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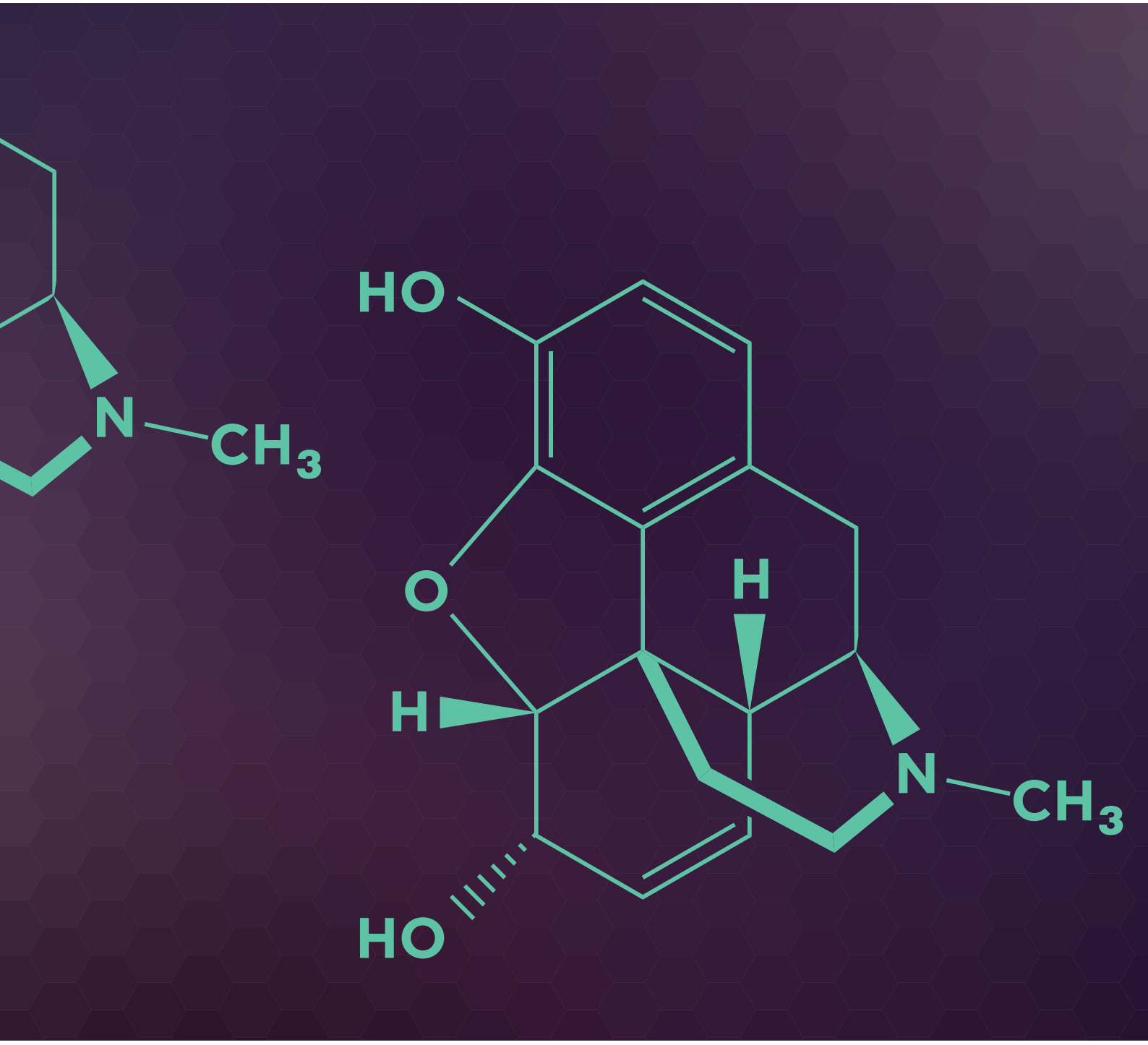
Royal Australian College *of* General Practitioners

Prescribing drugs of dependence in general practice, Part C1

Opioids



Prescribing drugs of dependence in general practice, Part C1: Opioids

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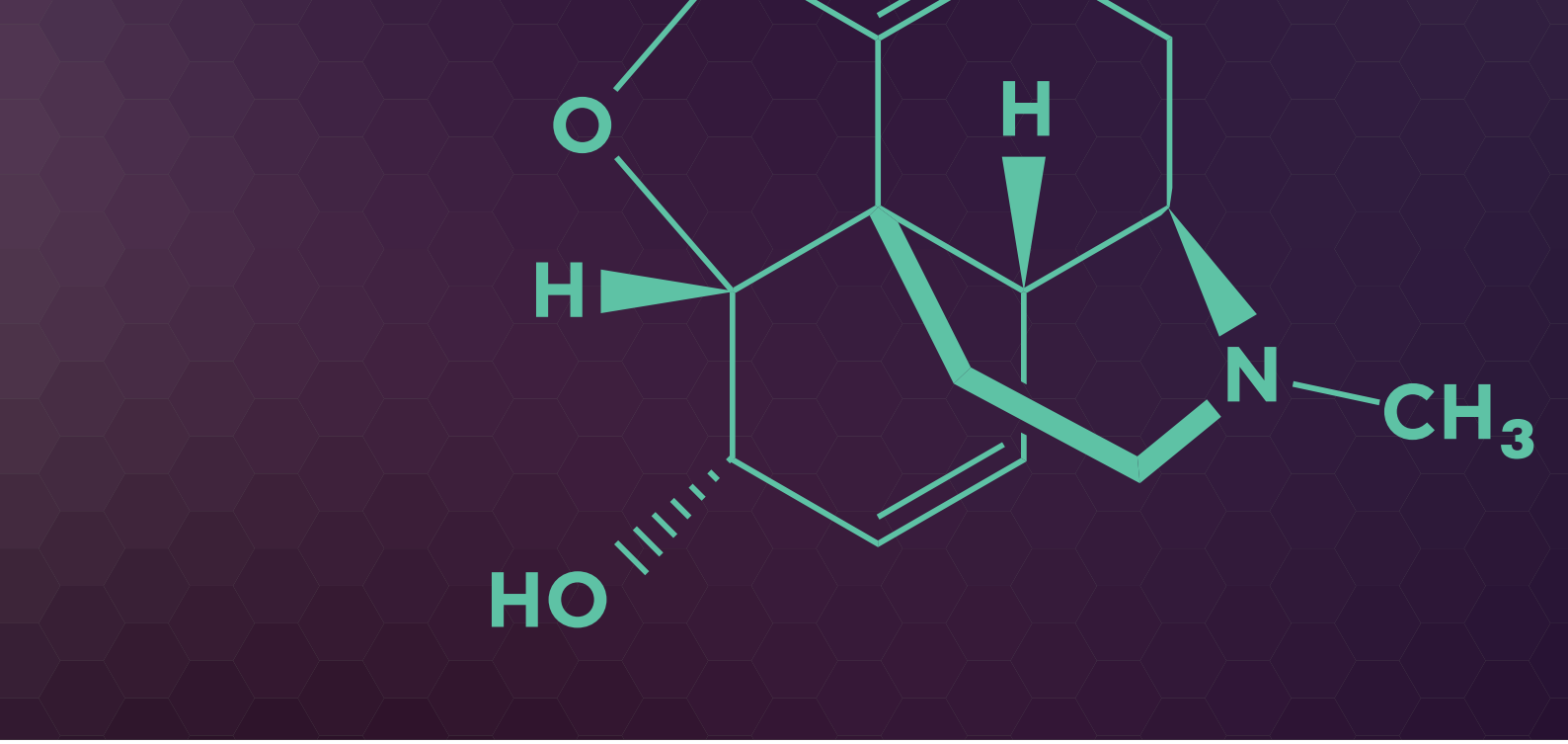
We acknowledge the Traditional Custodians of the lands and seas on which we work and live, and pay our respects to Elders, past, present and future.



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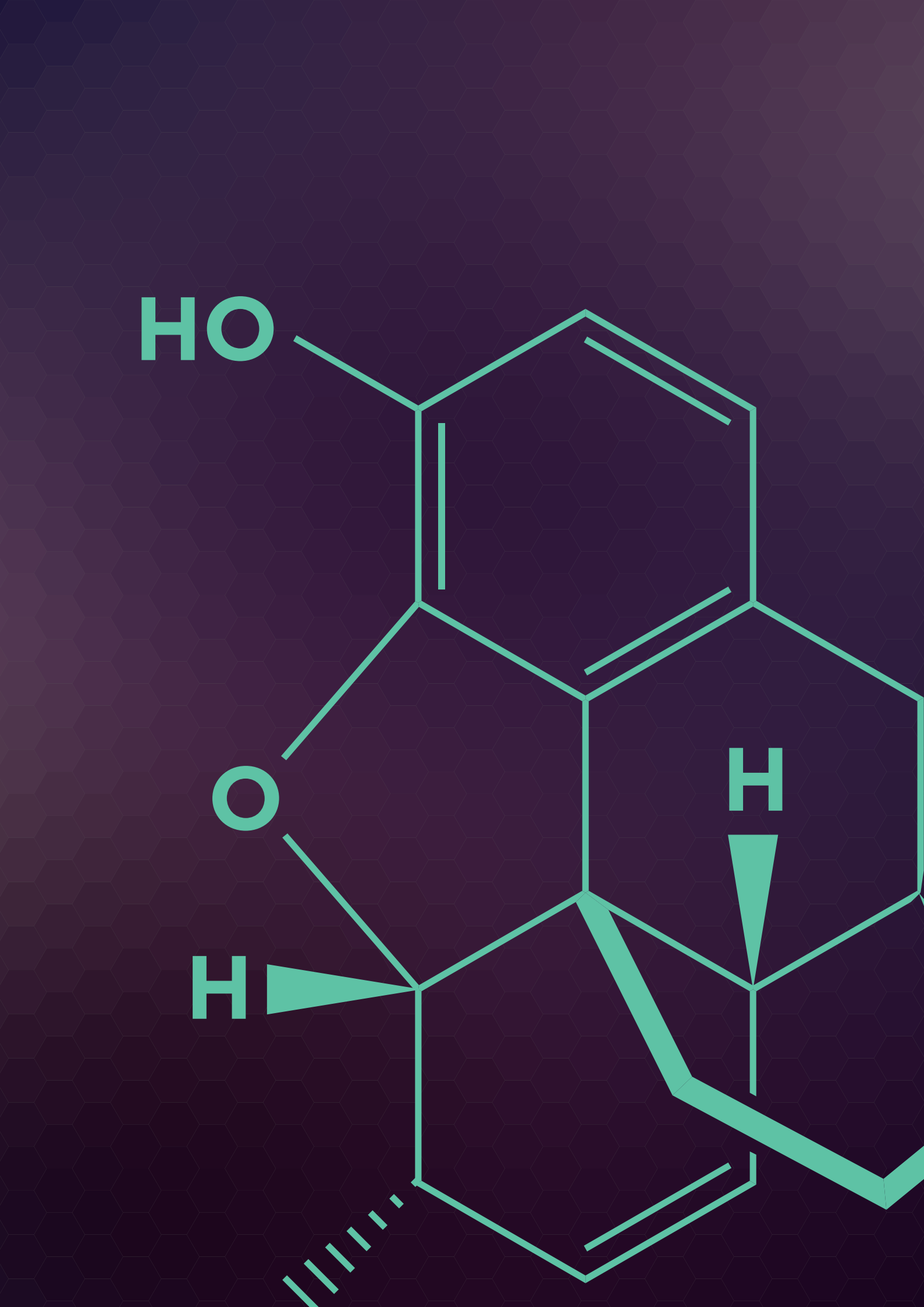
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Foreword

This guide has been produced largely in response to increasing community and clinical concerns about the use and safety of opioids. This isn't a new problem. We've been exploiting the analgesic (and other) properties of the opium poppy since prehistoric times. Perhaps the peak of use was during the Great Binge (~1870–1914) when opium and its derivatives were hailed as medical miracles and used by young and old. Mothers gave opium to their 'fussy' infants and Bayer made heroin for headaches, coughs, period pains and even as a cure for morphine addiction.

Today, opioids are 'controlled' through both medical and legal systems. Despite this, opioid use has been fuelled by drug company marketing, inappropriate therapeutic ideals, and a broad public demand for analgesia for chronic pain. The use of opioids has increased to a point where inappropriate prescribing and harm has ensued.

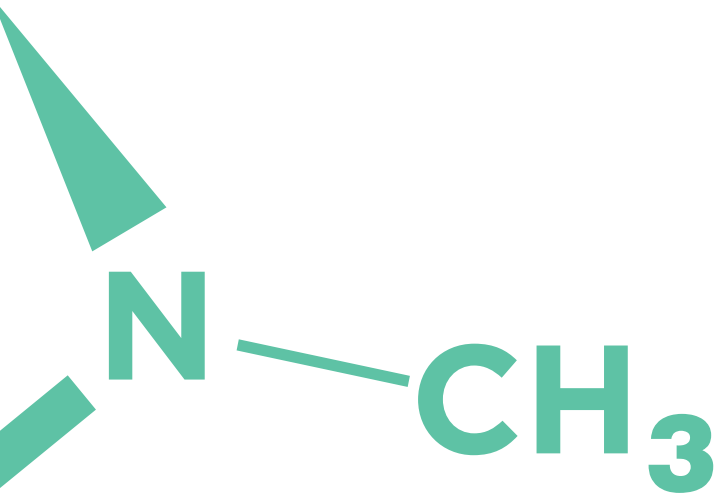
Clinical governance has never been more important. General practitioners (GPs) must prescribe these drugs judiciously in order to protect patients from harm. This means acting in accordance with national and state regulations, accountable prescribing, and particularly with opioids, understanding pain and pain management.

GPs should also 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.

This guide, and its companion, *Part C2: The role of opioids in pain management*, is a synthesis of the clinical standards and best available evidence for opioid use in the primary care setting.

In completing this guide, The Royal Australian College of General Practitioners (RACGP) acknowledges the work of the key advisers and reviewers, and the many people who have provided constructive feedback.

The 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.



Contents

Figures

Boxes

Tables

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Conflicts of interest

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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Central and Eastern Sydney Primary Health Network, New South Wales

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

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 patients 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, undertaken 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, then 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.

Introduction

Aims

This guide aims to help general practitioners (GPs) prescribe opioids appropriately in the general practice context. It is designed to discourage inappropriate use and reduce harms by providing GPs with guidance and practical advice regarding opioid therapy. It is complemented by *Part C2: The role of opioids in pain management* and aligns with *Prescribing drugs of dependence in general practice, Part A: Clinical governance framework*, which is available at www.racgp.org.au/your-practice/guidelines/drugs-of-dependence-a

Scope

This document provides an overview of clinical standards for opioid use in general practice.

The guide covers:

- the evidence base for opioid prescribing
- opioid pharmacology
- common concerns regarding opioid prescribing
- the place for opioids (and other interventions) in general practice
- clinical governance strategies that support accountable prescribing of opioids within general practice.

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

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 an RACGP series for 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 of 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 C2: The role of opioids in pain management*

  Part C2 is a companion to Part C1. However, unlike this guide, Part C2 provides broader guidance on pain management. Part C2 is available at www.racgp.org.au/download/Documents/Guidelines/Addictive-drugs/Addictive-drugs-guide-C2.pdf

Recommendations should be considered and implemented based on individual conditions and circumstances.

How was this guide developed?

As this is primarily a clinical governance document, the RACGP performed systematic searches on PubMed and Medline for national and international governance documents regarding opioids in primary care. We also reviewed government publications (including drug utilisation data), coroners' proceedings and state health laws and regulations. Further, we sought advice from a range of experts.

All conflicts of interest were managed according to RACGP policies, available at www.racgp.org.au/support/policies/organisational

The Expert Committee 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.

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

1. Overview of opioid use in Australia

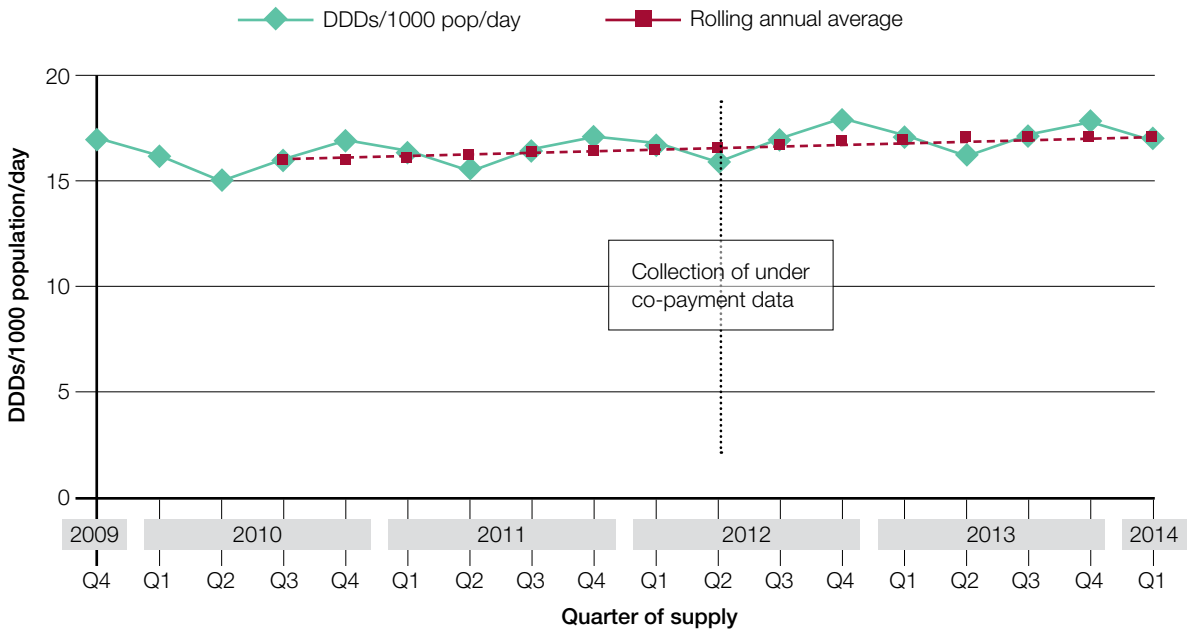
1.1 Trends in opioid use in Australia

Worldwide opioid use has increased significantly, with a doubling of opioid analgesic prescriptions recorded between 2001–03 and 2011–13.[1] While Australia only has around one-third the opioid consumption of the United States (US), opioid use here is still considered high and is on par with many European countries.[1]

Almost three million Australians received at least one Pharmaceutical Benefit Scheme (PBS) listed opioid analgesic between April 2013 and March 2014.[2] Of these three million, around 150,000 people (5%) accounted for 61% of opioid use in terms of opioid defined daily doses (DDDs) supplied.[2]

Australian use of opioids is also increasing at a marginal rate. The rolling annual average of DDDs/1000 population/day supplied has increased from 15.73 to 17.06 in the 10-year PBS data collection period (Figure 1).[2] Paracetamol with codeine and tramadol were the two most commonly supplied opioids for most of that period.[2]

Figure 1. Repatriation Pharmaceutical Benefits Scheme opioid utilisation in DDDs/1000 population/day



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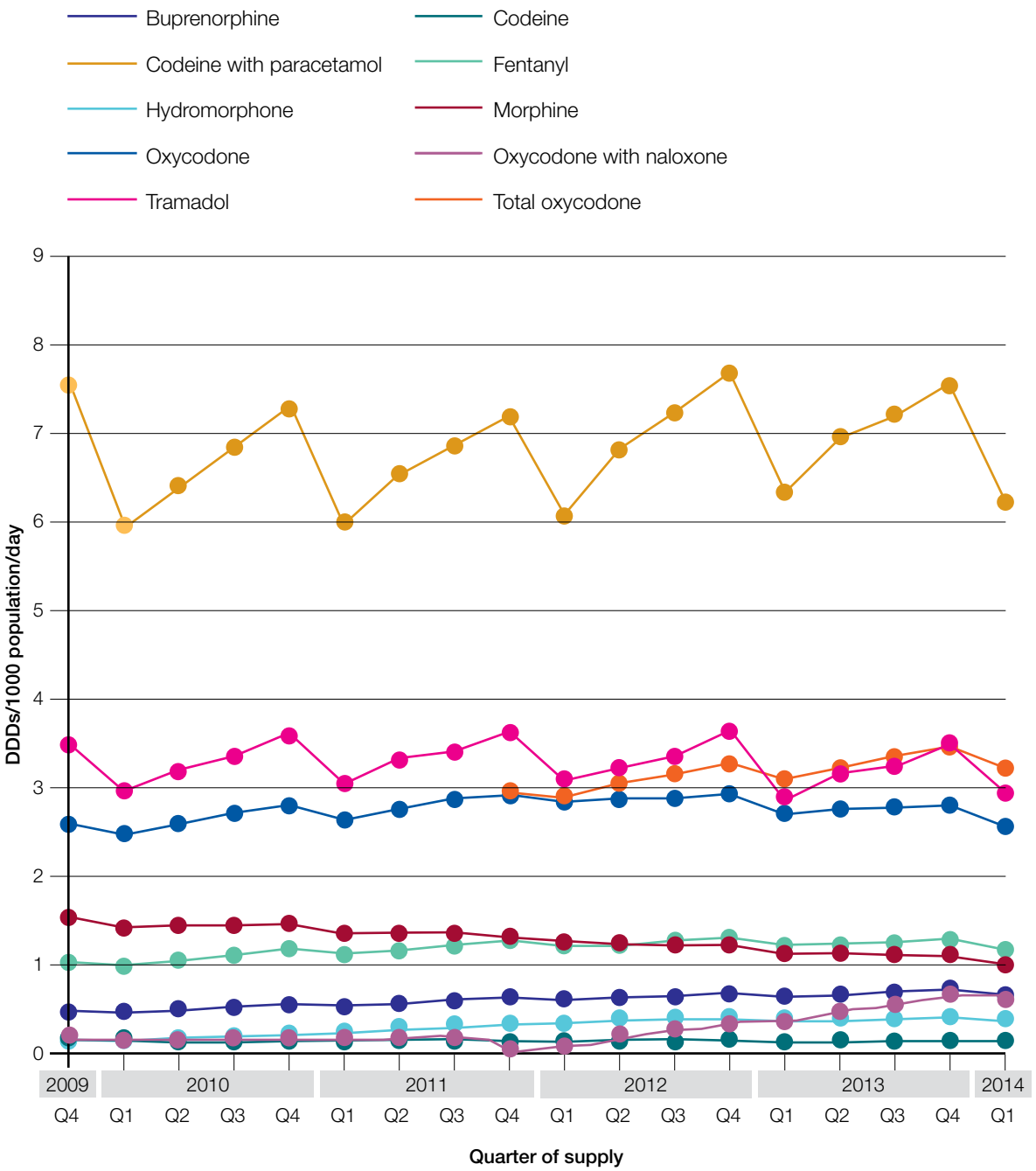
While overall use is only marginally increasing, there are changes in prescribing habits. The use of tramadol and morphine is decreasing, while use of fentanyl, buprenorphine, oxycodone with naloxone and hydromorphone is increasing (Figure 2).[2,3] In particular, oxycodone prescribing has increased: since 2013, oxycodone has become the second most commonly used opioid.[2] Numbers of oxycodone prescriptions are highest among older Australians.[3]

Figure 2. Repatriation Pharmaceutical Benefits Scheme opioid utilisation in DDDs/1000 population/day by drug



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The most commonly sold opioid is over-the-counter (OTC) codeine. It is also the most accessible opioid in the community setting. Despite effectiveness and adverse event concerns, codeine is still used in quite high volumes.[4] There has been a decision to up-schedule codeine to Schedule 4 (S4).[5] This will come into effect in 2018.

Trends in non-medical use of opioids in Australia

The prevalence of non-medical use of pharmaceutical opioids (such as oxycodone and morphine) remains relatively low among the general Australian population.[3] However, significant increases have been reported: between 2007 and 2010 the prevalence doubled from 0.2% to 0.4%.[3]

Refer to Problematic use of opioids

1.2 Why are opioids prescribed, and to whom?

Around half (52%) of PBS-listed opioids are used for the treatment of acutely painful conditions. The other half is almost equally divided between episodic and long-term treatment (25% and 23% respectively).[6] However, it is difficult to determine what proportion of opioids is being used for acute pain, cancer pain, addiction medicine, chronic pain and self-management of pain in Australia.[6]

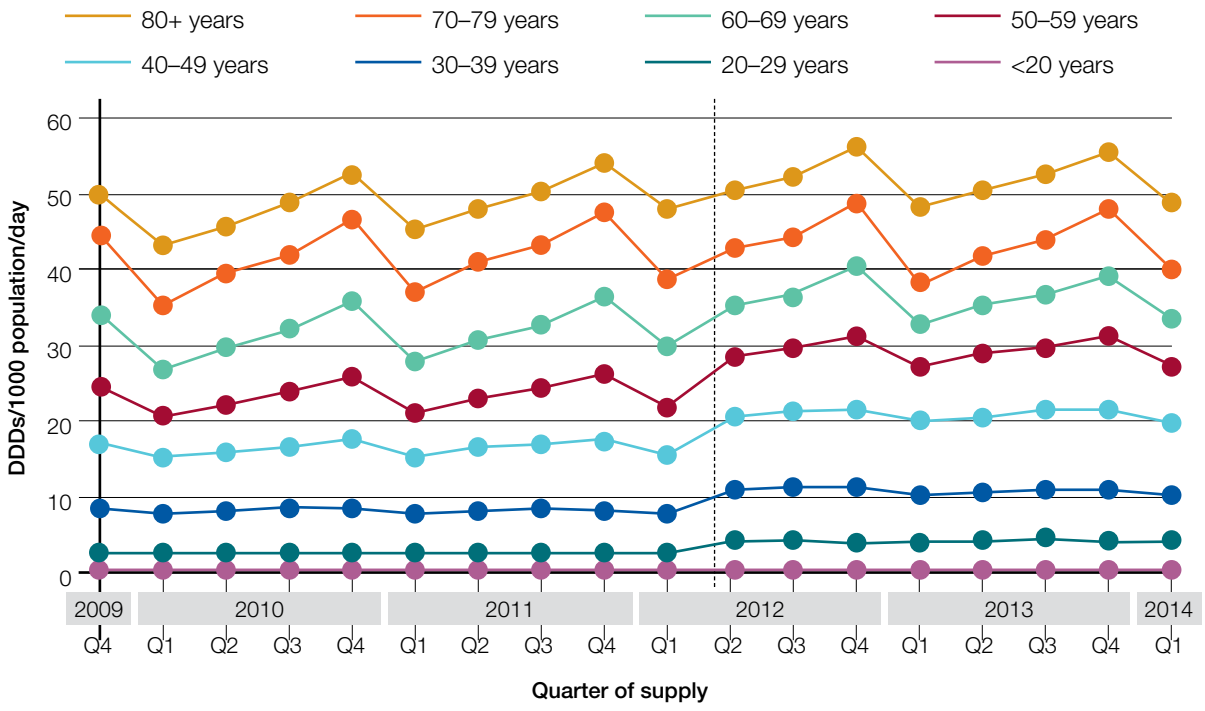
Compared to people not receiving opioid analgesics, people prescribed opioids have been shown to be in poorer health with poorer functioning and higher levels of distress. It is unknown if this is due to pain-related conditions or to medication.[6]

Opioid prescribing appears to vary depending on patient demographics and geography.

Demographics and opioid prescribing

Patients with higher socioeconomic status indicators (eg higher education and income levels, full-time work status, private health insurance) are less likely to be on longer-term opioid analgesic treatment than older patients (Figure 3) and patients who do not speak English at home.[6]

Figure 3. Repatriation Pharmaceutical Benefits Scheme opioid utilisation in DDDs/1000 population/day by age group



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Geography and opioid prescribing

Rates of opioid use are higher in areas that:[4]

- are outside of major cities
- are less populated
- have more men and older people
- have proportionally more low-income earning households
- have greater proportions of people in jobs requiring physical labour.

Implications of prescribing variation

Demographic and geographic findings suggest that longer-term opioid analgesic prescribing occurs in patient groups who might be at higher risk of poor health. This is based on a wide range of health and non-health factors.[6] Programs targeting inappropriate opioid prescribing and use need to focus on these groups and on areas outside of major cities.[4]

The RACGP is currently working with Primary Health Networks (PHNs) to address prescribing variation.

Refer to Strategies to improve appropriateness of opioid use

1.3 Problematic use of opioids

Prevalence of problematic use

The prevalence of non-medical use/misuse of pharmaceutical opioids (such as oxycodone and morphine) remains relatively low in Australia, despite a significant increase between 2007 and 2010 (from 0.2% to 0.4%).[3]

Incidence of problematic use

The incidence of problematic opioid use in primary care is hard to determine because terminology and classifications (eg 'misuse', 'abuse', 'addiction', 'dependence') are difficult to define or are very broad.[7] Reported rates of problematic use range from <1% to 81%.[7–9] Averaging across studies, the rate of misuse is between 21% and 29% and the rate of addiction is between 8% and 12%.[7–9]

Relationship between dose, duration of treatment and problematic use

Problematic use is dose dependent.[9] For example, the rate of opioid dependence or abuse with low-dose chronic therapy is around 0.7%, but this increases to around 6% with high-dose chronic therapy.[9] There are several factors associated with increased risk of problematic use. These include history of substance use disorder (SUD), younger age, major depression, and use of psychotropic medications.[10]

The mean duration between first use and problematic use of prescription opioids is 4.4 years (standard deviation 5.7 years), which presents a significant opportunity for intervention.[11]

Source of misused opioids

Medical practitioners are an important source of misused pharmaceuticals. However, they are not the main source of prescription opioids, with most misused opioids being obtained from dealers (via on-selling of prescribed opioids).[11] Family and friends are the next most common source after dealers.[11] This presents a challenge for strategies such as real-time prescription monitoring (RTPM) systems, as they will not pick up this activity.

RTPM is an important strategy in supporting safer opioid prescribing. While the RACGP strongly supports its implementation, it also recognises that this strategy is not the sole solution to curbing people misusing prescription opioids. It is therefore important for prescribers to recognise the limitations of these systems if solely relied on for the clinical assessment of drug-seeking behaviour.[11]

Refer to Real-time prescription monitoring

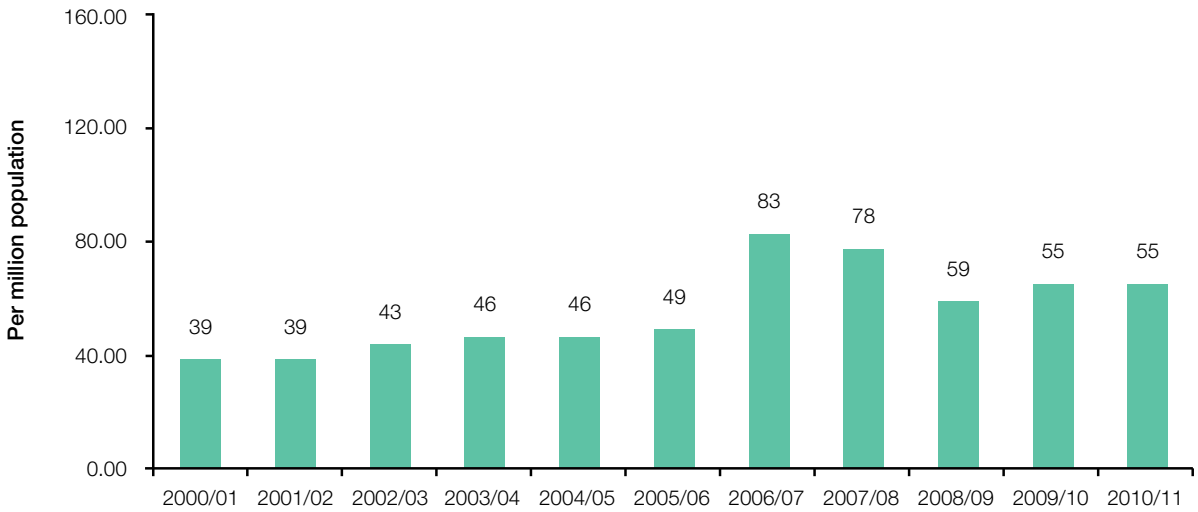
1.4 Treatment seeking for pharmaceutical opioids

Treatment seeking for pharmaceutical opioids increased from around 4800 to 7500 patients during the reporting period 2001/02 – 2011/12.[3] As a percentage of all treatment episodes, pharmaceutical opioids represented 4% in 2001/02 and 5.1% in 2011/12.[3] Morphine accounted for 25% of all treatment episodes for opioids other than heroin in 2011/12.[3]

1.5 Hospitalisation due to opioids

Hospitalisation for pharmaceutical opioid poisoning is not common. Rates peaked in 2006/07 (83 per million persons) and have declined more recently (65 per million persons).[12]

Figure 4. Rate of opioid* hospital separations for poisoning, per million persons, 2001 to 2011[12]



*'Opioid' includes morphine, oxycodone and codeine, and excludes heroin, methadone and pethidine

Reproduced from the Australian Institute of Health and Welfare. National hospital morbidity database (NHMD). Canberra: AIHW.

1.6 Overdose and mortality

Overall trend in overdose and age most affected

The number of deaths due to opioid overdose in Australia is growing. Between 2004 and 2014, there was a 61% increase in deaths due to accidental overdose (from 705 deaths in 2004 to 1137 in 2014).[13] Of the people who died in 2014, 78% were aged between 30 and 59 years.[13]

Geographical trend in overdose

The overall increase in overdose deaths is being driven by those occurring in rural and regional areas. Between 2008 and 2014, there was an 83% increase in deaths in these areas (from 3.1 deaths per 100,000 to 5.7 per 100,000).[13] In the same time period in metropolitan areas the rate changed from 4.2 per 100,000 to 4.4 per 100,000.[13]

Overdose trend in Aboriginal and Torres Strait Islander peoples

Accidental deaths due to opioid overdose per capita for Aboriginal and Torres Strait Islander peoples has increased substantially. Between 2004 and 2014 there was an increase of 141% across the five jurisdictions with Aboriginal data; from 3.9 deaths per 100,000 in 2004 to 9.4 per 100,000 in 2014.[13]

Relationship between patient factors, opioid characteristics and overdose

Higher opioid dosages are associated with an increased risk of fatal overdose. There is a three-fold increase in mortality when comparing high-dose opioid (>200 mg oral morphine equivalent daily dose [OMEDD]) relative to low-dose opioids (<20 mg OMEDD); however, the differences in absolute rates are quite low.[14]

Refer to Metabolism and duration of activity

Additionally, the risk of fatal overdose increases with:[15]

- slow-release and long-duration opioids
- co-prescription of opioids and benzodiazepines
- sleep-disordered breathing
- reduced renal or hepatic function
- older age
- pregnancy
- mental health disorders including SUDs.

In Victoria, 80% of all drug overdoses from 2001 to 2013 involved prescription medications, and pharmaceutical opioids contributed to half of all drug-overdose deaths during that time.[3] Fatal overdosing with pharmaceutical opioids is related to dose and duration of action.[3,16,17]

Table 1. Annual frequency of overdose deaths involving most frequent contributing individual drugs, Victoria 2009–16[18]

Individual drugs	2009	2010	2011	2012	2013	2014	2015	2016
Benzodiazepines	**160**	**169**	**180**	**199**	**212**	**215**	**238**	**258**
Diazepam	104	109	124	133	164	169	192	200
Alprazolam	62	56	43	57	45	28	23	21
Temazepam	28	22	48	35	22	20	25	25
Oxazepam	18	19	44	41	17	19	34	26
Nitrazepam	17	16	11	24	26	13	17	22
Clonazepam	7	9	14	18	19	25	33	30

Table 1. Annual frequency of overdose deaths involving most frequent contributing individual drugs, Victoria 2009–16[18]

Individual drugs	2009	2010	2011	2012	2013	2014	2015	2016
Opioids	**177**	**145**	**183**	**212**	**192**	**186**	**199**	**183**
Codeine	76	57	66	93	71	54	64	47
Methadone	50	55	72	75	70	67	67	70
Oxycodone	41	39	46	46	61	46	58	52
Tramadol	22	9	15	18	24	23	32	26
Morphine	22	11	10	13	7	12	8	13
Fentanyl	1	2	5	17	11	11	23	13
Illegal drugs	**147**	**149**	**153**	**133**	**166**	**164**	**227**	**257**
Heroin	127	139	129	111	132	136	172	190
Methamphetamine	23	14	29	36	51	53	72	116
Amphetamine	4	4	19	11	10	8	9	1
Cocaine	7	1	2	4	5	7	15	10
MDMA	5	1	1	1	3	4	5	13
Antidepressants	**122**	**106**	**101**	**142**	**134**	**144**	**161**	**156**
Mirtazapine	23	21	23	26	30	29	50	24
Amitriptyline	24	26	22	32	25	41	28	31
Citalopram	17	22	21	25	24	25	26	27
Venlafaxine	25	12	16	15	20	19	10	21
Fluoxetine	8	9	8	14	10	7	12	14
Duloxetine	3	5	7	15	11	12	12	14
Sertraline	6	6	4	12	13	9	12	11
Desvenlafaxine	0	1	3	6	8	11	15	17
Alcohol	**94**	**85**	**88**	**80**	**94**	**94**	**106**	**118**
Antipsychotics	**63**	**64**	**65**	**78**	**75**	**81**	**91**	**104**
Quetiapine	28	37	34	41	41	48	49	55
Olanzapine	19	18	17	22	15	21	30	36
Risperidone	6	3	11	8	10	7	9	13
Chlorpromazine	5	2	4	10	6	3	5	5
Zuclopenthixol	5	4	4	6	3	3	5	4
Clozapine	5	5	–	4	6	2	4	5

Table 1. Annual frequency of overdose deaths involving most frequent contributing individual drugs, Victoria 2009–16[18]

Individual drugs	2009	2010	2011	2012	2013	2014	2015	2016
Non-benzodiazepine anxiolytics	**35**	**28**	**33**	**38**	**56**	**48**	**60**	**37**
Doxylamine	13	16	11	21	23	13	14	12
Pentobarbitone*	4	5	11	1	8	15	18	9
Zopiclone	6	3	6	13	14	11	17	11
Zolpidem	11	3	5	5	4	6	11	5
Non-opioid analgesics	**26**	**25**	**30**	**52**	**41**	**49**	**46**	**35**
Paracetamol	23	21	24	50	39	37	42	30
Ibuprofen	5	5	4	5	2	7	5	4
Anticonvulsants	**18**	**14**	**13**	**10**	**37**	**45**	**51**	**52**
Pregabalin†	–	–	–	–	17	27	34	32
Sodium valproate	9	9	5	6	13	9	9	7
Carbamazepine	7	3	6	1	3	3	2	8

* Pentobarbitone prescribing to humans is not permitted in Australia, and the drug could be alternatively classified as illegal

† Routine post-mortem testing for pregabalin did not commence in Victoria until 2013

Reproduced from the Coroners Court of Victoria. Submission to the Inquiry into Drug Law Reform: Coronial recommendations on drug harm reduction. Melbourne: Coroners Court of Victoria, 2017.

In February 2017, the Coroners Court of Victoria in partnership with Turning Point Alcohol and Drug Centre concluded a study that examined the circumstances in which overdose deaths involving pharmaceutical drugs occur in Victoria. Regarding victims of overdose deaths:[18]

- 71% had an SUD
- 73% had a diagnosed mental illness
- 49.6% had both a diagnosed mental illness and a documented SUD.

These patients often had a long-established clinical history of mental illness and drug dependence and had in most cases been known to the health system for extended periods of time (ie longer than 10 years).[18]

This conclusion underpins advice to 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.

1.7 Strategies to improve appropriateness of opioid use

To support quality use of opioid medication and to reduce inappropriate opioid use, the RACGP supports:

- standardised regulatory definitions of dependency and laws regarding drugs of dependence across all state and territory jurisdictions
- an effective, national RTPM system and surveillance program
- up-scheduling of codeine
- improved analysis of PBS prescriptions to detect variation in prescribing drugs of dependence
- improved categorisation of deaths from prescription drugs by the National Coronial Information System
- state and territory health systems that support continual and coordinated care for patients with complex and/or multiple problems (eg combined SUDs, chronic pain and mental illness) in conjunction with general practice
- improved use and management of opioids in acute settings
- robust handover standards between primary, secondary and tertiary care
- a national set of clinical indicators that monitors general practice prescribing drugs of dependence
- national support for the 'medical home' concept (ie a patient having one general practice and preferably one GP to provide ongoing care and accountable prescribing of drugs of dependence)
- improved governance and monitoring of opioid prescribing at a general practice level
- adequate resourcing of systems of care within general practice for patients with
  - chronic non-cancer pain (CNCP)
  - SUDs
- improved collaboration with pharmacies regarding use of drugs of dependence
- education of consumers and health professionals, and expansion of non-pharmaceutical evidence-based treatments for chronic pain as crucial elements in preventive activities.

Real-time prescription monitoring

The RACGP is currently working with the Australian Institute of Health and Welfare (AIHW) to improve monitoring of opioids nationally.

The RACGP strongly supports the introduction of RTPM while recognising that the current state of research[19] with evidence on effectiveness in reducing inappropriate prescribing,[20] abuse, and opioid-related deaths is still evolving.[21,22] Consumer impact and experiences with RTPM are not always positive.[23] Administrators and clinicians should be clear about the intended objectives, risks and benefits of RTPM prior to implementation.[24–26] While it is not a panacea to reduction in prescription drug harm, RTPM has a key role in supporting the high-quality use of drugs of dependence.

2. Clinical governance

2.1 Patient focus

2.1.1 Patient perspectives

Patients have the right to best practice care that is respectful and promotes their dignity, privacy and safety. Those who misuse medication and/or illicit drugs have the same entitlement as other patients to respectful care. Treatment should aim to optimise outcomes across a range of areas including health, problematic drug and alcohol use, social functioning and crime.

Good pain management or opioid replacement therapy (ORT) can have significant benefits. For many people, effective therapy can transform quality of life: it can allow people to function and participate in their families, communities and workplaces. Some patients have experienced clinical improvement from opioid therapy, but have also experienced stigma and/or difficulties in accessing long-term care.[27] Patients report being continually judged or shamed by the media, society and the medical profession. Care should be undertaken not to stigmatise patients with these complex conditions.

This means balancing patient-centred care, evidence-based practice, legislative requirements and partnerships with other healthcare providers to patients across the spectrum. Further considerations when balancing patient care and legal requirements include such things as drivers licence requirements and potential risks to others (eg children and others in the patient's care).

Maintaining a patient focus ensures that care is provided in partnership with patients and their families and carers, respecting their diverse needs, preferences and choices, and in coordination with other organisations whose services impact on patient wellbeing.[28] 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.[29]

The healthcare provider may be faced with misaligned expectations of opioid therapy, especially where patients are either reluctant to consider therapeutic alternatives to opioids or to participate in a time-limited therapeutic trial of the opioid. Clinical discipline is required as there can sometimes be elements of manipulation behind patient requests for opioids. Patient-centred care does not mean professional boundaries can be crossed, laws ignored or therapy continued if it is considered detrimental to the patient's health.

2.1.2 Setting patient behaviour standards for patients on opioid therapy

When prescribing drugs of dependence or when changing a prescription (to manage risk), prescribers have a responsibility to make patients aware of expected standards of behaviour. This process is best undertaken in an empathetic, non-judgemental manner, where there is a good therapeutic alliance with the patient. Having practice policies will help this process.

Patient behaviour standards may include:

- only obtaining scripts from one doctor and one pharmacy
- receiving a staged supply through the pharmacy
- a supervised dose taken by the patient at the pharmacy

- attending appointments regularly
- engaging with other supports
- engaging with psychological supports
- agreement when a therapeutic trial of treatment will cease
- the consequences of inappropriate patient behaviour (eg formal review, possible referral or cessation of clinical relationship).

Any coercion or threat (physical or verbal) in order to manipulate the doctor to prescribe is an immediate red flag and a breach of the therapeutic alliance. A GP has the right to discontinue the care if a patient has crossed boundaries and behaved in a violent or threatening manner.[30]

The therapeutic relationship may be ended by the GP during a consultation or by letter or telephone.[30] Safety determines which method is used. Practices should consider having a process that staff can follow if the patient makes any further contact.[30]

2.1.3 Shared decision making around opioid therapy

Shared decision making (SDM) is vital to patient-centred care. For patients to be an active partner in their care, they need to be well informed.

SDM is the 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.[31–33]

Very few clinical situations surrounding opioid therapy involve consideration of just one option, and no treatments are 100% effective or 100% safe. When considering pain management options, often the evidence does not strongly support a single clinically superior option.[31,32,34] Hence, pain management typically involves a preference-sensitive decision that is likely to be strongly influenced by patients' beliefs and values.[34–36]

Information provided should allow realistic expectations about the likely or potential outcomes of the treatment. SDM has been shown to build trust, prevent harm and reduce surprise and distress if complications or adverse events occur.[37–41]

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).[42]

A caveat

While most patient involvement with opioids is clinically driven, there can also be elements of manipulation (and rarely, criminal intent) behind patient requests for opioids. The important caveat when prescribing opioids relates to healthcare benefits. Some patients with CNCP or drug dependence may request higher opioid doses on the basis that they have a 'right' to analgesic drugs for pain and are making a choice as an informed patient.

Patients do have a right to receive good healthcare, but not a right to access drugs of dependence. Patients need to be informed of this at the beginning of any trial using drugs of dependence. If the clinician feels that further therapy is detrimental to a patient's health, then clinical withdrawal of medication should begin.

Doctors typically have a strong desire to alleviate patient distress and suffering. There are GPs who find it difficult to set boundaries for patients and are at risk of being pressured to prescribe inappropriately. The psychological phenomenon of 'transference' in addiction, pain and mental illness can result in doctors having difficulty in these clinical areas. Others have difficulties in saying 'no' or hold the belief that they are 'helping' or using a harm minimisation approach by giving patients who are seeking drugs what they ask for.

All practitioners express difficulty responding to manipulative behaviours or techniques posed by some patients seeking opioids inappropriately. GPs should educate themselves about appropriate responses to common

manipulative techniques and behaviours posed by some patients to access opioids. To aid GP negotiation skills, scripted replies have been developed to help with appropriate responses in difficult situations.

Box 1. 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

2.2 Laws and regulations

2.2.1 Legislative requirements for opioid prescribing in general practice

State and territory law

There are strict legal requirements around the prescription of drugs of addiction or controlled drugs, known as Schedule 8 (S8) medicines, which include opioid medications. Doctors must abide by the laws and regulations that govern prescribing. Those who disregard their responsibility risk civil, disciplinary or coronial proceedings.

Before prescribing an opioid, GPs must take all reasonable steps to ensure a therapeutic need exists. Once a therapeutic need is established, GPs are required to comply with state-specific or territory-specific health legislation and, in some cases, obtain a permit from the relevant health authority.

The legislative requirements vary across Australia. There are inconsistencies across states and territories regarding the definition of 'drug dependency', the authority required for prescribing, and the rules of interstate prescribing. It is the prescriber's responsibility to ensure that prescriptions comply with all aspects of their state or territory legislation.

Consistently, the state or territory legislative requirements for prescribing S8 drugs depend on the person's drug dependency status and the duration of opioid prescribing. That is:

- For people who are known or suspected to be drug dependent, S8 medications (and in some states and territories, certain S4 benzodiazepines) cannot be prescribed without a permit or an appropriate approval from the relevant state or territory health department's pharmaceutical services unit (PSU). A prescriber must understand the legislative definition of 'drug dependence' in their state or territory and use their clinical judgement to determine whether the patient is drug dependent in accordance with that definition. Patients currently or previously on opioid treatment programs need special consideration as some states consider these patients to be drug dependent.
- For people who are not drug dependent, S8 medications cannot be prescribed for a period greater than two months without an appropriate approval under current state and territory legislation. The New South Wales, Tasmanian and Northern Territory governments have subtle variations to this law and prescribers are referred to relevant legislation.

These approvals are distinct from, and in addition to, any authority under the PBS for scripts.

Box 2. Information needed for an S8 prescription to comply with state and territory standards

- The prescriber's full name, address and prescriber number
- Date the prescription was written
- The patient's full name, address and date of birth
- Description and quantity of the medicine of addiction to be dispensed
- Precise directions for use
- Number of repeats (if any) and intervals at which they may be dispensed
- Signature of the prescriber

For computer-generated S8 prescriptions, the information highlighted in italics (above) must be written in the doctor's own handwriting.

Adapted from the Government of Western Australia Department of Health. WA Regulatory requirements for prescribing Schedule 8 medicines (S8s). Perth: WA Drug and Alcohol Office, 2009. Available at ww2.health.wa.gov.au/Articles/N_R/Opioids-benzodiazepines-and-other-S8-medicines

It is important that prescribers are aware of and comply with the legislative restrictions that apply in the state where the prescription is dispensed. This is a particular issue for GPs working close to state or territory borders. To avoid potential issues, GPs should advise patients that prescriptions should be dispensed in the state or territory where the prescription is written.

GPs need to be aware of their obligations regarding the impact of medication on the patient's ability to safely perform usual activities such as driving (eg Jet's Law in Queensland – refer to www.legislation.qld.gov.au/LEGISLTN/CURRENT/T/TrantOpRUDLR10.pdf)

Table 2. Opioid prescribing in Australia: Definitions of drug dependence, state and territory authority requirements* and prescription rules

State	Statutory definition of 'drug dependent'†	Local authority required to prescribe opioids		Interstate prescription rules	Useful websites
		For drug-dependent patients	For non–drug-dependent patients		
ACT	A person who, due to the administration of the drug/substance, shows impaired control or drug-seeking behaviour suggesting impaired control; and due to the cessation of the drug/substance, is likely to experience symptoms of mental/physical distress or disorder	Approval is required for all S8 drugs, and will only be provided if prescribing is in accordance with opioid treatment guidelines	Approval is required if prescribing for longer than two months	Interstate prescriptions are allowed as long as the relevant approvals are fulfilled	ACT Health
NSW	A person who has acquired an overpowering desire for the continued administration of a drug of addiction or a prohibited drug listed in Schedule 1 of the *Drug Misuse and Trafficking Act 1985* (NSW)	Authority is required for all S8 drugs	Authority is required when prescribing the following drugs for more than two months: • any injectable form of any S8 drug • alprazolam • buprenorphine • flunitrazepam • hydromorphone • methadone	Interstate prescriptions require prior authorisation	NSW Ministry of Health

Table 2. Opioid prescribing in Australia: Definitions of drug dependence, state and territory authority requirements* and prescription rules

State	Statutory definition of 'drug dependent'†	Local authority required to prescribe opioids		Interstate prescription rules	Useful websites
		For drug-dependent patients	For non–drug-dependent patients		
NT	Addiction to a regulated substance means a state of physiological or psychological dependence on, or increased tolerance to, the habitual and excessive use of the substance, and includes pain and other symptomatic indications arising specifically from withdrawal of the substance	Authority is required	Authorisation is required when prescribing an unrestricted S8 drug for more than 15 patients. Notification is required when prescribing for more than eight weeks or in a specific example such as the replacement of lost or stolen prescriptions. Refer to the *Code of Practice: S8 Substances* for further examples	No interstate prescriptions are allowed unless the subject of an authorised exemption	NT Department of Health
Qld	A person who, as a result of repeated administration of dangerous drugs, demonstrates impaired control, or exhibits drug-seeking behaviour that suggests impaired control, over the continued use of dangerous drugs; and who, when the administration of those drugs ceases, suffers or is likely to suffer mental/physical distress or disorder	Approval is required to prescribe S8 and S4D drugs to registered drug dependent persons	Notification and treatment report are required if prescribed for longer than two months	Interstate prescriptions are allowed as long as the relevant requirements are fulfilled. No interstate prescriptions for methadone or buprenorphine will be allowed for patients on opioid treatment programs	Queensland Health
SA	A person who, due to repeated administration of prescription drugs or controlled drugs, has an overpowering desire for the administration of any such drug and is likely to suffer mental/physical distress or disorder upon cessation of administration of that drug; or has a history of consuming or using prescribed drugs in a manner that presents a risk to that person's health or which is contrary to a medical practitioner's instructions	Authority is required to prescribe all S8 drugs	Authority is required if prescribing for more than two months	Interstate prescriptions are allowed as long as the relevant notifications and permit requirements are fulfilled in line with SA legislative requirements	SA Health
Tas	A person who seeks to obtain a drug of dependence to sell or supply to another person, or for non-medical purposes, or as a result of administration exhibits impaired ability to manage properly the use of any such drug, or behaviour which suggests impaired ability. Failure to obtain drugs of dependence for a non-medical purpose, and consequent mental/physical distress or disorder, is also a sign	Authority is required immediately to prescribe S8 drugs. Notification of drug-seeking or other aberrant behaviour is also required	Authority is required to prescribe for more than two months. If alprazolam is concurrently prescribed, authority is required after one month	Interstate prescriptions of S8 or S4 drugs cannot be dispensed in Tasmania	Tasmanian Department of Health and Human Services

Table 2. Opioid prescribing in Australia: Definitions of drug dependence, state and territory authority requirements* and prescription rules

State	Statutory definition of 'drug dependent'†	Local authority required to prescribe opioids		Interstate prescription rules	Useful websites
		For drug-dependent patients	For non–drug-dependent patients		
Vic	Not defined in the *Drugs, Poisons and Controlled Substances Act 1981* (Vic)	A permit is required to prescribe S8 drugs	A permit is required to prescribe continuously for more than eight weeks	Interstate prescriptions are allowed as long as the relevant requirements are fulfilled	Victorian Department of Health and Human Services
WA	A person who, under a state of any periodic or chronic intoxication produced by a drug of addiction or any substitute, or is under a desire/craving to take that substance/any substitute until the desire or craving is satisfied, or is under a psychic‡/physical dependence to take a drug of addiction or any substitute; or is listed in the register for information kept under the *Drugs of Addiction Notification Regulations 1980*	Authority is required to prescribe S8 drugs	Authority is required when prescribing for longer than 60 days (or for more than 60 days in any 12-month period)	Interstate prescriptions can be dispensed in WA if they comply with regulations. Further restrictions on some S8 drugs apply	Western Australian Department of Health

* This does not refer to PBS requirements

† In Tasmania, the Act defines drug-seeking behaviour rather than drug-dependent behaviour

‡ Psychic is used to legally define a drug-addicted patient in the WA Regulations

Reproduced from Jammal W, Gown G. Opioid prescribing pitfalls: Medicolegal and regulatory issues. Aust Presc 2015;38:198–203.

2.2.2 Pharmaceutical Benefits Scheme requirements for opioid prescriptions

Under PBS categorisation, most S8 opioids are 'Restricted benefits' items and some are 'Authority required benefits' items. Before initial prescribing and before requesting repeats or increased maximum quantities, prescribers need to check the status of each item.

The following descriptions are taken from Western Australia and Queensland health department regulatory requirements for S8 medications.

- WA: ww2.health.wa.gov.au/Articles/N_R/Opioids-benzodiazepines-and-other-S8-medicines
- Qld: www.health.qld.gov.au/clinical-practice/guidelines-procedures/medicines/drugs-of-dependence?a=167256

Restricted benefits

Authorities for increased maximum quantities and/or repeats for restricted benefit items will be granted only for:

- chronic severe disabling pain associated with proven malignant neoplasia
- chronic severe disabling pain not responding to non-opioid analgesics where the total duration of narcotic analgesic treatment is less than 12 months

- first application for treatment beyond 12 months of chronic severe disabling pain not responding to non-narcotic analgesics where the patient's pain management has been reviewed through consultation by the patient with another medical practitioner, and the clinical need for continuing narcotic analgesic treatment has been confirmed. The date of the consultation must be no more than three months prior to the application for a PBS authority. The full name of the medical practitioner consulted and the date of consultation are to be provided at the time of application
- subsequent application for treatment of chronic severe disabling pain not responding to non-narcotic analgesics where a PBS authority prescription for treatment beyond 12 months has previously been issued for this patient.

Authority required benefits

Authority required benefits are restricted benefits that require prior approval from Medicare Australia or the Department of Veterans' Affairs (DVA).

When a PBS or Repatriation Pharmaceutical Benefits Scheme (RPBS) authority application is for an S8 opioid, the following guidelines apply:

- The supply quantity is generally for 14–28 tablets.
- Where supply for a longer period is warranted
  - telephone approvals are limited to one month's supply by calling the PBS Authority approvals enquiry line (1800 888 333)
  - quantities are usually for up to three months' therapy with written application posting an Authority prescription form to Medicare Australia. After approval, Medicare Australia will forward both copies of the prescription to the patient or the prescriber (if it is to be sent direct to the patient, the prescriber should mark the box next to the patient's details).

2.3 General practice responsibilities for safe opioid prescribing

The quality and safety of patient care is no longer confined to the individual practitioner. General practices have responsibilities to work collaboratively with practitioners to address the safety and quality of health services provided in their facilities.

A simple checklist has been included (Appendix B4) to inform practice owners of their position regarding drugs of dependence. It is not a standard or practice requirement; rather, it is designed to enable general practices to evaluate their status in managing drugs of dependence for their respective populations. As each general practice is different, findings should be interpreted individually.

Refer to Appendix B4: Simple checklist for a general practice to review its quality management of drugs of dependence.

Practice systems of care around opioids can be put in place to maximise health outcomes and social functioning for patients while minimising drug and alcohol misuse, abuse, diversion and crime. Systems of care also provide the necessary infrastructure and support for GPs to perform their jobs efficiently and effectively.

2.3.1 Staff education and competency

Practices should ensure they have the level of knowledge among team members and practice capacity to address the issues associated with opioid prescribing (eg identification of patients with more complex needs and those at higher risk). Prescriber education is particularly important.

GPs who are regularly involved in managing patients with problematic use of opioids or other drugs and alcohol should consider further training and developing good working relationships with addiction specialists.

Practices should promote the development of competency in prescribing opioids. Where potentially inappropriate and suboptimal prescribing is identified, practices and GPs have an opportunity to engage in education and support to improve patient outcomes.

2.3.2 Opioid dependence programs within the general practice

Access to relevant programs is limited in some areas of Australia. Opioid substitution therapy (ie using methadone and buprenorphine) is effective for the management of opioid dependence and is within the scope of most Australian GPs.[43] The training and regulatory requirements for prescribing opioids for substitution therapy varies between jurisdictions.

Opioid replacement and detoxification typically requires significant and frequent communication with patients, more regular visits with the GP and other clinical staff, on-call mechanisms, and management of patients who are often highly anxious.[44] Suitably qualified staff, organised support and ongoing quality assurance arrangements may be required. GPs involved in this type of program should feel comfortable prescribing adjunct medications.[45]

2.3.3 Balancing patients' needs with practice capacity (risk stratification)

Patients should be appropriately evaluated to determine the complexity of services required. A goal of the initial patient assessment is to make a reasonable determination of clinical complexity and risk in the context of concurrent SUD or psychopathology. From this, patients can be placed into one of three basic risk groups: patients who may be safely managed in the primary care setting, patients who should be co-managed with specialist support, and patients who should be referred on for management in a specialist setting (Table 3).

GPs with advanced training in addiction medicine and/or mental health management are suited to taking on higher responsibilities under this model.

Table 3. Patient risk groups[46]

Group I	Group II	Group III
Managed in primary care	Managed in primary care with specialist support	Managed by specialist services
Patients with no evidence of past or current history of SUD or mental illness, apart from the presenting problem	Patients may have a past history of a treated SUD or a significant family history of problematic drug use Patients may also have a past or concurrent psychiatric or chronic pain disorder While not actively addicted, these patients are at increased risk, but may be managed in consultation with appropriate specialist support	Patients with an active SUD or major untreated psychopathology These are the most complex cases to manage and patients pose significant risk to both themselves and to practitioners without appropriate resources or experience

These groups are dynamic and it is important to continually reassess risk over time.[46]

For example, a patient in Group II can relapse to active addiction, moving to Group III, or a patient in Group III can move to Group II with appropriate treatment. Sometimes, as more information is obtained over time, patients initially assessed as low risk (Group I) may be reclassified as Group II or even Group III.[46]

2.3.4 General practice policies regarding opioid prescribing

Good clinical governance is supported by comprehensive practice policies aimed at a unified approach to drugs of dependence, which support individual GPs to prescribe these drugs safely and appropriately. Practices may choose to display some of these policies on a sign in the waiting room.

Appendix B of this document provides example policies. At a minimum, general practices should consider having clinical policies regarding:

- Opioid prescribing policy for patients (Appendix B1)
- Requests for repeat scripts for drugs of dependence (Appendix B3)
- Reducing unnecessary opioid prescribing for acute conditions (Appendix B6)
- Risk assessment for patients with ongoing needs for drugs of dependence (Appendix B7)
- Opioid dosing thresholds (Appendix B8)
- One-year review of opioid prescribing (Appendix B9)
- Continuation of opioid therapy in a new patients (Appendix B10)
- Approach to drug-seeking patients (Appendix B11)
- Opioid reduction policy (Appendix B12)

2.4 Accountable prescribing of opioids in general practice

2.4.1 Key prescribing principles

As with any treatment, prescription of opioids 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 non-pharmacological treatments and interventions. GPs should be aware of
  - the characteristics of each opioid, its accepted indications for use, and its general and specific risks
  - patient groups or contexts which require additional caution or exclusion (eg pregnancy and lactation, workers' compensation injuries, patients who drive, patients with sleep apnoea or disordered breathing, patients over 65 years of age, patients with renal or hepatic disease, Aboriginal and Torres Strait Islander patients or culturally diverse populations, and patients with comorbid mental health disorders)
- a management plan derived through SDM and continual clinical monitoring.

Accountable prescribing also involves provision of adequate therapeutic monitoring, dose limitations and compliance with national and state law.

In acute pain, opioids should only be prescribed at the lowest effective doses and in amounts no more than the number of doses needed (and should not be *pro re nata* [PRN]). This should be based on the expected duration of pain that is severe enough to justify prescribing opioids for that condition.[47] Less than three days of opioid therapy will usually be sufficient for non-traumatic pain not related to major surgery, and continuing requirements for opioid therapy after this time should prompt review.[48]

2.4.2 Recognising patients at risk with opioid prescribing

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

- younger patients – substance use issues generally commence before 35 years of age
- patients without a definite diagnosis or pathology
- patients with active substance use problems or 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[10]
- patients with socioenvironmental problems.

Refer to Patient selection/exclusion process for opioid therapy.

2.4.3 Strategies to address risk with opioid prescriptions

The risk of opioid misuse is addressed by comprehensive assessment.[49,50] Although screening for opioid risk has been recommended, there is little current evidence that it is effective. Treatment agreements and urine testing have also been recommended, however do not appear to reduce overall rates of opioid prescribing, misuse or overdose.[51,52]

As patients with a history of SUD are at higher risk of harms, checking 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 routine urine drug screen may reveal evidence of substances of which the practitioner is not aware. Not all substances are routinely tested for (eg oxycodone, methadone and fentanyl testing may need to be specifically requested). If such drugs are found, whether illicit or legal, the patient should be referred for specialist assessment and management.

Alternatively, negative results on urine testing for specified prescribed medications may raise the possibility of diversion.

2.4.4 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, are likely to fail to provide adequate pain relief, or are contraindicated.

Table 4. Patient groups that require caution when considering opioid therapy[53]

- Pregnant and breastfeeding women
- Workers' compensation injuries
- Patients who drive
- Patients with obstructive sleep apnoea or disordered breathing
- Patients aged 65 years and over
- Patients with renal disease
- Patients with hepatic disease
- Aboriginal and Torres Strait Islander peoples
- Culturally and linguistically diverse populations
- Patients with mental health disorders
- Patients with an SUD, who are opioid tolerant or undergoing opiate withdrawal

Adapted from the Australian and New Zealand College of Anaesthetists. Guidelines on acute pain management. Melbourne: ANZCA, 2013.

Evaluate the risk factors for opioid-related harms in individual patients. This may include a review of the patient's history of controlled substance prescriptions using the Prescription Shopping Programme (PSP) or

state prescription drug monitoring program (PDMP) data to check if the patient is receiving other opioids or medications (especially benzodiazepines[54]) that increase risk of overdose.

Avoid prescribing opioids to patients with polydrug use or comorbid alcohol or substance use disorders. GPs should consider tapering benzodiazepines and seeking specialist opinion or a specialised pain management facility in the management of these patients.[55]

2.4.5 Prescribing practices to minimise risks in opioid therapy

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 time frame, but also by dispensing patients a manageable 'pill load' (ie dispense only the amount of opioid medication needed for a defined interval).

Prescribers can also decrease the risk of misuse by reducing access and temptation to overuse medication through much more frequent dispensing of smaller quantities of medications. This can range from weekly, twice weekly to daily (supervised) dispensing.

Prescriptions can also have 'Do not fill until [insert date]' instructions. This can reduce the number of tablets a patient is given at a time without requiring unnecessary visits for repeat prescriptions. This is aided by a one-practice and, preferably, one-GP approach, and the dispensing of medication through one pharmacy.

Refer to Appendix B7: Risk assessment for patients with ongoing needs for drugs of dependence

2.4.6 Getting urgent advice and support for patients on opioid therapy

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

Table 5. State and territory legislative frameworks and clinical advisory services

State/territory	Legislative framework	24-hour clinical advisory services
Australian Capital Territory	Pharmaceutical Services Section, ACT Health – 02 6205 0998	Drug and Alcohol Clinical Advisory Service – 03 9418 1082
New South Wales	Pharmaceutical Services Unit, NSW Health – 02 9391 9944	Drug and Alcohol Specialist Advisory Service – 02 9361 8006 (Sydney) 1800 023 687 (rural)
Northern Territory	Poisons Control Unit, Department of Health – 08 8922 7341	Drug and Alcohol Clinical Advisory Service – 1800 111 092
Queensland	Medicines, Regulation and Quality, Queensland Health – 07 3328 9890	Alcohol and Drug Information Service – 1800 177 833 (to be put through to Alcohol, Tobacco and Other Drugs for clinical advice)
South Australia	Drugs of Dependence Unit, SA Health – 1300 652 584	Drug and Alcohol Clinical Advisory Service – 08 8363 8633
Tasmania	Pharmaceutical Services Branch, Department of Health and Human Services – 03 6166 0400	Drug and Alcohol Clinical Advisory Service – 1800 630 093
Victoria	Drugs and Poisons Regulation, Department of Human Services – 1300 364 545	Drug and Alcohol Clinical Advisory Service – 1800 812 804
Western Australia	Pharmaceutical Services Branch, Department of Health – 08 9222 6883	Clinical Advisory Service – 08 9442 5042

2.5 Care coordination for patients prescribed opioid therapy

Clinical coordination needs to occur whenever care is to be delivered by different providers. Poor transfer of care risks patient safety and is a common cause of serious adverse outcomes. Inadequate handover can also lead to medication errors, wasted resources and unnecessary repetition of tests, delayed treatment or follow-up of significant test results, and increased risk of medico-legal action. Within general practices there should be an effective handover system that ensures safe and continuing healthcare delivery for patients in the event of staff absences.

GPs also work with a range of care facilities and other professionals who prescribe drugs of dependence, and may work as part of a wider organisation or in a multidisciplinary team. It is important to be aware of accepted best-practice protocols used in each setting and work in accordance with these.

It is usually good practice to ensure that clinical practices are standardised through local area policies and protocols.

2.5.1 Managing patients prescribed opioid therapy who see multiple providers

Occasionally, some complex patients are managed by several practitioners working in collaboration. It is important to determine and agree on a primary medication provider to avoid medication adverse events.

The doctor writing the prescription ultimately assumes responsibility for the prescription and its compliance with legislation. This is irrespective of whether another doctor at the practice primarily prescribes or a specialist has recommended the treatment.

When a GP does not feel happy to provide a prescription, they should not feel pressured to do so. The ideal situation is to have an independent drug and alcohol specialist review the case. Alternatively, referral back to the original provider for scripts may be warranted.

2.5.2 Referral of patients prescribed long-term opioid therapy

Inter-practice referral of patients prescribed long-term opioid therapy

Patients will travel within Australia and appropriate handover of care to another practice or practitioner is often necessary. For patients who are prescribed opioid therapy this can be complicated. Referral of patients should be both written to Australian Commission for Safety and Quality in Health Care (ACSQHC) handover standards, and assisted by GP-to-GP communication or practice-to-practice communication prior to the arrival of the patient at the new destination.

GPs at the new practice have an obligation to reassess the clinical context and prescribing appropriateness (refer to *Prescribing drugs of dependence in general practice, Part C2: The role of opioids in general practice* – Section 1.5.5 The inherited patient – Continuation of long-term opioid management plans initiated by other healthcare providers). All referrals should contain relevant information pertaining to short-term and long-term pain management including:

- a summary of biopsychosocial assessment and pain history
- a pain diagnosis, and the rationale and plan for pain management
- a medical summary including medications and known adverse reactions
- relevant specialists involved in care
- a copy of relevant state permits.

Deciding when to seek advice or consider referral to a specialist

Patients who are at higher risk for dependence or have more complex issues need to be jointly managed between primary care and specialised drug and alcohol addiction services. They also may also require the input of mental health and/or pain specialists.

The ongoing treatment of pain, addiction and mental illness comorbidities is a complex undertaking. Initial referral may be needed to obtain a comprehensive evaluation or to clarify the optimal therapeutic strategies.

Referral is typically considered for patients who are at higher risk, who have more complex needs or for patients at risk of adverse events. This includes patients who:[56]

- are relatively young (<35 years)
- have a comorbid psychiatric or psychological disorder
- have previous or current opioid (or other) SUDs
- have indeterminate pathology.

Once an optimal regimen and monitoring approach has been implemented, referral may be warranted in the case of:[56]

- unexpected drug dose escalation
- ceiling drug dosages reached
- suspected abuse or misuse
- risk category change
- high levels of patient distress
- unusual opioid requirements or suspicions of drug diversion
- poorly controlled comorbid psychiatric or psychological disorder.

Deciding when to refer a patient for hospital admission (through emergency departments)

Patients may need referral to hospital if they are at risk to themselves, pose risks to others or are at risk of harm by others. Typically, these situations are sensitive, and contact with state or territory helplines and accident and emergency staff may be appropriate.

Table 6. Identifying patient risk

Risk to self	Risk to others	Risk by others
• Self-harm and suicide, including repetitive self-injury • Self-neglect • Absconding and wandering (which may also be a risk to others) • Health, including: – drug and alcohol abuse – medical conditions (eg alcohol withdrawal, unstable diabetes mellitus, delirium, organic brain injury, epilepsy) • Quality of life, including dignity, reputation, social and financial status • During pregnancy (both risk to mother and foetus)	• Harassment • Stalking or predatory intent • Violence and aggression, including sexual assault or abuse • Neglect or abuse to children • Property damage, including arson • Public nuisance • Reckless behaviour that endangers others (eg drink driving)	• Physical, sexual or emotional harm or abuse by others • Social or financial abuse or neglect by others • Deviation of supply of medication from elders who are dependent on medication (form of elder abuse)

Adapted from Mental Health Division, Western Australia Department of Health. Clinical risk assessment and management (CRAM) in Western Australian mental health services: Policy and standards. Perth: WA Department of Health, 2008.

Hospital staff often find it difficult to manage referred patients with chronic pain on long-term treatment even when admission is not related to opioid use. Without the relevant information and a clear understanding of the patient's pain management, the patient's treatment may be stopped or altered, which may affect other treatment and outcomes and impact on morbidity, mortality, length of stay and discharge.

All referrals, whether for pain, trauma, injury or other reasons, should contain the relevant information pertaining to short-term and long-term pain management, including:

- medications and known adverse reactions
- diagnosis including reason for requiring inpatient pain management
- relevant specialists involved in care
- duration of treatment
- a summary of biopsychosocial assessment and forensic history.

Providing this information assists hospital teams to seek appropriate consults relevant to the patient's care and optimises outcomes and discharge. Patients with chronic pain may benefit from a chronic pain service consult while in hospital, and linking in with the service if required. The chronic pain service may request follow-up by a community-based chronic pain service on discharge.

2.5.3 Clinical handover of patients using opioid therapy to general practice

Overview

Clinical handover needs to occur whenever care is to be delivered by different providers.

Inadequate transfer of care is a major risk to patient safety and may result in delays in treatment or follow-up, medication errors and unnecessary repetition of tests. It also increases the risk of medico-legal action.

Patients on opioid therapy – handover from hospital clinics to general practice

An effective and efficient health system relies on high standards of care, particularly where handover of care from hospital to community is involved. General practices and GPs should insist on high standards for referral letters for clinical handover or shared-care arrangements from secondary care before accepting the ongoing care of a patient. This facilitates the continuity of care and transfer back to higher levels of care if the need arises.

A practice or GP may not accept the ongoing management of a high-risk patient referred from a public sector facility, unless there is:

- a medical summary
- a clear management plan, particularly with ongoing drugs of dependence including opioids
- patient-specific instructions, including specific clinical issues that would prompt referral back to secondary care
- contact details of a case manager and a clinically responsible person
- documentation that details mechanisms for rapid transfer back to specialty care if deterioration occurs.

These requirements should be supported by practice policies and communicated to referral agencies if information does not meet required standards. It might also be useful to document non-attendance by patients.

Refer to Appendix C: Preliminary RACGP position statements regarding health services integration.

ACSQHC handover standards are available at www.safetyandquality.gov.au/wp-content/uploads/2012/10/Standard6_Oct_2012_WEB.pdf

Patients on opioid therapy – handover from emergency departments to general practice

An effective and efficient health system relies on high standards of care, particularly where handover of care from hospital to community is involved. It is vital that hospitals make clear plans for analgesia reduction after discharge and have reliable systems for communication with usual treating practitioners.[57–59]

Problematic opioid use often has its origins in the acute pain setting.[15,60,61] Therefore, before prescribing opioids at discharge, possible adverse effects of opioids should be considered. These include potential risks of long-term opioid use, injury, drug diversion, misuse, abuse, and death from accidental overdose.[62] Three days or less of opioid therapy will often be sufficient for acute analgesia; more than seven days will rarely be needed.[15] The number of doses dispensed should be no more than the number needed. This prescription should be based on the expected duration of pain that is severe enough to justify prescribing opioids for that condition.[47]

Additionally, patients discharged from emergency departments (EDs) with opioids may not safely store and dispose of their medications.[63] One study found that after receiving opioid prescriptions for an acute episode, 64% of patients kept unused opioids and 34% shared them with others.[64] Patients should be advised of the risks associated with these behaviours and what they should do with unused opioids (ie return them to a pharmacy).[62]

When patients present for acute exacerbation of chronic pain, it is important to identify the source of the pain rather than just treating for acute pain, since treatment for the chronic pain patient can be significantly different. Clinicians should:

- consult the patient's pain care plan prior to prescribing any medications
- confer with the clinician managing the patient's chronic pain, their interdisciplinary team or available resources to provide appropriate chronic pain management
- avoid prescribing increased dosage or additional opioids
- manage exacerbations of pain with non-opioid therapy[65]
- check state-based prescription monitoring services for history of opioid prescriptions
- assess the patient's mental health status and social situation to determine if additional resources may be appropriate.

Patients on opioid therapy – handover from hospital surgical and rehabilitation units

An effective and efficient health system relies on high standards of care, particularly where handover of care from hospital to community is involved. Over-prescription of opioids has been noted for surgical discharges.[66–68] For example, 19% of postoperative patients were prescribed oxycodone upon discharge from a large Australian teaching hospital even though they had not needed any opioid treatment in the 24 hours prior to discharge.[69]

In part due to the increase in the number of patients and procedures considered suitable for short stay or early discharge, the number of patients discharged from hospital or rehabilitation units with opioid medication is rising.[62] There is an association between long-term use of analgesics and early discharge after day-stay surgery with a prescription of opioids, with up to 8% of patients continuing to use opioid medication for months or even years after surgery.[70–72]

In a population of almost 400,000 opioid-naïve patients over 65 years of age who underwent short-stay surgery, the patients who received an opioid prescription within seven days after surgery were more likely to become long-term opioid users within one year, in comparison to those without a prescription.[70] In another study of 39,000 opioid-naïve patients having major elective surgery, 3.1% showed prolonged opioid use after discharge.[72]

In the majority of cases, opioid therapy can be stopped within one week of surgery or injury.[73] With more complex cases, opioids should be weaned and ceased within three months at the most.[73]

A clear plan for analgesia reduction after discharge and good communication with usual treating practitioners will assist in avoiding long-term treatment and unintended dose escalation.[57–59]

Patients on opioid therapy – handover after admission with intentional non-fatal overdose of opioids

Patients who have had a presentation or admission for opioid overdose are at significant risk for another overdose and further harms.[74]

At two years, the cumulative incidence of repeated overdose was:[74]

- 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.[74] Non-fatal opioid overdose is an opportunity to identify and treat SUDs, as patients often have both pain and substance abuse issues.

Alternatively, 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.[75] Please refer to 'Naloxone therapy' in Part C2: The role of opioids in pain management for further information.

All patients presenting to hospital EDs with non-fatal opioid overdose should undergo a full pain and psychiatric evaluation, including consideration of opioid cessation or naloxone therapy. A clear plan for opioid safety after discharge and communication with the patient's usual treating GP in the community is essential.

Box 3. Summary of requirements for effective handover from hospital to general practice

- Hospitals should develop robust communication systems for transfer of care to usual treating practitioners in the community consistent with ACSQHC standards for handover, available at www.safetyandquality.gov.au/wp-content/uploads/2012/10/Standard6_Oct_2012_WEB.pdf
- Patients discharged from hospitals (including EDs, rehabilitation units and day care facilities) on opioids should be educated regarding the safe and optimal use of the pain medications that have been prescribed
- Patients discharged from hospitals (including EDs, rehabilitation units and day care facilities) on opioids should have a clear plan of pain management to facilitate handover of care:
  - A post-surgery discharge letter must accurately reflect information on opioid dose frequency and suggested duration of treatment, including plan for dose reduction
  - Patients commenced on long-term opioids in hospital for chronic (cancer or non-cancer) pain should contain detailed documentary support justifying continued opioid use
  - Psychiatric patients, or patients who were admitted with opioid overdose, should have clear justifications for opioid use and clear plans for future monitoring
- Prescriptions of opioids on discharge should, in most cases, not exceed seven days' supply (or until earliest office opening and follow-up from the patient's usual GP)
- If a patient with a history of chronic pain is admitted to a hospital for non-fatal overdose:
  - the patient should have a full pain and psychiatric evaluation, and consideration of opioid cessation or provision of naloxone therapy for peer or family administration in situations of overdose
  - the patient's usual GP or care team should be notified.

2.6 Discontinuing opioids

2.6.1 Managing opioid discontinuation

Where there is evidence of substance use disorder

The legislative requirements vary in each state and territory. 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.[76] 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).[15]

Where there are complex patient comorbidities

Referral to an addiction or pain specialist is advised.[15,52]

Where there is no evidence of substance use disorder

A commonly used approach is decreasing the original dose by 10% every five to seven days until 30% of the original dose is reached.[77] Then, decreasing the remaining dose by 10% each week.[77] This approach rarely precipitates withdrawal symptoms and facilitates adherence.[77]

If discontinuation is required after a shorter period of opioid therapy then a faster rate of weaning is generally appropriate.[52] One option is reducing the daily opioid dose each week by 10–25% of the starting dose.[52]

3. Clinical pharmacology

3.1 General opioid pharmacology

3.1.1 Mode of action

Opioids act as either pure or partial agonists on opioid receptors in the central and peripheral nervous system. There are three main types of opioid receptors: mu, kappa and delta (μ,κ and δ). Receptor affinity varies with individual opioids. Action at receptors produces the range of opioid effects including:[2,77,78]

- analgesia (analgesic activity of most clinically used opioids is due to their agonist activity at the mu receptor)
- respiratory depression
- cough suppression
- euphoria
- sedation
- decreased gastrointestinal motility (leading to constipation)
- physical dependence.

3.1.2 Metabolism and duration of activity

The response to opioids depends on many factors.[79,80] Variations in response related to age and gender, combined with the significant individual (genetic) differences in opioid effects seen clinically, mean that doses need to be titrated to effect for each patient.

Age

Age is a better determinant than weight for the amount of opioid an adult is likely to require for effective analgesia. This appears to be mainly due to differences in pharmacodynamics of brain penetration rather than systemic pharmacokinetic factors.[81–83]

Gender

Gender also plays a complex role. Potentially due to interaction between oestrogen and opioid receptors, some studies have shown that women report more severe pain than men with similar disease processes or in response to painful stimuli.[84,85]

Genetics

Genetic differences influence opioid pharmacokinetics (metabolising enzymes, transporters) and pharmacodynamics (receptors and signal transduction elements). These contribute to the large inter-patient variability to opioid therapy.[86,87]

Most medicines are metabolised by the hepatic cytochrome P450 enzyme system. Within this system, and most relevant to opioid analgesia, is the CYP2D6 enzyme, which has over 100 allelic variants.[88] These polymorphisms influence the speed of opioid metabolism, including the production of active metabolites, and severity of pain:[48,89]

- Ultrarapid metabolisers (ie carriers of the *CYP2D6* gene duplication) have significantly higher levels of morphine and morphine metabolites after administration of codeine and tramadol, increasing their risk of respiratory depression and death.[90–93]
- Poor metabolisers are likely to have more severe postoperative pain than those who have other variants.

Table 7. Genetics of *CYP2D6*

Genetic type	*CYP2D6* activity	Proportion of the population (approximate)
Poor metabolisers	None	6–10% of Caucasian population[94–96] 0–34% of African population[97,98] ~1% of Asian population[97–99]
Intermediate metabolisers	Low	Not established
Extensive metabolisers	Normal	Most people in the general population
Ultrarapid metabolisers	High	3–5%[94–96] of Caucasian population (note: higher in Southern European [7–10%][99]) 5–30% of African population[98–100] 0.5% of Asian population[98,100]

3.2 Specific opioids

Presented in alphabetical order.

Table 8. Therapeutic Goods Administration approved indications[2]

Drug	Indication
Buprenorphine	Moderate to severe pain Opioid replacement therapy
Codeine	Mild to moderate pain
Fentanyl	Moderate to severe acute or chronic pain
Hydromorphone	Moderate to severe pain
Methadone	Opioid replacement therapy 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.

3.2.1 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 oral and sublingual formulations are usually used.

Musculoskeletal pain

There is limited evidence regarding buprenorphine for CNCP due to a lack of high-quality randomised controlled trials (RCTs).[101] However, transdermal buprenorphine for osteoarthritis has been shown to be effective and well tolerated, with analgesic effects similar to tramadol.[102]

Neuropathic pain

Case reports suggest that buprenorphine is effective in peripheral[103,104] and central neuropathic pain in the clinical setting.[105] However, large trials are lacking and currently there is not enough evidence to support or dispute efficacy of buprenorphine in any neuropathic pain condition.[106]

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.[107]

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.[108] There is a ceiling effect for respiratory depression but not for analgesia.[109] If buprenorphine-induced respiratory depression occurs it may be completely reversed with naloxone,[107] although higher than usual doses and a longer duration infusion of naloxone are required.[110]

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.[108]

Buprenorphine binds strongly to the mu receptor site, but does not fully activate it.[111] 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.[111]

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.

3.2.2 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.[96,112] Ultrarapid metabolisers have significantly higher levels of morphine and morphine metabolites after the same dose of codeine.[91] Poor metabolisers do not produce any morphine or gain any analgesic effect.

Codeine is subject to misuse and dependence, and is the most common prescription opioid associated with fatal overdoses in Victoria.[7] Rates of misuse average between 21% and 29%, and rates of dependence average between 8% and 12%.[7]

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.[113]

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.[114] 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.[114,115]

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

3.2.3 Dextropropoxyphene

In November 2011, the Therapeutic Goods Administration (TGA) decided to remove the registration of dextropropoxyphene in Australia.[116] 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.[117] In combination with paracetamol, it also provides little benefit above paracetamol alone.[118]

In practice

Dextropropoxyphene has now been limited to authorised prescribers 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 painkillers
- have considered the contraindications for the medicine outlined in the product information, and have explained these 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 every time a patient presents for a prescription.

3.2.4 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.[119]

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.[119]

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.[3] 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.

3.2.5 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.[120,121] 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.[76]

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.

3.2.6 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.[122] But it also has a long and unpredictable half-life (mean of 22 hours; range 4–190 hours), which increases the risk of accumulation.[123]

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, some antiretroviral agents) may increase methadone metabolism, which lowers methadone blood levels and leads to potential reduced efficacy or even withdrawal.[124] Use of P450 inhibitors (eg other antiretroviral agents, some selective serotonin reuptake inhibitors [SSRIs], grapefruit juice, antifungal agents) may lead to raised methadone levels, which increases risk of adverse effects or overdose.[124] 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 are typically used three to four times daily to manage persistent pain.[73]

Methadone use is usually confined to specialist pain medicine areas[125] 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.[73]

3.2.7 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.[126] 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.[112] 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.[127,128]

While the clinical significance is uncertain, morphine is the most immunosuppressive of the currently available opioids.[129,130]

There has been a decrease in morphine prescribing in Australia.[3] Prescriptions are most prevalent among older Australians.

Musculoskeletal pain

The evidence for morphine in managing CNCP, including low back pain, is poor.[101]

Neuropathic pain

Strong opioids including morphine have weak Grading of Recommendations Assessment, Development and Evaluation (GRADE) recommendations for use and are recommended as third line mainly because of safety concerns.[131]

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.

3.2.8 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.[132,133]

Paradoxically, in acute postoperative pain, the *CYP2D6* genotype does not appear to influence oxycodone requirements.[134] 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.[134–136]

Oxycodone-related deaths are currently relatively low in Australia; they are not comparable to numbers reported in the US.[3]

Musculoskeletal pain

The evidence for oxycodone in the management of CNCP is poor.[101]

Neuropathic pain

Strong opioids including oxycodone have weak GRADE recommendations for use and are recommended as third line mainly because of safety concerns.[131]

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,[137] but the risks of misuse and diversion still exist.

Note that St John's wort (*Hypericum perforatum*) induces metabolism of oxycodone, significantly reducing its plasma concentrations and efficacy.[138]

3.2.9 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.[139]

When used parenterally, pethidine does not provide better analgesia than morphine, but does induce more nausea and vomiting than morphine.[140]

In practice

Use of pethidine is discouraged in favour of other opioids.[141,142]

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.

3.2.10 Tapentadol

Tapentadol is a combined weak mu agonist and noradrenaline reuptake inhibitor (acting on descending pain inhibition pathways) with no active metabolites.[143–145] 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.[146]

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.[147] However, as it is metabolised by the liver, impaired hepatic function may require dose adjustment.[148]

Despite widespread use over several years in the US and Europe, there are only two reported cases of an overdose death.[149] 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.[150,151]

There are limited data to support a role for tapentadol in cancer pain.[152]

Musculoskeletal pain

Currently, relatively few RCTs have studied tapentadol. There is evidence of benefit in osteoarthritis, low back pain and postoperative pain.[153–156] 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.[101]

Neuropathic pain

Due to the effect of noradrenaline uptake inhibition on descending pathways of pain, tapentadol modulates increased conditioned pain seen with neuropathic pain.[157] This effect has been confirmed in diabetic neuropathy.[144]

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 OMEDD dose of 125 mg/day is reached.

3.2.11 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.[145,158]

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.[159] Hence, patients who are poor metabolisers receive less analgesic effect from tramadol.[160]

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.[161,162] However, tramadol has less effect on gastrointestinal motor function than morphine.[162,163] It causes less respiratory depression than other opioids at equianalgesic doses.[164,165] Tramadol does not increase the incidence of seizures compared with other analgesic agents,[166,167] although there is a risk of inducing serotonin toxicity when tramadol is combined with other serotonergic medicines, in particular SSRIs.[168]

Tramadol has a lower potential for misuse than conventional opioids.[169]

Musculoskeletal pain

There is fair evidence for tramadol in managing osteoarthritis.[101]

Neuropathic pain

Tramadol has a weak GRADE recommendation for use in neuropathic pain,[131] and is regarded as generally second line due to tolerability and safety.[131,170]

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.

3.3 Opioid formulations and doses

3.3.1 Formulations

The practical usefulness of opioids is related to the available formulations (Table 9).

Table 9. Opioid formulations[171]

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.

3.3.2 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.[172] However, accurate determination of equianalgesic doses is difficult due to individual variability in pharmacokinetics and dynamics.[173]

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.[76] They also do not take into account incomplete cross-tolerance and patient-specific factors.[125]

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 4. Useful tools for calculating equivalent doses

- The Faculty of Pain Medicine at the Australian and New Zealand College of Anaesthetists (ANZCA) 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

3.3.3 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 oral morphine equivalent (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.[15] Higher opioid doses may be acceptable in cancer-related pain.

Table 10. Opioid doses[15,52,174]

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

3.4 Tolerance and opioid-induced hyperalgesia

Tolerance is a predictable state of adaption where exposure to a drug induces changes that result in reduction of one or more of the drug's effects over time.[175] The patient becomes '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).[76] However, it is now known that administration of opioids can also result in opioid-induced hyperalgesia (OIH), which is at sensitisation of pro-nociceptive pathways leading to pain hypersensitivity. Both tolerance and OIH can significantly reduce the analgesic effect of opioids.[176,177]

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.[178,179]

Opioids appear to differ in both the ability to induce tolerance and the degree of OIH. For example, methadone and fentanyl are less likely to lose effect over time as they promote opioid receptor internalisation, which results in receptor recycling. In contrast, the activation of opioid receptors by morphine leads to little or no receptor internalisation and thereby increased risk of development of tolerance.[179–181]

There is some evidence that administration of 'commonly used' dosages of oral opioids does not result in abnormal pain sensitivity.[182]

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.[178] 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, but there is little change in miosis or constipation.[178]

3.5 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.[77]

Opioid withdrawal syndrome is characterised by signs and symptoms of sympathetic stimulation due to decreased sympathetic antagonism by opioids (Table 11).[77] 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.[77] Timelines and symptoms vary depending on the duration of action,[65] specific dose, speed of taper, and duration of use.[77]

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.[65,77] 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.[77] Reassurance and comfort measures may also be required.[77]

Table 11. Opioid withdrawal syndrome signs and symptoms[77]

- Anxiety (which can also enhance other symptoms)
- Hypertension
- Tachycardia
- Restlessness
- Mydriasis
- Diaphoresis
- Tremor
- Piloerection
- Nausea, abdominal cramps and diarrhoea
- Anorexia
- Dizziness
- Dysphoria
- Hot flashes
- Shivering
- Myalgias or arthralgias
- Rhinorrhoea, sneezing
- Lacrimation
- 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 substance use disorder for up to six months,[77] but is uncommon in other patients.[77]

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.

3.6 Harms associated with opioids

3.6.1 Adverse effects

Common opioid-related adverse effects are sedation, pruritus, nausea, vomiting, slowing of gastrointestinal function and urinary retention.[183–185] Uncommonly, opioids (methadone, oxycodone) are associated with prolonged QT-interval with a risk of TdP and cardiac arrest.[186,187] These effects are dose related.

Table 12. 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 controlled-release (CR) oxycodone and naloxone has been studied in patients with CNCP, producing similar analgesic efficacy but less bowel dysfunction[188]
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 may 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 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

Table 12. Adverse effects of opioids	
Side effect	**Notes**
Falls	Newly prescribed opioids (alone or in combination with other medications) may trigger injurious falls (especially in the first two weeks). The effect is reduced with duration of use and is less pronounced with increasing age (ie it is most common in young adults). The risk is also higher for fall from height[189]
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[190–193]
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)	

3.6.2 Other harms

Refer to Treatment seeking for pharmaceutical opioids

Refer to Hospitalisation due to opioids

Refer to Overdose and mortality

4. 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.

4.1 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.[194] GPs should access appropriate expertise if considering tapering opioids because of possible risk to the woman and to the fetus if withdrawal occurs.[15]

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.[77]

4.2 Opioid use in workers' compensation injuries

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.[195]

It is well recognised that patients who are psychologically distressed after a work injury have poorer outcomes.[196,197] 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.[198] 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.[199,200] However, recovery rates are not improved by commencing a new activity program in the first 4–6 weeks after injury.[201,202]

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.

Returning to as much usual activity as soon as possible is the most important treatment for musculoskeletal injuries. For cases of increased complexity multidisciplinary involvement is beneficial, (refer to *Prescribing drugs of dependence in general practice, Part C2: The role of opioids in general practice* – Section 3.2 Multidisciplinary approach) including teamwork with specialists and a physiotherapist (refer to *Prescribing drugs of dependence in general practice, Part C2: The role of opioids in general practice* – Section 4.2 Activity and exercise interventions) with pain management experience.

4.3 Prescribing opioids to patients who drive

Opioids can interfere with complex tasks such as driving due to sedation; diminished reaction times, reflexes and coordination; reduced peripheral vision due to the persistent miotic effects;[203] and decreased ability to concentrate.[204]

There is little direct evidence that opioid analgesics (eg hydromorphone, morphine or oxycodone) have direct adverse effects on driving behaviour.[205] The risk of accidents appears to increase in the first weeks of starting opioid therapy or after increasing the dose.[204,206,207] This may be dose dependent.[14]

There does not appear to be evidence that any one opioid has less impact than another.[208] However, stable doses of sustained-release opioids do not appear to impair driving activity.[204,206,209–211]

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.[205,212]

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:[212]

- 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.[207,213–215] 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.[204,211] Driving at night may be a problem due to the persistent miotic effects of opioid drugs reducing peripheral vision.[203]

4.4 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.[216]

Compared to people without OSA, people with OSA are at higher risk of increased sensitivity to opioid analgesia and decreased sensitivity to pain.[217] Administration of opioids may also exacerbate OSA.[218,219]

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.[220–222]

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.[15,223]

The use of opioids in patients with severe untreated sleep apnoea is not recommended.[54]

4.5 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,[224,225] 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.[226] 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.[15,226]

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.[226] However, analgesics should be:[226]

- 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.[15]

Opioid therapy

Appropriate precautions must be taken when considering opioid therapy for older patients.[227] These precautions include lower starting doses, slower titration, longer dosing intervals, more frequent monitoring and tapering of benzodiazepines.[194,227] There is an increased risk of adverse effects including cognitive impairment, sedation, respiratory depression and falls.[228,229] The risk of respiratory depression is minimised by monitoring the patient for sedation and reducing the dose of opioid if this occurs.[228]

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,[81] morphine, oxycodone[230] and buprenorphine.[108] However, in the clinical setting, there is evidence of an age-related 2–4-fold decrease in morphine and fentanyl requirements.[231,232] In patients older than 75 years, the elimination half-life of tramadol is slightly prolonged[233] and lower daily doses have been suggested.[234]

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.[231,232,235] However, inter-patient variability exists in all age groups and doses must be titrated to effect in all patients.

4.6 Opioid therapy in patients with renal disease

Prescribers should use additional caution and increased monitoring to minimise risks of opioid therapy in patients with renal insufficiency.[15] 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.[236] These include morphine, diamorphine and codeine derivatives.[236]

Hydromorphone, methadone, morphine and tramadol have been used in patients with renal disease but with dose adjustments depending on the degree of impairment.[76] Tapentadol is not recommended for use with creatinine clearance <30 mL/min. Alternates to pethidine and dextropropoxyphene are recommended.[237,238]

In practice

The safest analgesics for patients with renal impairment are buprenorphine, fentanyl and paracetamol.[76] 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.[76] Hydromorphone is used for patients undergoing dialysis.

4.7 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.[239]

Prescribers should use additional caution and increased monitoring to minimise risks of opioids in patients with hepatic insufficiency.[15] 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 (CR) formulations are advised.[240]

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.[240] 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.

4.8 Opioid therapy for culturally and linguistically diverse patients

4.8.1 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.[241,242]

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.[243,244]

There are genetic differences in the metabolism of opioids,[88,94,133] which also need to be considered.

4.8.2 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.[245–248]

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.[249]

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).[250,251]

4.9 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.[27] 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.[252]

Depression is the most common mental health comorbidity with long-term pain. It is associated with poorer quality of life and increased functional impairment.[253] Diagnosis may be challenging as there are indistinct symptom boundaries between chronic pain, distress and depression.[254]

Chronic pain is associated with a range of other psychological problems including anxiety, somatisation, fear of pain, anger and hostility.[255] Around one-third (31.8%) of people with a psychotic disorder in Australia are also experiencing chronic pain.[256]

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.[201]

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.[15,194]

Before prescribing opioids, a thorough evaluation for contraindications to opioids is recommended.[54] Treatment of anxiety and depression should be optimised prior to initiation of opioids.[15] The concomitant use of benzodiazepines should be avoided;[54] tapering of benzodiazepines or referral is suggested before starting opioid therapy.[55]

GPs should review patients' histories of controlled substance prescriptions using state PDMP data to determine whether patients 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 a mental health and/or pain medicine specialist is recommended for patients with:[54]

- mental and behavioural health disorders
- SUDs
- uncontrolled or severe psychiatric disorders
- suicidal ideation or action
- 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.

4.10 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 13. Patient risk categories[257]

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

Appendix A

A1 Pharmaceutical Benefits Scheme listing of opioid analgesics

Table A1. PBS 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 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 Chronic severe pain (palliative care)
Oral liquids	
Morphine hydrochloride oral liquid (standard release)	Severe disabling pain

Table A1. PBS 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 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 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) 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 Opioid medicines cause constipation. You may need to be treated for this while you are taking opioids. **Sedation** 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. 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 Dry eyes Blurred vision Nausea and vomiting Inability to urinate Low blood pressure Slow heartbeat Depressed mood Slowed breathing Problems with balance Decreased sex drive (decreased testosterone) Decreased immune function Swelling in hands and feet Jerking of arms and legs Increased sensitivity to pain Disruption of normal sleep Dental problems Apathy Falls resulting in fractures	Sweating Nausea Abdominal pain/cramping Diarrhoea Trouble sleeping Muscle aches Fast heartbeat Anxiety Runny nose 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 – Example practice policies

B1 Opioid prescribing policy for patients

Purpose

To inform patients about the practice's standards regarding the prescription of drugs of dependence.

Example policy

[insert practice name]

Date effective:

Review date:

OPIOID PRESCRIBING POLICY

Many of our patients require strong, potentially addictive medication to help manage their condition(s). Of concern are 'drugs of dependence' (eg opioid medications and benzodiazepines), particularly when these are prescribed on an ongoing basis. Due to increasing reports of abuse of prescription drugs and patient behavioural problems, [insert practice name] has established a policy to ensure adequate treatment of your condition, while reducing the risk of problems with drug prescriptions.

The major points are described below.

For new patients to the practice:

- It may take time to get accurate medical information about your condition. Until such information is available, your GP may choose not to prescribe any medication. It is our policy that GPs do not prescribe drugs of dependence until they have a full clinical picture.
- Your GP may decide not to continue prescribing an opioid medication previously prescribed for you. It may be determined that such a medication is not suitable. It is our policy that GPs do not prescribe drugs of dependence if they feel that previous prescriptions were inappropriate.
- Your GP will evaluate your condition and only prescribe an opioid of the strength necessary for you. This may be different than what another doctor may have given you in the past.

General practice standards:

- If the decision to prescribe is taken after a shared discussion of goals, plans, risks and benefits, you may be required to confirm your consent in writing.
- You may be asked to sign an agreement that will detail our practice's expectations when prescribing drugs of dependence. This contract details your responsibilities as a patient taking a drug of dependence, any prescriptions issues, advice on taking your medications, how we will monitor your care, and the standards of behaviour that are expected. The agreement is not a legally binding contract.
- You may need to acknowledge that your care requirements are complex, and that referral for ongoing care for all or part of your healthcare may be required. It is our practice policy that patient care is matched with the level of complexity.
- Patients are reminded that we have a zero tolerance policy on issues relating to staff abuse. Any threats to staff will result in transfer of your care.

B2 Drugs of dependence treatment agreement/ contract

GPs should use their discretion in deciding which patients may benefit from a treatment agreement. Currently there is no evidence to show that treatment agreements lead to less opioid misuse. However, treatment agreements for patients at high risk are recommended.

Purpose

To inform patients about their responsibilities and expected behaviours regarding drugs of dependence.

Example agreement

This treatment agreement is based on the standard treatment contract developed by the Government of Western Australia Department of Health.

[insert practice name]

Date effective:

Review date:

PATIENT AGREEMENT FOR DRUGS OF DEPENDENCE THERAPY

Treatment contract

for the use of an opioid medicine (morphine-like painkiller) for the management of chronic pain

Patient name:_____

Address:_____

Date of birth:_____

PLEASE COMPLETE ALL DETAILS

I, ... , understand that an opioid medicine is to be prescribed to me in an attempt to improve my level of functioning and reduce my pain. My medical practitioner and I have discussed that strong opioid (morphine-like) medicines may only be partially helpful in achieving this goal and on occasion will not help at all. I understand that an opioid medicine is only one part of the management of my chronic pain. My medical practitioner and I agree to the following conditions regarding my treatment and the prescribing of an opioid medicine for my pain:

1. My medical practitioner is responsible for prescribing a safe and effective dose of an opioid medicine. I will not use an opioid medicine other than at the dose prescribed and I will discuss any changes in my dose with my medical practitioner.
2. I am responsible for the security of my opioid medicine. Lost, misplaced or stolen medicines or prescriptions for opioid medicines will not be replaced.
3. I will only obtain my opioid medicine from the medical practitioner who signs this contract, or other doctors in the same practice authorised to prescribe to me. I understand that no early prescriptions will be provided.
4. While most people do not have any serious problems with this type of medicine when used as directed, there can be side effects. My medical practitioner has explained the main ones to me, and I will tell him or her if I experience what could be side effects.
5. I am aware that my medical practitioner is required to gain authorisation from the Department of Health for continued prescription of an opioid medicine.
6. As possible dependence is an important consideration in the management of my pain, I have informed my medical practitioner of any present or past dependence on alcohol or drugs that I may have had, and of any illegal activity related to any drugs (including prescription medicines) that I may have been involved in.
7. I am aware that providing my opioid medicine to other people is illegal and could be dangerous to them.
8. My medical practitioner respects my right to participate in decisions about my pain management and will explain the risks, benefits and side effects of any treatment.
9. My medical practitioner and I will work together to improve my level of functioning and reduce my pain.
10. I understand that my medical practitioner may stop prescribing my opioid medicine or change the treatment plan if my level of activity has not improved, if I do not show a significant reduction in my pain, or if I fail to comply with any of the conditions listed above.

Patient's signature:_____

Patient's name: _____ Date: _____

Medical practitioner's signature: _____

Medical practitioner's name: _____

Medical practitioner's provider number: _____ Date: _____

Please provide a copy of the signed contract to the patient.

Why do I need to sign a treatment contract?

Both you and your doctor are subject to strict regulations when an opioid medicine is prescribed. Your doctor needs to get special approval from the Department of Health in order to continue prescribing an opioid medicine to you after a trial period. A treatment contract is used so that your doctor is sure that you understand what is expected from you while you take this type of medicine, and that you consent to the requirements described in this contract.

There needs to be **trust, honesty** and **good communication** between you and your doctor when an opioid medicine is prescribed.

The doctor who prescribes you an opioid medicine is expected to:

- do his or her best to prescribe the opioid medicine safely and effectively
- arrange your appointments and prescriptions so that you do not run out of your medication.

In order to receive these drugs it is normal to sign a treatment contract with your doctor. This will list some important conditions you will need to accept, which include the following:

- Agree to get all of your prescriptions for your opioid medicine(s) from one doctor only. This may be a specialist doctor or your GP. You should fill all your opioid prescriptions at the same pharmacy.
- Agree to take the opioid medicine only as prescribed for pain relief and not to change the dose.
- If you are travelling away from home for long periods of time, you will need to discuss your opioid medicine requirements with your doctor so arrangements can be made if ongoing supply is required.
- If you have ever been dependent on alcohol or other drugs (including prescription medicines) you need to tell your doctor **before** signing the contract. A past problem of this nature does not mean that you cannot have opioid medicines for pain relief; however, it does mean that you could be at risk of developing another drug problem and your doctor needs to know this. Past problems you must tell your doctor about include any illegal activity involving drugs.

B3 Requests for repeat scripts for drugs of dependence

Purpose

To inform patients about practice policies regarding repeat prescriptions for drugs of dependence.

Example policy

[insert practice name]

Date effective:

Review date:

REQUESTS FOR REPEAT DRUG OF DEPENDENCE PRESCRIPTIONS

Patients should be aware of their responsibilities in requesting prescriptions for drugs of dependence. These responsibilities are explained in the practice 'Opioid prescribing policy for patients' and in the 'Patient agreement for drugs of dependence therapy'.

Patients should note the following:

- All requests for repeat scripts for drugs of dependence will go to your usual doctor.
- Requests may require a clinical review by your doctor. If it appears to your doctor that there is no improvement in your daily function or quality of life from these medications, your doctor will suggest weaning and discontinuing the medication.
- As a patient you understand that your usual doctor reserves the right to perform random or unannounced urine drug testing, and you agree to comply with this testing. This is a safety issue.
- Patients are responsible for their prescriptions. Lost prescriptions will not be replaced.
- Repeat prescriptions are generally written for a maximum of one-month's supply and will be filled at the same pharmacy.
- Patients have the responsibility to schedule appointments for the next opioid prescription before leaving the clinic or within three days of the last clinic visit. No walk-in appointments for medication refills will be granted.
- Patients have the responsibility for keeping medications in a safe and secure place, such as a locked cabinet or safe. If medications are lost, misplaced, or stolen your doctor may choose not to replace the medications or to taper and discontinue the medications.
- Patients have the responsibility for taking medications as directed and understand that increasing the dose without the close supervision of your doctor could lead to the cessation of prescribing. Early requests for repeat scripts will not be performed.

B4 Simple checklist for a general practice to review its quality management of drugs of dependence

This simple checklist was developed from content in this guide. It is designed to enable general practices to evaluate their status in managing drugs of dependence for their respective populations. As each general practice is different, findings should be interpreted individually.

Table B4. Practice management of drugs of dependence checklist

1. Quality and safety infrastructure (tick each item that applies)	
Is your practice accredited to The Royal Australian College of General Practitioners' (RACGP's) *Standards for general practices*?	☐
Is there a clinical leader responsible for safety and quality within your general practice?	☐
Is the acquisition, use, storage and disposal of Schedule 4 and Schedule 8 medicines made in accordance with legislative requirements?	
If your general practice contains a drugs of dependence management program: • Does it ensure staff are suitably qualified? • Is there organised support? • Are there ongoing quality assurance arrangements?	☐ ☐ ☐
Does your general practice have strategies to ensure the occupational health and safety of GPs and other members of the practice team?	☐
2. Clinical policy	
Does your general practice have agreed clinical policies regarding prescribing drugs of dependence?	☐
3. Organisation of services	
Does your general practice have an effective handover system (eg during staff absence) to ensure safe and continuing healthcare delivery for patients (eg a buddy system for continued care in the GP's absence)?	☐
Does your general practice facilitate GPs' access to information management data to monitor potential prescription drug abuse (eg state and territory health ministries' drug units and Prescription Shopping Information Service [PSIS])?	☐
Does your general practice allow GPs the right to discontinue care of a patient who has behaved in a violent or threatening manner?	☐
4. Preventive health and screening	
Is there evidence that GPs use urine drug screening to detect misuse or abuse of drugs of dependence?	☐
5. Clinical documentation	
Do GPs ensure patient records are clear, up to date and contain sufficient information for another practitioner to take over care?	☐
6. Clinical assessment	
Is there evidence of an adequate assessment and management plan for each patient taking a drug of dependence?	☐

Table B4. Practice management of drugs of dependence checklist	
7. Clinical management	
Do GPs use principles of universal precautions to guide their approach to patients who require drugs of dependence?	☐
Do GPs use specialist support to manage problematic drug use in patients with more complex issues or if the clinical situation deteriorates?	☐
8. Prescribing safety	
Do GPs prescribe within legislative frameworks and comply with professional standards and approved clinical guidelines?	☐
Do GPs ensure a permit or authority is obtained from the relevant state or territory health department when prescribing a Schedule 8 drug to a patient who is drug dependent?	☐
Do GPs inform patients that drugs of dependence are to be prescribed from one practice and preferably by one GP, and drugs should be dispensed from one pharmacy?	☐
9. Clinical practice review	
Do GPs have a structured approach to reviewing opioid prescriptions after 12 months? (eg similar to Appendix B9)	☐
10. Populations for intervention	
Does your general practice engage in practice population interventions to reduce use of drugs of dependence?	☐

B5 Restriction of prescribing rights for drugs of dependence

Purpose

To specify the scope of, and limitations to, prescribing drugs of dependence by general practice registrars.

Example policy

[insert practice name]

Date effective:

Review date:

POSITION STATEMENT REGARDING PRESCRIBING AUTHORISATION OF REGISTRARS

Registrars at [insert practice name] are restricted in prescribing drugs of addiction and drugs of dependence to levels determined by [insert practice name] clinical governance team or supervising GP.

Quality use of these drugs is an essential component of primary care. Ongoing experience, training and self-education in the use of these medications is required as part of training at [insert practice name].

Drugs restricted under this policy:

- Opioid analgesics
- Benzodiazepines

Scope and limitations [may be changed according to individual practice circumstances.]

Opioid analgesics

Registrars are permitted to **initiate opioid** analgesics as specified below, informing a senior GP at the next most convenient time.

To which patients	For what reason	Using which medications
Hospitalised and residential aged care facility patients	Acute analgesia – on call	Tramadol (currently S4) – ceiling dose 200 mg per day Morphine – ceiling dose 20 mg per day (Note that combinations of drugs that result in higher than 40 mg morphine equivalent per day will require senior GP review)
General practice patients		Paracetamol 500 mg codeine 30 mg – limited to 20 tablets Tramadol 100 mg – limited to 20 tablets (Note that higher dose tramadol requires consultation with a senior practitioner within the practice. Codeine, oxycodone, buprenorphine patches, fentanyl patches and hydromorphone use require discussion with a senior practitioner within the practice.)

Registrars are permitted to provide **opioid analgesic continuation** as specified below.

To which patients	Comment
Long-term patients of the practice who are on stable medication regimens, in the absence of their usual practitioner	Patients requesting increased analgesia will need to be referred back to their usual practitioner
Patients requiring continued postoperative analgesia (ie patients discharged from hospital)	Provided: • there is no increase in opioid analgesic requirements • a plan is undertaken to reduce and cease all opioid analgesia within a fortnight for most surgery, but up to six weeks for joint replacement or thoracotomy • a consultation with a senior GP at [insert practice name] has occurred Registrars are not permitted to continue analgesic plans initiated at other practices or healthcare facilities without the review of a senior GP at [insert practice name]

Benzodiazepines

Benzodiazepine initiation:

- Initiation is limited to a single pack (25 tablets) of temazepam 10 mg tablets with no repeats for short-term intermittent use.
- This is in association with a full clinical assessment and documentation of indication for use as a therapy adjunct to addressing the primary causal issue.

Benzodiazepine continuation:

- Registrars are permitted to supply continuation therapy to long-term patients of the practice who are on stable medication regimes, in the absence of their usual practitioner.
- The continuation of alprazolam is restricted to the usual senior GP in the practice.

Refer to the RACGP's *Prescribing drugs of dependence in general practice, Part B: Benzodiazepines* and Part C1: Opioids for other relevant information to include (eg driving ability).

B6 Reducing unnecessary opioid prescribing for acute conditions

Purpose

This policy aims to minimise inappropriate use of opioids in acute presentations at this practice.

Example policy

[insert practice name]

Date effective:

Review date:

MINIMISING INAPPROPRIATE PRESCRIBING OF OPIOIDS

1. In this practice, opioid medications should not routinely be prescribed for:

- uncomplicated back and neck pain
- uncomplicated musculoskeletal pain
- headache/migraine
- renal colic
- non-traumatic tooth pain
- self-limited illness (eg sore throat)
- dental pain
- trigeminal neuralgia
- primary dysmenorrhea
- irritable bowel syndrome
- shoulder pain
- any functional or mental disorder of which pain is a leading manifestation
- an exacerbation of chronic non-malignant pain
- chronic visceral pains (eg chronic pelvic pain, chronic abdominal pain).

2. When opioids are prescribed for acute pain, GPs should prescribe:

- the lowest effective dose of immediate-release opioids
- no greater quantity than needed for the expected duration of pain – three days or less will often be sufficient; more than seven days will rarely be needed. This often requires limits put on dispensed medication.

3. Patients with existing chronic pain sometimes present with acute pain, which is a specific area of pain management. 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.

B7 Risk assessment for patients with ongoing needs for drugs of dependence

Purpose

To identify key risk situations to enable appropriate care provision for patients.

Example policy

[insert practice name]

Date effective:

Review date:

PATIENTS WITH COMPLEX NEEDS – RISK ASSESSMENT FOR ONGOING MANAGEMENT

This practice deems the following patients to be at high clinical risk and in need of referral to public alcohol and drug facilities, or to a GP with advanced training in addiction medicine:

- Patients discharged from other general practices due to problematic behaviour
- Patients recently discharged from a correctional services facility
- Patients with a past family or personal history of substance misuse
- Patients using drugs of dependence with serious mental health comorbidities, or who are on antipsychotic medication
- Patients using a mix of opioids and illicit drugs
- Patients using a mix of opioids and benzodiazepines

B8 Opioid dosing thresholds

Purpose

To detail safe limitations for prescribing opioid medication in this practice. The policy relates to chronic non-malignant pain.

Example policy

[insert practice name]

Date effective:

Review date:

SAFE LIMITS FOR OPIOID PRESCRIBING

The practice policy is to:

- provide ongoing structured review in all patients on long-term opioid therapy (ie monitoring the 5As of pain management: analgesia, activity, aberrant behaviour, adverse effects, affect) before every prescription
- exercise caution in prescribing patients over 50 mg average daily oral morphine equivalent (OME) dose, particularly in those patients with significant comorbidities or at higher risk for opioid misuse
- not prescribe more than an average daily OME dose of 100 mg without further validation from specialist involvement.

Opioids should be reserved for patients who have not responded to non-opioid treatments and who have defined pain conditions for which opioids have been shown to be effective. Prescribed opioids have an accepted individual and combined morphine equivalent threshold, above which the risk of adverse events significantly rises.

Most patients' pain will be controlled on a dose of less than 50 mg OME.

Before prescribing an opioid:

- a diagnosis of the source of the pain must be made
- simple analgesia and other appropriate treatments should have been trialled
- there should be regular assessment of the patient using the 5As.

Patients who have chronic pain and experience an exacerbation of pain or a new painful condition should preferably not be treated with additional opioids.

Calculation of OME dose

For patients taking more than one opioid, the morphine equivalent dose of the different opioids must be added together to determine the cumulative dose.

For example, if a patient takes four codeine 30 mg combined with paracetamol 500 mg and two 20 mg oxycodone extended-release tablets per day, the cumulative dose may be calculated as follows:

- Codeine 30 mg x 4 tablets per day = 120 mg per day
- Using the OME dose table, 120 mg of codeine = 15 mg morphine equivalents
- Oxycodone 20 mg x 2 tablets per day = 40 mg per day
- Using the OME dose table, 20 mg oxycodone = 30 mg morphine, so 40 mg oxycodone = 60 mg morphine equivalents
- Cumulative dose is 15 mg + 60 mg = 75 mg OME per day.

B9 One-year review of opioid prescribing

Purpose

This policy details a protocol that [insert practice name] feels is appropriate to make an informed evaluation of long-term opioid therapy.

The policy relates to chronic non-cancer pain.

Example policy

[insert practice name]

Date effective:

Review date:

REVIEW OF OPIOID PRESCRIBING

If opioid therapy is required for longer than 12 months, the Pharmaceutical Benefits Scheme (PBS) requires clinical review of the case and support by a second medical practitioner. The standards required for evaluation for the PBS review have not been documented. [insert practice name] believes this protocol should be considered for peer clinical review on a regular basis (eg every two years).

Table B9. Evaluation criteria – Review of opioid prescribing (tick if applies)	Yes	No
1. Clinical diagnosis		
a. Is there a comprehensive documentation of the patient's pain condition, general medical condition, psychosocial history, psychiatric status and substance use history?	☐	☐
b. Is the indication/diagnosis for prescribing opioids clearly supported and documented?	☐	☐
c. Is opioid medication clinically appropriate in this condition?	☐	☐
2. Opioid treatment		
a. Has opioid therapy produced and maintained a measurable improvement in the patient's functional capacity?	☐	☐
b. Are the total doses of all opioids below 'ceiling' dose levels? (ie for [insert practice name]) 100 mg morphine equivalent a day)	☐	☐
c. Is the patient substantially free from adverse side effects of opioid therapy?	☐	☐
d. Is there continued absence of inappropriate dose escalation, aberrant behaviour, misuse or abuse of opioids?	☐	☐
e. Have urine drug screens been used to investigate possible diversion, compliance, or other illicit drug use?	☐	☐
3. Additional treatment		
a. Are non-drug therapies maximised?	☐	☐
b. Given the clinical complexity and risk, is the current level of specialist care and multidisciplinary intervention adequate and appropriate? In general, the following scenarios are considered as complex and high risk by [insert practice name], and indicated for specialist and multidisciplinary review: • Patients who use two or more psychoactive drugs in combination (polydrug use) (eg opioid, benzodiazepines, antipsychotic, anti-epileptics, and depressants) • Patients with serious mental illness comorbidities, or who are taking antipsychotic medication • Mixed use of opioids and illicit drugs • Recent discharge from a correctional services facility • Discharged from other general practice/s due to problematic behaviour • Signs of potential high-risk behaviours	☐	☐
4. Compliance		
a. Is current opioid prescribing compliant with relevant state and territory laws and regulations for controlled substances?	☐	☐
Answering 'no' to any of the above options should prompt a consideration to alter the management plan.		

Recommendations

- Continue therapy
- Reduce opioid dose
- Reduce and cease opioids
- Pursue alternate therapies
- Suggest specialist review

B10 Continuation of opioid therapy in new patients (originating from external healthcare providers)

Purpose

To document the standards under which this practice agrees to continue the management of opioid treatment programs for patients with chronic non-cancer pain (CNCP) who present or who are transferred to the practice.

Example policy

[insert practice name]

Date effective:

Review date:

CONTINUATION OF OPIOID MANAGEMENT PLANS INITIATED BY EXTERNAL PROVIDERS

Patients often arrive from other practices or institutions requesting continuation of their opioid management programs. These practices and institutions can have prescribing practices which are variable, and may not be evidence based or safe. To ensure the safety of these programs and the quality of services provided by this practice, the following standards are to be observed.

Policy statement – Doctors at this practice should not prescribe drugs of dependence until evidence of clinical need is established.

If opioids were commenced for acute nociceptive pain (eg after surgery or trauma) 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. Even in complex cases this should be within 90 days.

If opioids were commenced for chronic pain:

- further opioids should not be prescribed until satisfactory evidence of need is established. Such evidence may be in the form of a full clinical assessment, medical records or direct communication with the previous prescriber. This is necessary to avoid the risk of outdated records, recent changes to therapy or aberrant drug-seeking behaviour
- and it is difficult to confirm prior appropriate prescribing, you may request that the patient ask previous prescribers or pharmacists to contact you before you will continue the purported prescribing. Difficulty in obtaining this information may signal that the patient may be involved in deceptive behaviour. Drug-seeking patients often attend a practice after hours or when such information is difficult to obtain. Do not allow the patient to pressure you into prescribing. Politely inform the patient that a prescription will be considered only when the information becomes available
- all records are required to enable a comprehensive evaluation of the patient. A signed release of information form is required.

Policy statement – Doctors at this practice should not continue to prescribe drugs of dependence until reasonable steps have been undertaken to exclude problematic drug use.

- Given that there is a high prevalence of drug-seeking behaviour for opioids, and there is a high risk that these drugs may be sought and diverted for misuse or trafficking, it is important that each doctor independently makes a thorough clinical assessment of each patient's opioid use, and develops a pain management treatment plan consistent with clinical guidelines. Doctors must satisfy themselves that the full range of treatment options is used, which may or may not include opioid medications.
- Examination of the patient should include checking for evidence of IV or other injecting drug use, or drug or alcohol intoxication.
- Check if the state or territory drugs and poisons unit or pharmaceutical services unit has a notification of dependence or has issued a permit for long-term opioid prescribing (refer to www.tga.gov.au/industry/scheduling-st-contacts.htm).
- Seek information from the Prescription Shopping Information Service (PSIS) operated by the PBS. This requires prior registration with the PSIS (call 1800 631 181 or visit www.medicareaustralia.gov.au/provider/pbs/prescription-shopping/index.jsp).
- Perform a baseline urine drug test (UDT) at the initial visit, with a request to include detection of oxycodone and other drugs not usually recognised by immunoassay. Detection of oxycodone requires a gas chromatography–mass spectrometry (GC–MS) test.
- Schedule a follow-up visit for when UDT results and medical records are available.
- Provide a patient information leaflet regarding the practice policies and procedures for pain management.

Policy statement – In the event of problematic drug use being identified, doctors at this practice should:

- offer opioid replacement therapy if this is within the practitioner's skill set
- offer referral to appropriate drug misuse agencies. Appropriate nearby referral agencies include:

[insert appropriate local agencies]

Policy statement – This practice deems the following scenarios to be high risk and in need of referral to public alcohol and drug facilities, or to a GP with advanced training in addiction medicine:

[Strike out or add as required]

- Serious mental illness, or antipsychotic medication
- Past family or personal history of substance misuse
- Mixed use of opioids and illicit drugs
- Mixed use of opioids and benzodiazepines
- Recent discharge from a correctional services facility
- Discharge from other general practices due to problematic behaviour

Policy statement – If clinical need for opioid therapy is justified, doctors at this practice should observe the following practice requirements:

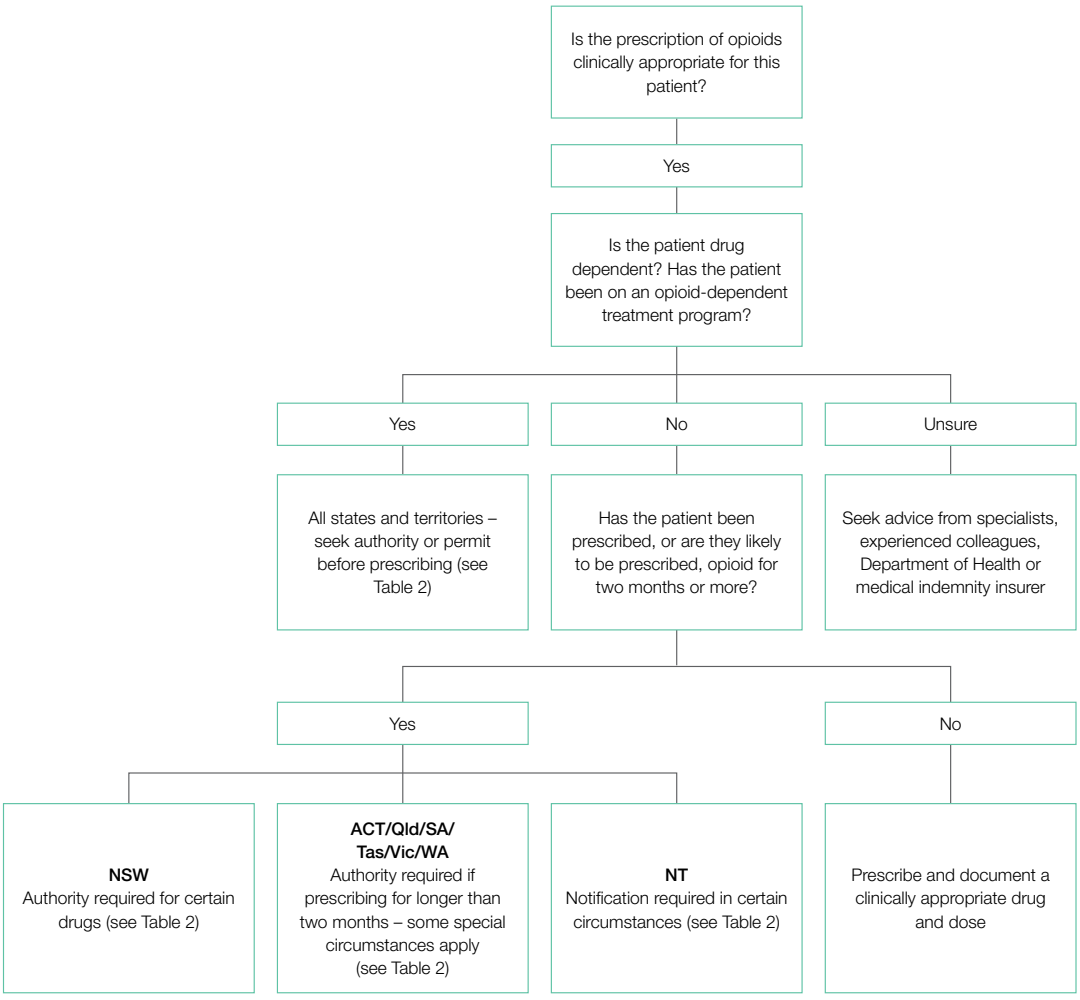
- There is a comprehensive evaluation of the patient's condition and analgesic modalities which are documented within a treatment plan and recorded in the notes.
- Doctors should prescribe opioids according to their best clinical judgement, including if this is less than the wishes of patients, the recommendations of consultants, or the practices of the patient's previous doctors.
- Patients taking inappropriate doses should be advised that the dose will be tapered in the near future.
- Patients who are unwilling to comply with the taper should be referred to specialist or public health services.

- Relevant permits to prescribe should be obtained from the state or territory drugs and poisons unit or pharmaceutical services (see flow chart below). In the case of continuing prescribing, these permits should be sought immediately if the patient has been receiving opioid treatment for eight weeks or longer. This will enable coordination of treatment and reduce the risk that previous prescribers will continue prescribing concurrently.

Policy statement – Patients who satisfy the criteria and are accepted under the continued care of a single doctor will be prescribed ongoing medication according to the practice protocols. This includes:

- continued prescribing and management by a single GP within the practice
- a comprehensive assessment
- a continued use of allied therapies
- the adoption of universal precautions
- a treatment agreement based on informed consent regarding the risks of dependence
- clear boundaries surrounding the use of opioids
- registration with or under state or territory health laws.

Figure B10. Permits required to prescribe opioids



Reproduced from Jammal W, Gown G. Opioid prescribing pitfalls: Medicolegal and regulatory issues. Aust Presc 2015;38:198–203.

B11 Approach to drug-seeking patients

Purpose

To guide prescribers in the respectful approach of patients who display drug-seeking behaviour.

Example policy

[insert practice name]

Date effective:

Review date:

Policy statement – All patients have the right to professional respectful care that promotes their dignity, privacy and safety.

In the event of problematic drug use being identified, doctors at this practice should offer:

- remedial programs if this is within their skill set
- referral to appropriate drug misuse agencies.

Rationale

All patients, including those with drug-seeking behaviour, have the right to respectful care that promotes their dignity, privacy and safety.

Patients with substance use disorders have diverse needs and often complex social and psychological issues. Respecting their circumstances and assisting in offering referral to other organisations for support and management of their substance use disorder is recommended at this practice.

These patients have a medical condition (substance use disorder) characterised by presentation with manipulative or deceptive behaviour. Some doctors get offended by and upset with this sort of behaviour, but it is important to remember that these are the presenting symptoms of a condition and a professional, non-judgemental approach is necessary.

This patient will be someone's son or daughter, sister or brother, etc. Their family will be hoping that you will provide appropriate care for the patient. Getting upset, angry or being offended does not help with the rapport needed to facilitate appropriate care.

This presentation may be the one opportunity in which proper care can be organised for these patients.

Verbal scripts

Some doctors have difficulty in knowing what to say in these circumstances. The following is a suggestion only:

- *[Patient name], I am very concerned about your health. From what you have told me today, and from what I can gather from the material you have here, I am concerned you may have a substance use disorder.*
- *This is quite concerning, as ongoing use of [drug of concern] in the manner you have described may result in long-term harm for you or your health.*
- *I do not have state authorisation. Under the state law, in these circumstances, it is actually forbidden for me to prescribe these medications to you.*
- *The level of care needed to properly manage your case is outside my area of expertise, but I am happy to refer you to [insert local drug and alcohol services] to ensure that you get the care you need. I am also quite happy to provide other care outside these medications. Are you interested in that? Unfortunately, I cannot prescribe any tablets in the interim.*

B12 Opioid reduction policy

Purpose

This policy details a protocol for tapering or withdrawal of opioid medication.

Example policy

[insert practice name]

Date effective:

Review date:

TAPERING OR DISCONTINUING OPIOIDS

- If benefits do not outweigh harms of continued opioid therapy, this practice policy supports GPs to work with patients to taper opioids to lower dosages or to taper and discontinue opioids.
- Continued pain management, including optimised non-opioid regimens and interventional approaches, should be offered for patients undergoing tapering of opioids.
- Where there is no evidence of substance use disorder, tapers can be initiated using the patient's usual long-term opioid treatment medication.
- Where there is evidence of substance use disorder, doctors are reminded of their obligations under state or territory legislation, and advised that referral to clinics experienced in substance use disorder or to GPs specifically trained in this area is required.

Details

Depression, high pain scores and high opioid doses are key predictors of opioid tapering dropout or relapse. Addressing these factors through pharmacologic and psychological support might improve outcomes, although there is no research yet to validate this hypothesis.

Withdrawal symptom management using a2-adrenergic agonists (eg clonidine) is well supported by the literature. These drugs reduce sympathetic activity and therefore reduce symptoms of withdrawal.

Where there is no evidence of substance use disorder

If weaning is required after a short 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.

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 five to seven 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.

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. Depression, high pain scores and high opioid doses are key predictors of opioid tapering dropout or relapse.

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

Doctors are advised to adhere to the legislative requirements of each state or territory regarding opioid therapy for patients with a substance use disorder (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. Doctors are advised that referral to clinics experienced in SUD or to GPs specifically trained in this area is required.

Appendix C – Preliminary RACGP position statements regarding health services integration

C1 Handover of care standards

Purpose

To ensure high-quality continuity of care for patients who require drugs of dependence by complying with the Australian Commission on Safety and Quality in Health Care's (ACSQHC's) handover standards.

Example policy

[insert practice name]

Date effective:

Review date:

HANDOVER POLICY

Background

Clinical handover needs to occur whenever care is to be delivered by different providers. Within general practices there should be an effective handover system that ensures safe and continuing healthcare delivery for patients in the event of staff absences.

Failure of transfer of care, or inadequate transfer of care is a major risk to patient safety and a common cause of serious adverse patient outcomes. Inadequate handover can also lead to wasted resources, delayed treatment, delayed follow-up of significant test results, unnecessary repetition of tests, medication errors and increased risk of medico-legal action.[20]

It is recommended that general practices and GPs insist on high standards for referral letters for clinical handover or shared-care arrangements from secondary care before accepting the ongoing care of a patient. This facilitates the continuity of care and transfer back to higher levels of care if the need arises.

Handover within the general practice

Practice standards are required to ensure the ongoing provision of care in the event of the absence of the patient's usual doctor. These standards include:

- having an effective handover system to ensure safe and continuing healthcare delivery for patients (eg a buddy system for continued care in the usual GP's absence)
- ensuring each patient's medical records contain up-to-date healthcare notes (that allow continuity of care in the usual GP's absence).

Handover from external healthcare facilities (hospitals, rehabilitation units, specialist outpatients)

With respect to new patients presenting to the practice, or being referred by other agencies, it is our practice policy that:

- the practice reserves the right not to accept these patients if either the practice or the practitioner is of the view that the current treatment plan is inconsistent with evidence-based guidelines, and the level of complexity exceeds the practice's capacity to manage the patient
- if a doctor feels that a referral letter from an external agency does not meet handover standards, then communication should be sent to the original referrer seeking additional information.

A practice or GP should not accept the ongoing management of a high-risk patient referred from a public sector facility, unless the referral includes:

- a medical summary
- a clear management plan
- patient-specific instructions, including specific clinical issues that would prompt referral back to secondary care
- contact details of a case manager and a clinically responsible person
- documentation that details mechanisms for rapid transfer back to specialty care if deterioration occurs.

This requirement should be supported by practice policies and communicated to referral agencies if information does not meet required standards.

Handover to external healthcare centres (specialist outpatients)

It is our practice policy that all patients regularly using drugs of dependence have their problems and needs assessed based on levels of complexity (ie low, medium or high). Patients in medium-complexity or high-complexity groups should have an appropriate specialist review.

Practice policy requires that patients with medium-complexity or high-complexity problems are managed in a manner consistent with the universal precautions of pain medicine. That is:

- a clear diagnosis and reasons for prescription are documented
- a full psychosocial assessment is conducted, including risk of addictive disorders
- informed consent for treatment plans is used
- pre-intervention and post-intervention assessments of pain level and function are undertaken
- opioid therapy with or without adjunctive medication is commenced on a trial basis
- levels of pain and function are constantly assessed
- the '5As' of pain medicine (analgesia, activity, adverse effects, aberrant behaviour, affect) are constantly assessed
- the diagnosis is periodically reviewed and comorbidities are managed appropriately
- the level of documentation standard is high.

The ACSQHC handover standards are available at www.safetyandquality.gov.au/wp-content/uploads/2012/10/Standard6_Oct_2012_WEB.pdf

C2 Request to hospital accident and emergency departments regarding opioid analgesia

Background

An effective and efficient health system relies on high standards of care, particularly where handover of care from hospital to community is involved.

Before prescribing opioids as a discharge medication, consideration needs to be given to possible opioid adverse effects, which include the potential risks of long-term opioid use, drug diversion, misuse/abuse and death from accidental overdose.[62] The risk of falls should also be considered: the overall risk is greatest in the first week following the initial prescription, and decreases over time.[190]

A small pilot study has shown that patients discharged from emergency departments (EDs) with opioid medication do not safely store and dispose of these medicines.[63] After receiving opioid prescriptions for an acute episode, 64% of patients kept unused opioids and 34% shared them with others.[64] Patients should be educated about not compiling or distributing medications and also of the safe way to dispose of unused opioid medicines, which, in Australia, is to return them to a pharmacy.[62]

A clear plan for analgesia reduction after discharge and robust systems for communication with usual treating practitioners in the community are essential and will assist in avoiding unintended dose escalation.[57-59]

Evidence statements

- The efficacy of opioid therapy in acute pain is supported by strong evidence from randomised controlled trials.[48,52]
- Long-term opioid use often begins with treatment of acute pain.[15] 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.[15]

RACGP requests of hospital accident and EDs

- A clear plan for analgesia reduction after discharge and robust systems for communication with usual treating practitioners in the community are essential.[57-59]
- Patients presenting with an acute exacerbation of existing chronic pain should be assessed with caution and usually by or in conjunction with their usual doctor or healthcare team.
- A prescription for three days or less will often be sufficient; more than seven days will rarely be needed.[15]

Acute exacerbation of existing chronic pain

It is important to identify the source of pain rather than just treating for acute pain, since treatment for the chronic pain patient can be significantly different. Because of potential risks and adverse effects, clinicians are encouraged to avoid prescribing increased dosage or additional opioids. Assess the patient's mental health status and social situation to determine if additional resources may be appropriate.

Consult the patient's pain care plan prior to prescribing any medications:

- Exacerbations of pain should be managed with non-opioid therapy[65]
- Confer with the clinician managing the patient's chronic pain, their interdisciplinary team or available resources to provide appropriate chronic pain management
- Check state-based prescription monitoring services for history of opioid prescriptions

C3 Request to hospital and rehabilitation units regarding discharge analgesia

Background

The number of patients discharged from hospital or rehabilitation units with opioid medication is rising because the range of patients and procedures considered suitable for short stay or early discharge are increasing.[62]

Before prescribing opioids as a discharge medication, consideration needs to be given to possible opioid adverse effects, which include the potential risks of long-term opioid use, drug diversion, misuse/abuse and death from accidental overdose.[62]

Postoperative opioids

Opioid therapy can usually be ceased within one week of surgery or injury. In more complex cases opioids should be weaned and ceased within 90 days at most. However, following postoperative initiation, up to 8% of patients continue to use opioid medication for months or even years.[70–72]

Early discharge after day surgery with a prescription of opioids or non-steroidal anti-inflammatory drugs (NSAIDs) carries an increased risk of subsequent long-term use of these analgesics. In a population of 391,139 opioid-naïve patients over 65 years of age who underwent short-stay surgery, patients who received an opioid prescription within the seven-day period after surgery were more likely to become long-term opioid users within one year in comparison to those without a prescription.[70]

Of 39,000 opioid-naïve patients having major elective surgery, 3.1% showed prolonged opioid use after discharge.[72]

Additionally, after receiving opioid prescriptions for an acute episode, 64% of patients kept unused opioids and 34% shared them with others.[64]

This rate of 'over-prescription' has been noted for surgical discharges.[66–68] Indeed, it is often completely unnecessary: 19% of postoperative patients prescribed oxycodone upon discharge from a large Australian teaching hospital had not needed any opioid in the 24 hours prior to discharge.[69]

A clear plan for analgesia reduction after discharge and robust systems for communication with usual treating practitioners in the community are essential and will assist in avoiding unintended dose escalation.[57–59]

Evidence statements

- The efficacy of opioid therapy in acute pain is supported by strong evidence from randomised controlled trials.[48,52]
- Long-term opioid use often begins with treatment of acute pain.[15] 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.[15]

RACGP requests to hospitals regarding handover on patient discharge

- Hospitals and rehabilitation units should develop robust communication systems for transfer of care to usual treating practitioners in the community consistent with the ACSQHC's standards for handover.
- Patients discharged from hospital or day care facilities on opioids should be educated regarding the safe and optimal use of the pain medications that have been prescribed.
- Patients discharged from hospital or day care facilities on opioids should have a clear plan of pain management to facilitate handover of care.

- A post-surgery discharge letter must accurately reflect information on opioid dose frequency and suggested duration of treatment, including a plan for dose reduction.
- Patients commenced on long-term opioids in hospital for chronic (cancer or non-cancer) pain should receive a detailed discharge summary justifying opioid use.
- Psychiatric patients, or patients who were admitted with opioid overdose, should have clear justifications for opioid use and clear plans for future monitoring.
- Discharge prescriptions for opioids should:
  - (in most cases) not exceed seven days' supply (or until earliest office opening and follow-up from the patient's usual GP)
  - be communicated to the patient's usual GP or care team.
- If a patient with a history of chronic pain is admitted for non-fatal overdose:
  - hospital staff should conduct a full pain and psychiatric evaluation, and consider opioid cessation or naloxone therapy. These deliberations should be documented on the discharge summaries to GPs
  - the usual GP or care team should be notified.

C4 Admissions with intentional non-fatal overdose of opioids

Patients who have had a presentation or admission for opioid overdose are at significant risk for another overdose and further harms.[74] Almost all patients continue to receive prescription opioids after an overdose.

At two years, the cumulative incidence of repeated overdose was:[74]

- 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% to 11%) for those receiving no opioids.

Opioid discontinuation after overdose is associated with lower risk for repeated overdose.[74]

Non-fatal opioid overdose is an opportunity to identify and treat substance use disorders, as patients often have both pain and substance abuse issues.

The use of naloxone falls within harm reduction strategies and patient-centred care. It is safe, effective, inexpensive, and relatively easy to administer via intramuscular (IM) injection.[75]

The RACGP requests that for all patients presenting to hospital EDs with non-fatal opioid overdose, hospital staff conduct full pain and psychiatric evaluations, and consider opioid cessation or naloxone therapy. It is essential for practitioners in the ED to develop a clear plan for opioid safety after discharge and to communicate with the patient's usual treating practitioners in the community.

Appendix D

D1 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.[258,259]

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 D1. Drug misuse behaviours

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

Table D1. 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 medication 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 concerning 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 E

E1 Urine drug testing in patients using opioids for chronic pain

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.

E1.1 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 E1.1 Length of time drugs of dependence can be detected in urine[260]

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.

E1.2 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.[261]

Table E1.2. Interpreting unexpected results of urine drug tests[227]

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

UDS, urine drug screen; UDT, urine drug test

Appendix F

F1 Criteria for substance (opioid) use disorder

Table F1. DSM-5 criteria for diagnosing a substance use disorder – Opioids

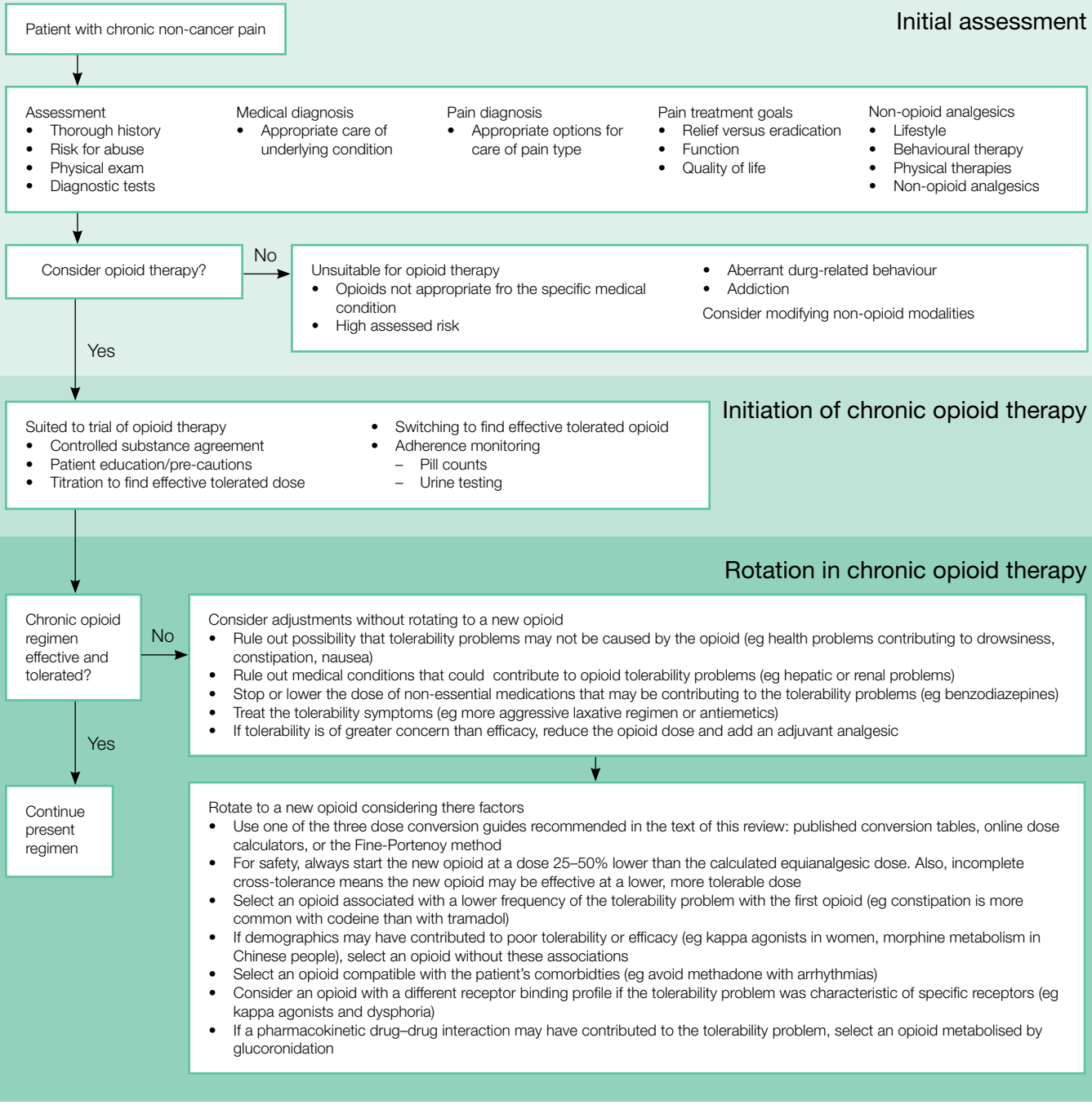
A problematic pattern of substance use leading to clinically significant impairment or distress, as manifested by at least two of the following 11 criteria, occurring within a 12-month period:	
Impaired control criteria	1. Substances are often taken in larger amounts or over a longer period than was intended 2. There is a persistent desire or unsuccessful efforts to cut down or control substance use 3. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects 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) 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) 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) 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: a. A need for markedly increasing amounts of the substance to achieve intoxication or desired effect b. A markedly diminished effect with continued use of the same amount of the substance Note: Criterion 10 is not considered to be met for individuals taking substances under medical supervision 11. Withdrawal, as manifested by either one of the following: a. The characteristic withdrawal syndrome for the substance b. Substance (or a closely related substance) is taken to relieve or avoid withdrawal symptoms
Specifiers: '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) '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) 'In a controlled environment': This additional specifier is used if the individual is in an environment where access to substance is restricted Current severity: '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 G

G1 Opioid rotation therapy algorithm

Figure G1. Algorithm for initial patient assessment and initiation and rotation of opioid therapy[263]



Reproduced from Smith HS, Peppin JF. Toward a systematic approach to opioid rotation. J Pain Res 2014;7:589–608.

Appendix H

H1 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).[262]

Table H1. 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

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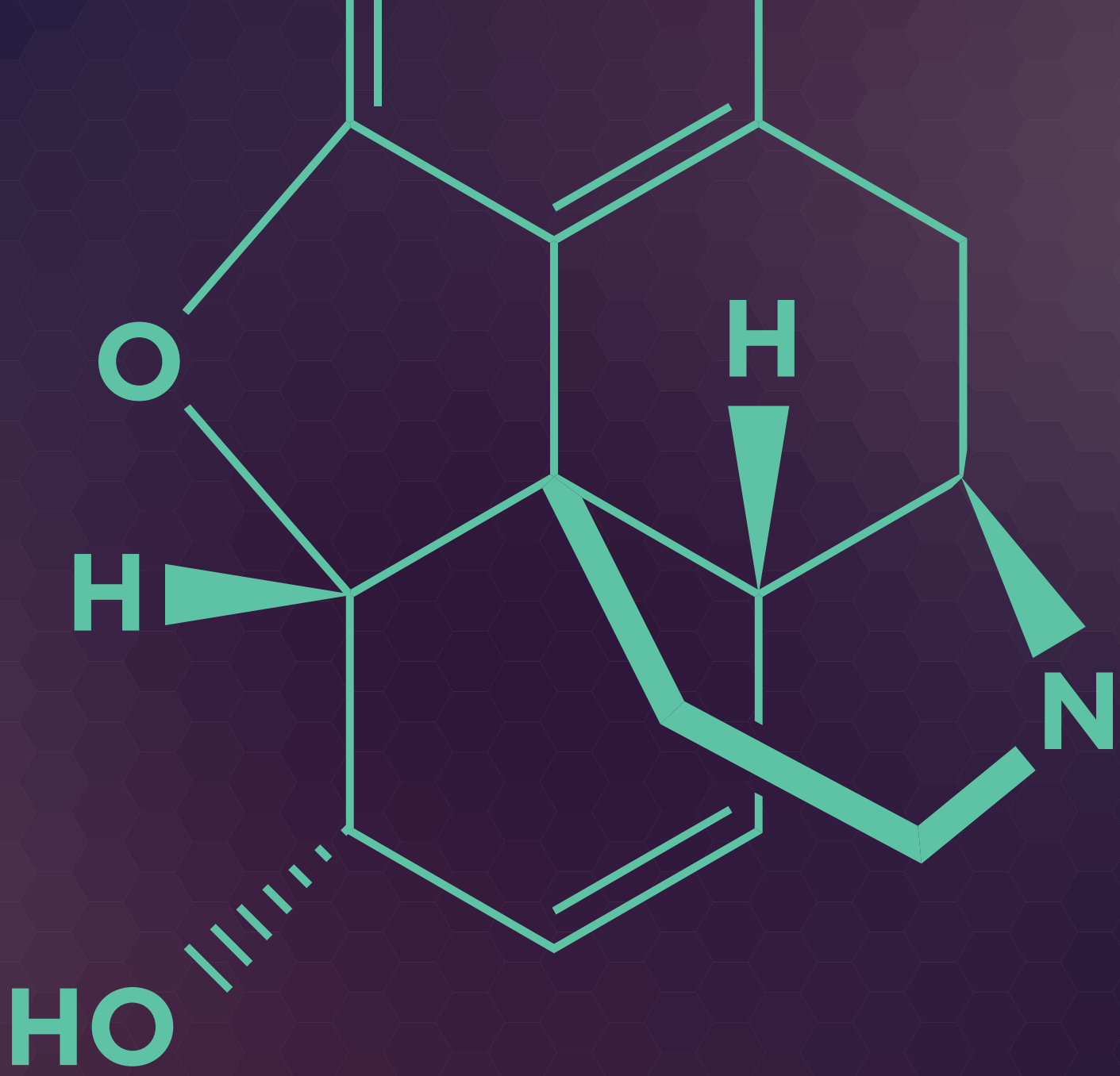

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