks.

There is moderate, generally consistent evidence that driving performance of patients on long-term opioids for chronic pain may not be negatively affected by their medication.[413,425] Driving at night may be a problem due to the persistent miotic effects of opioid drugs reducing peripheral vision.[412]

# 7.4 Opioid therapy in sleep apnoea or disordered breathing

Sleep-disordered breathing describes a spectrum of disorders, including obstructive sleep apnoea (OSA). One in 15 adults has moderate or more severe OSA, experiencing partial or complete cessation of breathing many times during sleep, and around 80% of those who could benefit from treatment remain undiagnosed.[426]

Compared to people without OSA, people with OSA are at higher risk of increased sensitivity to opioid analgesia and decreased sensitivity to pain.[427] Administration of opioids may also exacerbate OSA.[428,429]

Experts in this area recommend non-opioid analgesics, and other pain management techniques should be used as either an alternative to opioids or to help limit the amount of opioid required.[430–432]

## In practice

If opioids are prescribed for patients with mild sleep-disordered breathing, careful monitoring and cautious dose titration should be used. Prescribing opioids to patients with moderate or severe sleep-disordered breathing should be avoided whenever possible to minimise risks for opioid overdose.[8,433]

The use of opioids in patients with severe untreated sleep apnoea is not recommended.[101]

# 7.5 Opioid therapy in patients aged 65 years and over

As the population ages the challenge of safe and appropriate pain management increases. Management challenges include age-related changes in physiology, increased risk of falls,[434,435] pharmacodynamics and pharmacokinetics, higher prevalence of comorbidities and concurrent medications, altered responses to pain, and difficulties with assessment of pain severity and response to treatment, including problems related to cognitive impairment.

Consider the use of non-drug strategies such as movement, exercise, physiotherapy and psychological therapies as alternatives to, or in combination with, medication.[436] Where opioids are used, consider risk assessment for falls and interventions to mitigate common risks of opioid therapy such as constipation. Also, monitor older patients for the presence of cognitive impairment.[8,436]

Despite the higher incidence of side effects with drug therapy in older people, analgesics may still be safely and effectively used if tailored for the individual patient and comorbidity and other medications are considered.[436] However, analgesics should be:[436]

- initiated one at a time using a low dose
- monitored regularly and adjusted as needed to improve efficacy and limit adverse events
- titrated slowly according to response
- used in combination where synergistic effects provide improved pain relief with fewer side effects than higher doses of a single drug.

When prescribing opioids to older adults, it is important to provide education about risky medication-related behaviours such as obtaining controlled medications from multiple prescribers and saving or stockpiling unused medications.[8]

## 7.5.1 Analgesics for older patients

In general, there is limited evidence about the use of analgesic medications in older patients. Older patients are often specifically excluded from clinical trials because of their age, comorbidities or concurrent medications.

For all patient groups, timing of medication administration and duration of action is important. Severe, episodic pain requires treatment with medicines with a rapid onset of action and short duration. However, if a patient is experiencing continuous pain, regular analgesia is the most effective, possibly using modified-release formulations.[436]

### Paracetamol

Paracetamol is recommended as a first-line therapy in older adults for mild to moderate pain. There is no evidence to support a need for dosage reduction of paracetamol in this group. Although there is emerging evidence of ineffectiveness of paracetamol in low back pain and some osteoarthritis conditions,[295] these findings are disputed.

### Non-steroidal anti-inflammatories

The use of non-selective NSAIDs is relatively contraindicated in older patients due to increased risk of gastric and renal side effects, as well as cardiovascular and cerebrovascular effects.[437] However, individual circumstance and context may make these drugs an appropriate choice. A large 2010 study of patients with arthritis (mean age 80 years) found that overall, patients on NSAIDs appear to fare better than those taking opioids: the opioid cohort showed higher rates of fracture, hospital admission and all-cause mortality with similar or higher rates of cardiovascular, renal and gastrointestinal adverse effects.[438]

Judicious use is advised particularly in older patients;[439] support with protective proton pump therapy is advised.[440]

### Adjuvant therapies – Anticonvulsants

An increase in adverse effects with pregabalin appears to be dose related rather than associated with patient age. However, the initial doses of anticonvulsant drugs should be low and increases in dose should occur slowly. The reduction in renal function that occurs with increasing age means that the elimination of gabapentin and pregabalin may be reduced and lower doses required.

Monitoring of side effects is important, particularly for somnolence and dizziness with pregabalin, but the lack of hepatic metabolism and low drug interactions makes gabapentin and pregabalin useful in older patients.

### Adjuvant therapies – Antidepressants

Caution should be exercised with TCAs as their clearance may decrease in older patients. Confusion and hypotension are more likely in this group due to increasing anticholinergic load. Lower initial doses are recommended with careful monitoring for side effects. Contraindications to TCAs include prostatic hypertrophy, narrow angle glaucoma, cardiovascular disease and impaired liver function.

Other antidepressants may be more appropriate: SNRIs (duloxetine) have shown to be effective and safe in older patients though care should be taken with poor renal function.

### Opioid therapy

Appropriate precautions must be taken when considering opioid therapy for older patients.[102] These precautions include lower starting doses, slower titration, longer dosing intervals, more frequent monitoring and tapering of benzodiazepines.[78,102] There is an increased risk of adverse effects including cognitive impairment, sedation, respiratory depression and falls.[441,442] The risk of respiratory depression is minimised by monitoring the patient for sedation and reducing the dose of opioid if this occurs.[441]

While there are large individual differences, older patients are more sensitive to opioids and dose requirement decreases progressively with age, often reduced by 50% or more. There may be fewer pharmacokinetic differences between older and younger patients with fentanyl requirements.[445,446] In patients older than 75 years, the elimination half-life of tramadol is slightly prolonged[447] and lower daily doses have been suggested.[448]

### In practice

Older patients require less opioid medication than younger patients to achieve the same degree of pain relief; harms can also occur at lower doses than they occur in younger patients.[445,446,449] However, inter-patient variability exists in all age groups and doses must be titrated to effect in all patients.

## 7.6 Opioid therapy in patients with renal disease

Patients with chronic renal disease frequently report pain[450] and patients with cancer often develop severe renal impairment.[451]

## 7.6.1 Analgesics for patients with renal disease

### Pain adjuvants

Pain adjuvants gabapentin and pregabalin require dose adjustments dependent on creatinine clearance.[452]

There is limited data on TCAs. Metabolite accumulation may occur and increase the risk of adverse effects but there is little evidence to indicate need for dose reduction. Duloxetine is avoided in patients with creatinine clearance <30 mL/min.[453]

### Opioids

Prescribers should use additional caution and increased monitoring to minimise risks of opioid therapy in patients with renal insufficiency.[8] While all patients on opioids should be monitored for adverse effects, there are particular opioids (or their metabolites) that are more likely to cause toxicity in patients with renal impairment.[454] These include morphine, diamorphine and codeine derivatives.[454]

Hydromorphone, methadone, morphine and tramadol have been used in patients with renal disease but with dose adjustments depending on the degree of impairment.[337] Tapentadol is not recommended for use with creatinine clearance <30 mL/min. Alternates to pethidine and dextropropoxyphene are recommended.[455,456]

### In practice

The safest analgesics for patients with renal impairment are buprenorphine, fentanyl and paracetamol.[337] These analgesics are not associated with high active metabolite load or significantly prolonged clearance. Oxycodone can usually be used without any dose adjustment as its metabolites do not appear to contribute to any clinical effect.[337] Hydromorphone is used for patients undergoing dialysis.

## 7.7 Opioid therapy in patients with liver disease

Liver disease does not always equate with hepatic dysfunction, and there is no accurate measure of liver disease severity that can be used to guide dose adjustment.[457]

### 7.7.1 Analgesics for patients with liver disease

#### Paracetamol

Paracetamol is safe in patients with chronic liver disease, but a reduced dose of 2–3 g daily is recommended for long-term use.[457]

#### Pain adjuvants

Adjuvant analgesics such as TCAs and anticonvulsants may be used cautiously for cirrhotic patients with neuropathic pain.[458] Gabapentin or pregabalin may be better tolerated in cirrhosis because of non-hepatic metabolism and a lack of anticholinergic side effects.[458]

#### Opioids

Prescribers should use additional caution and increased monitoring to minimise risks of opioids in patients with hepatic insufficiency.[8] In these patients, opioids are well known to cause sedation, constipation and precipitate encephalopathy. There is an increased risk for patients with hypoalbuminaemia, and immediate-release as opposed to controlled-release formulations are advised.[458]

Mild pain not controlled with paracetamol may be best managed with either low-dose tramadol or oxycodone (not slow-release formulation) with an increase in laxatives.[458] Fentanyl and buprenorphine are also considered relatively safe. However, combined preparations of slow-release oxycodone and naloxone are not recommended.

#### In practice

Co-prescription of laxatives is mandatory to avoid constipation and encephalopathy in patients with hepatic insufficiency.

## 7.8 Opioid therapy for culturally and linguistically diverse patients

### 7.8.1 Culturally responsive care

Culture, language and religious convictions have an impact on pain sensitivities, assessment and management. There are significant cultural differences in self-care when managing pain, which affect pain relief seeking behaviour.[459,460]

Given the large inter-individual differences in pain behaviours and analgesic requirements in any patient group, pain should be assessed and managed on an individual basis rather than expectations associated with any cultural or ethnic group.[461,462]

There are genetic differences (refer to *Prescribing drugs of dependence in general practice, Part C1: Opioids* – Section 3.1.2 Metabolism and duration of activity) in the metabolism of opioids,[349,463,464] which also need to be considered.

### 7.8.2 Prescribing opioids to Aboriginal and Torres Strait Islander peoples

High-quality literature to inform acute pain management and opioid use in Aboriginal and Torres Strait Islander peoples is limited or conflicting.[465–468]

As with all patients, comorbidities need to be considered when selecting analgesics. Higher levels of medical comorbidities such as renal failure have been identified within the Aboriginal and Torres Strait Islander population.[469]

### In practice

Non-Indigenous GPs should consider seeking the assistance of an Aboriginal health worker or an interpreter to assist in communication and cross-cultural understandings (as needed).[470,471]

## 7.9 Prescribing opioids to patients with mental health conditions

Many people experiencing long-term pain may have a range of chronic health conditions, including mental health issues.[472] For example, the AIHW (2016) reports that three in 10 people living with back pain are living with mental health issues, which is twice the rate of the general population.[473]

Depression is the most common mental health comorbidity with long-term pain. It is associated with poorer quality of life and increased functional impairment.[474] Diagnosis may be challenging as there are indistinct symptom boundaries between chronic pain, distress and depression.[475]

Chronic pain is associated with a range of other psychological problems including anxiety, somatisation, fear of pain, anger and hostility.[476] Around one-third (31.8%) of people with a psychotic disorder in Australia are also experiencing chronic pain.[477]

Patients may present with pain as a manifestation of mental health problems. However, opioids should be reserved for well-defined somatic or neuropathic pain conditions.[411]

Patients with a mental health disorder, including SUDs, are at greater risk of adverse effects from opioid treatment. Prescribers should use additional caution and increased monitoring: titrate more slowly and seek consultant advice where feasible.[8,78]

Before prescribing opioids, a thorough evaluation for contraindications to opioids is recommended.[101] Treatment of anxiety and depression should be optimised prior to initiation of opioids.[8] The concomitant use of benzodiazepines should be avoided;[101] tapering of benzodiazepines or referral is suggested before starting opioid therapy.[90]

GPs should review patients' histories of controlled substance prescriptions using PDMP data to determine whether they are receiving opioid dosages or dangerous combinations that put them at high risk for overdose.

### In practice

Prescribers should use additional caution and increased monitoring: titrate more slowly and seek appropriate advice. Referral to mental health and/or pain medicine specialist is recommended for patients with:[101]

- mental and behavioural health disorders
- SUDs
- uncontrolled or severe psychiatric disorders
- suicidal ideation or actions
- significant medical comorbidities
- adverse behavioural or cognitive effects.

There is an issue with accessibility to services in many areas, but this should not be a reason for lack of consultation.

Multidisciplinary care and maximal use of non-pharmacological and non-opioid therapies to address analgesia should be undertaken. Optimise therapies to address mental health conditions. Consider low ceiling doses for opioids and naloxone therapy.

# 7.10 Risk stratification of patients for opioid therapy

Stratification of patients into high-risk, medium-risk, and low-risk categories is important prior to consideration of initiation and maintenance of opioid therapy. Risk stratification is justified in all patients who are likely to undergo long-term opioid therapy due to the significant proportion of potential harm, misuse and abuse.

**Table 14. Patient risk categories[478]**

| Low risk | Medium risk | High risk |
|---|---|---|
| Low-risk patients include those:<br>• with a definable physical pathology<br>• with clinical correlation with diagnostic testing including MRI, physical examination, and interventional diagnostic techniques<br>• with or without mild psychological comorbidities<br>• with or without mild co-existing medical disorders<br>• with no or well-defined and controlled personal or family history of alcoholism or substance abuse<br>• aged 45 years or higher<br>• with high levels of pain acceptance and active coping strategies<br>• who are well-motivated with a willingness to participate in multimodal therapy and attempting to function at normal levels | Medium-risk patients include those:<br>• with significant pain problems with objective signs and symptoms confirmed by radiological evaluation, physical examination, or diagnostic interventions<br>• with moderate psychological problems well-controlled by medical therapy<br>• with moderate co-existing medical disorders well controlled by medical therapy and which are not affected by chronic opioid therapy such as central sleep apnoea<br>• who develop mild tolerance but not hyperalgesia, without physical dependence or addiction<br>• with a past history of personal or family history of alcoholism or substance abuse<br>• with multiple pain sites<br>• with defined pathology and moderate levels of pain acceptance and coping strategies<br>• who are willing to participate in multimodal therapy and attempting to function in their normal daily lives | High-risk patients include those:<br>• with widespread pain without objective signs and symptoms (involvement of more than three regions of the body)<br>• with aberrant drug-related behaviour<br>• with a history of misuse, abuse, addiction, diversion, dependency, tolerance and hyperalgesia and alcoholism<br>• with major psychological disorders<br>• aged less than 45 years<br>• with HIV-related pain<br>• with high levels of pain exacerbation and low levels of coping strategies<br>• who are unwilling to participate in multimodal therapy<br>• who are not functioning close to a near normal lifestyle |

Adapted from Manchikanti L, Kaye AM, Knezevic NN, et al. Responsible, safe, and effective prescription of opioids for chronic non-cancer pain: American Society of Interventional Pain Physicians (ASIPP) guidelines. Pain Physician 2017;20(2S):S3–92.

## In practice

Risk stratification should be considered as part of a clinical evaluation for opioid therapy. Stratifications aids in decisions regarding risk modification therapies (eg naloxone) and referral.

# *Appendix A*

## A1 Pharmaceutical Benefits Scheme listing of opioid analgesics

**Table A1. Pharmaceutical Benefits Scheme listing of opioid analgesics**

| Drug and dosage form (brand) | Restrictions (abridged) |
|---|---|
| **Buprenorphine** | |
| Buprenorphine patches | Chronic severe pain |
| **Codeine** | |
| Codeine phosphate tablets | Unrestricted benefit |
| **Fentanyl** | |
| Fentanyl patches | Chronic severe pain |
| Fentanyl lozenge | Breakthrough pain (palliative care) |
| **Hydromorphone** | |
| Hydromorphone tablets (standard release) | Severe disabling pain |
| Hydromorphone tablets (modified release) | Chronic severe pain |
| Hydromorphone injection | Unrestricted benefit |
| Hydromorphone oral liquid | Severe disabling pain |
| **Methadone** | |
| Methadone tablet | Severe disabling pain |
| Methadone oral liquid | Chronic severe pain (palliative care) |
| Methadone injection | Severe disabling pain |
| **Morphine** | |
| ***Standard-release tablets*** | |
| Morphine sulphate tablet (Anamorph) | Severe disabling pain |
| Morphine sulphate tablet (Sevredol) | Severe disabling pain due to cancer<br>Severe disabling pain (palliative care) |
| ***Modified-release tablets or capsules*** | |
| Morphine sulphate modified tablets (up to 120 mg/tablet) | Chronic severe pain |
| Morphine sulphate modified tablets 200 mg | Chronic severe pain due to cancer<br>Chronic severe pain (palliative care) |
| ***Oral liquids*** | |
| Morphine hydrochloride oral liquid (standard release) | Severe disabling pain |

| Table A1. Pharmaceutical Benefits Scheme listing of opioid analgesics | |
|---|---|
| **Drug and dosage form (brand)** | **Restrictions (abridged)** |
| Morphine controlled release granules for oral suspension (up to 100 mg) | Chronic severe pain |
| Morphine controlled-release granules for oral suspension (200 mg) | Chronic severe pain due to cancer |
| ***Injections*** | |
| Morphine sulphate injections | Unrestricted benefit |
| **Oxycodone** | |
| Oxycodone tablet or capsule (standard release) | Severe disabling pain |
| Oxycodone tablet (modified release) | Chronic severe pain |
| Oxycodone oral liquid | Severe disabling pain |
| Oxycodone suppository | Severe disabling pain |
| **Oxycodone + naloxone** | |
| Oxycodone + naloxone tablet | Chronic severe pain |
| **Paracetamol + codeine** | |
| Paracetamol 500 mg + codeine phosphate 30 mg – 20 tablets | Unrestricted benefit |
| Paracetamol 500 mg + codeine phosphate 30 mg – 60 tablets | Authority required listing<br>Severe disabling pain |
| **Tramadol** | |
| Tramadol capsule 50 mg (standard release) | Acute pain not responding to aspirin and/or paracetamol |
| Tramadol tablet (modified release) | Pain not responding to aspirin and/or paracetamol<br>Dose titration in chronic pain not responding to aspirin and/or paracetamol (50 mg strength) |
| Tramadol oral liquid | Pain not responding to aspirin and/or paracetamol |
| Tramadol injection | Unrestricted benefit (Doctor's bag)<br>Short-term treatment of acute pain |
| **Tapentadol** | |
| Tapentadol tablet (modified release) | Chronic severe pain |

Adapted from the Pharmaceutical Benefits Scheme Drug Utilisation Sub-committee (DUSC). Opioid analgesics: Overview. Canberra: Commonwealth of Australia, 2014. Available at www.pbs.gov.au/industry/listing/participants/public-release-docs/opioids/opioids-dusc-prd-2014-10-final.pdf

# A2 Opioid fact sheet for patients

## Using opioid medicines to treat your pain

You and your doctor have decided that opioid pain medicine might help reduce your pain and improve your functioning in daily life.

It is important to understand that opioids are not likely to make your pain go away completely, and that this treatment involves potential risks and benefits. It is also important that you follow the guidelines in this handout and let your doctor know what you expect from your treatment. Your doctor may ask you to sign an 'Opioid patient care agreement'.

## What are the goals and possible benefits of opioid treatment?

The goals of treatment are to reduce your pain and improve how you function on a day-to-day basis. The benefits of opioid medicines vary from person to person. Opioids typically reduce chronic pain by about 30%, and some people find that they can function better day to day, but research has shown this is not achieved in all patients.

Experts agree that opioids may make pain worse, especially at high doses. 'Flare-ups' are common and should not usually be treated by increasing the dose or taking extra medicine.

Your doctor will monitor how you are doing by asking you to rate your pain level and your daily functioning. They may want to know how far you can walk, how long you can sit, whether you are able to work or do housework, and what kinds of activities you do alone or with family and friends.

## What are the common side effects and risks of opioids?

Opioids cause common side effects that can be unpleasant. They can also increase risks of serious health issues. Because opioids have risks that can be serious, your doctor may ask you for a urine or blood sample to help protect your safety.

Side effects vary from person to person. You and your doctor will work together to monitor how opioids affect you. Your doctor may need to adjust your dose until you find the right balance between pain reduction, improved function and side effects.

It is normal to develop physical dependence on opioids. Physical dependence means your body has adapted to the medicine and you will experience tolerance and withdrawal. Tolerance means you need to take more of the medicine to get the same effect. Withdrawal means you will have symptoms when you stop using the medicine.

Withdrawal symptoms are usually the opposite of the effects of the medicine. For example, if the medicine causes constipation, the withdrawal symptom would be diarrhoea. If the medicine reduces pain, the withdrawal symptom would be increased pain. Withdrawal from opioids is temporary and usually not dangerous.

If you do get pregnant while taking opioids, let your doctor know right away. Babies born to mothers taking opioids will be dependent on opioids at birth. You should not take opioids if you are trying to get pregnant.

People who have had problems with mental health, drugs or alcohol are more likely to have problems with opioids. You must tell your doctor about any mental illness, substance abuse or addiction of any type you have experienced in the past. You must also tell your doctor if anyone in your family has had these problems. Research shows these problems sometimes run in families.

Experts agree that people with active substance abuse or addiction problems should not use opioids for chronic non-cancer pain (CNCP). If you have problems with substance abuse or addiction, it is important to let your doctor know so you can get the help you need. Tell your doctor right away if you feel you are becoming addicted to opioids.

| Common side effects | Other side effects | Withdrawal symptoms |
|---|---|---|
| **Constipation**<br>Opioid medicines cause constipation. You may need to be treated for this while you are taking opioids.<br><br>**Sedation**<br>Many opioid medications can make you feel drowsy, slow your reaction time, and cause loss of coordination. They can also make it hard to concentrate and think clearly.<br>Do not drive or use dangerous equipment until you are sure that opioids do not affect your reaction time or thinking ability. It may take a week or longer before you know if you can drive safely while taking opioids. If you are in a traffic accident while driving on opioids, you may be considered to be driving under the influence. | Rash and/or itching<br>Dry eyes<br>Blurred vision<br>Nausea and vomiting<br>Inability to urinate<br>Low blood pressure<br>Slow heart beat<br>Depressed mood<br>Slowed breathing<br>Problems with balance<br>Decreased sex drive (decreased testosterone)<br>Decreased immune function<br>Swelling in hands and feet<br>Jerking of arms and legs<br>Increased sensitivity to pain<br>Disruption of normal sleep<br>Dental problems<br>Apathy<br>Falls resulting in fractures | Sweating<br>Nausea<br>Abdominal pain/cramping<br>Diarrhoea<br>Trouble sleeping<br>Muscle aches<br>Fast heart beat<br>Anxiety<br>Runny nose<br>Goose bumps |

## Risk of serious bodily harm or death

Opioid pain medicines can cause serious bodily harm or death. Higher doses appear to cause more side effects, leading to sedation, injuries and serious fractures due to falls. Higher doses increase the risk of overdose. An overdose of opioids, whether by accident or on purpose, can cause serious bodily harm or death. Research continues to show more and more problems with long-term opioid use, especially at high doses.

Using more opioids than your doctor prescribes can cause you to become dangerously sedated, stop breathing or overdose. Combining opioids with certain other medicines or with alcohol or drugs can have the same effect.

## Are there alternatives to opioid treatment for chronic non-cancer pain?

Your doctor may prescribe other treatments to help your pain and to help you do daily activities better. These may include exercise, psychological counselling and medicines that are not opioids. Please be sure to discuss these options with your doctor.

# *Appendix B*

## B1 Drug misuse behaviours

Drug-seeking patients can often provide well-developed clinical histories that may sound very 'real'. These patients may aim to exploit doctors' desires to minimise patients' distress, but rather than being aggressive, many drug-seeking patients will be very pleasant.

Not all drug-seeking patients are faking symptoms. They may have a legitimate complaint and, over time, have become dependent or tolerant and require larger doses of medication to function in their daily lives.[479,480]

The RACGP advises a one-doctor policy within the practice for prescribing any drugs of dependence unless special arrangements are made to cover leave. The aim of this practice is to minimise drug-seeking behaviour and its resulting harms and costs to the healthcare system.

There is a wide spectrum of drug misuse behaviours – many will not be obvious during the consultation. Behaviours are described below.

**Table B1. Drug misuse behaviours**

| Typical requests and complaints |
|---|
| • Aggressively complaining about need for medication<br>• Complaining of lost or stolen scripts<br>• Asking for specific medications by name<br>• Asking for non-generic medication<br>• Requesting to have medication dose increased<br>• Claiming multiple pain medicine allergies<br>• Anger or irritability when questioned closely about pain |
| **Inappropriate self-medicating** |
| • Taking a few extra, unauthorised doses on occasion<br>• Hoarding medication<br>• Using a controlled substance for non-pain relief purposes (eg to enhance mood, sleep aid)<br>• Injecting an oral formulation |
| **Inappropriate use of general practice services** |
| • Visiting multiple doctors for controlled substances (doctor shopping)<br>• Frequently calling the clinic<br>• Frequent unscheduled clinic visits for early refills<br>• Consistently disruptive behaviour when arriving at the clinic<br>• Consistently calling outside of clinic hours or when a particular physician is on call who prescribes controlled substances |
| **Resistant behaviour** |
| • Unwilling to consider other medications or non-pharmacologic treatments<br>• Frequent unauthorised dose escalations after being told that is inappropriate<br>• Unwilling to sign controlled substances agreement<br>• Refusing diagnostic workup or consultation |

**Table B1. Drug misuse behaviours**

| Manipulative or illegal behaviour |
| --- |
| • Claiming to be on waiting list or unable to afford dental work and needing to manage dental pain |
| • Obtaining controlled substances medications from family members (including stealing from older relatives) |
| • Using aliases |
| • Forging prescriptions |
| • Pattern of lost or stolen prescriptions |
| • Selling medications |
| • Obtaining controlled substance analgesics from illicit sources |
| **Other typical behaviours** |
| • Being more concerned about the drug than their medical problem that persists beyond the third clinic visit |
| • Deterioration at home or work or reduction of social activities because of medication side effects |

# *Appendix C*

## C1 Urine drug testing

A baseline urine drug test (UDT) should be performed at the initial visit, with a request to include detection of oxycodone and other drugs not usually recognised by immunoassay such as fentanyl, tramadol, methadone and buprenorphine. These additional tests will be at extra cost to the patient.

### C1.1 Screening and testing

Most urinalysis procedures are carried out using gas chromatography in specialist laboratories and there is usually a delay in receiving a result. The result establishes whether the drug/s is/are present but does not measure the amounts in which the drug/s has/have been taken. It can therefore be very helpful to have a supply of onsite urine testing strips that, within a couple of minutes, provide a basic guide to the drugs being used. This is a screening tool: it is not confirmatory, and should always be used in conjunction with clinical signs and history. False positives and negatives can occur with onsite tests, though they are rare.

**Table C1.1 Length of time drugs of dependence can be detected in urine[481]**

| Drug | Time |
|---|---|
| Alcohol | 7–12 hours |
| Amphetamine | |
| • Methamphetamine | 48 hours |
| Benzodiazepine | |
| • Ultra-short acting | 12 hours |
| • Short acting | 24 hours |
| • Long acting | 3 weeks |
| Marijuana | |
| • Single use | 3 days |
| • Moderate use (4 times/week) | 5–7 days |
| • Daily use | 10–15 days |
| • Chronic heavy use (>3 times/day) | >30 days |
| Opioids | |
| • Buprenorphine (and metabolites) | 8 days |
| • Codeine | 48 hours |
| • Heroin (morphine) | 48 hours |
| • Hydromorphone | 2–4 days |
| • Methadone | 3 days |
| • Morphine | 2–3 days |
| • Oxycodone | 2–4 days |

Adapted from Moeller KE, Lee KC, Kissack JC. Urine drug screening: Practical guide for clinicians. Mayo Clin Proc 2008;83(1):66–76.

## C1.2 Interpreting urine drug tests

Unexpected results from such screens should be interpreted within their limitations: fentanyl, buprenorphine, synthetic drugs, anabolic steroids, and usually oxycodone are not routinely detected and must be requested as additional tests (at extra cost to the patient). Drug misusers may adopt a variety of methods, such as switching urine samples, to influence results.[148]

**Table C1.2. Interpreting unexpected results of urine drug tests[102]**

| | Unexpected result | Possible explanations | Actions to take |
|---|---|---|---|
| 1 | UDT *negative* for prescribed opioid | • False negative<br>• Non-adherence<br>• Diversion<br>• Urine replacement or dilution (see below) | • Repeat test using chromatography; specify the drug of interest (eg oxycodone often missed by immunoassay, unless specifically ordered)<br>• Take a detailed history of the patient's medication use for the preceding seven days (eg could learn that patient ran out several days prior to test)<br>• Ask patient if they've given the drug to others<br>• Monitor compliance with pill counts |
| 2 | UDS *positive* for non-prescribed opioid or benzodiazepines | • False positive<br>• Patient acquired opioids from other sources (doctor shopping, street) | • Repeat UDT regularly<br>• Ask the patient if they accessed opioids from other sources<br>• Assess for opioid misuse/addiction<br>• Review/revise treatment agreement |
| 3 | UDS *positive* for illicit drugs (eg cocaine, cannabis) | • False positive<br>• Patient is occasional user or addicted to the illicit drug | • Repeat UDT regularly<br>• Assess for abuse/addiction and refer for addiction treatment as appropriate<br>• Seek information on false positives |
| 4 | Urine creatinine is lower than 2–3 mmol/L | • Patient added water to sample | • Repeat UDT, consider supervised collection or temperature testing<br>• Take a detailed history of the patient's medication use for the preceding seven days<br>• Review/revise treatment agreement |
| 5 | Urine sample is cold | • Delay in handling sample (urine cools within minutes)<br>• Patient added water to sample | • Repeat UDT, consider supervised collection or temperature testing<br>• Take a detailed history of the patient's medication use for the preceding seven days<br>• Review/revise treatment agreement |

UDS, urine drug screen; UDT, urine drug test

# *Appendix D*

## D1 Criteria for substance (opioid) use disorder

**Table D1. DSM-5 criteria for diagnosing a substance use disorder – Opioids**

| | |
|---|---|
| **A problematic pattern of substance use leading to clinically significant impairment or distress, as manifested by at least two of the following 11 criteria, occurring within a 12-month period:** | |
| Impaired control criteria | 1. Substances are often taken in larger amounts or over a longer period than was intended<br>2. There is a persistent desire or unsuccessful efforts to cut down or control substance use<br>3. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects<br>4. There is a craving or strong desire or urge to use the substance |
| Social impairment criteria | 5. Recurrent substance use is resulting in a failure to fulfil major role obligations at work, school or home (eg repeated absences from work or poor work performance related to substance use; substance-related absences, suspensions or expulsions from school; neglect of children or household)<br>6. Substance use is continued despite having persistent or recurrent social or interpersonal problems caused by or exacerbated by the effects of substances (eg arguments with a spouse about consequences of intoxication; physical fights)<br>7. Important social, occupational or recreational activities are given up or reduced because of substance use |
| Risky use criteria | 8. Recurrent substance use in situations in which it is physically hazardous (eg driving an automobile or operating a machine when impaired by sedative, hypnotic or anxiolytic use)<br>9. Substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance |
| Pharmacological criteria | 10. Tolerance, as defined by either of the following:<br>a. A need for markedly increasing amounts of the substance to achieve intoxication or desired effect<br>b. A markedly diminished effect with continued use of the same amount of the substance<br>Note: Criterion 10 is not considered to be met for individuals taking substances under medical supervision<br>11. Withdrawal, as manifested by either one of the following:<br>a. The characteristic withdrawal syndrome for the substance<br>b. Substance (or a closely related substance) is taken to relieve or avoid withdrawal symptoms |
| Specifiers:<br>'In early remission': After full criteria for SUD were previously met, none of the criteria for SUD have been met for at least three months but for less than 12 months (with the exception that Criterion 4 may be met)<br>'In sustained remission': After full criteria for SUD were previously met, none of the criteria for SUD have been met at any time during a period of 12 months or longer (with the exception that Criterion 4 may be met)<br>'In a controlled environment': This additional specifier is used if the individual is in an environment where access to substance is restricted<br>Current severity:<br>'Mild': Presence of 2–3 criteria 'Moderate': Presence of 4–5 criteria 'Severe': Presence of 6 or more criteria | |

Reproduced with permission from the American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th edn. Arlington, VA: APA, 2013.

# *Appendix E*

## E1 PEG pain tool

The PEG is a practical tool to assess and monitor chronic pain by measuring three items: average pain intensity (P), interference with enjoyment of life (E), and interference with general activity (G).[109]

**Table E1. PEG pain tool**

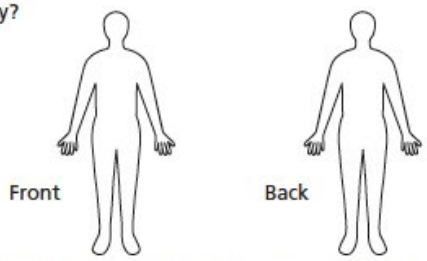
| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **1. What number best describes your pain on average in the past week?** | | | | | | | | | | |
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| No pain | | | | | | | | | | Pain as bad as you can imagine |
| **2. What number best describes how, during the past week, pain has interfered with your enjoyment of life?** | | | | | | | | | | |
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Does not interfere | | | | | | | | | | Completely interferes |
| **3. What number best describes how, during the past week, pain has interfered with your general activity?** | | | | | | | | | | |
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Does not interfere | | | | | | | | | | Completely interferes |

# E2 Brief pain inventory

## Brief Pain Inventory

Name _____ Date _____ Time _____

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, toothaches). Have you had pain other than these everyday types of pain today?
   1. Yes 2. No
2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.




3. Please rate your pain by circling the one number that best describes your pain at its worst in the past 24 hours.

   0 1 2 3 4 5 6 7 8 9 10
   *No pain* — *Pain as bad as you can imagine*

4. Please rate your pain by circling the one number that best describes your pain at its least in the last 24 hours.

   0 1 2 3 4 5 6 7 8 9 10
   *No pain* — *Pain as bad as you can imagine*

5. Please rate your pain by circling the one number that best describes your pain on average.

   0 1 2 3 4 5 6 7 8 9 10
   *No pain* — *Pain as bad as you can imagine*

6. Please rate your pain by circling the one number that tells how much pain you have right now.

   0 1 2 3 4 5 6 7 8 9 10
   *No pain* — *Pain as bad as you can imagine*

7. What treatment or medication are you receiving for the pain?

   _____

   _____

   _____

   _____

   _____

8. In the past 24 hours, how much relief have pain treatments or medication provided? Please circle the one percentage that most shows how much relief you have received.

   0% 10 20 30 40 50 60 70 80 90 100%
   *No relief* — *Complete relief*

9. Circle the one number that describes how, during the past 24 hours, pain has interfered with your:

   A. General activity

   0 1 2 3 4 5 6 7 8 9 10
   *Does not interfere* — *Completely interferes*

   B. Mood

   0 1 2 3 4 5 6 7 8 9 10
   *Does not interfere* — *Completely interferes*

   C. Walking ability

   0 1 2 3 4 5 6 7 8 9 10
   *Does not interfere* — *Completely interferes*

   D. Normal work (includes both work outside the home and housework)

   0 1 2 3 4 5 6 7 8 9 10
   *Does not interfere* — *Completely interferes*

   E. Relations with other people

   0 1 2 3 4 5 6 7 8 9 10
   *Does not interfere* — *Completely interferes*

   F. Sleep

   0 1 2 3 4 5 6 7 8 9 10
   *Does not interfere* — *Completely interferes*

   G. Enjoyment of life

   0 1 2 3 4 5 6 7 8 9 10
   *Does not interfere* — *Completely interferes*

   H. Ability to concentrate

   0 1 2 3 4 5 6 7 8 9 10
   *Does not interfere* — *Completely interferes*

   I. Appetite

   0 1 2 3 4 5 6 7 8 9 10
   *Does not interfere* — *Completely interferes*

# E3 McGill pain questionnaire[482,483]

## Overview

The McGill pain questionnaire can be used to evaluate a person experiencing significant pain. It can be used to monitor the pain over time and to determine the effectiveness of any intervention. It was developed by Dr Ronald Melzack at McGill University in Montreal, Canada, and has been translated into several languages.

Sections:

- What does your pain feel like?
- How does your pain change with time?
- How strong is your pain?

## What does your pain feel like?

Statement: Some of the words below describe your present pain. Circle ONLY those words that best describe it. Leave out any category that is not suitable. Use only a single word in each appropriate category – the one that applies best.

| Group | Descriptor | Points |
|---|---|---|
| 1 (temporal) | flickering | 1 |
| | quivering | 2 |
| | pulsing | 3 |
| | throbbing | 4 |
| | beating | 5 |
| | pounding | 6 |
| 2 (spatial) | jumping | 1 |
| | flashing | 2 |
| | shooting | 3 |
| 3 (punctate pressure) | pricking | 1 |
| | boring | 2 |
| | drilling | 3 |
| | stabbing | 4 |
| | lancinating | 5 |
| 4 (incisive pressure) | sharp | 1 |
| | cutting | 2 |
| | lacerating | 3 |
| 5 (constrictive pressure) | pinching | 1 |
| | pressing | 2 |
| | gnawing | 3 |
| | cramping | 4 |
| | crushing | 5 |

| Group | Descriptor | Points |
|---|---|---|
| 6 (traction pressure) | tugging | 1 |
| | pulling | 2 |
| | wrenching | 3 |
| 7 (thermal) | hot | 1 |
| | boring | 2 |
| | scalding | 3 |
| | searing | 4 |
| 8 (brightness) | tingling | 1 |
| | itchy | 2 |
| | smarting | 3 |
| | stinging | 4 |
| 9 (dullness) | dull | 1 |
| | sore | 2 |
| | hurting | 3 |
| | aching | 4 |
| | heavy | 5 |
| 10 (sensory miscellaneous) | tender | 1 |
| | taut | 2 |
| | rasping | 3 |
| | splitting | 4 |
| 11 (tension) | tiring | 1 |
| | exhausting | 2 |
| 12 (autonomic) | sickening | 1 |
| | suffocating | 2 |
| 13 (fear) | fearful | 1 |
| | frightful | 2 |
| | terrifying | 3 |
| 14 (punishment) | punishing | 1 |
| | gruelling | 2 |
| | cruel | 3 |
| | vicious | 4 |
| | killing | 5 |
| 15 (affective-evaluative-sensory: miscellaneous) | wretched | 1 |
| | blinding | 2 |
| 16 (evaluative) | annoying | 1 |
| | troublesome | 2 |

| Group | Descriptor | Points |
|---|---|---|
| | miserable | 3 |
| | intense | 4 |
| | unbearable | 5 |
| 17 (sensory: miscellaneous) | spreading | 1 |
| | radiating | 2 |
| | penetrating | 3 |
| | piercing | 4 |
| 18 (sensory: miscellaneous) | tight | 1 |
| | numb | 2 |
| | drawing | 3 |
| | squeezing | 4 |
| | tearing | 5 |
| 19 (sensory) | cool | 1 |
| | cold | 2 |
| | freezing | 3 |
| 20 (affective-evaluative: miscellaneous) | nagging | 1 |
| | nauseating | 2 |
| | agonizing | 3 |
| | dreadful | 4 |
| | torturing | 5 |
| Pain score = SUM (points for applicable descriptors) | | |

## How does your pain change with time?

| Question | Response | Points |
|---|---|---|
| Which word or words would you use to describe the pattern of your pain? | Continuous steady constant | 1 |
| | Rhythmic periodic intermittent | 2 |
| | Brief momentary transient | 3 |

Do the following items increase or decrease your pain?

- Liquor
- Stimulants (eg coffee)
- Eating
- Heat
- Cold
- Damp
- Weather changes
- Massage or use of a vibrator
- Pressure
- No movement
- Movement
- Sleep or rest
- Lying down
- Distraction (eg tv, reading)
- Urination or defecation
- Tension
- Bright lights
- Loud noises
- Going to work
- Intercourse
- Mild exercise
- Fatigue

## How strong is your pain?

Statement: People agree that the following five words (mild, discomforting, distressing, horrible, excruciating) represent pain of increasing intensity. To answer each question below, write the number of the most appropriate word in the space beside the question.

| Question | Response | Points |
|---|---|---|
| Which word describes your pain right now? | mild | 1 |
| | discomforting | 2 |
| | distressing | 3 |
| | horrible | 4 |
| | excruciating | 5 |
| Which word describes it at its worst? | mild | 1 |
| | discomforting | 2 |
| | distressing | 3 |
| | horrible | 4 |
| | excruciating | 5 |
| Which word describes it when it is least? | mild | 1 |
| | discomforting | 2 |
| | distressing | 3 |
| | horrible | 4 |
| | excruciating | 5 |
| Which word describes the worst toothache you ever had? | mild | 1 |
| | discomforting | 2 |
| | distressing | 3 |
| | horrible | 4 |
| | excruciating | 5 |
| Which word describes the worst headache you ever had? | mild | 1 |
| | discomforting | 2 |
| | distressing | 3 |
| | horrible | 4 |
| | excruciating | 5 |
| Which word describes the worst stomach ache you ever had? | mild | 1 |
| | discomforting | 2 |
| | distressing | 3 |
| | horrible | 4 |
| | excruciating | 5 |

Interpretation

- Minimum pain score: 0 (would not be seen in a person with true pain)
- Maximum pain score: 78
- The higher the pain score, the greater the pain

## E4 DN4 neuropathic pain questionnaire

To estimate the probability of neuropathic pain, please answer yes or no for each item of the following four questions.

**INTERVIEW OF THE PATIENT**

**QUESTION 1:**

| **Does the pain have one or more of the following characteristics?** | **YES** | **NO** |
|---|---|---|
| Burning | ❑ | ❑ |
| Painful cold | ❑ | ❑ |
| Electric shocks | ❑ | ❑ |

**QUESTION 2:**

| **Is the pain associated with one or more of the following symptoms in the same area?** | **YES** | **NO** |
|---|---|---|
| Tingling | ❑ | ❑ |
| Pins and needles | ❑ | ❑ |
| Numbness | ❑ | ❑ |
| Itching | ❑ | ❑ |

**EXAMINATION OF THE PATIENT**

**QUESTION 3:**

| **Is the pain located in an area where the physical examination may reveal one or more of the following characteristics?** | **YES** | **NO** |
|---|---|---|
| Hypoesthesia to touch | ❑ | ❑ |
| Hypoesthesia to pinprick | ❑ | ❑ |

**QUESTION 4:**

| **In the painful area, can the pain be caused or increased by:** | **YES** | **NO** |
|---|---|---|
| Brushing? | ❑ | ❑ |

**YES = 1 point**
**NO = 0 points**

**Patient's Score: /10**

# E5 Örebro musculoskeletal pain questionnaire[484]

1. **Name** _____ **Phone** _____ **Date** _____
2. **Date of Injury** _____ **Date of birth** _____
3. **Male** ☐ **Female** ☐
4. **Were you born in Australia*?** Yes ☐ No ☐

These questions and statements apply if you have aches or pains, such as back, shoulder or neck pain. Please read and answer questions carefully. Do not take long to answer the questions, however it is important that you answer every question. There is **always** a response for your particular situation.

| | |
|---|---|
| 5. **Where do you have pain?** Place a tick (✓) for all appropriate sites.<br>☐ Neck ☐ Shoulder ☐ Arm ☐ Upper Back<br>☐ Lower Back ☐ Leg ☐ Other (state) | 2x (max 10) |
| 6. **How many days of work have you missed because of pain during the past 18 months?** Tick (✓) one.<br>☐ 0 days (1) ☐ 1-2 days (2) ☐ 3-7 days (3) ☐ 8-14 days (4)<br>☐ 15-30 days (5) ☐ 1 month (6) ☐ 2 months (7) ☐ 3-6 months (8)<br>☐ 6-12 months (9) ☐ over 1 year (10) | |
| 7. **How long have you had your current pain problem?** Tick (✓) one.<br>☐ 0-1 week (1) ☐ 1-2 weeks (2) ☐ 3-4 weeks (3) ☐ 4-5 weeks (4)<br>☐ 6-8 weeks (5) ☐ 9-11 weeks (6) ☐ 3-6 months (7) ☐ 6-9 months (8)<br>☐ 9-12 months (9) ☐ over 1 year (10) | |
| 8. **Is your work heavy or monotonous?** Circle the best alternative.<br>0 1 2 3 4 5 6 7 8 9 10<br>Not at all Extremely | |
| 9. **How would you rate the pain that you have had during the past week?** Circle one.<br>0 1 2 3 4 5 6 7 8 9 10<br>No pain Pain as bad as it could be | |

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| | |
|---|---|
| **10. In the past three months, on average, how bad was your pain on a 0-10 scale?** Circle one.<br>0 1 2 3 4 5 6 7 8 9 10<br>No pain — Pain as bad as it could be | |
| **11. How often would you say that you have experience pain episodes, on average, during the past three months?** Circle one.<br>0 1 2 3 4 5 6 7 8 9 10<br>Never — Always | |
| **12. Based on all things you do to cope, or deal with your pain, on an average day, how much are you able to decrease it?** Circle the appropriate number.<br>0 1 2 3 4 5 6 7 8 9 10<br>Can't decrease it at all — Can decrease it completely | 10 - x |
| **13. How tense or anxious have you felt in the past week?** Circle one.<br>0 1 2 3 4 5 6 7 8 9 10<br>Absolutely clam and relaxed — As tense and anxious as I've ever felt | |
| **14. How much have you been bothered by feeling depressed in the past week?** Circle one.<br>0 1 2 3 4 5 6 7 8 9 10<br>Not at all — Extremely | |
| **15. In your view, how large is the risk that your current pain may become persistent?** Circle one.<br>0 1 2 3 4 5 6 7 8 9 10<br>No risk — Very large risk | |
| **16. In your estimation, what are the chances that you will be able to work in six months?** Circle one.<br>0 1 2 3 4 5 6 7 8 9 10<br>No chance — Very large chance | 10 - x |
| **17. If you take into consideration your work routines, management, salary, promotion possibilities and work mates, how satisfied are you with your job?** Circle one.<br>0 1 2 3 4 5 6 7 8 9 10<br>Not satisfied at all — Completely satisfied | 10 - x |

| | |
|---|---|
| Here are some of the things that other people have told us about their pain. For each statement, circle one number from 0 to 10 to say how much physical activities, such as bending, lifting, walking or driving, would affect your pain. | |
| **18. Physical activity makes my pain worse.**<br>0 1 2 3 4 5 6 7 8 9 10<br>Completely disagree ... Completely agree | |
| **19. An increase in pain is an indication that I should stop what I'm doing until the pain decreases.**<br>0 1 2 3 4 5 6 7 8 9 10<br>Completely disagree ... Completely agree | |
| **20. I should not do my normal work with my present pain.**<br>0 1 2 3 4 5 6 7 8 9 10<br>Completely disagree ... Completely agree | |
| Here is a list of five activities. Circle the one number that best describes your current ability to participate in each of these activities. | |
| **21. I can do light work for an hour.**<br>0 1 2 3 4 5 6 7 8 9 10<br>Can't do it because of pain problem ... Can do it without pain being a problem | 10 - x |
| **22. I can walk for an hour.**<br>0 1 2 3 4 5 6 7 8 9 10<br>Can't do it because of pain problem ... Can do it without pain being a problem | 10 - x |
| **23. I can do ordinary household chores.**<br>0 1 2 3 4 5 6 7 8 9 10<br>Can't do it because of pain problem ... Can do it without pain being a problem | 10 - x |
| **24. I can do the weekly shopping.**<br>0 1 2 3 4 5 6 7 8 9 10<br>Can't do it because of pain problem ... Can do it without pain being a problem | 10 - x |
| **25. I can sleep at night.**<br>0 1 2 3 4 5 6 7 8 9 10<br>Can't do it because of pain problem ... Can do it without pain being a problem | 10 - x |

## Explanatory notes

The Örebro musculoskeletal pain questionnaire (ÖMPQ) is a 'yellow flag' screening tool that predicts long-term disability and failure to return to work when completed 4–12 weeks following a soft tissue injury.[485] A cut-off score of 105 has been found to predict (with 95% accuracy) those who will recover, those who will have no further sick leave in the next six months (with 81% accuracy), and those who will have long-term sick leave (with 67% accuracy).[484]

The ÖMPQ predicted failure to return to work six months after compensable musculoskeletal injury in a NSW population of workers. The injuries in the study group were mixed, and the ÖMPQ was found to be more specific and sensitive for back injuries. In workers with back injuries screened at 4–12 weeks, a cut-off score of 130 correctly predicted 86% of those who failed to return to work.[486]

Identification through the ÖMPQ of workers at risk of failing to return to work due to personal and environmental factors provides the opportunity for treating practitioners to apply appropriate interventions (including the use of activity programs based on cognitive behavioural strategies) to reduce the risk of long-term disability in injured workers. Evidence indicates that these factors can be changed if they are addressed.[487–489]

## Administering the questionnaire

The ÖMPQ is designed to be a self-administered tool completed by the worker in a quiet environment without assistance from any other person. A detailed explanation is provided by the person administering the questionnaire:

*Information from this questionnaire helps us understand your problem better, and it especially helps us evaluate the possible long-term consequences your pain may have. It is important that you read each question carefully and answer it as best you can. There are no right or wrong answers. Please answer every question. If you have difficulty, select the answer that best describes your situation.*

Where uncertainty or a request for more information is expressed, encouragement is provided to 'answer as best you can'. The questionnaire item may be read aloud to assist; however, the question should not be rephrased. All questions should be answered, as missing values will reduce validity.[490]

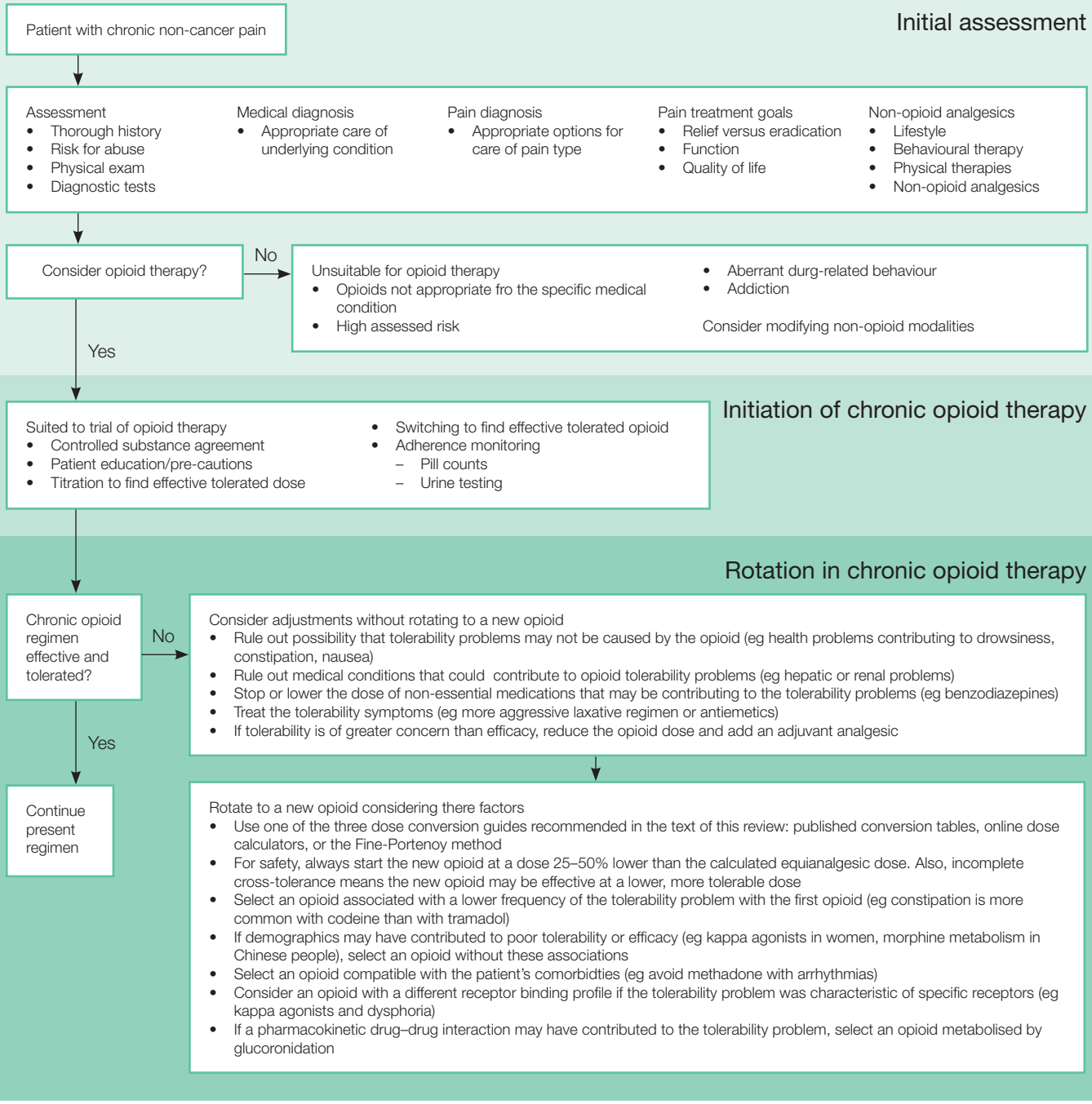
## Scoring instructions

- For Question 5, count the number of pain sites and multiply by two – this is the score (maximum score allowable is 10).
- For Questions 6 and 7 the score is the number bracketed after the ticked box.
- For Questions 8, 9, 10, 11, 13, 14, 15, 18, 19 and 20 the score is the number that has been ticked or circled.
- For Questions 12, 16, 17, 21, 22, 23, 24 and 25 the score is 10 minus the number that has been circled.
- Write the score in the shaded area beside each item.
- Add up the scores for Questions 5 to 25 – this is the total ÖMPQ score.

# *Appendix F*

## F1 Opioid rotation algorithm

**Figure F1. Algorithm for initial patient assessment and initiation and rotation of opioid therapy[263]**

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