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Prescription opioid misuse Contemporary challenges – 2

Supplement

**The rise and rise of prescription opioid use
in Australia**

**Long-term opioid use in patients with chronic
noncancer pain. Who is experiencing problems?**

Tapering off opioid analgesia

**Clinical care and regulation of opioid use:
the Tasmanian model**

**Over the counter, under the radar:
nonprescription codeine dependence**

**Drug misuse and addiction. What is out there
to support GPs?**

**Prescription opioid management in chronic
noncancer pain: case studies**

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SUPPLEMENT

**PRESCRIPTION OPIOID MISUSE:
CONTEMPORARY CHALLENGES – 2
MARCH 2017**

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Medicine Today

THE PEER REVIEWED JOURNAL OF CLINICAL PRACTICE

FOREWORD FROM THE SUPPLEMENT EDITOR

Doctors are often called upon to perform a delicate balancing act between providing adequate analgesia to the patient in pain versus prescribing excessive medication. This is a major problem in contemporary practice and the second time we address this topic in *Medicine Today*.*

This supplement addresses a number of current issues. It looks at the evidence that the use of prescription opioids in patients with chronic noncancer pain is still growing in Australia and at the risk factors, identified by the POINT study, for developing problems, and presents an approach to tapering patients off opioid drugs that can be used in general practice. It describes clinical and regulatory systems that can promote safer prescribing of opioids, using the model in place in Tasmania as an example, and considers the resources that are available to help GPs in providing safe clinical care. It takes a detailed look at codeine dependence and the controversy regarding the recent change to its scheduling. Finally, three case studies, drawn from general practice and a hospital outpatient service, demonstrate a recommended clinical approach. I hope these articles will help you to manage your patients with a little more confidence.



Professor Paul Haber

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The rise and rise of prescription opioid use in Australia

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There have been marked increases in prescription opioid use in Australia since 1990, with corresponding increases in opioid-related harms. Understanding the drivers of these changes is an important step toward improving the quality of opioid prescribing in Australia.

KEY POINTS

- The use of opioid analgesics is increasing globally, with accompanying increases in extra-medical use, overdoses, hospitalisations and deaths.
- In Australia, prescription opioid use increased almost fourfold between 1990 and 2014, with particularly large increases in use of strong and long-acting opioids.
- The subsidy of long-acting formulations for the treatment of patients with chronic noncancer pain has been a key driver of the increasing use of opioids in Australia.
- This rise in prescription opioid use and harms requires targeted intervention at the clinical and population levels.

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The past two decades have seen global increases in prescription opioid use. The USA is in the midst of a 'prescription opioid epidemic' and opioid harms have increased with burgeoning use. In 2014, more than two million people in the USA abused or were dependent on prescription opioids, and more than 14,000 died after a prescription opioid overdose.¹

Although per capita opioid consumption in Australia is only one-third that of the USA and about half that of Canada, Australia ranks eighth out of 168 countries globally.² Recent studies have shown ongoing increases in opioid use in this country, accompanied by a rise in extra-medical use, overdoses, hospitalisations and deaths.³ Prescription opioids now account for about four times as many hospitalisations in Australia as heroin.^{3,4} These trends raise questions about how opioids are prescribed in Australia, how changes in clinical practice and policy have contributed to increasing use, and how we might curtail further increases in opioid-related harms.

We recently published an analysis of prescription opioid use in Australia over the past 25 years.⁵ Here, we present some of our key findings from that study, providing an overview of trends in opioid use since 1990 (see Boxes 1 and 2 for explanatory notes about the data reported here).^{5,6} Additionally, we draw on our analysis and other key literature to discuss the role of various factors in driving the observed changes.

The changing landscape

In 2014, almost three million people in Australia received at least one PBS-listed opioid, and more than 15 million opioid prescriptions were dispensed.^{5,7} Our study detailed the dramatic changes in the landscape since 1990, when the number of prescriptions was about one million.

In 1990, only six opioid analgesics were available on the PBS for acute and malignant pain, and the weak opioids codeine and dextropropoxyphene dominated the market, together comprising over 90% of use. Since then, five new opioids and multiple formulations have been introduced, and others phased out (Figure 1).

1. A NOTE ABOUT THE STUDY DATA⁵

Our estimates of prescription opioid use in Australia over the past 25 years are based on data on prescriptions dispensed from community pharmacies and private hospitals.⁵ Data came from two sources:

- records of prescriptions dispensed under the PBS and the RPBS
- data on nonsubsidised prescriptions; these include low-cost medicines priced below the PBS general beneficiary co-payment and private prescriptions.

The estimates of nonsubsidised medicine dispensing in our study were derived from a survey of a representative sample of community pharmacies, which was conducted by the Pharmacy Guild of Australia until mid 2012. Thereafter, actual under co-payment dispensing volumes were also recorded in the PBS and RPBS dataset, but data on private prescriptions were no longer available. We have indicated the timing of these changes in data capture on the graphs.

The data from our study used in this article have the following limitations:

- limited capture of opioid use in public hospitals
- no information on over-the-counter opioid use; about 40 to 50% of codeine is obtained over-the-counter⁶
- no records of private prescriptions from August 2012 (as noted above); as it is difficult to predict the impact of this change in data capture, we have largely confined our discussion of trends to the period 1990 to 2011.

Abbreviation: RPBS = Repatriation Pharmaceutical Benefits Scheme.

Between 1990 and 2000, opioid analgesic use increased by over 150% in Australia. This increase was primarily driven by growth in use of strong and long-acting opioids, particularly morphine and methadone; use of each increased more than 10-fold in this decade. By 2000, the three most prescribed opioids were codeine (58% of opioid use), morphine (14%) and methadone (14%).

Significant changes in opioid availability occurred toward the end of the 1990s. Fentanyl transdermal patches, tramadol and controlled-release oxycodone and hydromorphone were registered and subsidised on the PBS between 1997 and 2000, followed by long-acting formulations of tramadol, hydromorphone and buprenorphine in the 2000s. In 2010 and 2013, new formulations of oxycodone (oxycodone–naloxone and tamper-resistant tablets, respectively) were introduced. Accordingly, we found marked increases in tramadol, oxycodone, buprenorphine, fentanyl and hydromorphone use between 2001 and 2011, and a further shift toward strong and long-acting opioids.

In 2011, the weaker opioids codeine and tramadol accounted for about 40% and 20% of prescription opioid use, respectively, and oxycodone was by far the most common strong opioid (42% of strong opioid use and 16% of opioid use overall). Our analysis found a fourfold increase in total opioid use between 1990 and 2011, with a 15-fold increase in the use of strong opioids.

2. MEASURING OPIOID USE: EXPLAINING DDD/1000 POP/DAY

Opioid use in this article is presented in terms of defined daily doses per 1000 population per day (DDD/1000 pop/day).

The WHO allocates each medicine a 'defined daily dose', which is said to represent the mean daily dose of the drug when used for its main indication in adults. Most of the DDDs for strong opioids were developed when they were used primarily for treating patients with cancer pain, so the DDD may be higher than the actual dosing used for patients with chronic noncancer pain, resulting in some underestimation of use.

Despite these limitations, DDD/1000 pop/day remains the 'gold standard' in drug utilisation research for standardising measures of medicine use across different countries, formulations and medicine strengths.

Drivers of change Paradigm shifts

Information on the use of opioid analgesics in Australia before the 1990s is limited. Concerns about addiction, dependence and extra-medical use were commonly documented and formed a barrier to the effective treatment of pain. In 1986, however, the WHO introduced guidelines for the management of patients with cancer pain to improve its treatment worldwide. The WHO's three-step analgesic pain ladder legitimised the use of both weak and strong opioids, particularly morphine, in cancer pain management and was a major step toward combating opiophobia in the medical profession.⁸

However, the undertreatment of pain remained a concern. The mid to late 1990s brought attempts to deal with this issue through altering the prevailing views on pain and its treatment. In the USA, this paradigm shift began with the American Pain Society's endorsement of pain as a 'vital sign' in 1996, leading to initiatives, guidelines and mandates endorsing the routine assessment of pain.⁹ Concurrently, a widespread movement began promoting the treatment of pain as a fundamental human right. Statements endorsing this right were released throughout the USA, Europe and Australasia. Examples from Australia include the Medical Treatment Act 1994 (ACT) and a statement from the newly formed Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists and its Joint Faculty of Intensive Care Medicine.¹⁰ In 2000, the US Congress declared that the Decade of Pain Control and Research would commence in 2001, and in 2004 the WHO and the International Association for the Study of Pain launched the Global Day Against Pain, with the theme that 'the relief of pain should be a human right'. The day not only promoted the treatment of pain in people with cancer and AIDS but also called for recognition of chronic noncancer pain as a treatable disease in its own right.¹¹ This movement has continued, culminating in the 2010 Declaration of Montreal that 'access to pain management is a fundamental human right'.

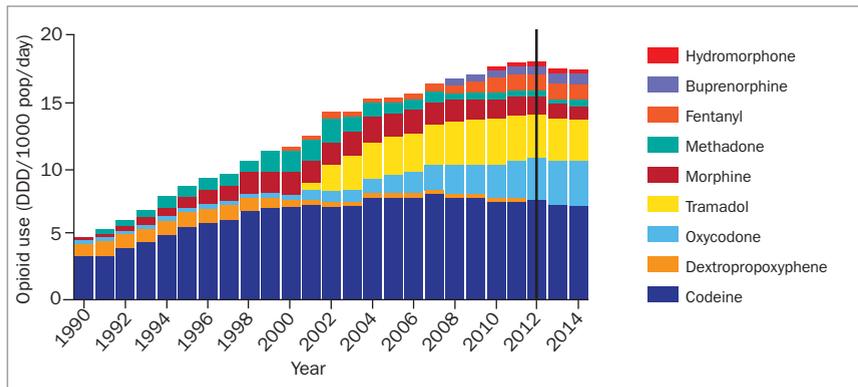


Figure 1. Trends in the use of prescription opioid analgesics by drug, 1990 to 2014. Pethidine and tapentadol not shown; pethidine use dropped from a maximum of about 1% of total opioid use in 1990 to <0.1% in 2005, and tapentadol use was 0.3% of total opioid use in 2014. The vertical line indicates the loss of data on private prescriptions in 2012 (Box 1).⁵
 Abbreviation: DDD/1000 pop/day = defined daily doses per 1000 population per day.

This ongoing encouragement to treat pain, fuelled and exploited by the pharmaceutical industry through opinion leaders, pain societies and initiatives, contributed significantly to the increasing use of opioids, especially for the management of patients with chronic noncancer pain. Additionally, concerns about the addictive properties of opioids were allayed by clinical trials, pharmaceutical marketing and treatment guidelines incorrectly claiming a low risk of addiction in patients without a history of substance misuse.¹² Aggressive treatment of pain was further encouraged with the

emerging belief that rapid pain management could prevent the transition from acute to chronic pain.¹³

Increasing availability of long-acting formulations

In our study, we showed that the introduction and PBS subsidy of long-acting formulations was a major driver of increasing opioid use over the past 25 years.⁵ In 1990, the only long-acting opioids available were methadone and oxycodone suppositories. Accordingly, more than 95% of prescribed opioids were short-acting (Figure 2). The

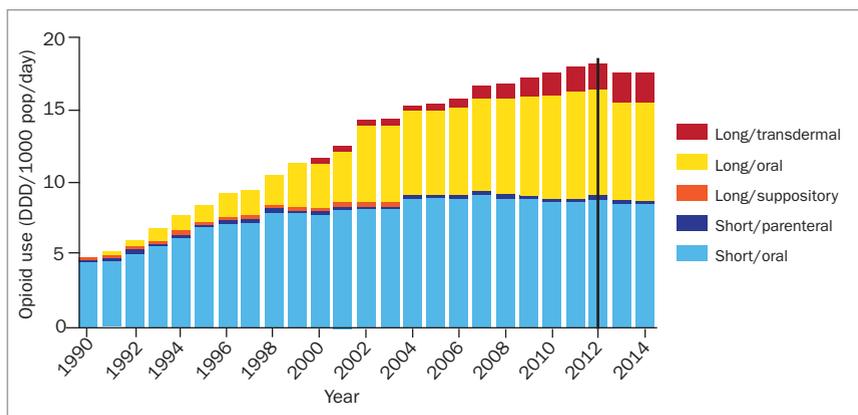


Figure 2. Trends in the use of prescription opioid analgesics by duration of action and route of administration, 1990 to 2014. Long-acting parenteral formulations (methadone) not shown (<0.1% of total opioid use). The vertical line indicates the loss of data on private prescriptions in 2012 (Box 1).⁵
 Abbreviation: DDD/1000 pop/day = defined daily doses per 1000 population per day.

registration and PBS subsidy of long-acting morphine tablets and capsules (subsidised in 1991 and 1994, respectively) was instrumental in driving the 12-fold increase in morphine use in Australia between 1990 and 2000. These formulations provided ‘around-the-clock’ therapy with once or twice daily oral dosing, enabling more stable blood concentrations and greater patient compliance. Aided by pharmaceutical marketing and the WHO’s endorsement of morphine as the preferred opioid in the third step of the analgesic ladder, these formulations quickly became the treatment of choice for patients with moderate to severe chronic cancer pain and those with chronic non-cancer pain.¹⁴

Similarly, the subsidy of controlled-release oxycodone tablets in 2000 contributed greatly to oxycodone’s initial rise in popularity. Controlled-release oxycodone (OxyContin) was promoted as the ‘ideal analgesic’, purportedly having a short half-life, long duration of action, rapid analgesic activity, no active metabolites, predictable pharmacokinetics and fewer side effects than morphine.¹⁵ These and other claims were often incorrect or even mutually incompatible.^{16,17} In particular, OxyContin was aggressively marketed as having a very low risk of addiction, abuse and dependence; unsubstantiated claims that resulted in the 2007 prosecution of its manufacturer Purdue Pharma in the USA for misbranding.¹⁷ As such, oxycodone use increased rapidly from 2000, overtaking morphine as the most dispensed strong opioid in Australia in 2007. Although morphine is still considered the strong opioid of choice for patients with moderate to severe pain,¹⁸ oxycodone comprised more than 40% of opioid use in Australia in 2011, and about 80% of this was the controlled-release formulation.

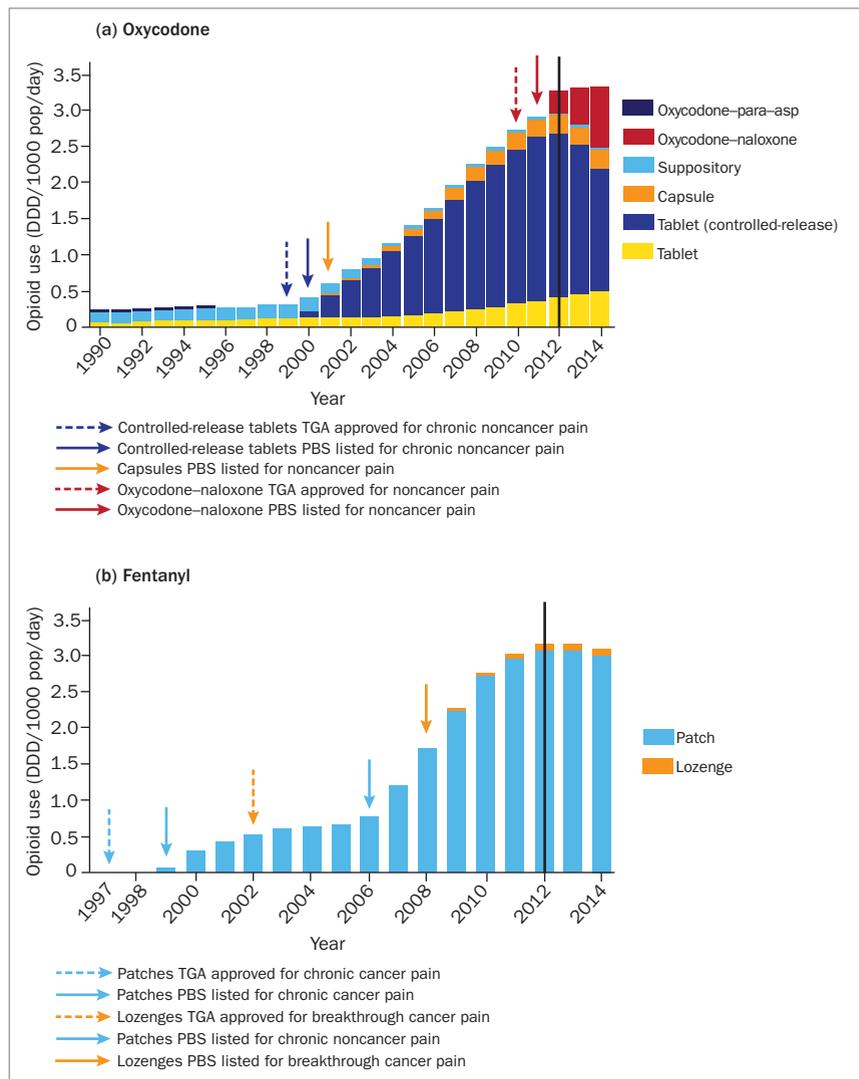
The success of controlled-release formulations of morphine and oxycodone sparked the release of various other long-acting formulations. Fentanyl transdermal patches, PBS subsidised in 1999, were the first nonoral long-acting alternative to methadone and oxycodone suppositories for treating

patients with cancer pain. Their slow-release delivery over several days is particularly suited to patients with chronic continuous pain, especially where oral administration is not possible. A dramatic increase in dispensing followed the subsidy by the PBS of sustained-release tramadol tablets in 2001, and tramadol soon replaced dextro-propoxyphene as the weak opioid of choice after codeine. Similarly, hydromorphone use increased markedly after modified-release tablets were subsidised in 2009. This growth in hydromorphone was almost entirely attributable to increasing use of the modified-release formulation.

Most Australian and European guidelines still recommend the use of oral long-acting opioids for chronic pain because of their ability to maintain more stable blood concentrations, although short-acting opioids still have a place in treating acute and breakthrough pain and, in some guidelines, for dose titration in chronic pain.¹⁸ However, in light of the high rates of extra-medical use, especially of controlled-release oxycodone, and the increased risk of overdose in patients who commence therapy with extended-release formulations, the USA has recently tightened its guidelines on the use of long-acting formulations.¹⁹ These guidelines now recommend initiation on immediate-release formulations, with long-acting opioids restricted to patients with pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.²⁰

Increasing use in chronic noncancer pain

The increases in opioid use over the past two decades are also attributable to their increasing use in patients with chronic noncancer pain. Until the late 1990s, opioids were predominantly reserved for treating those with acute and malignant pain. However, growing concerns about undertreatment of pain and the aggressive marketing of opioids, particularly OxyContin, for nonmalignant pain opened up a whole new market.¹⁷



Figures 3a and b. Trends in the use of (a) oxycodone and (b) fentanyl in Australia following changes in regulatory approval by the TGA and PBS subsidy. Note the increase in use after PBS subsidy for noncancer pain. Data for oxycodone ampoule and oral solution not shown (ampoule, <0.001% of use; oral solution, ≤0.3% of use). The vertical line indicates the loss of data on private prescriptions in 2012 (Box 1).⁵

Abbreviations: DDD/1000 pop/day = defined daily doses per 1000 population per day; Oxycodone-para-asp = oxycodone with paracetamol and aspirin; PBS = Pharmaceutical Benefits Scheme; TGA = Therapeutic Goods Administration.

The PBS subsidy of opioids for noncancer pain facilitated their increased use in Australia. After the subsidy of tramadol capsules and controlled-release oxycodone tablets for noncancer pain in 2000, their use increased sixfold and eightfold, respectively, by 2011. Similarly, use of buprenorphine and fentanyl patches remained low until their PBS indications expanded in 2005 and 2006, respectively (Figures 3a and b).⁵

Estimates suggest that chronic noncancer pain now accounts for almost half of opioid prescriptions written by GPs in Australia, although the true rates are likely higher.²¹ The duration of opioid treatment is also increasing. Although there is strong evidence for the effectiveness of opioids in the short-term treatment of patients with noncancer pain, evidence supporting their long-term use is lacking. Select patient groups may maintain

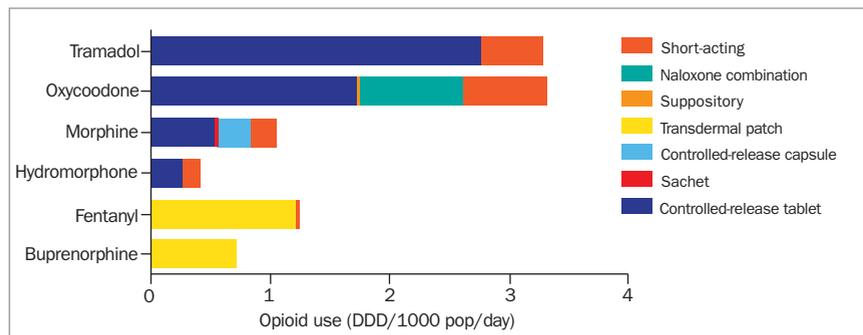


Figure 4. Use of different long-acting formulations and short-acting formulations (combined) of opioid analgesics in 2014. Only opioids with both short- and long-acting formulations are shown.⁵

Abbreviation: DDD/1000 pop/day = defined daily doses per 1000 population per day.

lasting benefit, but insufficient pain relief or intolerable adverse effects are a common cause of treatment discontinuation.²² Long-term opioid use has been associated with increased risk of overdose, extra-medical use, falls and fractures, myocardial infarction, depression, hyperalgesia and hormonal or sexual problems.²³ Chronic use can also have negative effects on day-to-day functioning, quality of life, mood, physical activity and pain severity.²⁴ Interestingly, tapering or withdrawing high-dose opioid treatment has been associated with improvements in these markers.²⁵

Recent developments

Oxycodone–naloxone

Oxycodone–naloxone controlled-release tablets were TGA approved and PBS listed in Australia for chronic severe pain in 2010 and 2011, respectively. The addition of naloxone (an opioid antagonist) to oxycodone (a full agonist opioid) in a 1:2 ratio decreases oxycodone-induced constipation by antagonising opioid receptors in the gut. Also, the low oral bioavailability of naloxone prevents it acting centrally and permits equivalent analgesia as oxycodone alone at standard doses.²⁶ It has also been suggested that oxycodone–naloxone tablets are tamper-resistant, deterring against extra-medical use through snorting and injection (but not orally), although little evidence is available. In the USA, oxycodone–naloxone has recently been labelled ‘abuse-deterrent’ based on a clinical trial submitted by

Purdue Pharma to the US Food and Drug Administration.²⁷

By 2014, the controlled-release oxycodone–naloxone formulation comprised one-quarter of all oxycodone use (Figure 4).⁵ Given the concerns about opioid-induced constipation and extra-medical use, this dramatic rise in oxycodone–naloxone use is unsurprising. There has been an accompanying decline in the use of other controlled-release oxycodone tablets (Figure 3a).

Tapentadol

Tapentadol received PBS subsidy for chronic severe disabling pain in 2014. It has a novel mode of action, acting as an opioid receptor agonist and noradrenaline reuptake inhibitor. Tapentadol has apparent efficacy in a variety of pain states, including neuropathic, osteoarthritic, cancer and nociceptive pain, and may produce fewer gastrointestinal side effects than other opioids.²⁸ We found that, in 2014, tapentadol was rarely used in Australia, comprising less than 1% of total opioid use.

Tamper-resistant oxycodone

Concerns about the extra-medical use of opioids have led to efforts to produce abuse-deterrent formulations. Mundipharma released a tamper-resistant form of oxycodone (Reformulated OxyContin) in the Australian market in April 2014. The reformulation is more difficult to crush and solubilise, releases oxycodone less rapidly upon tampering and forms a gel when

dissolved in water. These properties have been effective in decreasing extra-medical oxycodone use through injection and inhalation, although tampering is still possible.^{29,30}

Where to from here?

Pain is a common complaint encountered in general practice, with approximately one in five patients presenting with chronic non-cancer pain.³¹ However, the effective treatment of pain is challenging, particularly given its varied presentations and causes, and the interplay between the experience and impact of pain and biopsychosocial factors. GPs report feeling under-equipped to deal with patients experiencing chronic noncancer pain, yet the lack of accessible pain management clinics leave them frequently responsible for its treatment.

Several factors have contributed to legitimising and facilitating the use of opioids for patients with chronic noncancer pain. The pharmaceutical industry has played an undeniable part, both contributing to and capitalising on changing ideas regarding pain and the role, efficacy and safety of opioids in the treatment of affected patients. In our study, we also showed the importance of regulatory approval and subsidy for chronic noncancer pain indications in driving the increased access to opioids in Australia.

There is increasing recognition that opioids have a limited role in the treatment of patients with chronic noncancer pain and should even be avoided in certain conditions, such as chronic low back pain, headache and fibromyalgia. Optimal pain treatment should focus initially on pain education and nonpharmacological physical and psychosocial strategies. Where medication for chronic pain is required, many PBS restrictions and treatment guidelines stipulate a trial of opioids only after other pharmacological treatments have failed. Yet nonopioid alternatives for severe pain are limited and often lack PBS subsidy. Although pregabalin is PBS subsidised for refractory neuropathic pain, neither serotonin and noradrenaline reuptake inhibitors nor gabapentin are available on the general PBS.

Clearly, the management of patients with chronic pain is complex, and equipping GPs with adequate resources and training is paramount to ensure optimal treatment and evidence-based use of opioids. Educational resources for GPs are available through various sources, including the NSW Agency for Clinical Innovation Pain Management Network, the Better Pain Management program of the Australian and New Zealand College of Anaesthetists Faculty of Pain Medicine, and the Royal Australian College of General Practitioners' pain management active learning module.

Strategies are also being implemented in Australia to curb the increasing use of and harms associated with opioids, such as the introduction of a national controlled drug monitoring program, revised treatment guidelines, promotion of tamper-resistant formulations and the rescheduling of codeine and naloxone.

Ultimately, however, it is clinicians who have the power to enact change. As part of the launch of a new initiative against the opioid crisis in the USA, the US Surgeon General called on the medical profession to pledge their commitment to 'turning the tide' on the opioid epidemic.³² He said: 'We often struggle to balance reducing our patients' pain with increasing their risk of opioid addiction. But, as clinicians, we have the unique power to help end this epidemic. As cynical as times may seem, the public still looks to our profession for hope during difficult moments. This is one of those times.'³²

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Long-term opioid use in patients with chronic noncancer pain

Who is experiencing problems?

GABRIELLE CAMPBELL PhD
LOUISA DEGENHARDT PhD

An increase in opioid prescribing for chronic noncancer pain has led to increased concern regarding opioid dependence. The POINT study aims to identify risk factors associated with the development of dependence.

Chronic noncancer pain is common and burdensome. In 2010, low-back pain, neck pain and migraines were the first, fourth and eighth largest contributors, respectively, to the global nonfatal health burden (years lived with disability).¹ Chronic noncancer pain has a major impact on the patient in terms of quality of life, mental health, health status, relationships and employment.²⁻⁴

Despite limited evidence of efficacy, there has been a considerable increase in the long-term prescribing of opioids for patients with chronic noncancer pain in several countries.⁵⁻⁹ There has also been professional and public concern about concomitant increases in problematic opioid use and harms, including dependence.^{6,10-12}

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Data on the patterns of opioid prescribing and related harms for individual patients over the longer term are limited.¹³ Clinical trials typically find far lower rates of aberrant drug-related behaviours and opioid dependence than have been reported in some observational studies, because controlled trials often exclude more complex patients and rarely follow up patients for long enough to capture behaviours indicative of abuse or dependence.^{14,15} Physicians, specialists and academics have repeatedly called for better quality studies to contribute to understanding the nature and extent of opioid dependence in people prescribed opioids for chronic noncancer pain.¹⁶

This article reports on a study carried out by the authors and other investigators on opioid prescribing for chronic noncancer pain in Australia.

The POINT study

The Pain and Opioids in Treatment (POINT) cohort study was designed to document patterns of pharmaceutical opioid prescribing for, and risk of adverse events in, patients



KEY POINTS

- Concern about the appropriateness of prescribing pharmaceutical opioids for patients with chronic noncancer pain is rising, given the risks of problematic use and dependence.
- The Pain and Opioids in Treatment (POINT) study included 1514 people in Australia who had been prescribed opioids for chronic noncancer pain.
- The POINT study showed:
 - current opioid consumption varied widely: 40% were taking 90 mg oral morphine equivalent (OME) or more daily.
 - greater daily consumption was associated with higher odds of multiple physical and mental health issues, aberrant opioid use, problems associated with opioid medication and opioid dependence.
 - a significant minority (8.5%) met criteria for lifetime pharmaceutical opioid dependence and 4.7% met criteria for past-year pharmaceutical opioid dependence.
 - past-year dependence was independently associated with being younger, exhibiting more aberrant behaviours and having a history of benzodiazepine dependence.



prescribed Schedule 8 opioids for chronic noncancer pain.¹⁷ The study has received international recognition for its efforts to delineate issues related to opioid prescribing for patients with chronic noncancer pain.¹⁸

The POINT study is a prospective cohort study of people across Australia who have been prescribed opioids for chronic noncancer pain; the study methodology and cohort characteristics have been described in detail elsewhere.^{17,19} The study was approved by the Human Research Ethics Committee of the University of New South Wales.

Participants were recruited through community pharmacies. Of all community pharmacies across Australia, 33% agreed to assist with recruitment of the cohort. To check how similar the POINT study cohort might be to patients prescribed opioids overall, a random sample of 71 pharmacies across Australia were asked to collect data on the number and characteristics of all patients with chronic noncancer pain who were prescribed opioids during their six-week recruitment window.²⁰ We found that, of the total number of such patients having opioids supplied by these pharmacies, 52% were female (the POINT cohort was 55% female); and 7% were 18 to 34 years of age, 55% were 35 to 64 years and 38% were 65 years or older (*vs* 5%, 62% and 33%, respectively, in the POINT cohort). Of these patients, 63% were prescribed oxycodone (*vs* 62% in the POINT cohort), 16.5%

were prescribed morphine (*vs* 15%), 21% fentanyl patches (*vs* 15%) and 24% buprenorphine patches (*vs* 21%). These findings suggest similarity between the POINT sample and people prescribed opioids for chronic noncancer pain more generally.

Participant eligibility and recruitment

Participants were eligible for the POINT study if they were:

- 18 years of age or older
- fluent in English
- mentally and physically able to complete telephone and self-complete interviews
- without obvious cognitive impairment (determined by researchers at the time of obtaining consent)
- living with chronic noncancer pain
- prescribed an opioid such as morphine, oxycodone or fentanyl (Schedule 8 in the Australian classification of drugs of dependence; namely, drugs that are subject to additional regulatory controls regarding manufacture, supply, distribution, possession and use²¹)
- more than six weeks into a course of taking such opioids for chronic noncancer pain.

A history of injecting drug use was not an exclusion criterion, but people currently prescribed methadone or buprenorphine as treatment for heroin dependence were not eligible. Patients taking opioids for cancer pain were also excluded.

Around 2700 participants were referred to the study. POINT study staff determined the eligibility of potential participants, and the 2091 eligible participants underwent a voluntary informed consent process. The 1873 people who were willing to participate underwent an initial telephone interview that took about one to one-and-a-half hours. Of those who were eligible, 81% (1514 participants) completed the baseline interview.¹⁸

Early findings from the POINT study

Patient characteristics

The POINT study has found that people who have been prescribed strong opioids for chronic noncancer pain have complex

demographic and clinical profiles.¹⁹ Overall, participants reported a low rate of employment, and most were on low weekly incomes similar to the amounts received for aged or disability pensions. About two-thirds of participants reported that their pain had impacted on their employment status. Additionally, one in six reported some barriers to pain treatment and one-third reported that they were unable to afford nonopioid prescription pain treatments. Our findings are consistent with other research that suggests chronic noncancer pain has a major impact on the ability to work, and patients with chronic noncancer pain experience significant socioeconomic disadvantage.²²

Demonstrating the complexity of the cohort, most participants experienced multiple pain conditions, reported poor physical health and had experienced childhood abuse or neglect. Just under half met criteria for current moderate to severe depression. Substantial minorities among participants met criteria for current moderate to severe anxiety or agoraphobia, reported attempted suicide, and reported alcohol or cannabis use disorder (*International Classification of Diseases*, 10th edition [ICD-10]) criteria.

Complex clinical profiles were more prevalent among the younger age groups. These groups reported more mental health problems, more experience of childhood abuse or neglect and lifetime suicidality, and more substance use than the older age groups. Younger participants were prescribed higher doses of opioids, were more likely to also be prescribed codeine, and were likely to be taking concurrently prescribed benzodiazepines or other antidepressants, or antipsychotic medications. Taken together, these characteristics suggest a very high-risk group, with multiple concomitant risk factors for overdose due to polypharmacy.^{23,24} Although diversion and injection prevalence were low among POINT participants, the younger age groups were more likely to engage in nonadherent behaviours. A more detailed examination of diversion in the POINT cohort has been published previously.²⁵

This complex picture highlights the need for greater recognition of the social and

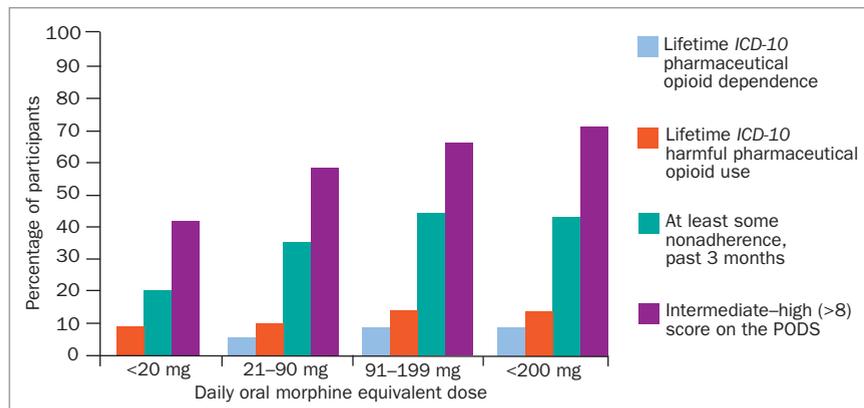


Figure. Proportion of Pain and Opioids in Treatment (POINT) study participants with lifetime opioid dependence, harmful use, nonadherence and an intermediate–high Prescribed Opioid Difficulties Scale score, by oral morphine equivalent.³⁴

Abbreviations: ICD-10 = International Classification of Diseases, 10th edition; PODS = Prescribed Opioid Difficulties Scale.

psychological contributions to the experience of chronic noncancer pain and also indicates the need for multifaceted (and multidisciplinary) healthcare approaches that address the numerous comorbidities seen in people with chronic noncancer pain.

Opioid consumption

Universal precautions in opioid prescribing have been widely endorsed internationally and in Australian national guidelines, and provide a uniform approach to risk management based on the fact that chronic pain and substance use disorders often co-occur.^{26,27} Guidelines based on universal precautions often suggest consultation with a pain specialist for patients in whom high doses (usually more than 91 mg oral morphine equivalent [OME] daily) appear to be required and in whom improvement in pain and function are not seen.²⁸ Uptake of these guidelines in practice is generally low, possibly because of challenges in prescriber confidence in managing identified risks.

The POINT study provides a unique perspective, reporting on actual consumption of all pharmaceutical opioids, including those obtained without prescription (i.e. over-the-counter opioids sold in pharmacies). Participants record all medications they consume in a seven-day medication diary that includes dosages.

This detailed assessment revealed some concerning patterns of opioid consumption,

and clear associations between high-level consumption and a range of indicators of poorer functioning.³⁴ About 15% of the cohort were taking daily doses of more than 200 mg OME, and around 40% of the cohort were consuming 90 mg OME or more daily. Those taking higher doses had the highest rates of problems associated with opioid medication, such as aberrant behaviours and opioid dependence. Of concern, participants taking higher OME doses (greater than 90 mg OME daily) reported less pain relief from their medications than participants taking lower doses.

Higher current opioid consumption was associated with a range of demographic and substance use characteristics (respectively, being younger, male and unemployed; and lifetime history of alcohol and substance use disorders and use of alcohol and illicit drugs in the past month). Correlates of higher opioid consumption were also consistent with factors identified in the literature as being associated with increased overdose mortality risk, including young age, male sex, lower socioeconomic status and psychiatric comorbidity.^{22,29–31} They were also consistent with characteristics identified in risk screening tools for opioid prescribing.³²

The association of higher opioid consumption with increasing levels of aberrant behaviours (e.g. tampering and nonmedical use) suggests that monitoring by prescribers is warranted.³³ Conversely, the finding that

some behaviours such as doctor shopping were rarely reported suggests that, at least in this sample, strategies such as prescription drug monitoring would provide limited ability for identifying patients at risk.

Pharmaceutical opioid dependence

A minority (8.5%) of participants met criteria for lifetime ICD-10 pharmaceutical opioid dependence, and 4.7% had features of dependence within the past year. The median age of onset for ICD-10 opioid use disorder was 40 years (interquartile range, 32–49 years).³⁴ This is consistent with research suggesting that pharmaceutical opioid use disorders affect a minority of patients with chronic noncancer pain who are prescribed opioids.³⁵

In this study, past-year dependence was associated with indicators of adverse psychosocial, mental and physical functioning, including younger age, unemployment, mental health problems and a history of substance use and dependence. Those who met criteria for past-year opioid dependence were also currently prescribed a higher median opioid consumption, reported more problems and concerns associated with their opioid use, and were more likely to engage in aberrant behaviours. The most common aberrant behaviours among participants meeting dependence criteria were asking for an early prescription renewal (33 participants; 48.5%) and asking the doctor for an increase in dose (27 participants; 39.7%). Past-year opioid dependence was independently associated with being younger and having lifetime benzodiazepine dependence, which has important clinical implications for the safety of opioid prescribing.³⁴

‘Adverse selection’?

The term ‘adverse selection’ has been coined to describe this apparent contradiction in which the likelihood of a patient receiving opioid therapy, and at greater doses, increases as the number of risk factors for adverse outcomes increases.³¹ The POINT study found strong evidence for this, whereby participants consuming higher levels of opioids were clearly those with a more complex picture of physical and mental health problems, as well

as social disadvantage.³⁴ Importantly, higher opioid consumption was related to increasing levels of aberrant behaviour, opioid dependence and problems associated with opioid medication (Figure 1).³⁴ Further, in this sample many of the patients with chronic non-cancer pain prescribed higher doses of long-term opioids were concurrently taking other medications (e.g. benzodiazepines) in doses that are considered high-risk for adverse outcomes, and levels of concomitant medications were higher among participants taking higher amounts of opioids.

Conclusion

The POINT study has clearly demonstrated the complex nature of patients with chronic noncancer pain, involving multiple socio-demographic, physical and mental health problems. A significant proportion of patients with chronic noncancer pain taking very high doses of opioids had multiple risk factors for potential adverse outcomes, such as dependence and overdose. Similarly, patients meeting criteria for dependence had higher levels of most indicators of poorer wellbeing. Higher opioid consumption was also strongly associated with risk for dependence; and patients on higher opioid doses had a different clinical profile compared with those on lower doses. There is clearly a need for increased vigilance and reassessment of the progress and functioning of patients with chronic noncancer pain in whom opioid consumption is considerable and problems related to opioid consumption are prominent.

Many patients with chronic noncancer pain are treated in primary care. Education and training of primary care physicians in chronic noncancer pain and addiction medicine is crucial; the risks of high-dose consumption of pharmaceutical opioids need to be weighed against clinical evidence that patients are deriving net benefit from their use. It is crucial for primary care physicians to routinely collect detailed histories of their patients in order to determine the most appropriate treatment plan, and to consider involving specialist mental health, addiction or other services when appropriate and available.

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Tapering off opioid analgesia

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Opioids are being increasingly used for treating chronic noncancer pain but adverse events outweigh the benefits of long-term opioid treatment in these patients. As abrupt cessation of opioid analgesia can lead to unpleasant withdrawal symptoms, tapering off opioid therapy is the preferred strategy.

The past 20 years have seen an unprecedented expansion in the use of opioid analgesics in Australia, with opioid dispensing episodes increasing by at least 15-fold.¹ One of the most important changes in clinical practice during this period has been the long-term use of opioid analgesics in treating chronic noncancer pain. Although the efficacy of opioids for short-term pain relief from acute pain conditions and the necessity of their regular use in the treatment of cancer pain has been well established, there is insufficient evidence for the long-term benefits of opioid analgesia in the treatment of chronic noncancer pain.

Almost half of the opioids prescribed in general practice are for chronic noncancer pain.² Increased patient awareness of and demand for the right to pain relief, along with ongoing problems of access to multidisciplinary chronic pain management services, may be adding to the over-reliance of GPs on opioid analgesia when treating this type of pain.

There are almost 250 preparations of 12 opioid analgesics on the market in

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Australia, leading to aggressive marketing strategies. These strategies potentially contribute to the overuse of opioid analgesics for treating chronic noncancer pain in the time-constrained setting of general practice, where prescribing a pain killer for a pain problem may be the expected clinical outcome for all involved. It is also important to acknowledge that both undergraduate medical training curricula and vocational GP training curricula in Australia lack a focused pain management component.

There is a consensus that adverse events outweigh the benefits of long-term opioid treatment.³ Misuse of, dependence on and addiction to these medications present an alarming public health problem in Australia. A major concern is the recent upsurge in serious harms associated with opioids, particularly the substantial increases in opioid-related hospitalisations and death rates.¹ Hospitalisations related to pharmaceutical opioids now outnumber those related to heroin use in Australia.¹

In patients for whom the long-term use of opioid analgesics is problematic, due to either adverse effects or aberrant behaviour, abrupt cessation is not an ideal option because of the associated withdrawal symptoms (Box 1). Tapering off these medications is an alternative strategy that can prevent discomfort and complications related to withdrawals.

This article provides a practical overview of best practice for tapering opioid therapy in the general practice setting.

KEY POINTS

- The long-term use of opioids for analgesia in patients with chronic noncancer pain is associated with health and social problems.
- Ceasing opioids abruptly after prolonged use may cause withdrawal symptoms.
- Tapering opioids may improve mood and function as well as pain outcomes.
- A structured tapering program can prevent an unpleasant withdrawal experience for the patient.

Indications for tapering

There are many valid reasons to consider tapering a patient's opioid analgesics, including the following:

- the patient may decide that they do not want to be taking any medication
- the side effects of an opioid medication may be intolerable (Box 2)
- despite regular dose increases, opioids may not be yielding the desired pain relief and functional outcomes
- the patient's condition may improve to a level where the pain medication is no longer necessary
- the patient may be misusing the medication or exhibiting aberrant drug-related behaviour.⁴

An appropriate specialist's input and further attention may be required in planning and conducting the tapering process in some clinical situations.

- **Unstable medical and psychiatric conditions.** As opioid withdrawal is associated with anxiety and insomnia, if the patient has a condition that would be worsened with anxiety, such as a poorly-controlled arrhythmia or



untreated mood disorder, it is essential to deal with these problems first.

- **Concomitant sedative medications.** It is best to avoid the use of sedatives during opioid tapering; however, if there is a clinical indication for these medications, staged dispensing might help reduce the risk of overdose.
- **Pregnancy.** Severe, acute opioid withdrawal has been associated with premature labour and spontaneous abortion, especially during the first trimester. Specialist advice should be sought or relevant guidelines referred to before tapering in pregnant women.⁵
- **Polysubstance use or access to opioid medications from other sources.** These patients are best managed in consultation with addiction services, possibly within a substitution treatment framework involving methadone or buprenorphine. An inpatient admission to a residential drug and alcohol facility may be warranted if the polysubstance use (especially the use of other sedating agents) is prominent.

Preparation for tapering

As soon as a valid indication for tapering of opioid analgesics is established, it is important to have a conversation with the patient to explain the process and develop a treatment agreement. This agreement could include:

- time frame for the agreement
- goals of the taper
- agreed frequency of dose reduction
- requirement for obtaining the prescriptions from a single clinician and a named pharmacy
- scheduled appointments for regular review
- expected effects of the taper
- disallowing increasing the medication dose without first discussing it with the prescriber
- consent for urine drug screening
- possible consequences of not following the treatment agreement.

Before starting tapering, it needs to be clearly emphasised to the patient that reducing the dose of opioid analgesia will not necessarily equate to increased pain and that it will, in effect, lead to improved mood and

1. SIGNS AND SYMPTOMS OF OPIOID WITHDRAWAL

- Drug craving
- Anxiety
- Insomnia
- Abdominal pain
- Vomiting
- Diarrhoea
- Diaphoresis
- Mydriasis
- Tremor
- Tachycardia
- Piloerection

functioning as well as a reduction in pain intensity. The prescriber should establish a therapeutic alliance with the patient and to develop a shared and specific goal. For example, a patient may decide to withdraw completely from opioids by the end of the year. The prescriber can advise clinically appropriate goals. In some cases, the goal might be to reduce the dose to a certain level if the patient cannot completely withdraw from the medication.

The prescribing of opioid analgesia for a prolonged period (usually more than eight weeks) on a regular basis is regulated by state and territory health authorities in Australia.⁶ It is important that the prescribing doctor is familiar with the regulation in their state or territory and that the parameters surrounding prescribing practice are clearly discussed with the patient.

Principles of tapering

To improve patient safety and achieve a practical positive outcome, consolidating all opioid analgesia into a single long-acting agent is recommended.⁵ The main objective of tapering is to reduce the dose of medication at an interval that will not cause any withdrawal symptoms.

Type of opioid, dosing and dispensing schedule

Unless there is a contraindication, the Royal Australian College of General Practitioners guidelines recommend all patients beginning opioid tapering be switched to controlled-release morphine tablets.⁵ For converting any opioid analgesic dose to the appropriate dose of oral morphine, the general principle is to calculate the total daily morphine-equivalent dose by using a conversion table (e.g. see opioid calculators in Box 3), then starting at half of this calculated dose of oral, controlled-release morphine, with a view to adjusting the dose

2. SIDE EFFECTS OF OPIOIDS

Common	Less common
• Sedation	• Hyperalgesia
• Dizziness	• Delayed gastric emptying
• Nausea	• Hormonal dysfunction
• Vomiting	• Muscle rigidity
• Constipation	• Myoclonus
• Tolerance	
• Physical dependence	
• Addiction	
• Respiratory depression	

to avoid withdrawal or sedation. It is important to choose the timing of this opioid rotation so that a dose review in three to four days is possible for both patient and prescriber. If prescribers do not feel confident about opioid rotation (switching from one opioid to another), they can contact their local pain management centre for further advice.

Prescribing scheduled doses is potentially more helpful for the patient than prescribing as required, as it provides a structure for the reduction. Organising pharmacy dispensing at frequent intervals, such as once- or twice-weekly, will help the patient comply with the tapering plan. It is important to support the patient in this by not providing them with extra prescriptions without a review if they run out of medication before the scheduled time. At the review, reasons for the extra use should be explored, and the frequency of dispensing might be increased. In this way, patients would have fewer tablets available to them and, if they did take more than prescribed, they would not experience major withdrawal by the time of the next scheduled dispensing.

Taper rate and duration

A 10% reduction of daily dose of any opioid every one to two weeks is usually well tolerated, with no significant withdrawal. When one-third of the initial daily dose is reached, slow the tapering to half the previous rate to minimise withdrawal-related anxiety.⁷

The pace of the taper depends on the patient and the reason for tapering. If the patient is experiencing serious opioid-related side effects, a faster taper is necessary. An even more rapid tapering might be warranted if the patient is refusing to see an addiction

3. WEANING OFF OPIOID THERAPY: USEFUL RESOURCES

Professional resources

- Opioid Tapering Calculator (Victoria State Government and NPS MedicineWise)
 - www2.health.vic.gov.au/Api/downloadmedia/%7B91501663-EA0B-4985-B996-74C159487EE3%7D
- Opioid Calculator App (FPM; ANZCA)
 - <http://fpm.anzca.edu.au/front-page-news/free-opioid-calculator-app>
- *A Guide to Deprescribing Opioids* (Tenni P, Orlikowski C; Deprescribing Clinical Reference Group; Primary Health Tasmania; 2016)
 - www.primaryhealthtas.com.au/sites/default/files/A%20Guide%20to%20Deprescribing%20Opioids.pdf
- *Recommendations Regarding the Use of Opioid Analgesics in Patients with Chronic Non-Cancer Pain* (FPM; ANZCA; 2015)
 - <http://fpm.anzca.edu.au/Documents/PM1-2010.pdf>
- *Quick Reference Recommendations for Conduct of an Opioid Trial in Chronic Non-Cancer Pain* (FPM; ANZCA; 2015)
 - http://fpm.anzca.edu.au/Documents/4462_001.pdf

Patient resource

- *Pain and Role of Medications* (Pain Management Network [Agency for Clinical Information])
 - www.aci.health.nsw.gov.au/chronic-pain/for-everyone/pain-and-role-of-medications

Abbreviations: ANZCA = Australian and New Zealand College of Anaesthetists; FPM = Faculty of Pain Medicine.

specialist after exhibiting aberrant behaviour, such as injecting, or breaching the treatment agreement by obtaining medications from multiple sources. A slower rate of tapering is advisable for patients who are highly anxious about the process and who might have psychological dependence on the pain medications, or for those who have significant cardiorespiratory conditions.⁷

For patients who experience severe withdrawal symptoms or a worsening of function because of an increase in their pain levels or deterioration of their mood, it is best to hold the daily dose or increase it to a level at which they are comfortable. Slowing down the taper or lessening the amount of dose reduction at each taper might help in this scenario. Clinical reviews before each dose reduction

ensure safety and help reduce anxiety. If the patient is adherent with the treatment agreement but cannot complete the taper, maintaining a lower dose with the same treatment structure may be an option.

It is advisable to suggest the option of substitution (also called 'maintenance') treatment as soon as failure to taper opioids or heavy reliance on opioid analgesia is observed.⁸ As regulation and legislation regarding substitution treatment are governed by the states and territories in Australia, it is best to discuss the practicalities of this with a local addiction specialist or treatment centre.

The duration of the taper would depend on the initial dose and the patient's condition and adherence with the plan. It is advisable to include the intended taper duration in the initial treatment agreement and revise it if the plan changes.

Monitoring

Scheduling frequent visits for the patient, in keeping with the tapering rate and, if possible, before each dose reduction (e.g. weekly or fortnightly), will allow the prescribing doctor to monitor the patient's pain status, withdrawal symptoms and benefits of the taper, such as reduced pain and improved mood, energy level and alertness. These consultations should focus on the benefits of the taper, rather than simply the medication dose and rate. Using a urine drug screen to assess adherence for every patient who has been taking opioid analgesia for more than three months has now been accepted as good practice.⁹ Medicare covers 36 urine drug screens within a period of 12 months if they are used for monitoring purposes. It is important to ask for testing of the exact agent used in the taper, as most pathology services do not routinely test for synthetic opioids such as oxycodone. The expectation is that the urine will test positive for the prescribed drug and negative for other opioids.

Involving allied healthcare professionals, especially a psychologist, during the taper is likely to increase the patient's capacity to deal with the negative thoughts and stress associated with the change in treatment. Excessive reliance or dependence on medication is often a stigmatised disorder to which patients cannot easily admit. It can

be helpful to listen with empathy and without passing judgement, to acknowledge the patient's difficulty in controlling the medication use and to encourage their efforts.

Finally, it is essential to clearly explain to the patient, and document in the patient record, that alongside the reducing dose of opioids, the patient's tolerance for opioids will be altered as well. If the patient returns to taking the initial dose after a period of reduction, this reduced tolerance makes it likely that they may experience serious adverse effects, including opioid overdose and respiratory depression.

Conclusion

There are valid reasons to wean patients off their long-term use of opioid analgesics. A structured and well-planned tapering program will improve treatment outcomes and reduce the complications associated with opioid withdrawal. **MT**

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Clinical care and regulation of opioid use

The Tasmanian model

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In 2009, Tasmania enhanced its clinical-regulatory processes for long-term opioid prescribing, including implementing real-time prescription monitoring – the only such system to date in Australia – and improved training on management of patients with chronic noncancer pain. Since then, prescription opioid-related mortality has fallen in this state, whereas it increased in Australia as a whole.

KEY POINTS

- Long-term prescribing of opioid medications for patients with persistent noncancer pain has questionable benefits and significant risks.
- Real-time prescription monitoring programs such as Tasmania's DORA (Drugs and Poisons Information System [DAPIS] Online Remote Access) can help doctors, pharmacists and regulators identify and respond earlier to patients with emerging or established drug-related problems.
- Clinicians also need to draw on their clinical skills to prevent, better identify and appropriately respond to patients with drug-related problems.
- Evidence suggests that Tasmania's integrated, proactive clinical-regulatory system for opioid prescribing linked to its prescription monitoring system has improved standards of care in the clinical management of patients with chronic noncancer pain.



In recent decades, prescribing rates for analgesic and psychotropic medicines such as opioid analgesics have increased significantly in Australia, presumably based on the assumption that this prescribing represents good, empathetic care. However, over time it has become evident that this increased prescribing is often associated with poor clinical outcomes and serious harms. Opioid therapy can adversely affect the respiratory, gastrointestinal, musculoskeletal, cardiovascular, immune, endocrine and central nervous systems.

Opioid-related harms include increased sensitivity to pain (opioid-induced hyperalgesia) and opioid tolerance, leading to worsening of the pain experience and reduced function, unsanctioned use (e.g. injecting use), limb ischaemia, androgen deficiency, sleep-disordered breathing, xerostomia with dental decay, intestinal obstruction, falls and accidents, and diversion to the illicit market. These harms all contribute to the reality that, in attempting to treat pain effectively with these agents, we may substantially increase our patients' likelihood of a poor outcome, including premature death from overdose.^{1,2}

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Patients with emerging or well-established prescription drug problems are complex and often technically and emotionally challenging to manage. Patient requests for opioid and other psychotropic medications may place significant pressure on prescribers. A high-functioning, well-resourced clinical-regulatory system can provide doctors with crucial and timely clinical information and other support to help them deliver safe, good care. Tasmania has paid particular attention to developing an integrated, proactive clinical-regulatory model. This was further enhanced in 2009 by the introduction of real-time prescription monitoring accessible to medical practitioners and pharmacists in Tasmania – the first (and to date only) real-time prescription reporting system in Australia. This has improved the capacity to assess patient risk and support clinicians in the safe clinical management of patients at risk from co-occurring pain, addiction and other morbidity, in turn reducing opioid-related harms.

This article discusses the Tasmanian clinical-regulatory model for the management of patients with, or at risk of, problematic use of prescription opioids for noncancer pain. It also outlines evidence about the impact of the model on opioid use and related harms.

Why regulate use of Schedule 8 medicines?

In a recent Tasmanian coronial finding, Coroner Stephen Carey addressed the issue of prescription medication overdose.³ He suggested that we should stop using the term ‘accidental’ when referring to prescription drug overdose deaths, based on the assumption that the overdose was not deliberate, and instead refer to these overdoses as ‘likely and avoidable’. This proposal bears careful consideration. Coroner Carey’s observation is consistent with our national shift away from referring to motor vehicle ‘accidents’, towards the term motor vehicle ‘crashes’, in recognition that many of these events are preventable rather than unforeseeable and unavoidable.³

The Penington Institute recently published Australia’s Annual Overdose Report 2016, in which it stated that, between 2008 and 2014:⁴

- Australia experienced an increase of 87% in prescription opioid-related deaths
- rural/regional Australia experienced an increase of 148% in prescription opioid-related deaths
- more Australians died from prescription medication overdose than from illicit drugs
- more Australians died from prescription medication overdose than from car crashes.

On the release of the US guideline for prescribing opioids for chronic pain in 2016, the Director of the US Food and Drug Administration commented regarding opioids: ‘We know of no other medication that’s routinely used for a nonfatal condition that kills patients so frequently’.^{5,6} If we accept the validity of

this statement then we are compelled to move beyond the status quo in current clinical and regulatory practices to respond to the problems we are witnessing.

The Pharmaceutical Services Branch (PSB) in Tasmania continues to identify patients in whom the treating doctor has not recognised or has not been able to safely manage emerging or well-established drug problems. Substantial attention has been paid to enhancing Tasmanian undergraduate and postgraduate medical education and training in addiction, pain medicine and the overlap. However, this is clearly insufficient to solve the problem in isolation, and further attention has been considered necessary to upstream health system and other structural factors that can influence clinician and patient behaviours.

How do we support best practice use of Schedule 8 medicines in Tasmania?

The Poisons Act (or equivalent) in each Australian jurisdiction provides a legal basis for protecting clinical and public safety in relation to the handling of drugs and poisons. The value of this legislation in supporting good clinical practice is often underestimated, and it is sometimes criticised as unnecessary ‘red tape’.

In Tasmania, a range of additional clinical and regulatory processes have been established for overseeing the treatment of patients with pain and opioid dependence. This was prompted by the recognition in 2007 that Tasmania had by far the highest per capita consumption of opioid and benzodiazepine medicines in Australia and the highest opioid-related mortality rate. Internal analysis of data by the Department of Health and Human Services (DHHS) Tasmania suggests that, in 2003, Tasmanian doctors were prescribing opioid medications at a level that was 50% higher by weight than the Australian average (measured as the oral morphine equivalent daily dose in g/1000 population). Something had to be done to address this serious public health problem.

The clinical-regulatory process

In Tasmania, long-term prescribing (more than two months) of Schedule 8 drugs such as opioid analgesics requires an authority, issued in accordance with specific provisions within the Poisons Act. A small team of DHHS pharmacists are appointed as delegates to administer the Act and grant authorities to prescribe. For an authority to be issued, a doctor must provide sufficient information demonstrating that the proposed Schedule 8 prescription regimen meets quality and safety standards. Although the focus is on the safety of the regimen, the regulation of medicines with high potential for abuse has evolved into a broader set of metrics and integrated clinical-regulatory processes that focus on best (evidence-based) clinical practice, particularly in the clinical management of patients with persistent noncancer pain and co-occurring opioid dependence.

If, after receiving an application, a pharmacy delegate identifies that a particular patient is at higher than standard risk of harm based on commonly identified behavioural indicators (often referred to as 'red flags' and 'yellow flags') then the delegate will ask one of a panel of specialist consultant medical officers to review the case and provide advice. Patients with particularly complex pain conditions and high-risk behaviours concerning their prescribed and nonprescribed drug use or management are referred to an expert advisory panel consisting of a pain medicine specialist, addiction medicine specialist, GP and one or more of the pharmacy delegates. This panel scrutinises a range of clinical reports and information before providing advice to the delegate.

The pain specialist focuses on whether the current or proposed medication regimen is likely to be effective in treating this patient's pain in the context of current best practice and, where feasible, considers what treatment might be appropriate in the context of a broader multimodal, multidisciplinary treatment framework. Among other matters, the addiction medicine specialist focuses on whether this regimen is likely to be safe and appropriate in the context of any evidence of co-occurring drug dependence and associated clinical or public health risk. The GP focuses on whether the particular patient is, from a practical perspective, able to be safely managed in the manner proposed, in the primary healthcare setting. A recommendation may be made for further specialist assessment to map out a best-practice treatment approach.

The expert advisory panel meets fortnightly to consider applications for an authority to prescribe opioid analgesics. They examine a wide range of electronically recorded clinical information, including GP and specialist medical reports, electronically recorded ambulance and hospital notes, alcohol and drug service clinical notes and reports, radiology and pathology reports and detailed real-time information on all Schedule 8 medicines that have been dispensed to the particular patient. The system captures both public (PBS funded) and private prescriptions.

The advisory panel follows a process of detailed inductive reasoning, piecing together all the information related to benefit, risk and harm in association with the patient's clinical presentation and treatment. The group makes carefully structured and documented recommendations, describing their basis, to the delegate, after considering all the information available to it. In making these recommendations, the group considers clinical and other evidence of positive or adverse treatment outcomes both in terms of the pain condition(s) and any aberrant behaviours that might signal the existence or emergence of a substance use disorder.

Undergraduate and postgraduate medical training

The nature and extent of prescribing problems for Schedule 4 and Schedule 8 drugs in Tasmania have led to more attention to this

area in medical training. All University of Tasmania medical students, medical registrars in psychiatry, general practice, pain and addiction medicine, and to a lesser extent GPs and doctors working in Tasmanian hospitals now receive teaching from addiction and pain medicine specialists about:

- the importance of undertaking a careful and ongoing assessment of benefit, risk and harm in their prescribing of analgesic and psychotropic medicines
- rapidly deprescribing when there is evidence of risk and harm and an absence of clear evidence of benefit.

Although the problems are by no means adequately addressed, Tasmania has worked towards adopting a more thoughtful, clinical duty-of-care approach to assessing and responding to these health and human problems.

We were not surprised to see a transition in clinical thinking from one in which there was no opioid ceiling dose and a common scenario of opioid medicines titrated to effect, leading to very high doses, to one in which recommended ceiling doses are clearly described in the pain management literature and are continuing to drop. Moreover, contemporary pain management guidelines highlight the risks and evidence of limited benefit and significant harms associated with the use of opioid medicines in the longer-term treatment of patients with persistent noncancer pain.⁵⁻¹¹ They display a parallel transition from a medicines focus to approaches involving multimodal self-management, physical therapy and psychological pain management.

Electronic recording and reporting of prescriptions

Real-time information on prescriptions for controlled drugs is made possible by Tasmania's leading-edge development of its Drugs and Poisons Information System (DAPIS). Medical practitioners and pharmacists in Tasmania are able to access a light version known as DAPIS Online Remote Access (DORA). This suite of software was developed in 2009 to 2011. It formed the basis for the development of the National Electronic Recording and Reporting Controlled Drugs (ERRCD) system, which the Australian Government has made available to all states and territories with a view to establishing a nationwide interconnected system of real-time reporting for controlled drugs. Currently, DORA remains Australia's first (and only) real-time reporting system.

All doctors and pharmacists in Tasmania can apply for access to DORA and can then view their patient's file when there is a legitimate clinical need. DORA is accessed by clicking on a hyperlink installed on the doctor's or pharmacist's computer desktop. It is a secured site with contemporary access and encryption protections. DORA allows doctors to see within seconds:

- what opioid medications have been dispensed for their patient and the doses and quantities
- when the medications were dispensed
- whether there is an authority held by another doctor to

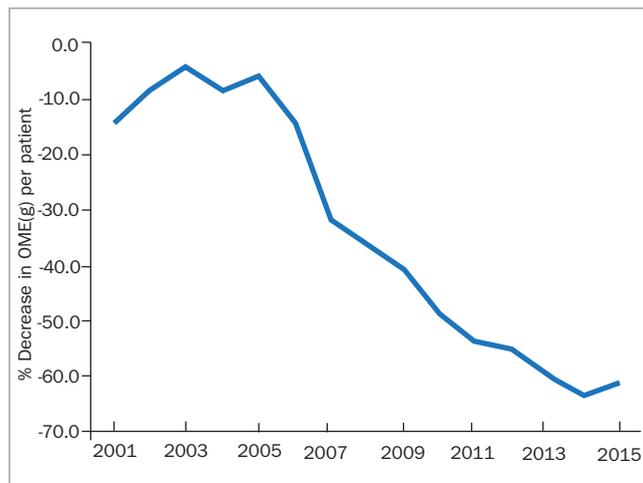


Figure 1. Percentage decrease in oral morphine equivalents (OME) in grams per patient with chronic pain treated with opioids in Tasmania. The OME was calculated as the total amount of opioid medication supplied in Tasmania per year divided by the number of authorities issued to medical practitioners to prescribe opioids for patients with chronic pain. It was compared with the value for the year 2000.

prescribe (in which case the second doctor cannot prescribe unless it is a medical emergency)

- whether there are any 'drug seeking' alerts or whether the patient has been declared 'drug dependent' within provisions of the Poisons Act (Tasmania).

This information assists doctors in their decision-making on prescribing.

Similarly, pharmacists who are presented with a prescription for a Schedule 8 drug (and any other medication that is deemed a declared restricted substance) can check DORA to see what Schedule 8 medicines have been dispensed recently to the patient and the details. This can alert pharmacists to the possibility of a problem. They can then make a decision about the appropriateness of dispensing and, if necessary, also contact the Pharmaceutical Services Branch by telephone or email, to safeguard the patient and community and to assist in their decision-making and clinical management.

Impact of the clinical-regulatory system and real-time prescription reporting

Real-time prescription reporting has attracted significant attention among health practitioners and coroners in Australia. Tasmanian authorities have been at pains to point out that the information provided by prescription reporting does not of itself address or solve prescription drug risk and harm. It is what the clinician and regulators working with clinicians do with this information that can enhance the quality use of medicines and clinical outcomes. Tasmania witnessed an end to doctor shopping for Schedule 8 medicines when it implemented real-time prescription processes

linked to proactive clinical-regulatory monitoring combined with timely communication and practical support to doctors and pharmacists to enhance their awareness of the risks and harms associated with a patient's current or proposed treatment regimen.

It is pleasing to observe that momentum is building nationally for the adoption of ERRCD. Coroners and professional bodies continue to agitate for ERRCD's timely implementation.

It is important to note that the clinical-regulatory interface is not about denying access to opioids when they are indicated and beneficial. In fact, Tasmania has continued to see an ever-increasing number of authorities being requested and granted for the long-term prescribing of opioid medicines, as is the case nationwide. However, although the number of authorities issued to doctors to prescribe opioid medicines to patients with chronic pain continues to increase in Tasmania, the average dose prescribed has trended downwards since 2005 (Figure 1).

Between 2005 and 2015, there was a trebling of patients prescribed opioids for chronic pain in Tasmania (from 2061 to 6207). Over 95% of these authorities were issued for the management of persistent noncancer pain. At the same time, the average authorised daily dose per patient (calculated as the crude oral morphine equivalent daily dose) decreased from 71 mg to 44 mg – a reduction of about 38%.

This reduction in average opioid doses in Tasmania occurred during a period of continuous and substantial increases in the prescribing of opioid medicines across the country. An internal analysis of primary data provided by the Australian Office of Drug Control indicates that the average quantity of opioids (oral morphine equivalents in grams) per 1000 people supplied by pharmaceutical wholesalers to pharmacies in Tasmania declined from 140% to 95% of the national average between 2005 and 2015 (Figure 2).

These changes in prescribing are consistent with evidence-based decreases in the maximum opioid doses and duration of opioid prescribing recommended in Australian and international pain management guidelines.⁵⁻¹¹

A study authorised by the Tasmanian Coroner's Office shows that Tasmania has successfully reduced deaths associated with prescription opioids. In the period before the implementation of DORA (2005 to 2009), prescription opioid-related deaths in Tasmania averaged 25 each year, with a peak of 33 deaths in 2007. In the period 2010 to 2014, prescription opioid-related deaths averaged 17 each year, a reduction of 34%. We are cautious in our interpretation of these data, but they do appear to run counter to trends in other states and territories.

An improved clinical-regulatory interface is important for prevention

There has been substantial national interest in Tasmania's clinical and regulatory responses. We caution against the idea that the provision of real-time information through a national ERRCD

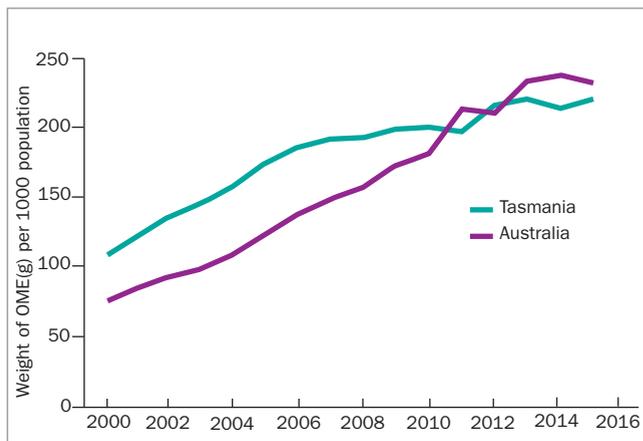


Figure 2. Annual weight of opioids supplied by pharmaceutical wholesalers to Tasmania and to Australia per 1000 population (expressed as oral morphine equivalents [OME] in grams). Data were obtained from the Australian Office of Drug Control and analysed by the Tasmanian Pharmaceutical Services Branch.

married with clinician self-regulation will of itself solve doctor shopping and broader prescription drug problems in Australia. If clinicians routinely embrace the use of ERRCD as part of their broader ‘tools of the trade’ then we can reasonably expect a significant reduction in Schedule 8 doctor shopping and a portion of the associated harms. However, the ERRCD will not in isolation address the significant harms occurring through injudicious or unsafe prescribing to patients (e.g. the use of high opioid doses or prescribing despite significant risk factors for drug overdose, misuse or diversion).

Adoption of the Tasmanian model throughout Australia might well prevent the high mortality from opioid overdose currently experienced in the USA. This was described by the US Surgeon General in his 2016 letter to all American doctors as an ‘opioid epidemic’, adding that doctors have prescribed opioids with good intentions, coinciding with heavy marketing of these medicines, and without sufficient training or other support to treat pain safely and effectively.¹²

Conclusion

The Tasmanian clinical-regulatory model has improved standards of care in the clinical management of patients with chronic noncancer pain, although there is more to be done. A persistent and consistent message has been communicated to doctors about the importance of safe and appropriate treatment of patients with persistent noncancer pain, which appears to be having an impact on clinical practice, including lowering the average prescribed opioid doses and reducing opioid-related mortality. It is our collective challenge to maintain and build on these evidence-guided improvements in clinical practice.

We believe Tasmania has demonstrated the benefits of a

comprehensive approach to prescription drug problems. The Tasmanian approach involves increased attention to undergraduate and postgraduate medical teaching about assessment and clinical management of patients with co-occurring persistent noncancer pain and opioid dependence, along with implementation of an ERRCD system and evolution of a high-functioning clinical-regulatory interface that utilises the skills and knowledge of our pain and addiction consultants, GPs and regulatory affairs pharmacists. **MT**

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COMPETING INTERESTS: None.

Over the counter, under the radar

Nonprescription codeine dependence

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Addiction to combination codeine-containing products is associated with potentially life-threatening gastrointestinal, hepatic and renal complications. Effective treatment of codeine dependence can be initiated and maintained by GPs.

Codeine is methylmorphine, a low-potency opiate that is indicated for treating moderate pain in oral doses of 30 to 60 mg. In lower doses, evidence of analgesic efficacy is unclear when compared with simple analgesics, such as ibuprofen and paracetamol.^{1,2} Codeine's usefulness is further limited by genetic polymorphism of its metabolism that can vary with ethnic background. Individuals who efficiently convert codeine to morphine may be at risk of toxicity while poor metabolisers may find the drug relatively ineffective.

Codeine is not available as an over-the-counter (OTC) pharmacy product in the USA or in most of the European Union. Australia, however, is one of a handful of countries where low-dose, codeine-containing analgesic and antitussive preparations can still be purchased without prescription. Despite known risks and limited evidence of benefit, OTC codeine products generate many millions of dollars annually and comprise a significant component of pharmacy medication sales in Australia.

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Over-the-counter codeine addiction

Problems with the nonmedical use of combination analgesics surfaced in the 1970s, when kidney disease associated with phenacetin-containing OTC painkillers – analgesic nephropathy – was identified. (Nonmedical use is use that is not of medical benefit or based on medical advice.) In Australia, analgesic nephropathy became the most common cause of renal failure for decades.^{3,4} The popularity of OTC pain medication in Australia has continued into the 21st century.

In recent years, the misuse of codeine, usually characterised by consumption of supratherapeutic daily doses of combination OTC analgesics (and, occasionally, antitussives), has been reported in many Australian and New Zealand case series.^{5,6} In these series, some codeine users have reported taking more than 10 times the recommended daily doses of these preparations.

The range of serious harms from taking high doses of combination nonprescription analgesics are mostly due to constituents other than codeine, such as paracetamol and, in particular, ibuprofen. Renal and hepatic impairment, profound hypokalaemia, gastrointestinal ulceration and perforation, and anaemia from blood loss have been reported in long-term users (Box 1).



KEY POINTS

- Combination products containing low-dose codeine are currently available without a prescription in a handful of countries, including Australia.
- Codeine is a weak opioid and its metabolism is subject to genetic variation.
- Addiction to over-the-counter codeine is a well-recognised problem in Australia.
- Long-term high-dose intake of NSAIDs in combination codeine-containing products can lead to life-threatening gastrointestinal, renal and hepatic damage.
- Opioid maintenance therapy offers good outcomes for patients with codeine dependence.
- In Australia, the TGA has recently reviewed codeine scheduling, and codeine products will become prescription-only (Schedule 4) from 2018.



Coronial reports of multi-drug toxicity cases have implicated codeine products as contributing to deaths.

A hidden population

Nonprescription codeine users may be considered a 'hidden population' because sales to individuals are not routinely recorded or monitored. There are anecdotal reports of unrecognised and untreated addiction to codeine in patients admitted for life-threatening complications of high-dose ibuprofen–codeine products. Individuals who are addicted to codeine may not identify as drug users. They can also stay under the diagnostic radar by concealing their use because of shame and embarrassment.^{7,8}

Recently, in response to concerns about 'pharmacy shopping' for these products, the retail pharmacy industry developed a medication-monitoring package, 'MedsAS-SIST'. This is a recording and monitoring system for medications containing codeine. It involves the pharmacist recording the transaction and an identification number

from photographic identification (with the patient's consent) in a database.⁹ Pharmacists who elect to use this system may be better able to identify individuals purchasing large amounts of codeine analgesics.

The role of the GP

Identifying patients with codeine dependence

Given that the harmful use of codeine combination analgesics does not require a consultation with a medical practitioner, how can GPs address OTC codeine dependence and its related morbidity? Specific questioning about use of OTC medicines for pain is key to identifying and managing a codeine-related opioid use disorder. In some settings, this questioning is routine – the absence of OTC codeine use is a 'relevant negative' in a drug and alcohol history. This line of enquiry is particularly important in patients with features of NSAID toxicity. Once use of a pharmacy-purchased medication is established, further information on frequency and pattern of use, dose and total daily intake should be obtained.

In patients who are using very high doses of codeine combination products, a typical history is escalation of doses following self-initiated management of persisting pain. Other drivers of nonmedical use include attempts to attenuate opioid withdrawal symptoms and to self-treat anxiety, insomnia or low mood. In all these settings, high doses of codeine, particularly in combination with ibuprofen, paracetamol or doxylamine, are likely to have limited or no benefit while carrying significant risks. Codeine users may attempt to reduce intake of ibuprofen or other drugs by tampering with tablets, for example through so-called 'cold-water extraction', but this does not eliminate the risks of codeine addiction.

Managing patients with suspected codeine misuse

It can be challenging to manage patients with suspected alcohol or drug misuse, particularly when trying to obtain an accurate history. Some patients understate intake or problems associated with substance use. However, many patients, especially those

contemplating or seeking treatment of OTC opioid addiction, provide an accurate history. An open approach, vigilance and specific questioning when seeing patients with a background of dependence on OTC or prescription medicines for pain may yield benefit.

A GP who is concerned about OTC codeine use should take a detailed history, paying particular attention to:

- precipitants, triggers and symptoms related to codeine-product use (e.g. anxiety, chronic pain, insomnia)
- daily intake and pattern of dose increases, including:
 - number of packs purchased
 - number of pharmacies visited
 - duration of use
- other drug and alcohol use.

Principles of management of OTC codeine dependence follow the same model as treatment of illicit opioid use, with some specific considerations. Unlike illicit opioids, nonprescription codeine analgesics are particularly accessible and relatively affordable; therefore, treatment approaches may need to focus on longer-term care and education (Box 2).

Initial management of the adverse effects of long-term high-dose ibuprofen or paracetamol is often required. This ranges from assessing severity (e.g. renal and liver function tests and full blood count) and managing symptoms (e.g. prescribing gastric mucosa-protecting medications) to referral to a specialist physician. The patient with codeine addiction in the setting of persisting pain will benefit from a management plan that focuses on functional improvement and physical and psychological therapies.

In some cases, treatment of addiction will result in resolution of symptoms such as insomnia, anxiety and low mood. However, specific measures to address comorbid mental health problems are often required.

Opioid maintenance therapy

Opioid maintenance therapy (sometimes called substitution or replacement treatment) is a valuable, practical intervention in the management of OTC codeine addiction. Buprenorphine–naloxone sublingual film

1. SOME SERIOUS COMPLICATIONS OF HIGH DOSES OF ANALGESIC INGREDIENTS

NSAID-related effects

- Hypertension
- Cardiac failure
- Peptic ulcer disease with or without perforation
- Gastrointestinal and other haemorrhage
- Anaemia
- Renal toxicity/failure
- Liver toxicity/failure

Paracetamol-related effect

- Liver toxicity/failure

Codeine-related effects

- Dependence
- Respiratory depression

as an opioid maintenance medication is effective at managing opioid withdrawal symptoms and blocking or reducing the reinforcing, euphoric effect of opioid agonists such as codeine. Buprenorphine, a partial opioid agonist, carries a relatively low risk profile and significant benefits for patients with codeine dependence. Methadone liquid has also been used in the treatment of OTC codeine addiction with positive outcomes. However, buprenorphine–naloxone preparations carry benefits over methadone, including:

- easier access: buprenorphine–naloxone is often available to GP prescribers with less intensive specialist training compared with methadone
- less stigma: methadone treatment is associated with community stigma as being a treatment of heroin addiction
- less clinical risk: methadone toxicity is more frequently associated with significant morbidity and mortality than toxicity from buprenorphine–naloxone.

Treatment of any opioid-use disorder with opioid maintenance therapy is well within the scope of specialist and non-specialist GPs. However, opinion from an addiction medicine specialist physician or support from a specialist alcohol and drug service may be indicated in complex cases, such as where there is a high risk of other

2. WHAT TO TELL PATIENTS

- Codeine is an addictive drug that is converted to morphine in the body
- Taking codeine painkillers for more than a few weeks increases the risk of addiction
- Long-term use of high doses of codeine combination painkillers can cause liver and kidney damage, stomach ulcers, anaemia, fatigue, depression and worsening of pain symptoms
- Your doctor can talk to you about tests and treatment if you are finding it difficult to stop taking codeine painkillers

drug use, lack of response to treatment or significant comorbidities.

GPs may be frustrated when patients continue to use high doses of OTC codeine products while resisting treatments such as opioid maintenance therapy. However, providing information about risks, monitoring with blood tests and maintaining engagement are still valuable interventions while treatments such as buprenorphine–naloxone or specialist referral are offered as an option.

The future for OTC codeine

At the time of writing, the TGA has announced a change to codeine scheduling. This follows a change in regulation of some codeine-containing products to Schedule 3 in 2013 which put them ‘behind the counter’, requiring a pharmacist’s intervention before sale and limiting quantities to a few days’ supply. The TGA’s decision in late December 2016 will further restrict the availability of codeine-containing products to Schedule 4: from early 2018, patients will require a doctor’s prescription to obtain codeine-containing analgesics.¹⁰

How this change will affect general practice is unclear. One possibility is an increase in patient presentations for medical management of pain. Patients who have been self-managing pain with opioid medication may be a particular challenge for GPs. The role of opioids in pain management is being scrutinised, and treatment guidelines are recommending increasingly

conservative doses of opioids in the treatment of nonmalignant persisting pain.^{5,11}

Changes to scheduling may also cause an increase in patient presentations for opioid-use disorders, particularly codeine-related. Knowledge and experience in opioid maintenance therapy prescribing, including within shared care arrangements with addiction medicine specialist physicians, is likely to be a valuable clinical skill for GPs into the future. **MT**

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COMPETING INTERESTS: NONE.

Drug misuse and addiction

What is out there to support GPs?

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Assisting distressed patients with problems of drug misuse or addiction can be difficult for nonspecialists, but there are many resources available to help busy GPs provide appropriate care for these patients and deal with inappropriate requests for drugs of dependency.

Various supports are available for GPs who are dealing with issues of drug misuse and addiction in their patients. Although it is not possible to present an exhaustive list, this article provides details of some of the services available to support GPs and suggests simple responses to inappropriate requests from patients for drugs of addiction.

It is a good idea for GPs to familiarise themselves with the available resources and to keep the service contact details and links to online resources handy, to ensure they are prepared during a clinical encounter with a distressed patient.

Local services

The services available in the local area differ depending on the location.

Local government services

Some local health districts have specialist drug and alcohol services, which may offer outpatient and inpatient options. The local hospital can advise what is available.

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Local nongovernment services

Nongovernment services may be outpatient or inpatient, and can provide detoxification, rehabilitation and counselling. The Australian Drug Information Network (www.adin.com.au) can help identify these services locally.

Primary Health Networks

Many Primary Health Networks (www.health.gov.au/internet/main/publishing.nsf/Content/PHN-Home) are developing online 'health pathways' through their intranet sites, to offer simple management tips, specific local referral options and referral processes.

Primary Health Networks may also be able to help identify a local GP, addiction psychiatrist or addiction specialist who takes referrals.

In Victoria, pharmacotherapy networks have been established to assist the Primary Health Networks.

Private counselling services

There may be psychologists or other counsellors in the local area to whom patients can be referred through Medicare for outpatient counselling. GPs should check whether local providers have the skills to assist people with dependent or problematic drug use.



KEY POINTS

- Many services and supports are available to assist GPs and their patients with drug and alcohol issues.
- GPs should be aware of regulatory and legal requirements when prescribing drugs of addiction.
- It is important to understand how to say no to inappropriate requests for drugs of dependency and to keep all practice staff safe.

Private psychiatrists

Some psychiatrists have additional training in addiction and offer treatment for substance use disorders.

Private hospitals

There may be private hospitals in the local area that offer inpatient treatment. The Federal Government's MyHospitals website (www.myhospitals.gov.au/search/hospitals) lists all private and public hospitals.

Specialist GPs and private addiction specialists

Some GPs have a special interest or specialist training in substance use disorders and take referrals from other GPs. Addiction medicine is a small but growing specialty in Australia. The Royal Australasian College of Physicians provides a list of all addiction specialists in Australia (www.racp.edu.au/about/racps-structure/adult-medicine-division/australasian-chapter-of-addiction-medicine/)

list-of-acham-fellows). However, only a few of these work privately and take referrals.

As the government is establishing Medicare item numbers for addiction specialists, there may be an increase in doctors entering private practice to assist people with drug and alcohol issues.

State- and territory-based information services

Some state- and territory-based information services are run by state and territory governments, whereas others are contracted out to other services. They can provide support and information about treatment options. These 24-hour clinical advisory services provide telephone advice, generally from an on-call roster of specialists in addiction medicine. They include:

- Victorian Drug and Alcohol Clinical Advisory Service – 1800 812 804
- NSW Drug and Alcohol Specialist Advisory Service – 02 9361 8006 (Sydney), 1800 023 687 (regional NSW)
- Queensland Alcohol and Drug Information Service – 1800 177 833 (GPs should ask to be put through to Alcohol, Tobacco and Other Drugs)
- WA Clinical Advisory Service – 08 9442 5042 (Perth), 1800 688 847 (regional WA)
- SA Drug and Alcohol Clinical Advisory Service – 08 8363 8633
- ACT Health 24 Hour Helpline (Alcohol and Other Drugs Services) – 02 6207 9977
- Tasmanian Drug and Alcohol Clinical Advisory Service – 1800 630 093
- NT Drug and Alcohol Clinical Advisory Service – 1800 111 092.

State and territory government regulatory services

State and territory government regulatory services can provide support on the basis of their legislative authority. This includes state or territory 'authorities' or 'permits' to prescribe drugs of addiction. The state or territory authority provides permission to prescribe for a defined period, typically 12 months, whereas a PBS authority provides

a subsidy for medication supply for a period of typically one month. Generally, GPs need an authority/permit to prescribe a drug of addiction to a drug-dependent person and may need an additional authority/permit to prescribe it for any length of time.

Each state or territory has slightly different laws and different forms to complete. As the staff of these services understand the regulatory framework for their jurisdiction, it is advisable to check with the relevant authority before prescribing.

- **Victoria.** Drugs and Poisons Regulation, Department of Health and Human Services – 1300 364 545 (www2.health.vic.gov.au/public-health/drugs-and-poisons)
- **NSW.** Pharmaceutical Services, NSW Health – 02 9391 9944 (www.health.nsw.gov.au/pharmaceutical/pages/default.aspx)
- **Queensland.** Medicines and Poisons, Queensland Health – 07 3328 9890 (www.health.qld.gov.au/system-governance/licences/medicines-poisons)
- **WA.** Pharmaceutical Services Branch, Department of Health – 08 9222 6883 (www.health.wa.gov.au/services/detail.cfm?Unit_ID=2301)
- **SA.** Drugs of Dependence Unit, SA Health – 1300 652 584 (www.sahealth.sa.gov.au and search for 'Prescribing medicines and drugs: regulations and requirements')
- **ACT.** Pharmaceutical Services, ACT Health – 02 6205 0998 (www.health.act.gov.au/public-information/businesses/pharmaceutical-services)
- **Tasmania.** Pharmaceutical Services, Department of Health and Human Services – 03 6166 0400 (www.dhhs.tas.gov.au/psbtas)
- **NT.** Medicines and Poisons Control, Department of Health – 08 8922 7341 (<https://health.nt.gov.au/professionals/environmental-health/medicines-and-poisons-control>).

Federal Government services

The Prescription Shopping Programme (PSP; www.humanservices.gov.au/

health-professionals/services/medicare/prescription-shopping-programme) helps prescribers identify and reduce the number of patients who acquire, either deliberately or unintentionally, more PBS-subsidised medicines than they medically need. Patients may access more medicines than they need for reasons that include:

- dependency
 - stockpiling for later use
 - intention to sell, exchange or give medicines to relatives
 - sending medicines illegally overseas.
- The PSP has a 24-hour Prescription Shopping Information Service (PSIS) and a Prescription Shopping Alert Service. Both prescribers and pharmacists can access these services. The PSIS is a 24-hour telephone service (1800 631 181) that gives prescribers information (accurate up to the past 24 hours) on whether patients meet at least one of the criteria of the PSP. These criteria are that the patient has received:
- pharmaceutical benefits prescribed by six or more different prescribers
 - a total of 25 or more target medicines on the PBS (including analgesics, central nervous system drugs, antiepileptic drugs, anti-Parkinson disease drugs, antihypertensive drugs)
 - a total of 50 or more medicines on the PBS.

In addition, GPs can ask patients to complete an 'Authority to release personal Medicare and Pharmaceutical Benefits Scheme claims information to a third party' form to obtain their PBS and Medicare claims information for a defined period. The form should be sent to Medicare Australia with a letter on the practice's letterhead, and the requested information will be received about six weeks later. This report can be requested periodically (e.g. annually, for a patient in an ongoing treatment program).

Online services

There are several useful websites for practitioners and patients that give information about pain management and drugs of dependency. Use of Australian websites is generally recommended.

Websites for practitioners

- NSW Agency for Clinical Innovation Pain Management Network
 - www.aci.health.nsw.gov.au/chronic-pain
- Pain Australia
 - www.painaustralia.org.au
- National Prescribing Service (NPS) MedicineWise
 - www.nps.org.au/medicines/pain-relief/opioid-pain-relievers
- International Association for the Study of Pain
 - www.iasp-pain.org
- Australian and New Zealand College of Anaesthetists (ANZCA) and ANZCA Faculty of Pain Medicine, *Acute Pain Management: Scientific Evidence*, 4th edition, 2015
 - www.anzca.edu.au/resources/college-publications
- Cancer Council Australia, Cancer Guidelines Wiki: Cancer pain management in adults
 - http://wiki.cancer.org.au/australia/Guidelines:Cancer_pain_management
- Hunter Integrated Pain Service
 - www.hnehealth.nsw.gov.au/Pain/Pages/Health-professional-resources.aspx
- NSW Therapeutic Advisory Group, *Preventing and Managing Problems with Opioid Prescribing for Chronic Non-Cancer Pain*
 - www.ciap.health.nsw.gov.au/nswtag/documents/publications/practical-guidance/pain-guidance-july-2015.pdf

Websites for patients

- Alcohol and Drug Foundation
 - www.adf.org.au
- Chronic Pain Australia
 - www.chronicpinaustralia.org.au
- NSW Agency for Clinical Innovation Pain Management Network
 - www.aci.health.nsw.gov.au/chronic-pain
- Pain Australia
 - www.painaustralia.org.au

- Hunter Integrated Pain Service
 - www.hnehealth.nsw.gov.au/Pain/Pages/Community-resources.aspx

How to say no

It can be difficult to say no to patients seeking psychoactive medications. The resources mentioned above can assist the busy GPs with this. Following are some suggested responses to patients who try to obtain medications that the GP believes are inappropriate or put the patient at risk of harm.

At the practice level

General practices should have and should advertise a policy regarding drugs of dependence, such as the example in the Box.¹ All practice staff should agree on and follow the practice policy. The policy should also be communicated to specialists external to the practice, particularly neurologists and psychiatrists, to avoid patients receiving mixed messages. The practice should also have a process for patient review, so there is support in place for both practitioner and patient if anyone in the practice is struggling to manage a patient with complex needs.

For individual practitioners Script responses to drug-seeking behaviour

Establishing prepared 'scripts' can help practitioners have a ready response to drug-seeking behaviour. For new patients, the practice administrator or nurse and the doctor can both enforce the message, as follows.

- Practice administrator or nurse: 'The doctor, when seeing you for the first time, will do a detailed assessment and may need additional information from your previous doctors before making any treatment decisions, including prescribing medicines.'
- Doctor: 'I want to help you; however, we have a practice policy that we do not provide opioid medications to new patients. I will need to undertake a comprehensive assessment and seek information from your previous health team. I will not be giving you a prescription today.'

EXAMPLE OF GENERAL PRACTICE DRUGS OF DEPENDENCE POLICY

Painkiller and sleeping pills policy

Except for terminal cancer, our policy is that we will not prescribe these medicines (e.g. oxycodone and morphine):

- at your first appointment
- on a phone request
- without a proper assessment
- over the long term (we prefer safer and better options).

Explain why you are unwilling to give prescriptions

GPs need to be able to explain why they are not willing to give prescriptions.

- 'We are now aware that these medicines can cause significant and serious side effects and so are very cautious about prescribing them. It has become clear that opioids are not very effective in the treatment of chronic pain. In fact, the risks of opioid treatment outweigh the benefits, and people do better with other options. I'm happy to discuss these options with you.'

Devise responses to often used statements

Patients may arrive with an often used statement, such as: 'I need this for my pain', 'I can't cope without it', 'You'll force me to go out and buy drugs', 'You've given them to me in the past, why won't you give them to me now?', 'I've tried everything else, nothing else works' or 'I'm using the drugs to detox, they really help'. There are various responses that GPs can make to this kind of approach.

- 'I understand that you're struggling with this; however, we now know that the use of this medication is not the best approach to help people to improve and maintain their health and wellbeing. I want to help but can only do what is effective and safe.'
- 'I am not prepared to prescribe these medicines in the way you suggest. These medicines have a risk and I need to create greater safety by changing the way this medicine is prescribed.'

- 'I want to help you but I cannot continue to prescribe this medication in this way, as I am concerned that you may come to harm.'
- 'I am concerned for your safety and think these medicines may be causing you harm. I think you have become dependent and there are other options that may work better. I am going to ask for advice from an addiction specialist and suggest treatment changes, which may include referral or alternative medications, including opioid substitution treatment.'

Offer alternatives

Another mechanism that GPs can use is 'borrowed protection'.

- 'I can't prescribe that medication because of health department regulations. However, I do want to help you and can offer other, safer options.'

Explain why you cannot provide what the patient wants

It is best to explain why it is not possible to provide what the patient wants. Providing a clear explanation of the clinical reasons for the decision and why it is in the patient's best interests can help the patient understand why the GP has made the decision. The patient may not agree, but it shows them a clear position that is based on safety and care rather than what can otherwise seem like practitioner whim. It is also important to offer the patient alternatives. Even if they do not want to take these up, they may in future remember the help offered and return for further assistance.

It is important to understand that the drugs have a role in patients' lives and asking them to do things differently can be hard for them.

Opioid prescribing tips

Practitioners who do prescribe opioids should consider the following options to decrease harm. The Royal Australian College of General Practitioners (RACGP) guide for drugs of dependency has more details that may be helpful.²

- **Assess function.** GPs should explain to patients that opioids may help improve function but will not cure pain.
- **Offer a time-based trial.** A time-based trial of treatment with function-based outcomes can be offered. This can use an outcomes measure, such as the Brief Pain Inventory (www.hnehealth.nsw.gov.au/Pain/Documents/BPI.dec06.pdf) or the even briefer three-question Pain intensity, Enjoyment of life, General activity (PEG) assessment tool (<https://ndarc.med.unsw.edu.au/content/gp-toolkit-resources>).
- **Limit supply.** GPs should check with the PSIS that the patient has only one prescriber and one pharmacy. The prescription should be faxed directly to the pharmacy, and the prescriber liaise regularly with the pharmacist.
- **Stop prescribing if the functional outcomes are not achieved.** This plan is best discussed and agreed with the patient before commencing treatment.
- **Limit dose.** If the patient is not doing well with 40 mg of oral daily morphine equivalent, it is unlikely that increasing the dose will help.
- **Request staged supply.** Pharmacies can dispense small amounts of medication. The prescriber can ask the pharmacist to dispense medications daily or to give a few days to a week's supply. Pharmacies receive some funding from the federal government to do this, but some pharmacies may charge for this service (from \$1 to \$5 per dispensing).
- **Organise supervised dosing.** Pharmacists can oversee the taking of medication by having the patient attend the pharmacy and take the medication while the pharmacist watches.
- **Wean slowly to cessation.** The dose can be reduced by 10 to 25% per month.

Keeping practice staff safe

All staff have a right to a safe workplace and it is important for general practices to implement strategies to ensure the occupational health and safety of their staff. Such risk

management may include a duress alarm system in each consulting room. Practitioners may need training to feel confident that they could use this system in any situation in which they feel under threat.

If practitioners feel under threat from patients inappropriately requesting drugs of dependence then it may be safest to provide a prescription for a small amount of medication. Police can be contacted after the patient has left the surgery, and the patient can be discharged from the practice or other arrangements made.

An RACGP guide *General Practice – A Safe Place: A Guide for the Prevention and Management of Patient-Initiated – Violence* provides more tips and tools, and *The Aggressive, Violent or Intimidating Patient* offers advice on managing aggressive or threatening patients.^{3,4}

Conclusion

With appropriate handling of legislative and practice boundaries, addiction treatments can be incorporated into general practice. Although it may at times seem that there are too many hurdles, treatment of addiction can become a fulfilling, rewarding facet of a GP's patient care. MT

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Prescription opioid management in chronic noncancer pain

Case studies

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All GPs have a role at some level in caring for patients who are taking opioids for chronic noncancer pain, including those who develop opioid dependence. Three cases of opioid dependence managed in the outpatient setting are discussed.

Up-titration of full agonist opioids (e.g. oxycodone, methadone, codeine and morphine) for the treatment of patients with chronic pain is common and usually done with good intentions but leads to dependence on prescription opioids, even though these agents have no proven benefit in treating those with chronic noncancer pain. The partial agonist buprenorphine has efficacy in treating patients with opioid dependence and chronic noncancer pain, and many patients can be converted to it from a full agonist in the outpatient setting.

Three cases of opioid dependence are discussed, one in which the care is completely general practice-based and the others where specialist services are involved.

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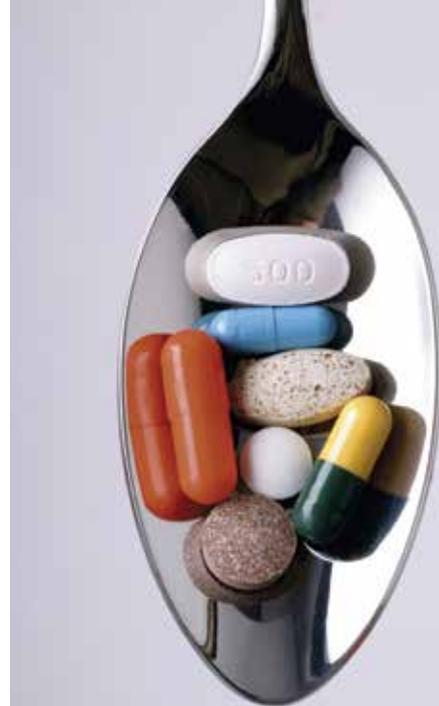
Case 1. Active management avoids opioid substitution

David, 38 years old, presents with lower back pain, requesting another script for oxycodone. You have been his regular GP for about six months, and last saw him three weeks ago. He has a 10-year history of episodic lower back pain, for which you provide monthly scripts on authority for 90 tablets of oxycodone 5 mg (allowing three tablets per day). He is also taking regular celecoxib 200 mg daily, paracetamol–codeine 500/15 mg as needed (up to four times daily) and diazepam 5 mg twice daily.

David says he has finished the medication a week early because of a flare-up in pain. Your records show that he has come a week early for his regular script several times now.

What would you do first?

You review David's history of back pain. David cannot remember the initial trigger but says this episode was triggered by undertaking simple household repairs, and has lasted for four months. He says it is probably his worst to date in terms of severity and duration. He says he 'feels his back go' and describes constant background pain, rating it as six to seven out of 10, with flares on activity and in some seated positions. He rates pain when driving as nine out of 10. The pain is only in the back; there is no leg pain.



KEY POINTS

- In patients taking opioids long-term for chronic noncancer pain, consider whether the drug use has become problematic.
- Precise diagnosis of opioid dependence is challenging and not essential to quality care.
- Consider nonpharmacological options for treating and emphasise appropriate physical and psychological therapy.
- Wean unhelpful nonanalgesic medications such as sedatives.
- Consider using the partial agonist buprenorphine, which is an effective analgesic with a prolonged duration of action and is frequently tolerated better than full agonists.
- Structured opioid treatment may be offered in general practice or by referral to specialist services.

David has tried a range of over-the-counter analgesics over the years, including paracetamol, ibuprofen and codeine, singly and in several combinations. These had an effect in earlier episodes, but David thinks they have become less effective in recent episodes. He has also tried physiotherapy, and this also has become less helpful.

Over time, David has seen several GPs and been prescribed several different analgesics (oxycodone, paracetamol–codeine, celecoxib and diazepam). The GPs had recommended specific doses for each medication, but he had been taking extra

medications when his pain flared.

David is a marketing executive and drives an hour to another office several times a week, which increases his lower back pain; sitting in long meetings is also often problematic. He wants to help his wife around the house and with their young children, but finds it nearly impossible to do strenuous housework or lift the children. He finds it difficult to even sit on the floor to play with his children. He is feeling increasingly run down and lethargic due to the length and severity of this episode, and is having difficulty sleeping.

David has no other significant medical or surgical history and is not taking any other medications; he knows not to take additional paracetamol or NSAIDs. His current dose of oxycodone is 5 to 15 mg daily, as needed. He has never smoked. He drinks five to 10 standard drinks once a week when he goes out, and only the occasional beer otherwise. He admits, however, that about once a month he might drink more when the pain is worse, to help him sleep.

This patient is the sole income earner in the household, and does not want to take time off work to see doctors.

What would you do next?

You take a history to investigate drug-related harms. David has no significant dyspepsia or history of ulceration. He denies symptoms of withdrawal if he runs out of opiate medication, and says that on good days he often does not take medication and does not become unwell. However, closer questioning reveals he has not had a drug-free day in the past six months. He has no history of alcohol-related harms. He smoked cannabis a few times in high school but denies any other illicit drug use and has never injected drugs. He does not think his medication use is a problem but is frustrated that he requires opiates on an ongoing basis because of continuing pain. He is also somewhat frustrated about his limitation of activities, as he has had to give up his weekly game of touch football with old friends. He is aware that opioid drugs can be addictive but he firmly believes he is not drug-dependent.

On examination, David looks uncomfortable sitting in the chair, and moves slowly and with difficulty. There is no obvious swelling or scars on the lower back but there is some tenderness, most pronounced in the L4 to L5 segment. The range of motion is reduced on flexion, extension, lateral flexion and rotation due to pain. Brief lower limb neurological examination seems normal bilaterally: sensation in all dermatomes is intact, power is 5/5 throughout and proprioception is normal. There are no red flags for cauda equina injury (i.e. no altered saddle sensation and no altered bowel or urine habit).

David tells you he had a 'normal' spinal MRI about a year ago at another practice. He has never seen a specialist for his back. He has not seen a physiotherapist for several years because it never seemed to help; it transpires he only attended a few times and did not do exercises at home as recommended.

What is your assessment?

Your assessment is that the drug use pattern does not match the history. David is taking, on average, more than four tablets of oxycodone 5 mg daily (equivalent to 30 mg of oral morphine daily), and has been doing so for about six months. He is not using any strategy to control his pain apart from medications. He has constipation, and often goes three to four days between bowel actions.

On further exploration, David acknowledges that he occasionally takes a tablet of diazepam to help him relax at work or at home. He admits he has dozed off during meetings a few times and even once when driving (fortunately not resulting in an accident).

How can you help this patient?

You have clear evidence of drug-related harms, potentially serious. You discuss with David your public duty to ensure that any patient who is not fit to drive does not drive. The conversation gets tense when he says there is no other way to get to work, and that he has to use these tablets because of his back problem, and he can easily get medication from other doctors. You

reassure him that you want to help him to solve these problems and that you are on his side.

You advise David to cease benzodiazepines as the combination of sedatives and opioids can contribute to daytime somnolence and benzodiazepines have no analgesic action. You and he reach an agreement to limit oxycodone use to three tablets per day and you write an authority script for a one-month supply of 90 tablets. You arrange for weekly pick-up of this medication by David from a local pharmacy that is open on the weekends. You urge David to resume physiotherapy to strengthen his core muscles, and find him a specialist back physiotherapist who is open on Saturdays. You encourage David to perform the exercises at home and to stick with it for three months before abandoning treatment. You offer referral to a private pain management service should this plan fail to help.

The outcome

At the next visit, David seems brighter. His pain is the same but he has been able to manage with slightly fewer oxycodone tablets. You recommend further dose reduction but he says he has just started physiotherapy and does not feel ready because he is doing the exercises at home and sometimes his back aches after a session.

Another month down the line, and David is responding to the physiotherapy program and is wondering why he relied on drugs to control his pain for so long. He now wants to come off all medication and asks how quickly can this be done. As David has been using opioids for several years, you consider switching him to a long-acting formulation of oxycodone to manage the withdrawal, a long-acting preparation providing steadier blood levels than a short-acting formulation. His bowel function is now normal so there is no indication for modified-release oxycodone-naloxone.

You consider conversion from oxycodone to the partial agonist opioid buprenorphine (opioid substitution treatment), using buprenorphine-naloxone (4:1; sublingual film). Naloxone is not absorbed orally, and

is instead present to deter intravenous diversion of the buprenorphine, as it is an opioid antagonist and can lead to a withdrawal syndrome if injected. As this patient's pattern of drug use seems to be improving already and the risk of intravenous diversion is minimal, the buprenorphine–naloxone combination is not indicated. You also consider buprenorphine patches but the patient prefers an oral formulation.

The patient agrees to switch to a long-acting formulation of oxycodone. You prescribe modified-release oxycodone 10 mg once daily for a month, aiming to reduce this to 5 mg once daily for another month before ceasing it completely.

Comment

The patient in this case study has relatively mild problems with prescription drug use and was easier to engage in treatment than many. He was initially demotivated and demoralised but not evidently depressed. The patient did not understand the limitations of drug treatment for chronic back pain, or the need for a sustained effort for physiotherapy to be effective. Once a more active management plan was developed, he responded well. As treatment progressed, his excessive use of drugs was exposed as a problem that was holding back his lifestyle. He became well motivated to address this and succeeded with minimal medical assistance and no specialist input.

Case 2. Opportunistic opioid substitution

Sue, a 24-year-old woman from rural NSW, has a chronic perineal sinus on a background of inflammatory bowel disease. She has had complex chronic pain issues for the past seven years. During this period, Sue underwent extensive surgical debridement and a series of reconstructive procedures. She had significant functional decline and became mostly bed-bound and dependent on her parents for assistance with self-care activities. Chronic pain was managed by her GP with some phone-based support from the local pain service. She was commenced on short-acting opioids (tramadol, oxycodone)

in the early stage and subsequently switched to longer-acting opioids (hydromorphone).

At presentation to a tertiary hospital for a further surgical revision, Sue is taking a high dose of opioids (equivalent to 400 mg oral morphine daily) in addition to a gabapentinoid, benzodiazepine and adjuvant agents (muscle relaxant, tricyclic antidepressant and NSAIDs). The hospital drug health and pain service is consulted.

How can Sue's opioid use be managed?

After a comprehensive review and multidisciplinary care planning, Sue consents to opioid substitution treatment with buprenorphine–naloxone. The decision to start opioid substitution is based on the duration of both pain and opioid use, the high doses of medications, the poor level of social functioning and the continuing need to provide optimal analgesia while Sue undergoes further surgical procedures.

Sue is apprehensive initially as to whether her analgesic needs will be met and the potential side effects. She is also concerned about the stigma attached to buprenorphine–naloxone as it is a 'drug for junkies'.

Sue starts on buprenorphine–naloxone in accordance with NSW guidelines, after cessation of other opioids. The starting dose is 4 mg and this is gradually uptitrated to 18 mg daily over six weeks. Other healthcare workers, including a clinical psychologist, a social worker, physiotherapists and occupational therapists, assist with psychological and functional requirements. Other medicines (benzodiazepine and adjuvant agents) are weaned and stopped before discharge.

The outcome

Sue's functional status improves with the opioid substitution treatment and interventions, as does her confidence level and self-efficacy.

During the eight-week hospital admission for revision surgery, Sue has weekly case conferencing involving the various team members. Clinical handover is provided to her GP, local pain team and pharmacy at

discharge. The local pain team had been contacted when considering opioid substitution and agreed to support the GP additional to outpatient review of the patient as required. It is agreed the buprenorphine–naloxone will be dispensed at Sue's local pharmacy on a twice-weekly basis. Sue comes from a small town and neither her GP nor the pharmacy is accustomed to managing patients on this regimen. However, her local GP is successfully continuing the program, and periodic specialist review will assist.

Comment

The above case highlights the role of opioid substitution in patients with chronic non-cancer pain. Sue was able to discontinue high-dose morphine and transfer to buprenorphine–naloxone. Given the recent increase in prescription opioid misuse, it is crucial to proactively identify opportunities to recognise opioid dependence and explore alternative pain management strategies. It is important to undertake a comprehensive assessment and management of patients with comorbid physical and mental health issues and to implement systems to support the individual.

Case 3. Opioid substitution

Harry, aged 60 years, has chronic right shoulder pain after an extensive rotator cuff tear 16 years ago. His injury required multiple surgical interventions and was complicated by postoperative septic arthritis. Over the years, Harry was treated with escalating doses of opioid medications, initially via his GP and subsequently via a chronic pain service at a tertiary referral hospital. He is now taking 80 mg of oxycodone twice daily (equivalent to 120 mg oral morphine twice daily). Harry's other medical history includes HIV infection, and he is on combined antiretroviral treatment with an undetectable viral load and a CD4+ T-lymphocyte count of above 500 x 10⁶. He has no history of AIDS-defining illnesses. He also has longstanding idiopathic epilepsy (well-controlled on lamotrigine), as well as depression (treated with venlafaxine).

Harry is a single homosexual man, living

alone in an apartment with his dog. He runs his own business, working as a hair and makeup artist. He has a close relationship with his parents, and good social supports from friends and family.

Harry was referred to the addiction medicine outpatient service by the chronic pain clinic at a tertiary centre because of the high dose of oxycodone that he was taking. He had refused to reduce medication and became hostile when the registrar in the pain clinic said he was drug-seeking.

What is the initial management?

In the addiction medicine outpatient setting, initial management of a patient likely to be opioid-dependent should focus on building rapport, discussing different forms of pain relief (pharmacological and non-pharmacological) and exploring the concept of planning opioid withdrawal.

How has opioid dependence developed?

Harry's opioid therapy for pain following a complex injury complicated by postoperative infection has escalated over the years, with little attention being paid to nonpharmacological strategies or de-escalating opioid treatment. Patients like Harry often develop opioid withdrawal pain, relieved by further opiates. This kind of pain may be mistaken for pain that is opioid-responsive, which can lead to a cycle of escalating full agonist opioid use that results in dependence. It should be noted that full agonist opioids are not effective in treating patients with chronic non-cancer pain; there are no clinical trials demonstrating long-term effectiveness.

What treatment is appropriate?

The appropriate treatment for Harry is a combination of effective nonpharmacological strategies of physiotherapy and psychotherapy and opioid substitution treatment.

There is recent evidence to support the use of sublingual buprenorphine in treating chronic pain in opioid-dependent patients.¹ The partial agonist blocks opioid withdrawal and has less severe side effects compared with full agonists. Conversion to

buprenorphine can, however, induce severe opioid withdrawal if the partial agonist is given while full agonist opioids are active. Therefore it is important to wait until the patient has ceased taking full agonist opioids and developed mild withdrawal symptoms before administering the first dose. Typical withdrawal symptoms include anxiety, diaphoresis, rhinorrhoea, lacrimation and muscle cramps. Buprenorphine should be commenced while these symptoms are still mild, and patients need to be advised that the first three days after starting buprenorphine may be unpleasant.

What are the goals of treatment?

Harry has a chronic condition and complete pain relief is not likely to be achieved, making complete freedom from pain an unrealistic therapeutic goal. In patients with longstanding pain, the focus of treatment should be to maximise function and minimise side effects. Focusing on complete relief of pain alone can lead to patient pressure and doctor perceived patient pressure to prescribe analgesics, and foster the notion that all treatment is unsuccessful even though functional gains have been achieved.

How is Harry treated?

Harry's initial pharmacological therapy focuses on de-escalating opioid treatment. Discussion with him revolves around the side effects of opioids, particularly the constipation that was causing him distress.

Harry becomes more motivated to titrate down his opioids, and a regimen is agreed upon. Oxycodone is weaned by 10 mg per week, until he is on a dose of 40 mg twice daily. This is the usual dose for successful outpatient conversion to buprenorphine-naloxone. Oxycodone is ceased and buprenorphine-naloxone commenced the following day, once mild withdrawal symptoms are present. Buprenorphine-naloxone is then gradually uptitrated to a dose of 20/5 mg daily over four weeks. Paracetamol is also prescribed, at 1 g four times daily, with monitoring of liver function tests.

Harry is also referred to a physiotherapist to maximise his range of movement,

strength and function. With ongoing physiotherapy, his function and pain improve moderately. Harry is also referred to a psychologist to explore various treatment approaches including distraction therapy, which he found useful in managing his pain.

The outcome

Harry's functional status and pain scores are at their all-time best when stabilised on buprenorphine-naloxone. His GP agrees to prescribe this medication under specialist supervision. Both the GP and Harry have mixed feelings about using buprenorphine-naloxone long-term; two years later and with referral to an addiction specialist, Harry is successfully weaned off this medication.

Comment

This case study highlights the common occurrence of an 'opioid prescribing cascade' that leads to dependence on prescription opioids. Although uptitration of full agonist opioids was likely done with good intentions by prescribers, these agents have no proven benefit in treating patients with chronic non-cancer pain. Conversion to buprenorphine resulted in treatment of the patients' opioid dependence and better pain control.

Patients such as Harry have often been taking full agonist opioids for many years, and are unaware of their dependence. Education around dependence and withdrawal pain is essential before converting to more appropriate therapy, as is building rapport.

Conclusion

The partial agonist buprenorphine has efficacy in treating opioid dependence and chronic noncancer pain. Conversion to a partial agonist from a full agonist can usually be done in the outpatient setting, with careful planning. Nonpharmacological treatments such as physiotherapy and psychotherapy also play a crucial part in treating chronic noncancer pain. **MI**

Reference

1. Chen KY, Chen L, Mao J. Buprenorphine-naloxone therapy in pain management. *Anesthesiology* 2014; 120: 1262-1274.

COMPETING INTERESTS: None.