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Prescription opioid misuse Contemporary challenges

Supplement

Use of opioids in chronic noncancer pain

Persistent noncancer pain in patients with addiction: reflecting on the challenges

Treatment of patients with opioid dependence

Benefits and challenges to the implementation of real-time prescription monitoring

Chronic pain, opioids and dependence: a role for every GP

The analgesia tango: chronic pain cases from a general practice



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SUBSCRIPTIONS

Amanda Goldsmith

PUBLISHER/EDITORIAL DIRECTOR

Judy Passlow

PUBLISHER/MANAGING DIRECTOR

Tony Scott

SYDNEY OFFICE

Suite 3, 134 Military Rd,

Neutral Bay NSW 2089

POSTAL ADDRESS

PO Box 1473, Neutral Bay

NSW 2089

TELEPHONE (02) 9908 8577

FACSIMILE (02) 9475 0645

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FOREWORD FROM THE SUPPLEMENT EDITORS

Opiates have always been an important part of a doctor's armamentarium, and are highly effective for managing pain that is severe and acute, or related to cancer. They have also been used historically by a broader population to alter mental states, and to cope with the many stressors that life brings. Opioids have a low therapeutic index and are a leading cause of drug-related harm. It is therefore no surprise that the dramatic rise in use of prescription opioids to manage chronic nonmalignant pain in recent times has been linked to a marked increase in morbidity and mortality, leading to the development of a national pharmaceutical misuse strategy. Unfortunately, the area of addiction is one that has traditionally been given little attention in medical curricula, leaving many doctors feeling underskilled or reluctant to manage addictive behaviours, and hence the low level of opiate substitution treatment available in primary care despite overwhelming evidence of its effectiveness as a medical treatment. This supplement provides a balanced discussion of the issues surrounding opiates, addiction and pain, and will hopefully help us consider our approach to opiates and management of their use within everyday practice.



Professor Dan I. Lubman and Professor Paul Haber

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Use of opioids in chronic noncancer pain

STEPHAN A. SCHUG MD, FANZCA, FFPMANZCA
MIR WAIS SEKANDARZAD MD, FANZCA, DESA

Opioids play a much smaller role in the management of chronic noncancer pain than they do in that of severe acute pain and cancer pain. They are beneficial in a small subset of patients with chronic noncancer pain but there are pharmacological, psychological and societal concerns about their current widespread use for this indication.

KEY POINTS

- There are pharmacological, psychological and societal concerns about the current widespread use of opioids for chronic noncancer pain.
- Opioids should not be regarded as the sole approach to managing chronic noncancer pain but as one component of a multidisciplinary management plan.
- They should only be used for this type of pain after an initial trial with defined positive outcomes, in particular improvement of function.
- They are not intended as life-long treatment and should be discontinued by tapering the dose when treatment goals are reached (or aberrant drug-taking behaviour becomes obvious).

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Professor Schug is Chair of Anaesthesiology in the Pharmacology, Pharmacy and Anaesthesiology Unit, School of Medicine and Pharmacology, The University of Western Australia, and Director of Pain Medicine at Royal Perth Hospital, Perth, WA. Dr Sekandarzad is Adjunct Senior Lecturer in Anaesthesiology and Critical Care at the School of Medicine Central, The University of Queensland, Brisbane, Qld.



There has been a dramatic increase in recent years in the use of opioids to treat chronic noncancer pain, particularly in the USA but also in Australia. This has led to increasing concerns about the usefulness versus risks of this approach, both for the individual patient and society as a whole. This review article outlines the controversies surrounding their use for treating chronic noncancer pain and summarises their role in this setting, the risks and complications regarding their use for this type of pain and the goals of such treatment, and its initiation and long-term use.

Different pain states

Chronic noncancer pain is a heterogenous disorder, characterised by a wide spectrum of pain states ranging from physiological pain with nociceptive and inflammatory origin (e.g. osteoarthritis) to pathological pain states of either neuropathic origin (i.e. caused by damage or disease of the somatosensory system, e.g. diabetic polyneuropathy) or dysfunctional origin (i.e. no such damage/disease and no nociception but caused by central sensitisation/insufficient endogenous inhibition, e.g. fibromyalgia).¹ It is therefore not surprising that the role of opioids in these different pain states is not the same.

Some principles of opioid therapy in the acute pain and chronic cancer pain setting, where they have well accepted analgesic efficacy and a good safety profile, may be transferred to the setting of nociceptive and neuropathic pain, where their use can lead to improved function and reduced pain in some patients, although long-term outcome data are limited or even contradictory.^{2,3} Dysfunctional pain states on the other hand are characterised primarily by central sensitisation and limited endogenous inhibition, and seem to be poorly responsive to opioid therapy. Furthermore, chronic pain is characterised as a biopsychosocial phenomenon, and the wide array of psychosocial factors, such as catastrophising, anxiety, mood states including depression, suffering and dependence on the healthcare system, are not really responsive to opioids and need to be addressed by multimodal, multidisciplinary interventions.⁴ Single modality opioid therapy

in dysfunctional pain states is both less successful in improving analgesia and functional outcome and also carries a significant risk of aberrant drug-taking behaviour and abuse.

Efficacy

As indicated above, opioids might confer a benefit and have some demonstrated efficacy in well-defined chronic pain states such as osteoarthritis and neuropathic pain.⁵⁻⁸ Despite opioids showing effectiveness and published guidelines supporting their use in osteoarthritis-related pain, a 2009 Cochrane review on the efficacy of opioids in osteoarthritis of the knee or hip found only small to moderate beneficial effects of opioids and an increased risk of adverse effects.^{2,9,10} Similarly, opioids are viewed in guidelines for neuropathic pain treatment as second- or third-line treatments because of their risk-benefit profile,¹¹⁻¹³ and therefore should only be used if first-line drugs (such as anticonvulsants and antidepressants) fail or are contraindicated.

The overall evidence for efficacy of opioids in chronic noncancer pain is even more disappointing. A 2010 Cochrane review on long-term opioid management of chronic noncancer pain that included a total of 4893 patients found only weak evidence for sustainable pain relief and an inconclusive benefit on functional improvement or quality of life.¹⁴ A similar outcome in relation to lack of improved pain control, function or quality of life in chronic noncancer pain patients treated with opioids was reported in a large epidemiological study from Denmark.¹⁵

In summary, the evidence in favour of use of opioids in the chronic noncancer pain setting is at best weak. This statement is further confounded by most trials assessing only short-term benefits, having methodological flaws and describing heterogeneous outcomes.

Risks and complications of opioid therapy

The most serious complication of opioid use is opioid-induced ventilatory impairment leading to death. Although this is unlikely to occur in patients who are taking a stable dose of opioid for long-term treatment, statistics for the USA and Australia show a dramatic increase in mortality linked to prescription opioids.^{16,17} Reasons for this increased mortality include incorrect opioid prescribing by doctors and incorrect intake by patients, and also diversion with use by others and coadministration with sedatives such as alcohol and benzodiazepines.¹⁸

Constipation is a major adverse effect of the long-term use of opioids and seriously affects patients' quality of life. Patients do not develop tolerance to opioid-induced constipation and need co-medication with appropriate laxatives. Opioid preparations with a reduced risk of constipation are transdermal patches or combinations with naloxone.¹⁹ Nausea, vomiting, sedation and cognitive impairment are often only short-term adverse effects; tolerance to these can develop and therefore interference with work or driving as well as the increased risk of falls occur primarily in periods of dose titration or dose escalation.^{20,21} Opioids, via direct effects on the μ -receptor, also cause significant impairments of immune and endocrine functions, particularly with long-term use. Impairment of endocrine function can lead to opioid-induced androgen deficiency requiring testosterone substitution.¹⁸

The phenomenon of opioid-induced hyperalgesia, a paradoxical

1. OPIOID THERAPY: USEFUL REFERENCE MATERIAL

- For Quick Clinical Guidelines for the use on opioids in patients with chronic noncancer pain, see for example the West Australian guidelines at: www.dao.health.wa.gov.au/DesktopModules/Bring2mind/DMX/Download.aspx?Command=Core_Download&EntryId=168&PortalId=0&TabId=211
- For a more detailed Prescription Opioid Policy, agreed upon by the Faculty of Pain Medicine of ANZCA, the RACGP, RACP and RANZCP, see: [www.fpm.anzca.edu.au/resources/professional-documents/documents/Prescription Opioid Policy.pdf](http://www.fpm.anzca.edu.au/resources/professional-documents/documents/Prescription_Opioid_Policy.pdf)
- For an example of a treatment contract for an opioid medicine, see: www.public.health.wa.gov.au/cproot/3590/2/Treatment_contract_for_opioid_medicine.pdf

increase in sensitivity to pain in patients on long-term opioid therapy, should also be mentioned.²² Attempts to treat this with increasing opioid doses can result in escalation of opioid doses without benefit for the patient.¹⁸ This therefore needs to be differentiated from development of tolerance to opioids.²³ Physiological dependence will also develop, but it and the potential withdrawal reactions can be overcome by tapering opioid doses slowly instead of discontinuing abruptly.

There are rather contradictory and inconsistent data on the prevalence of opioid abuse in patients using opioids for chronic noncancer pain. Addiction ('psychological dependence') is a behavioural pattern of drug use, characterised by overwhelming involvement with the use ('compulsive use') of a drug leading to physical, social and psychological harm.²⁴ A systematic review of trials of opioid therapy for chronic back pain showed a prevalence of lifetime substance abuse in the order of 36 to 56% and of current aberrant medication use of 5 to 24% in these patients.²⁵ Similarly, in a recent study, one in three patients undergoing long-term treatment with opioids for chronic pain met DSM-IV criteria for addiction.²⁶ On the other hand, a Cochrane review from 2010 reported an addiction rate of only 0.27% in patients undergoing long-term opioid therapy for chronic noncancer pain.¹⁴ Risk factors for the development of addiction are male gender, younger age, history of substance abuse disorder, mental health problems and use of higher doses of opioids.^{26,27}

Finally, there is a risk that long-term opioid therapy might contradict the goals of chronic pain management. These goals are not only pain reduction but also reduced pain behaviour, improved function and increased self-efficacy. Current data suggest that opioids are used particularly to treat patients who describe greater disability, distress and suffering and poorer functioning, which might set up a vicious cycle.²⁵ Rather than promoting self-efficacy and an internalised locus of control, opioid therapy leads to an externalised locus of control with increased dependence on the healthcare system, encouragement of passivity and reinforcement of pain behaviour proven to be counterproductive in patients with chronic pain.²⁸

2. OPIOID THERAPY: FACTORS TO CONSIDER PRIOR TO INITIATION*

- Pain diagnosis/psychological assessment
- Multidisciplinary pain treatment
- Assess baseline function and severity of pain
- Screen for addiction risk
- Determine treatment goals (focus on functional and quality of life improvement)
- Explain risks and benefits of opioid therapy
- Opioid treatment contract with patient: informed consent, rules for treatment and cessation, consequences of aberrant drug-taking behaviour

* Modified from multiple sources including references 3, 18 and 30.

Implementation of opioid therapy

The basis of good chronic pain management is a multidisciplinary and multimodal approach. Psychological therapy with emphasis on cognitive behavioural strategies to enhance coping mechanisms and reduce psychological stressors and physical therapy that includes exercise programs and physiotherapy form integral components of such an approach. Pharmacological therapy should be initiated according to

well-established guidelines, with paracetamol and NSAIDs/COX-2 inhibitors (coxibs) being used in nociceptive pain states and anticonvulsants and/or antidepressants in neuropathic pain states. As a small subgroup of patients with chronic pain may benefit from opioid use, this treatment should not be denied. However, in view of the risks described above, the introduction of opioids to treat chronic noncancer pain requires strict adherence to well-established guidelines.^{29,30} Details of examples of a quick clinical guideline for the use of opioids in patients with chronic noncancer pain, a prescription opioid policy and a treatment contract for an opioid medicine are given in Box 1.

Opioids should not be considered as a first-line treatment or a single treatment modality but as one component of multidisciplinary pain treatment. They should only be trialled after reasonable attempts at multidisciplinary pain management, including other pharmacological options, have failed. Their introduction requires a diagnosis of persistent nociceptive-inflammatory pain (e.g. osteoarthritis) or neuropathic pain, and even then they should only be considered second- or third-line treatment.^{18,31} They should not be used in dysfunctional pain states, including fibromyalgia, visceral and pelvic pain syndromes, headaches and nonspecific chronic low back pain. Factors to be taken into account before initiation of opioid therapy are listed in Box 2.

Initiation of opioid therapy for chronic noncancer pain should be in the form of a closely monitored trial period of around four weeks' duration of a transdermal or slow-release oral opioid.

Definitive endpoints such as improvement in quality of life and function, including mood, sleep, occupational and recreational activities, should be as important as simple pain reduction. Such endpoints along with risks, benefits and rules on supply should ideally be formulated as an opioid contract between the patient and the provider. Failure to achieve these treatment goals on reasonable opioid doses (less than 100 mg daily oral morphine equivalent) deems the patient's pain as not responsive to opioids and should lead to an agreed termination of opioid treatment via tapering doses. An approach to the initiation of opioid therapy is summarised in Figure 1.

If the agreed endpoints were reached, the patient should qualify for long-term treatment with opioids; however, this should not be seen as a decision for life-long treatment. Long-term treatment requires adherence to the opioid contract, including a single prescriber, a designated pharmacy and no unauthorised escalation of doses. Regular monitoring of the patient should assess the four 'As' of pain treatment outcomes: Analgesia, Activities of daily living, Adverse effects and Aberrant drug-taking behaviour. An approach to long-term opioid therapy is summarised in Figure 2.

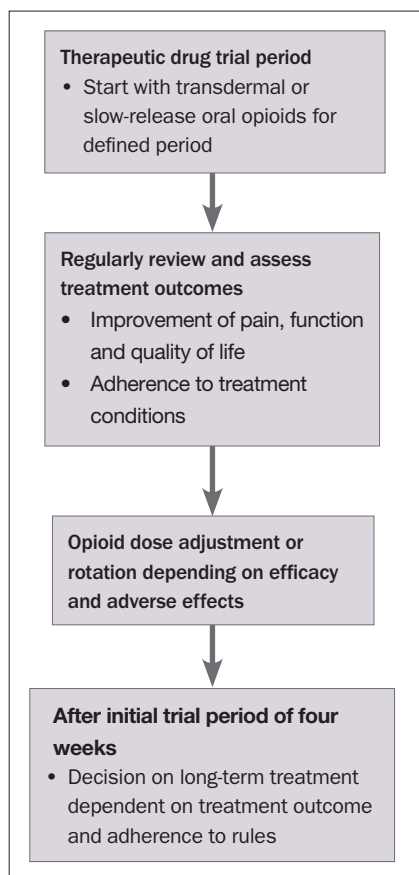


Figure 1. Initiation of opioid therapy.

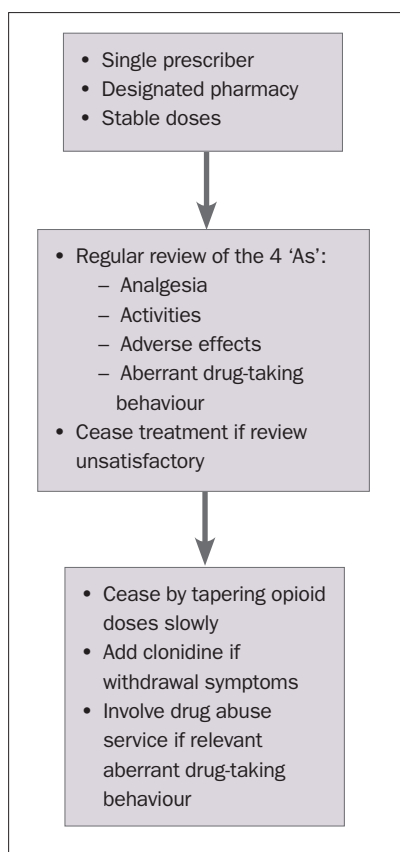


Figure 2. Long-term treatment/maintenance opioid therapy.

Indications for cessation of long-term opioid therapy are lack of improvement in function, lack of analgesia and aberrant drug-taking behaviour.^{18,31}

Conclusion

Opioids play a much lesser role in the management of chronic non-cancer pain than they do in the management of severe acute pain and cancer pain. Although they may be beneficial in a very small subset of patients with chronic noncancer pain, who should not be denied treatment of their chronic condition, there are pharmacological, psychological and societal concerns about their current widespread use for this indication. Their use in the management of chronic noncancer pain requires an established pain diagnosis, screening for increased risk of abuse, a good doctor–patient relationship and adherence to agreed rules, ideally formulated in a treatment contract. Opioids should only be used after an initial trial with defined positive outcomes, in particular improvement of function; a failed trial should lead to discontinuation by tapering the opioid dose.

Opioids should never be regarded as the sole approach to chronic noncancer pain but as one component of a multidisciplinary management plan. Even if used with benefits, they are not intended as life-long treatment and should be weaned when function has been stabilised (or aberrant drug-taking behaviour becomes obvious). This might be a particular challenge in the many patients who have been started on opioids inappropriately in the past.

PMT

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Persistent noncancer pain in patients with addiction

Reflecting on the challenges

SHALINI ARUNOGIRI MB BS(Hons), MPsychiatry, FRANZCP, CertAddictionPsych

MATTHEW FREI MB BS, FACHAM

DAN LUBMAN BSc(Hons), MB ChB, PhD, FRANZCP, FACHAM

Patients who present with persisting noncancer pain on a background of a past or current substance use disorder are a common management challenge. Often they are perceived as quintessential 'heartsink patients'. However, by maintaining an empathic perspective clinicians can help to create a productive therapeutic relationship.

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Dr Arunogiri is a Consultant Addiction Psychiatrist at Turning Point (Eastern Health), Melbourne. She also works in private practice and is a doctoral candidate at Monash University, Melbourne. Dr Frei is Clinical Director of Turning Point (Eastern Health) and Adjunct Senior Lecturer at Monash University, Melbourne. Professor Lubman is Director of Turning Point (Eastern Health) and Professor of Addiction Studies and Services at Monash University, Melbourne, Vic.



Over the past two decades, opioid prescribing for persisting noncancer pain has been increasing, both in Australia and internationally. This increase in prescribing may be justified by the evidence that oral opioids can be effective in controlling pain severity and improving function in the short term;¹ however, the associated increase in risks of morbidity and mortality in some patients is also well documented.² Long-term use of opioids for pain is associated with a wide range of harms, including addiction (characterised by physical and psychological dependence and aberrant behaviours related to opioids and pain), toxicity and overdose, drug–drug and drug–disease interactions, and problems of drug diversion and illicit use (e.g. the sale and purchase of opioid analgesics in black markets). Opioid misuse has become a major public health issue in Australia and in other countries – in the USA, for example, overdose deaths involving opioid analgesics now exceed deaths from heroin and cocaine combined.³

Risks of long-term opioid treatment

Any patient who is prescribed long-term opioid treatment can develop behavioural problems related to the medication, often termed 'aberrant behaviours', which are 'red flags' for the development of addiction (Box 1). Estimates vary, but researchers have found that up to 30% of individuals who are prescribed long-term opioid treatment have features of medication misuse.⁴ For individuals who have a history (current or previous) of a substance use disorder, the risk of developing such problems is higher. When prescribing opioid treatment, clinical vigilance is needed to identify individuals who may be at increased risk of developing problems associated with the medication and to determine when risk mitigation strategies are indicated.

ILLUSTRATION COMPOSITE: WHEEL WITH ADDICTIVE SUBSTANCES.
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Prescribing opioid analgesics

Initiating treatment

A standardised ‘universal precautions’ approach to opioid prescribing was first suggested in 2005 by Gourlay and colleagues.⁵ These authors advocated a structured assessment for all individuals, conducted in a nonjudgemental and evidence-based manner, prior to commencing treatment with an opioid medication (Box 2).

Current international consensus guidelines also discuss common principles of best practice that can be applied to mitigate the risks associated with prescribing opioids for noncancer pain.³ These guidelines recognise that special provisions are needed to manage persisting noncancer pain in patients at highest risk for addiction, such as those with a current or previous substance use disorder (including for alcohol and nicotine) or a family history of substance use disorder. Although a history of a substance use disorder does not entirely preclude patients from accessing opioid analgesia for persisting pain, it should alert a prescriber to the need for careful consideration of the risks and benefits of such treatment.

There are several useful screening instruments, available online, that can be used to identify individuals who are at risk of misusing opioids. These include the Opioid Risk Tool (<http://docs.health.vic.gov.au/docs/doc/Assessing-patients-when-considering-treatment-with-opioids>)⁶ and the Screener and Opioid Assessment for Pain (<http://bit.ly/1F6B2km>).² These instruments will usually place patients with a history of a substance use disorder in a high-risk category, but they may provide additional information and assist in the evaluation of other risk factors, such as comorbid mental health problems.

The assessment of a patient with pain on a background of substance use is complex. GPs may find it helpful to seek the opinion of an addiction medicine specialist or pain medicine specialist when formulating a management plan.

Continuing treatment

GPs often ‘inherit’ patients with active substance use problems who have already been commenced on opioid treatment. Rather than feeling compelled to continue high-risk management of pain with potent opioid analgesics, a GP can view this situation as an opportunity to discuss conditions for continuing treatment with the patient and to lay down ground rules. It may be that continuing opioid treatment should only be considered within the context of a gradual reduction or tapering plan or in the form of substitution treatment with opioid maintenance pharmacotherapy such as methadone or buprenorphine–naloxone. GPs may find it helpful to obtain the advice of an addiction medicine specialist to support them in this process.

Other aspects of management

An individual with a history of problematic substance use may have a limited repertoire of coping skills, a comorbid psychiatric illness or an acquired brain injury, which adds a degree of complexity when trying to deal with pain. It is important to explore psychological approaches to managing pain and comorbid issues as part of a management plan. Although a thorough discussion of such approaches is beyond the scope of this article, some considerations could include a focus on enhancing coping strategies (such as promoting exercise, distraction techniques, mindfulness and supportive social connections) and addressing negative schema. This can be supported by a focus on function (improving functional outcomes) rather than focusing solely on the experience of pain. A range of psychological therapies, including cognitive behavioural therapy and mindfulness or meditation-based approaches, can also help an individual develop skills to cope with pain. A multidisciplinary team model, with referral to psychologists, physiotherapists or other professionals can further support a comprehensive management plan.

1. EXAMPLES OF ABERRANT BEHAVIOURS IN PATIENTS PRESCRIBED LONG-TERM OPIOID TREATMENT

- Frequent unsanctioned dose escalations
- Obtaining of scripts from multiple doctors
- Obtaining of medication from nonmedical sources
- Stealing or borrowing of drugs from others
- Concurrent abuse of alcohol or illicit drugs
- Recurrent prescription loss
- Injecting of oral formulations
- Prescription forgery
- Selling of prescription drugs

Self-help and patient information websites, such as the American Psychological Association’s Pain Management Website (<http://www.apa.org/helpcenter/pain-management.aspx>) or the British National Health Service (NHS) Pain Toolkit (<http://www.paintoolkit.org>) can also be helpful, as can attendance at support groups for individuals with chronic pain.

The doctor–patient relationship

Patients who have co-occurring chronic pain and a substance use disorder can elicit a strong negative response in treatment providers. Often, they are quintessential ‘heartsink patients’.⁷ It is important to recognise a negative response when it occurs and to understand the reasons behind it. A patient’s problems may seem intractable and repeated visits without any improvement in symptoms or function can result in frustration and therapeutic nihilism. It can also take a great deal of time, effort and patience to comprehensively manage the range of problems associated with this group of patients. Clinicians may think that they are working harder to solve the problem than a patient and that

2. STRATEGIES TO MINIMISE HARMS ASSOCIATED WITH LONG-TERM OPIOID TREATMENT

Comprehensive assessment and examination

- Comprehensive pain and substance use history, including collateral history and communication with other treatment providers, to answer the following key questions:
 - what is the underlying pain diagnosis?
 - what are the current substance use problems?
 - what comorbidities require assessment and treatment (e.g. acquired brain injury, mental illness)?
 - what are the risks related to long-term opioid treatment for this patient (e.g. tolerance, addiction, diversion or selling of medication, toxicity, drug–drug interactions)?

Investigations and collateral history

- Appropriate investigations for pain (imaging, nerve conduction studies, etc)
- Urine drug screen to detect substance use
- History from previous prescribers and treatment providers, regulation authorities

Use of tools and instruments

- Pain – such as the Pain Assessment and Documentation Tool (PADT)
- Substance use – such as the Alcohol Use Disorders Identification Test (AUDIT) and Drug Use Disorders Identification Test (DUDIT)
- Mental health – such as the Kessler Psychological Distress Scale (K10)
- Opioid risk assessment tools, if opioid treatment is being considered – the Opioid Risk Tool (<http://docs.health.vic.gov.au/docs/doc/Assessing-patients-when-considering-treatment-with-opioid>)⁶ and the Screener and Opioid Assessment for Pain (<http://bit.ly/1F6B2km>)²

Adapted from: Gourlay DL, Heit HA. Universal precautions in pain medicine: the treatment of chronic pain with or without the disease of addiction. *Medscape Neurol Neurosurg* 2005; 7: 1-4 (reference 5).

Treatment plan and contract

- Identification of goals of treatment – specific goals with emphasis on functional outcomes
- Education regarding side effects and risks of treatment(s)
- Nonpharmacological pain management strategies
- Opioid analgesics – consider opinion from addiction medicine specialist, and following strategies to mitigate risks:
 - only one prescriber
 - only one dispensing point
 - no selling or giving of medication to others
 - no provision for early scripts
 - no replacement of lost scripts
 - consideration of limited dispensing (incorporate reasonable limits on the number of pills prescribed so the amounts prescribed match the number of treatment days/time between appointments)
 - consideration of random urine drug testing and random pill counts
 - consideration of use of a consent form for Prescription Shopping Information Service for higher risk patients (<http://www.medicare.australia.gov.au/provider/pbs/prescription-shopping>)

Treatment monitoring and review (4A's)

- Analgesia
- Activity
- Adverse events
- Aberrant behaviours – one or more 'red flags' (see Box 1) should trigger discussion with the patient and with regulatory authorities, consideration of referral to an addiction medicine specialist or pain medicine specialist, and consideration of methadone or buprenorphine–naloxone for opioid dependence
Note: Patients taking opioid doses ≥ 120 mg morphine equivalent should be referred for specialist review

Documentation

- Thorough documentation at all steps in the process

the patient is not actively participating in their recovery. Situations can arise where there is doubt about the veracity of the patient's history. The clinician may believe the patient is not reporting 'genuine pain' or is deliberately 'drug seeking'. Negative experiences can also colour future interactions with patients with similar problems. Many of these factors affect the dynamics of the doctor–patient relationship, and it can be helpful to consider strategies to address this.

Keys to fostering a therapeutic doctor–patient relationship are the same for this group of patients as for patients with any other clinical presentation. They include:

- open and honest communication
- consistent messages and plans
- consistent and frequent appointments for review and monitoring
- clear boundaries and conditions of treatment.

It is especially important to maintain a consistent and systematic approach in

managing this patient group because of the inherent level of complexity of care and the medicolegal and regulatory structures associated with opioid prescribing. Key approaches include:

- thorough and timely documentation
- familiarity and compliance with legislative and regulatory requirements
- communication and liaison with other treatment providers
- seeking of expert opinion and advice where necessary
- peer review and support.

By maintaining a clinical perspective of empathy with patients affected by pain and addiction, clinicians can help to create a productive therapeutic relationship. Reframing the ‘heartsink patient’ as an individual who produces a ‘heartsink reaction’ or engenders a ‘heartsink relationship’ can shift the focus of the ‘heartsink’ itself; these responses have been described as the responsibility of the treatment provider ‘rather than being an inherent characteristic of any particular patient’.⁸ The reactions that a patient provokes in the clinician may be similar to reactions that he or she elicits in others around them. Reflective practice, taking into account these reactions and feelings and pursuing support through discussion with peers and colleagues and/or exploring options for shared care with a psychologist or addiction medicine specialist, will result in effective practice and enable the clinician to remain a source of hope.

Conclusion

Prescribing opioid medications for individuals with co-occurring pain and a history of substance use disorder can be challenging for many doctors. However, incorporation of strategies to minimise physiological, psychological and medicolegal risks can make the treatment journey as painless as possible for both the doctor and patient.

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Treatment of patients with opioid dependence

NICHOLAS LINTZERIS BMedSci, MB BS, PhD, FACHAM

The prevalence of opioid dependence is growing in Australia with the increased use of pharmaceutical opioids. A number of effective interventions exist for patients with opioid dependence, including withdrawal services, opioid substitution treatment and psychosocial interventions, supported by self-help groups and harm-reduction services.

KEY POINTS

- Opioid dependence, a chronic condition characterised by impaired control over the use of opioids and related harms, is no longer the domain of heroin users but increasingly affects patients using pharmaceutical opioid analgesics.
- Patients with opioid dependence often have a range of medical and social comorbidities that need to be addressed, usually by a range of primary care and specialist services.
- There are effective treatment interventions available for opioid dependence, including detoxification, psychosocial interventions and opioid substitution treatment (OST) with methadone or buprenorphine–naloxone.
- OST treatment is safe and effective for patients with concomitant chronic pain and dependence on opioid analgesics.



Opioid dependence is a chronic relapsing condition that affects approximately 1% of the Australian adult population. It is characterised by regular opioid use, tolerance, impaired control over use, persistent use despite related harms, a characteristic withdrawal syndrome and relapse on attempts at stopping or reducing opioid use. Opioid dependence has historically been linked to illicit heroin use. However, over the past 15 years in Australia there has been a marked increase in the use of pharmaceutical opioids, both prescribed and over the counter, usually in the context of chronic pain. This has been associated with an increase in the numbers of individuals who develop opioid dependence and require management of that dependence in addition to any concomitant medical conditions (e.g. chronic pain or depression).

Opioid dependence is associated with a range of biological, psychological and social harms to the individual and wider community. There is a range of effective treatment interventions for opioid dependence, including opioid substitution treatment (OST; with methadone or buprenorphine–naloxone), management of opioid withdrawal (detoxification), psychosocial interventions (counselling or residential rehabilitation) and antagonist medication (naltrexone). Recent national clinical guidelines on medication-assisted treatment of opioid dependence are available from the National Drug Strategy (www.nationaldrugstrategy.gov.au).¹ Local regulations vary, and guidance can be obtained from state and territory health departments.

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Associate Professor Lintzeris is the Director of Drug and Alcohol Services, South East Sydney Local Health District, and Clinical Associate Professor in the Discipline of Addiction Medicine at the University of Sydney, Sydney, NSW.

Long-term opioid use: dependence and addiction

Tolerance and opioid withdrawal

The body adapts to regular and prolonged opioid use (neuro-adaptation), characterised by tolerance (diminished effects with repeated use, requiring increased doses to achieve the same effects) and withdrawal. Opioid withdrawal is a specific syndrome following the cessation or reduction in heavy and prolonged opioid use. It is characterised by a range of signs and symptoms that include generalised aches and pains, arthralgia, cravings, low mood, irritability, agitation, poor sleep, abdominal cramps, nausea, vomiting, diarrhoea, sweating, runny eyes and nose, dilated pupils and increased sensitivity to pain stimuli. The onset and duration of withdrawal symptoms depends on the duration of action of the opioid used (see below).

Addiction versus dependence

The diagnosis of dependence in patients using prescribed medications can be complex. Many pain specialists do not consider tolerance and withdrawal to be features of 'addiction' to prescribed opioids but rather normal physiological responses to long-term opioid use. For patients to qualify for a diagnosis of 'addiction' to prescribed opioids, they must have other psychosocial features of dependence. These include, most notably, impaired control over opioid use, cravings, continued use despite harms and failed attempts to reduce or cease opioid use. It is estimated that approximately 10% of Australian patients with chronic nonmalignant pain treated long term with opioids meet the criteria for dependence.²

Natural history of opioid dependence, morbidity and mortality

Long-term studies of opioid-dependent individuals indicate opioid dependence to be a chronic relapsing condition. Estimates suggest a 2 to 5% annual remission rate (i.e. 2 to 5% will stop using opioids in any one year).

In general, opioids are relatively safe drugs that have been used in many cultures for centuries and are widely prescribed by doctors today. Nevertheless, individuals may experience a range of harms arising from their opioid use. These are:

- physical (e.g. overdose and opioid side effects, including constipation, sedation, sleep and endocrine disorders and hyperalgesia)
- psychological (e.g. depression, anxiety, cognitive impairment and suicide)
- social (e.g. financial problems, impaired relationships or legal problems and stigma).

The harms vary according to type and route of opioid use, frequency of use and related behaviours.

The estimated mortality rate (from all causes) for untreated heroin users is around 1 to 2% per annum – approximately 10 to 15 times higher than mortality among age- and sex-matched control subjects in the community. The main causes of death in this

population are overdose and/or suicide (in approximately one-third of cases), trauma (in approximately one-third) and infectious diseases (e.g. hepatitis C-related liver disease, HIV infection and endocarditis). Much of the overdose-related mortality associated with dependence on opioids is linked to use of other sedative drugs (e.g. benzodiazepines, antidepressants) and drugs that contribute to hepatic toxicity (e.g. alcohol). Effective treatment (e.g. OST) is associated with a three to fivefold reduction in mortality.

Management of opioid dependence

Goals of treatment and treatment planning

Although many patients, their families and the broader community have the goal of sustained abstinence after a short treatment episode (e.g. a one-week withdrawal intervention), the chronic nature of opioid dependence suggests that effective treatment usually requires longer-term treatment, extended over months or years. More realistic and immediate goals for most people entering treatment include a reduction in high-risk patterns of drug use (e.g. polydrug use, injecting drug use), reductions in opioid use and improvements in health and psychosocial functioning. Patients with concomitant chronic pain and opioid dependence need treatment plans that address both conditions.

Opioid dependence is often associated with other harmful patterns of substance use (e.g. alcohol, tobacco, benzodiazepines, cannabis) and a range of medical, psychiatric and social problems. These also need to be addressed in any comprehensive treatment approach. Treatment planning should involve the patient and reflect their circumstances and case complexity, and also often involves co-ordination across multiple health and welfare providers.

Informed consent is important in the management of opioid dependence. Patients should understand the implications of different treatment options, including potential risks and benefits, side effects and financial and other commitments. Written information and opportunities to ask questions or consider alternatives should be provided. Cognition, literacy, language and cultural factors should be considered.

Assessment

A comprehensive assessment should be conducted, sometimes completed over several appointments depending on the health care setting and circumstances. Clinicians should initially aim to identify the patient's patterns of substance use and key medical, psychiatric and social complications, and to examine patient treatment goals and preferences. Referral or consultation with a specialist is recommended for patients with complex presentations. Key aspects of the clinical assessment of patients with possible opioid dependence are shown in Box 1.

Overview of treatment interventions

A range of service providers can be involved in delivering treatment services for opioid dependence, including primary care services

1. ASSESSMENT OF PATIENTS WITH POSSIBLE OPIOID DEPENDENCE

Presenting complaint

- Reason for presentation (this affects immediate treatment goals)
- Assessment of chronic pain (this is crucial in those using opioid analgesics)

History of substance use and previous drug and alcohol treatment

- Opioid use: quantity, frequency and route of use, duration of this episode
- Features and severity of dependence: evidence of tolerance, withdrawal, age at first use and first regular use, periods of abstinence, ability to control use, drug-related harms
- Use of other drugs (alcohol, benzodiazepines, cannabis, psychostimulants, tobacco) and other substance-use disorders
- Previous attempts at treatment: what has 'worked' and 'not worked' before

Medical and psychiatric history

- Particular attention to unstable or active conditions that may complicate or require treatment (chronic pain, hepatic and mood disorders are common)
- Risk behaviours, including risk of harm to self or others, polydrug intoxication, history of overdoses, injecting practices

Social circumstances

- Home environment, social supports, employment, financial and legal issues, child protection or domestic violence concerns, barriers to change
- Motivations and goals for treatment (an understanding of the reasons for seeking treatment and patient goals and expectations is essential to selecting the appropriate treatment)

Examination

- Vital signs (blood pressure, pulse, respiratory rate)
- Evidence of intoxication or withdrawal from opioids or other drugs
- Evidence of drug use and related complications (e.g. injection sites, hepatic disease, infections)
- Mental state and cognitive assessment

Investigations

- Urine drug screens (these can confirm or clarify recent substance use)
- Viral serology (HIV, hepatitis B and C) for patients with a history of injecting drug use
- Monitoring of hepatic function in patients with liver disease

(general practice, allied health, community pharmacy), specialist drug and alcohol services (government and nongovernment organisations) and hospital and other specialist providers (e.g. mental health and pain services).

Evidence-based interventions for opioid dependence are summarised in the flowchart. They include:¹

- withdrawal (detoxification) services – short-term interventions (usually five to 14 days) that aim to interrupt a pattern of heavy use, ameliorate the discomfort of withdrawal symptoms and link patients with ongoing services; these interventions may be delivered in outpatient, residential or hospital settings and usually achieve only short-term benefits
 - OST – a longer-term approach (months or years) that involves the use of methadone or buprenorphine–naloxone, regular clinical reviews and monitoring, and psychosocial interventions
 - psychosocial interventions – including counselling, case management and residential rehabilitation
 - antagonist-assisted treatment – involving the use of oral naltrexone and potentially useful for highly motivated patients with good social supports.
- Other important approaches include:
- self-help groups, which provide structure and support networks for patients (e.g. Narcotics Anonymous, SMART Recovery)
 - harm reduction services, which may be relevant for some individuals who continue to use opioids; they include access to a needle and syringe program, peer support and overdose prevention services, including prescription of take-home naloxone.

Interventions for opioid withdrawal

Withdrawal from short-acting opioids (e.g. heroin, oxycodone and codeine) generally starts within eight to 24 hours of last use and peaks at 48 to 96 hours. Most physical

symptoms subside within five to 10 days, although some symptoms (e.g. disturbed sleep and mood, and cravings) often persist for weeks. Withdrawal from long-acting opioids (e.g. methadone and buprenorphine) has a more protracted course.

Setting

Patients can usually safely complete opioid withdrawal as outpatients. Those with severe or unstable medical or psychiatric conditions may require hospitalisation. Residential services may be warranted for patients with unsupportive home environments (e.g. living alone or with other drug users) or following failed outpatient attempts. Many patients undergo opioid withdrawal during hospital admissions for other conditions, and hospital drug and alcohol consultation liaison services should be consulted.

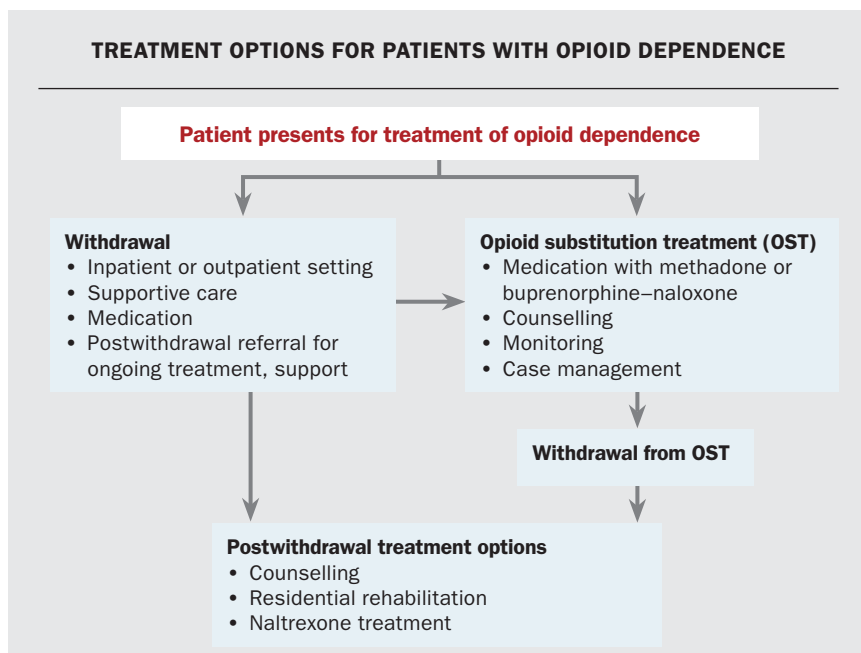
Supportive care

Supportive care includes daily review with a health worker (e.g. doctor, nurse or drug and alcohol worker, face to face or by telephone). Counselling during withdrawal focuses on coping with cravings, symptoms and maintaining motivation. Advice to patients includes avoiding dehydration (ensure fluid intake) or excessive caffeine, alcohol or other drug use. Social supports should be identified and plans developed for dealing with potential complications. Patients should also be warned about the risk of overdose if they resume opioid use after even a short period of abstinence.

Medication

Buprenorphine–naloxone is the preferred medication for managing opiate withdrawal, administered as a sublingual film. Evidence supports its use over symptomatic medications, and it is easier to use and to cease than methadone. Buprenorphine is a partial opioid agonist; naloxone is included to deter misuse by injection, as it is not absorbed after sublingual administration but may cause opioid withdrawal when injected. A short-term regimen of buprenorphine–naloxone should be

TREATMENT OPTIONS FOR PATIENTS WITH OPIOID DEPENDENCE



attempted (five to 14 days, depending on factors such as duration of inpatient admission), with progress reviewed within a few days. If buprenorphine is unavailable or contraindicated then methadone or medications to relieve symptoms may be used. Medication options for withdrawal are outlined in Box 2.³

Links to ongoing treatment and support

Withdrawal treatment can be life saving for some patients but on its own rarely results in long-term abstinence. Ongoing participation in treatment such as counselling, OST or residential rehabilitation is usually required to achieve long-term changes. Longer-term OST with buprenorphine or methadone is recommended for patients who:

- cannot stop or markedly reduce their opioid use during the withdrawal episode
- relapse into regular opioid use as the dose of buprenorphine is reduced or ceased, and/or
- do not feel confident about maintaining abstinence and want to avoid opioid relapse.

Patients should also be linked to services addressing broader health and welfare needs.

Opioid substitution treatment

OST is a long-term treatment approach (usually months or years) that involves daily dosing with a long-acting opioid medication such as methadone or buprenorphine (usually as buprenorphine–naloxone) to:

- prevent withdrawal
- reduce cravings
- reduce the reinforcing effects of any additional unsanctioned opioid use.

Although OST is still controversial in some quarters – being considered by some as ‘replacing one drug with another’ – extensive evaluation demonstrates it to be a safe and cost-effective treatment approach for most patients. OST reduces substance use, transmission of bloodborne viruses, mortality and crime, and improves general health, psychosocial function, community reintegration and quality of life.¹⁴

Methadone or buprenorphine–naloxone is usually administered as daily doses under supervision at a clinic or community pharmacy. However, as patients reduce their substance use and risk behaviours, medication can be dispensed in advance (take-away doses), enabling greater reintegration into activities such as work, study, parenting and social activities. Patients are reviewed regularly by a medical practitioner, nurse or

2. OVERVIEW OF MEDICATION REGIMENS FOR OPIOID WITHDRAWAL

Buprenorphine–naloxone sublingual film

- Initiate 4 to 8 mg buprenorphine–naloxone at onset of opiate withdrawal (use a clinical scale such as the Clinical Opiate Withdrawal Scale)³
- On days 2 to 4, titrate dose to achieve cessation of other opioid use and comfortable withdrawal symptoms (usually 8 to 16 mg per day)
- Taper dose over next two to seven days

Methadone oral liquid

- Use reducing doses over 10 to 20 days, commencing at 20 to 30 mg and reducing by 2.5 mg every one to two days

Symptomatic medications

- Antiemetic (e.g. metoclopramide 10 mg four times daily for up to three to four days)
- Antidiarrhoeal (e.g. atropine–diphenoxylate, one to two tablets three times daily for up to three to four days)
- Antispasmodic (e.g. hyoscine butylbromide 10 to 20 mg four times daily for up to three to four days)
- Anti-inflammatory (e.g. ibuprofen 400 mg four times daily for up to a week)
- Low dose benzodiazepines – can be useful but are not recommended beyond three to five days (e.g. diazepam 5 mg twice daily for two days, then 5 mg at night for two days)

drug and alcohol worker, and usually undergo regular urine drug testing to monitor their use of opioids and other drugs. The long-term nature of treatment provides opportunities to address related health and social problems, and engage with psychosocial interventions such as counselling.

The key elements of safe and effective OST include:

- establishing a safe and effective dosing regimen, including appropriate dosing conditions (pharmacy, clinic or take-away)
- undertaking regular clinical reviews and monitoring
- ensuring the patient participates in psychosocial interventions

3. METHADONE USE IN MANAGING OPIOID DEPENDENCE

Clinical pharmacology

- Methadone is a potent synthetic opioid agonist, well absorbed orally, with effects that are qualitatively similar to those of morphine and other opioids
- It has an onset of effects in 30 to 60 minutes, peak effects 2 to 4 hours after oral dosing, and a half-life of 15 to 30 hours
- Steady-state equilibrium is achieved three to seven days after daily dosing, with cumulative effects over this time
- It is metabolised by the hepatic cytochrome (CYP450) enzyme system to inactive metabolites, with important clinical implications for drug–drug interactions and particular disease states (e.g. liver failure)
- Methadone can also prolong QTc intervals, and electrocardiography monitoring may be required

Side effects and safety issues

- Side effects are similar to those of other opioids, most commonly constipation, sedation, sweating, nausea and reduced libido. These usually occur when starting treatment and often subside with time

- Methadone toxicity (severe sedation, respiratory depression, death) early in treatment is related to the use of other sedatives, inadequate assessment of tolerance, inadequate supervision of methadone dosing, starting on doses that are too high and/or too rapid dose escalation

Dosing

- Dosing usually commences at low doses (20 to 30 mg daily) and gradually increases by 5 mg every three to five days to achieve treatment objectives: reduction in withdrawal, cravings and cessation of additional opioid use. This is usually achieved for most patients with ‘maintenance’ doses of 60 to 100 mg daily

Issues in pain management

- Methadone oral tablets may be used for pain management only in nondependent patients; their use for pain management in drug-dependent patients requires specific local health department approval
- Effective pain management often requires lower methadone doses (e.g. 20 to 50 mg in two to three divided doses)

- addressing medical, psychiatric and social comorbidities
- attending to necessary regulatory issues in prescribing OST.

Practical aspects of the use of methadone and buprenorphine–naloxone in the management of opioid dependence are summarised in Boxes 3 and 4, respectively. The choice of methadone or buprenorphine–naloxone is generally driven by informed patient preference.

Eventually, most patients seek to exit OST after a period of reduced drug use and psychosocial stability. Optimal treatment outcomes are achieved in those who have remained in treatment for at least one to two years.⁴ Medication cessation usually involves a gradual dose reduction over weeks to months. Most patients experience a mild but prolonged opiate withdrawal syndrome on stopping methadone or buprenorphine–naloxone treatment. Without careful planning, this can serve

as a trigger for relapse to unsanctioned opioid use.

Psychosocial interventions

Counselling can be delivered in individual or group settings, targeting the patient’s substance use and related comorbidities, such as anxiety, depression, trauma or sleep problems. A range of counselling approaches can be effective. Motivational enhancement approaches can be used to encourage ambivalent patients to engage in treatment. Relapse prevention approaches aim to help patients identify and deal with situations or emotions that are associated with relapse to substance use. Cognitive behavioural therapy (CBT), mindfulness and narrative therapies are also supported by evidence.

Counselling approaches on their own have limited long-term benefit in treating heroin-dependent patients, and combining them with medication (e.g. OST or the opioid antagonist naltrexone) is often

recommended, as is common for patients with chronic biopsychosocial conditions such as depression and chronic pain disorders. Social, financial and occupational services are also important as many individuals have disrupted education and occupational backgrounds.

Residential rehabilitation programs have historically been medium- to long-term interventions (weeks to months) that involve treating patients in structured residential settings, using a variety of counselling and self-help or peer-led interventions. Residential rehabilitation programs generally target individuals with severe social problems who need an extended period of stability in a structured environment. Most programs also have community reintegration components to address the high rates of relapse on re-entry into the community.

Peer support approaches can be useful for some patients, particularly in providing social networks and structured activities removed from substance use. Notable examples include Narcotics Anonymous (a 12-step peer support approach similar to Alcoholics Anonymous) and SMART Recovery (a CBT-based peer support approach).

Antagonist-assisted treatment

Antagonist-assisted treatment involves the use of oral naltrexone to discourage the use of additional opioids. This long-acting opioid antagonist blocks the effects of opioid use for 24 to 48 hours, thereby reducing its reinforcing effects. Naltrexone treatment is usually integrated with psychosocial interventions (counselling) and regular clinical reviews with a medical practitioner. Oral naltrexone is usually taken once a day, although it should be administered only after completion of opiate withdrawal, and usually in consultation with a specialist. There is an increased risk of overdose with resumption of opioid use after ceasing naltrexone. Naltrexone is not subsidised by the PBS for opioid dependence, and its cost to consumers is a barrier to its use in Australia.

Because of the low rates of medication adherence with oral naltrexone by opioid users (estimated at less than 10% at six

months), it is usually reserved for individuals with exceptionally high levels of motivation and strong social supports. Furthermore, the role of naltrexone in individuals with concomitant pain conditions is unclear, and it may be contraindicated if continued or episodic opioid analgesia is required. Long-acting naltrexone depot injections (with one-month action) are licensed in some countries but not currently available in Australia. Naltrexone implants are not licensed in Australia.

Conclusion

Although historically most opioid-dependent users in Australia have used illicit opioids such as heroin as their primary drug, increasingly we are encountering patients who either misuse pharmaceutical opioid medications not prescribed for them or, alternatively, develop dependence on opioid medications used in the treatment of chronic pain. This last category is particularly important for all GPs and pain specialists, given the high prevalence of chronic pain in Australia. It is estimated that approximately 10% of patients with chronic nonmalignant pain using opioids long term will become opioid dependent.

Importantly, there are safe and effective treatment approaches for opioid dependence, irrespective of the source of the opioids (illicit, over the counter or prescribed). A trial of withdrawal is often warranted, but the long-term nature of opioid dependence generally requires long-term treatment approaches such as OST with buprenorphine–naloxone or methadone and psychosocial interventions.

Opioid dependence is often associated with a range of comorbidities, including pain, mental health problems, hepatic disease, cognitive impairment and impaired social relationships. It is crucial that these comorbidities are addressed, usually through networks of multidisciplinary treatment providers. Primary care practitioners working with patients with complex presentations should consult with addiction medicine and other specialists in developing and implementing effective treatment plans. **MI**

4. BUPRENORPHINE USE IN MANAGING OPIOID DEPENDENCE

Available formulations

- Buprenorphine is used as a sublingual formulation in treating opioid dependence
- Buprenorphine–naloxone combination sublingual film is the more commonly used formulation, containing dosages of 2/0.5 mg or 8/2 mg buprenorphine/naloxone
- Naloxone is included in the film to deter misuse and administration by injection; it is not absorbed after sublingual administration but may cause opioid withdrawal when injected

Clinical pharmacology

- Buprenorphine is a semisynthetic partial opioid agonist with high affinity for opioid receptors
- Peak clinical effects are achieved 1 to 4 hours after sublingual dosing
- Buprenorphine is metabolised principally in the liver to inactive metabolites, with an elimination half-life of 24 to 37 hours. CYP drug–drug interactions are usually not clinically significant

Side effects and safety issues

- Side effects are similar to those of other opioids, most commonly constipation, sedation, sweating, headaches, disturbed sleep and nausea. These usually occur when starting treatment and often subside with time
- Buprenorphine is less likely to cause respiratory depression and overdose than full agonists (e.g. methadone, oxycodone, heroin). Caution is still required in patients using sedatives (e.g. alcohol, benzodiazepines) and those with low or uncertain opioid tolerance

- The initial dose of buprenorphine can precipitate opioid withdrawal in patients who have recently used a full agonist (buprenorphine has higher receptor affinity but is a partial agonist). This is avoided by delaying the first buprenorphine dose until the patient is experiencing mild to moderate opioid withdrawal. Transfer from methadone to buprenorphine can be complicated, and specialist consultation is recommended

Dosing

- Doses of 4 to 8 mg are initiated when the patient is experiencing early to mild features of opiate withdrawal (e.g. 8 to 24 hours after last heroin use)
- Doses can be increased daily by 2, 4 or 8 mg per day until treatment goals are achieved: reduction in withdrawal and cravings, and cessation of additional opioid use. This is usually achieved for most patients with doses of 8 to 24 mg per day

Issues in pain management

- Buprenorphine transdermal patches or low dose (0.4 mg) sublingual tablets may be used for pain management only in nondependent patients; their use for pain management in drug-dependent patients requires specific local health department approval
- Buprenorphine has analgesic properties and there is emerging evidence that high doses can be effective in treating patients with both chronic pain and dependence⁵

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COMPETING INTERESTS: Associate Professor Lintzeris has received honoraria for presenting professional education in the area of opioid dependence, and educational grants for investigator-led research with buprenorphine–naloxone from Reckitt Benckiser, the manufacturer of Suboxone.

Benefits and challenges to the implementation of real-time prescription monitoring

ROWAN P. OGEIL BA, BSc(Hons), PhD

CHERIE HEILBRONN MB BS, MPH

BELINDA LLOYD BA(Hons), PhD

DAN I. LUBMAN BSc(Hons), MB ChB, PhD, FRANZCP, FACHAM

Harms linked to prescription drug misuse are rising in tandem with increased prescription availability. Individual practitioners and the healthcare system each have roles in reducing harms associated with pharmaceutical drugs and a real-time prescription monitoring system could help in this process.

KEY POINTS

- Benzodiazepines and opioids are efficacious medications for the short-term management of patients with anxiety, insomnia and pain, but are susceptible to being misused and abused.
- Recent studies have consistently identified increasing morbidity and mortality associated with these drugs in Australia.
- Real-time prescription monitoring (RTPM) has the potential to assist prescribers and dispensers in adhering to the quality use of medicines.
- RTPM also assists in the identification of those patients at risk of misuse or abuse of pharmaceuticals.
- Individual practitioners have an important role in minimising the misuse of pharmaceuticals by devising treatment plans and contracts and conducting ongoing monitoring of patients who are prescribed these medicines.



Prescription medications have made a significant and positive contribution to the health and wellbeing of Australians.^{1,2} However, some medications have the potential to cause harm when misused.¹ Pharmacological classes identified as being particularly susceptible to misuse, dependence or subsequent harm are the benzodiazepines and the opioid analgesics. Although these drugs can legitimately be used for the evidence-based short-term treatment of patients with anxiety, insomnia and chronic pain, recent data highlight increasing rates of harm associated with their use.³⁻⁵ Given the substantial increases in the prescription of opioids and benzodiazepines in Australia,^{6,7} there is a growing challenge for the Federal and the various state and territory governments to increase awareness about the potential misuse of prescription medications, and to implement mechanisms that promote quality use of medicine and minimise harm. This challenge is multifaceted and requires both system level (e.g. policies related to prescribing and dispensing and monitoring systems) and individual level (e.g. screening for appropriate behavioural markers, referral and treatments) actions to succeed.

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Dr Ogeil is an NHMRC Peter Doherty Early Career Fellow at Monash University, Melbourne, and Turning Point Alcohol and Drug Centre (Eastern Health), Melbourne. Dr Heilbronn is a Research Fellow at Turning Point, Melbourne; and Adjunct Lecturer at Monash University, Melbourne. Associate Professor Lloyd is Associate Professor of Addiction Studies, Monash University, Melbourne; and Head of Research and Workforce Development at Turning Point, Melbourne. Professor Lubman is Director of Turning Point, Melbourne; and Professor of Addiction Studies and Services at Monash University, Melbourne, Vic.

Benzodiazepines and opiate analgesics: benefits and risks

Benzodiazepines are widely prescribed and are efficacious in the treatment of patients with anxiety disorders and insomnia in the short term.^{8,9} Benzodiazepines also have significant side effect profiles if they are misused, most notably the development of tolerance and dependence with longer-term use.^{10,11} Chronic use of benzodiazepines is associated with cognitive impairment, falls and a diminished quality of life, especially in the elderly.^{6,7,12,13} In addition, short-acting benzodiazepines such as alprazolam, typically prescribed for the management of patients with anxiety, are more likely to be diverted for other uses, and are associated with both drug-related offending and increased utilisation of emergency resources.¹⁴

Opioids are efficacious analgesics and have legitimate and important treatment indications for the management of patients with pain.^{2,5} Misuse of opioids such as fentanyl, morphine and oxycodone is associated with significant side effects including respiratory depression, which can result in death.⁵ The long-term use of opioids for chronic pain is increasing in community settings, and has been associated with higher rates of fatal overdose.¹⁵ This has led to increasing debate about their efficacy and safety in the management of patients with chronic nonmalignant pain.¹⁶

Pharmaceutical drug use and associated harms in Australia

In 2013, 4.7% of people in Australia aged 14 years and older engaged in nonmedical use of analgesics, sedatives and/or corticosteroids, compared with 3.9% in 2001.¹⁷ This upward trend mirrors international patterns,⁸ and is occurring in parallel with rising supplies of commonly misused medications including opioids such as oxycodone and the antipsychotic quetiapine. In Australia, from 1992 to 2012, the number of dispensed PBS opioid prescriptions increased 15-fold (from 500,568 to 7,495,648 prescriptions), with dramatic increases in morphine prescription during the 1990s, oxycodone prescription from 2000 and fentanyl prescription from the mid-2000s.¹⁸ The concordant proliferation in the number of available opioid formulations from 11 preparations in 1992 to 146 preparations in 2013 was predominantly driven by the development of slow-release preparations.^{7,18}

Changing PBS regulations over the past 20 years have precipitated alterations in benzodiazepine prescribing patterns. For example, although the highest number of prescriptions per year in most years from 1992 to 2011 were for diazepam, there were notable shifts from the prescribing of oxazepam, nitrazepam and temazepam towards the prescription of alprazolam.¹⁹ The subsequent popularity of alprazolam and its well-documented harms resulted in its rescheduling to a restricted Schedule 8 drug in 2014.

Greater population-level prescription is not necessarily detrimental. Continued high benzodiazepine and opioid demand is expected as Australia's ageing population results in a greater prevalence of painful conditions and psychological disorders that

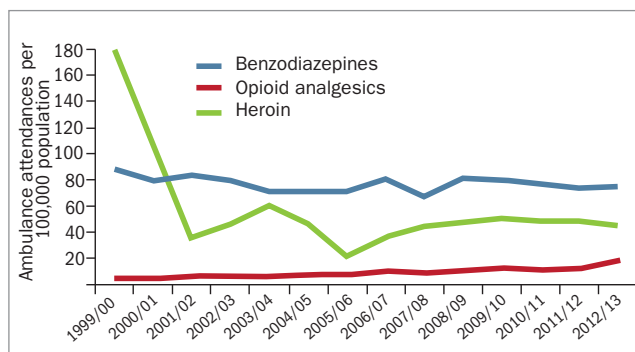


Figure. Benzodiazepine-, opioid analgesic- and heroin-related ambulance attendances per 100,000 population, metropolitan Melbourne, 1999/2000 to 2012/2013. Heroin included as a comparator drug. A substantial decline in harms during 2000/01 and 2001/02 reflected a drop in availability after the heroin 'glut' of the late 1990s.

peak during the middle and older years. If rising prescriptions reflect quality use of medicines, then people in Australia will profit from the advantageous potential of these drugs. Yet, as more people have engaged in nonmedical use of these medicines concomitant to their greater supply, associated harms have also increased.

Since the late 1990s, inappropriate benzodiazepine use has been involved in more ambulance attendances in Melbourne than any other drug except alcohol (Figure).^{20,21} Over this period, pharmaceutical opioid-related ambulance attendances have increased more than fourfold, whereas heroin-related events have halved.^{20,21} In parallel, hospitalisations in Australia for pharmaceutical opioid (excluding methadone) poisoning substantially increased from 1998 to 2009, these drugs superseding heroin as the leading cause of opioid-poisoning hospitalisations in 2001.¹⁸ Although hospital separations related to benzodiazepines remained stable, rates were consistently high and these drugs were the second leading drug cause of hospitalisation in Victoria (after alcohol) from 2000/01 to 2010/11.²² Perhaps most troubling is the growing rate of deaths in Australia involving oxycodone and fentanyl, as well as increased benzodiazepine involvement in heroin-related deaths over the past two decades.^{2,23-25}

Reducing harms associated with pharmaceutical drug misuse

Pharmaceuticals are often misused by individuals who do not typify those traditionally seeking treatment for alcohol and other drug problems.^{1,26} Pharmaceutical drugs may be conceived of as 'safe' and unlikely to lead to addiction by the general public because they have been prescribed by a physician.²⁷ Currently, information regarding pharmaceutical misuse relies on printed warnings on medication packaging and advice provided to the patient at either the point of prescription (e.g. by a physician) and/or the point of sale (e.g. by a pharmacist).¹ Accompanying this, information on regulation and monitoring of Schedule 8 drugs differs among the

BENEFITS, LIMITATIONS AND CHALLENGES TO THE IMPLEMENTATION OF REAL-TIME PRESCRIPTION MONITORING

Benefits

- Can alert prescribers to patient's prescription history
- Can alert prescribers to current prescriptions the patient has filled
- Has the ability to flag potential drug interactions
- Will make it more difficult for patients to engage in doctor shopping
- May identify patients who initially obtained drugs for genuine need but are at 'risk' of misuse or abuse

Limitations

- Proposed Australian system will monitor Schedule 8 drugs only
- It is unclear what the best practice is for patients at 'risk' of harm or misuse
- It is unclear how doctors and pharmacists will continue their support of individuals who are flagged in the system
- Patients with a genuine need may not be prescribed needed medications (the chilling effect)

Challenges

- At what threshold will a response be triggered?
 - Drug dose
 - Frequency of prescription
 - Comorbid use of prescription drugs
 - Comorbid mental health or physical condition
- Who will respond to a potential flag?
 - Prescribers
 - Pharmacists
 - Health services
 - Legal/law enforcement services
- Will the system be able to monitor shifts in drug prescribing?
- How will patient privacy be protected?
- What information about patients will be collected?
- Will the system be 'proactive' or 'reactive'?
- Who will develop and implement the system?
- Who will be responsible for training system users?

states and territories.²⁸ Such a system is limited in its ability to prevent misuse or abuse of medications, which may occur via the following mechanisms:^{2,27}

- doctor shopping
- drug theft
- prescription forgery
- inappropriate prescriptions by prescribers.

Given the large increases in harms associated with pharmaceutical drug misuse and abuse, and the increased number of opioid prescriptions filled in Australia, there has been considerable interest in strategies to minimise harms associated with long-term opioid use.^{18,29} This includes steps that can be taken by individual physicians (e.g. conducting a comprehensive pain and substance use history, devising a treatment plan and contract for those deemed at risk,

and conducting frequent monitoring and reviews) and by governments (e.g. requiring pharmacy and/or prescriber reports or use of wholesale data to monitor patterns of prescribing). One strategy that has received much interest in Australia is the implementation of real-time prescription monitoring (RTPM). RTPM systems collect information about the prescriber, the dispenser, the patient and relevant drugs.³⁰ The Royal Australasian College of Physicians and the Royal Australian College of General Practitioners both recommended the adoption of a real-time reporting system to operate nationally, and this is also supported by the Federal Government.²⁸

Prescription drug monitoring programs have been introduced in different jurisdictions to help control nonmedical use and/or medical abuse of prescription drugs.³⁰ In the USA, such systems originated in the early 20th century with the goal of detecting and prosecuting drug diversion and the abuse of controlled substances, with a secondary aim of providing information to prescribers in order to prevent the abuse of prescription medications.³¹ A RTPM system has recently been introduced in Tasmania to monitor Schedule 8 drugs prescribed alone or in combination with alprazolam.²⁸ However, there has been limited data examining the effectiveness of RTPM, with those studies completed focusing primarily on law enforcement rather than health outcomes.^{27,31,32}

Benefits and challenges to the implementation of RTPM

Multiple benefits, limitations and challenges will accompany the implementation of national RTPM in Australia (Box).²⁸ Potential benefits of RTPM include the ability of the system to inform prescribers about a patient's prescription history and their current filled prescriptions.³³ Such information is important in decreasing the incidence of 'doctor shopping', encouraging prescribing that concurs with relevant guidelines^{34,35} and alerting prescribers to potential drug interactions. Collection of this information may also help to identify people who use scheduled drugs for a genuine medical need initially and then go on to misuse or abuse these drugs.³⁰

One limitation involves the scope of drugs to be included in the Australian proposal.²⁸ The monitoring of Schedule 8 drugs means that some opioids (e.g. tramadol, codeine preparations) will be excluded despite their demonstrated roles in morbidity and mortality in Australia.³³ Another limitation concerns what is best practice for patients deemed to be 'at risk' of misuse or abuse of these medications. Current treatment pathways for such patients are not well defined, and referral pathways to other services and nondrug alternatives for managing chronic pain are not clear.³³ Addiction and chronic pain are often complex presentations and there is currently limited funding for addiction specialist expertise across Australia. There is also limited practical training opportunities for healthcare professionals in the management of patients with addiction and chronic pain, which means that there are real concerns about increasing stigma and the provision of adequate care to individuals

who are flagged in the system.²⁷ An additional concern is that patients with a genuine need for prescription medications may not be prescribed them for fear that an individual, or a prescriber, may become 'flagged' in the system.^{30,36}

Issues of privacy and confidentiality are clearly paramount to the success of RTPM, with a focus on health outcomes. This includes clear delineation of who will have access to the information, what information will be collected and stored, and how long records will be kept.³⁰ Finally, it is important to determine whether the system should be 'proactive' (e.g. generate reports for clinics or individual prescribers and identify those who may be at risk of dependence or abuse based on information provided to it) or 'reactive' (rely on user requests once someone is deemed at risk in order to identify potential problems from a patient or physician perspective).

Conclusion

With evidence of increasing misuse and harms associated with prescription medications, there has been a renewed interest in effective practitioner and system responses to promote quality use of medicines and minimise harm. Quality use of medicines by individual practitioners includes treatment plans, contracts and ongoing monitoring subsequent to a comprehensive pain, mental health and substance use history. In parallel, at the systems level the utility and value of RTPM must balance the needs of individual patients who require treatment with the public health ideal of reducing harm across the population. **MT**

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Chronic pain, opioids and dependence

A role for every GP

IAN THONG FPPMANZCA, FRACGP, MB BS, PhD, BSc(Hons)

VIVIENNE MILLER MB BS, FRACGP, DRACOG, DCH, MACPM, MWAME

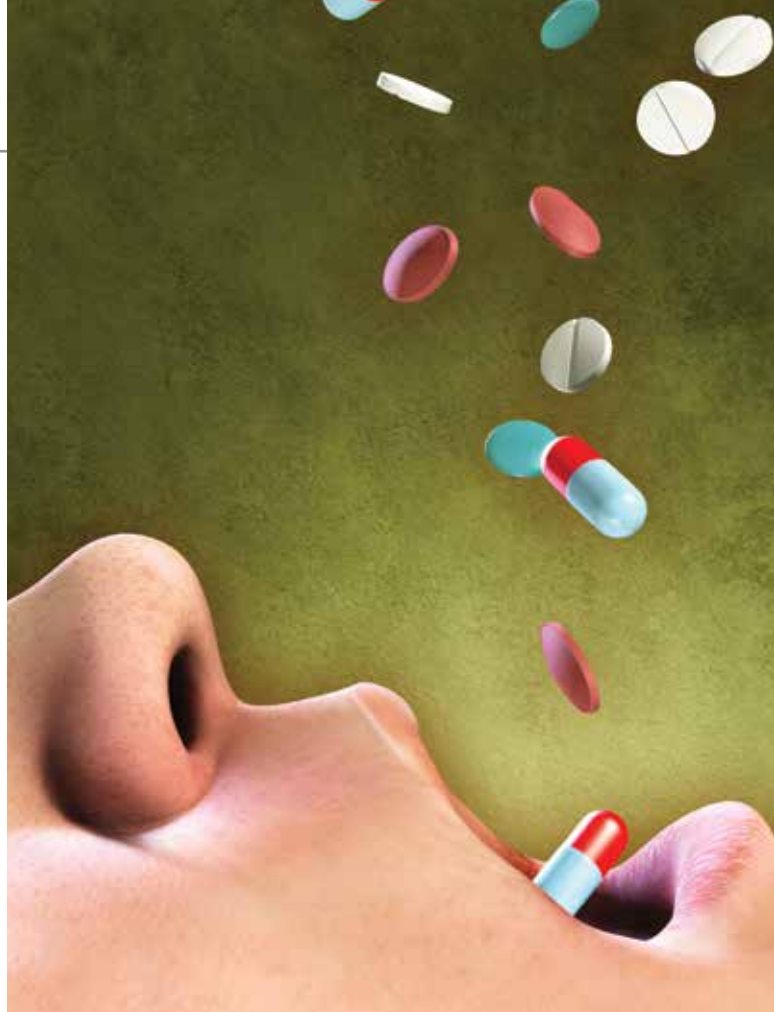
Every GP has a role at some level in caring for patients who develop opioid dependence while being treated with opioids for chronic pain. Two cases of opioid dependence managed in general practice with the assistance of pain and addiction specialists are discussed.

KEY POINTS

- Patients with opioid dependence are a common presentation in general practice.
- Stable patients taking medications for pain who are opioid dependent should ideally be managed in routine general practice.
- As well as usual primary care, opioid use or opioid substitution treatment needs monitoring in these patients.
- Shared care with pain and addiction specialists is an effective way for GPs to provide care to patients with addiction.

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Dr Thong is a General Practitioner in Bathurst with a special interest in drug and alcohol medicine; a pain specialist; Medical Director of Central West Pain Specialists; Chair of the Primary Care Pain Network, Agency for Clinical Innovation, NSW Health; and Conjoint Lecturer, The University of Sydney, Sydney. Dr Miller is a General Practitioner in Sydney; and an editor, author and medical journalist.



One of the many challenges in general practice is to supervise opioid use in patients who have chronic pain. In most individuals, this can be done with minimal issues and a low risk of complications; however, a small number of patients may become dependent on, or addicted to, these medications. For those who become addicted, opioid substitution treatment (OST) is a valuable option. OST is a program used by addiction specialists and authorised GPs to manage opioid addiction with controlled dosing of methadone, buprenorphine or buprenorphine with naloxone (the opioid antagonist naloxone discourages abuse of buprenorphine by injections).

The authors, one a GP with expertise in addiction medicine (IT), the other a suburban GP (VM), have coauthored this article with the purpose of showing how rewarding it can be for GPs to manage patients on an OST program.

Case 1

Mr BM, 38 years old, is a regular patient of your practice who was severely injured in a motorcycle accident nine months ago. He has worked as a storeman, is married with a supportive wife and has three young children and financial responsibilities. He had never used anything stronger than paracetamol for pain in the past. He has had no personal history of illicit substance use and there is no family history of opioid or other substance abuse. He is a nonsmoker and a social drinker only. There is also no history of mental health problems.

After the accident, Mr BM had many months of treatment in hospital and then was discharged on a high dose of oxycodone (oxycodone sustained release 40 mg twice daily and oxycodone 5 mg as needed, up to a maximum of 15 mg per day) to manage persistent post-traumatic and postoperative pain. He had returned to work but had been struggling with pain, and his opioid dose had gradually been increased under another GP's medical supervision to oxycodone sustained release 80 mg twice daily and oxycodone 10 mg as needed, up to a maximum of 40 mg per day.

After several months, it became apparent that Mr BM had features of addiction (Box 1).¹ He was using extra (nonprescribed) doses of short-acting opioid every time he felt pain (an additional 40 mg oxycodone per day) and would take another oxycodone sustained release 40 mg tablet (a leftover tablet) some days when the first tablet did not help, none of which he reported to his other GP. He was increasingly focused on his pain and was starting to present early for prescriptions. He was not coping at home or work. His wife had noticed these changes and called your practice to express her concerns.

At Mr BM's next attendance for his prescriptions, he admitted that he was struggling and relying on additional doses of medication to cope. After discussion with you, he acknowledged that he had an opioid dependence. On further questioning, he said he did not feel actually depressed, just flat due to pain. You contacted a pain specialist and an addiction specialist for advice, and they both agreed to see Mr BM urgently. As well as deciding on a treatment agreement, their advice was to refer Mr BM to a local clinical psychologist and physiotherapist for treatment recommended by the pain specialist. After seeing the addiction specialist, Mr BM's oxycodone was ceased and he was commenced on methadone tablets twice daily (this is prescribed for pain relief; liquid methadone is indicated daily for addiction only).

Mr BM returned to your care with clear recommendations, including a strategy to wean the methadone, and with the addiction specialist continuing to prescribe it. You contacted your local pharmacist and he became involved in Mr BM's care plan. You maintained a shared-care arrangement, consisting of the addiction specialist's support on the phone and his methadone prescriptions and your bimonthly reviews of Mr BM.

As the methadone dosage for pain was being decreased, Mr BM told you he was fighting the need to take oxycodone again; he was concerned that he would not cope if the methadone dose were reduced further. You discussed this with the addiction specialist and he transferred Mr BM to a daily liquid dose of methadone, with a plan to continue this for several months and then transfer Mr BM to buprenorphine-naloxone sublingual film daily, with the dose to be weaned down over another few months and then ceased. It should be emphasised that the TGA indication (and PBS listing) for buprenorphine-naloxone, as for methadone liquid, is for the treatment of opioid dependence (i.e. as an OST), not for analgesia. The buprenorphine component, like methadone, reduces withdrawal symptoms and the naloxone component deters misuse by injection (naloxone has little effect sublingually or orally because it is poorly absorbed via these routes but it will cause opioid withdrawal if injected).

After several months, Mr BM felt he could cope without oxycodone and the daily liquid methadone was then changed to buprenorphine-naloxone sublingual film, 24 mg/6 mg daily. Mr BM was relieved to have ceased the methadone, as he felt this was stigmatising. As part of his treatment agreement, Mr BM started with daily dosing of buprenorphine-naloxone, and over time he was able to increase the time between obtaining his medication doses. Several months later, Mr BM ceased all medication. He continued to work during this entire time. Psychological and physical therapy and

1. OPIOID TOLERANCE, PHYSICAL DEPENDENCE, ADDICTION AND PSEUDO-ADDICTION¹

Tolerance

Tolerance is a state of neurophysiological adaptation in which exposure to a drug induces changes that result in a reduction of the drug's effects over time so that the dose needs to be increased to obtain the same benefit. Patients with opioid tolerance have no clinical features of addiction. These patients are recognised as the ones who require a gradual increase in drug dosage over months or years. Opioid tolerance is neurophysiologically related to physical opioid dependence.

Physical dependence

Physical dependence refers to neurophysiological changes and withdrawal symptoms identified by cessation of the opioid or giving an opioid antagonist. It is reversed by re-administering an opioid medication. A patient with physical opioid dependence and adequate analgesia will be generally compliant with the treatment, often stable for months or years, and there are no features of addiction.

Addiction

Addiction (also often termed 'dependence') is recognised as compulsive use of an opioid that interferes with other activities and function, including caring for self, work or family, impaired control of use, cravings and continued use despite known harm. Addiction involves both physical and psychological dependence.

Pseudo-addiction

Pseudo-addiction is physical dependence with psychological and behavioural features of misuse or addiction that ends when an appropriate analgesic opioid dose is provided. It is seen in patients without tolerance or addiction and in those using subtherapeutic doses of opioid, and in patients with changed opioid tolerance. Aberrant or addiction behaviours stop once an adequate dose is provided, and usually only a small increment is required. If the doses keep increasing, consider addiction. If in doubt about the diagnosis, consider seeking a pain or addiction specialist's advice.

2. RECOGNISING PATIENTS AT RISK OF OPIOID MISUSE⁶

Behaviours

- Unscheduled visits
- Noncompliance with treatment
- Early prescription requests
- Lost or stolen medications
- Seeking medications from other sources
- Withdrawal symptoms at appointments
- Increasing pain without disease progression

Opioid assessment tools for patients with pain

- ORT – Opioid Risk Tool
- DIRE – Diagnosis, Intractability, Risk, Efficacy
- SOAPP – Screener and Opioid Assessment for Patients with Pain

the GP's counselling and advice assisted him to manage his persistent pain without opioid medications.

Case 2

Mr GW is a 65-year-old man with a past history of cannabis, heroin and prescription opioid abuse. He was born in a major city and raised in an impoverished and difficult home environment. He fell into opioid substance abuse initially after an injury, and this continued due to the influence of a girlfriend who was also addicted. He has been on methadone OST for many years and describes himself as a 'burnt-out drug user'. He has a regular addiction specialist, whom he sees every six months.

Mr GW has recently moved into your small rural town in the hope of a quiet life. He has not abused any illicit substance in years. He has no mental illness and no major health issues apart from being a cigarette smoker and having stable inactive hepatitis C. He has a supportive friend who lives locally and who has no significant health problems or addiction history.

3. RESOURCES FOR PRESCRIBING OPIOIDS

- NSW Chronic Pain website – the NSW Agency for Clinical Innovation (ACI) Pain Management Network (www.aci.health.nsw.gov.au/chronic-pain)
 - general information and resources for the public and health practitioners on the management of chronic pain
- National Guidelines for Medication-Assisted Treatment of Opioid Dependence – part of the Australian Government's National Drug Strategy (<http://nationaldrugstrategy.gov.au>)
- Opioid treatment accreditation training courses – vary between states and territories, e.g. NSW Health (www.otac.org.au)
- Opioid treatment programs – vary between states and territories, e.g. NSW Opioid Treatment Program – Health Practitioners (www.health.nsw.gov.au/pharmaceutical/doctors/Pages/otp-medical-practitioners.aspx)
- National Prescription Shopping Program (www.humanservices.gov.au/health-professionals/services/prescription-shopping-information-service/)
 - the Prescription Shopping Information Service (phone 1800 631 181) is a 24-hour, seven days a week telephone service to help prescribers assess if a particular patient meets the criteria of the Prescription Shopping Program; if the criteria are met then the patient's prescribed medications can be checked
- State and territory pharmaceutical services units*
 - information provided includes whether a patient is currently receiving opioid substitution treatment or has received it in the past
 - any patient treated with long-term opiate therapy must be registered with the local state or territory pharmaceutical services unit and the doctor must apply for authorisation to prescribe these medications – see the legislation requirements for each state or territory, e.g. NSW Health Form 1: Application for authority to prescribe a drug of addiction, available at www.health.nsw.gov.au/pharmaceutical/Documents/form1.pdf
- Tools for assessing patients with pain when considering opioid therapy
 - Opioid Risk Tool (ORT) – to predict which individuals may develop aberrant drug-related behaviours, e.g. www.aci.health.nsw.gov.au/chronic-pain/health-professionals/assessment

* For contact details of the various pharmaceutical units see Table 1 in the article by Holliday and Jammal titled 'The analgesia tango' in this supplement.

At his first appointment with you, Mr GW asked if you could become his regular GP. A few appointments later, he asked if he could be weaned off the methadone OST as he now felt well cared for and supported by his GP (you) and his addiction specialist. His specialist agreed and in a shared-care arrangement between the specialist and you the GP, Mr GW was gradually weaned off the methadone therapy, rotated to buprenorphine–naloxone and exited the OST program several months later.

Discussion

Prescription opioid drug addiction is an escalating problem.² The patient who

has chronic pain is at higher risk of addiction, and GPs and specialists must find the balance between good pain management and minimising opioid dependence.^{3,4} Patients at risk of developing opioid addiction may have a neurobiological predisposition.⁵ Some of these patients are identified by past and current behaviour, validated tools, regular clinical review and assessment, monitoring of dispensing of prescriptions and speaking with the local state or territory pharmaceutical services unit (Boxes 2 and 3).⁶

Although some patients' cases are more complex and these patients are best managed under the care of an addiction

specialist or a GP who has a special interest in addiction medicine, others can be managed in the community by their GP with support from other health professionals. Whether the problems are addiction, chronic pain or both pain and addiction, these patients also need a GP to provide routine health care.

The cases

In Case 1, Mr BM has a strong desire to reduce and cease opioid medication, as he is aware of the impact the medication is having on his quality of life, family and work. He can be managed in general practice, supported by the local pharmacy. His GP is able to contact both an addiction specialist and a pain specialist for advice. He has no significant mental health issues or other medical problems interfering with his care. There is a clear strategy for the future and Mr BM engages in non-pharmacological strategies to manage his pain, reducing his reliance on medication and assisting in the cessation of the opioid medication.

In Case 2, Mr GW has insight into his situation, recognises the error of his past use and accepts that he has opioid dependence. He has been compliant with treatment and medical advice and has some social support and a stable lifestyle. He, too, has no significant health problems and requires a GP to provide routine health care. He may have assumed that he needed to be on OST for life, but good care and support by his GP provides him with an opportunity to wean off OST.

GP-provided care

Examples of care that GPs can provide to opioid-dependent patients as well as monitoring their OST are:

- providing routine health checks
- treating health issues that may arise
- arranging supportive counselling (either by the GP or by a psychologist)
- co-ordinating specialist care and communication
- seeing patients regularly to assess pain management and medication use

- screening and early intervention if patients are using nonprescribed medications
- acting as a 'sounding board' for patients considering alternative therapy or complementary medicines
- keeping an accurate record of medications and health problems
- being a health professional the patient can trust and who provides support if he or she is going through a difficult time.

The management of these patients depends on you, the GP, as the specialists are unable to see these patients frequently. These patients require regular review and general health care. Stable patients with addiction issues or patients taking medications for pain who are opioid dependent can, and ideally should, be managed in routine general practice. Most of the care is the same as that which would be provided to other patients. The only difference is the need to monitor their OST or opioid use. This involves the occasional need for a longer consultation, with you, the GP, having the confidence to help these particular patients and the skill to establish a rapport with them, so that they feel comfortable with you as their doctor. It may encompass a good understanding of psychological medicine and counselling. It is useful to have affiliations with allied health professionals such as psychologists or physiotherapists with whom you could share the load. If managing these patients seems daunting, several educational resources can be of assistance (Box 4).⁷

Helping opioid-dependent patients also involves familiarity with the various state and territory regulations regarding prescribing opioids to patients with non-cancer pain and the management of patients with addiction. OST training and official recognition as an OST prescriber is required for GPs who would like to care for individuals on methadone (Box 3). Depending on legislation, other doctors may choose to care for patients on OST

4. POSTGRADUATE EDUCATION ON MANAGING PATIENTS WITH ADDICTION

- GP learning modules: Alcohol and other drug problems; Effective pain management in general practice; Addictions; Communication skills. (<http://www.racgp.org.au>)
- Discipline of Addiction Medicine, The University of Sydney (<http://sydney.edu.au/medicine/addiction/lectures/index.php>)
- ACRRM Addiction medicine online education modules (acrrm.org.au)

in a shared care arrangement with an addiction specialist. Some states and territories allow a GP this arrangement for up to five patients who are taking buprenorphine with naloxone. **MT**

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The analgesia tango

Chronic pain cases from a general practice

SIMON HOLLIDAY BMed(Newc), FACHAM, FRACGP, FACRRM, DA(UK), DipRACOG, GradDipA&DSt(Adel)

WALID JAMMAL MB BS, FRACGP, DCH, MHL

Complex cases of patients with pain who have developed opioid dependence are often managed by GPs with a special interest and expertise in pain and addiction issues, with specialist advice as needed. Four complex cases of opioid dependence are discussed.

KEY POINTS

- Opioids are indicated for acute analgesia, analgesia at the end of life and dependency management, and at times are prescribed for patients who have chronic pain resistant to other treatments.
- Opioid monotherapy for patients with chronic pain should not be relied on as the safety and efficacy of long-term use of opioids is not established. Other care for chronic pain should involve lifestyle and psychological management.
- The assessment and management of addictive behaviours requires a therapeutic, not a judgemental, approach.
- Addictive behaviours should determine how opioid analgesics are prescribed, rather than if they are prescribed. These behaviours determine the balance between usual prescribing and dispensing versus the structured approach of opioid substitution treatment.
- Training to become an authorised opioid substitution therapy prescriber may increase comfort about opioid management.



GPs face many clinical, ethical and regulatory challenges. These challenges often arise when treating patients with chronic nonmalignant pain. With the increasing use of pharmaceutical opioids, more patients are developing opioid dependence and need treatment for this as well as the condition for which they are taking the opioids. Opioid-dependent patients can be particularly demanding to treat, requiring quality time, and so may become our ‘heartsink’ patients. Becoming an authorised opioid substitution therapy (OST) prescriber should increase comfort about opioid management.

This article discusses several complex cases of patients with chronic pain who have developed dependence on their opioid analgesics. One author (SH) is a GP with expertise in the area of drugs and alcohol issues, and the other (WJ) is a GP with expertise in the medicolegal field. Here they reflect upon and discuss responses that ensure clinical safety and compliance with government regulations.

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Dr Holliday is a General Practitioner in Taree; Staff Specialist in Drug and Alcohol Clinical Services, Hunter New England Local Health District; and Conjoint Lecturer in the School of Medicine and Public Health at the University of Newcastle, Newcastle, NSW.

Dr Jammal is Senior Medical Advisor, Avant Mutual Group, Sydney; a General Practitioner in Bella Vista, Sydney; Clinical Lecturer, Faculty of Medicine, University of Sydney; and Conjoint Lecturer, School of Medicine, University of Western Sydney, Sydney, NSW.



Case 1

One Friday evening, before a long weekend, you are the only GP remaining in the surgery. A regular patient of a colleague telephoned reception late this afternoon and although there were no appointments she was told, as is the practice policy, that she would be seen if it was urgent.

The patient, 35-year-old Ms H, has now arrived in the surgery, with several of her very active children. She requests a prescription for her usual oxycodone tablets for her chronic neck and back pain, saying she needs it quickly, before the pharmacy closes. She explains that in response to leaving her violent partner, she prematurely ingested over the past few days a week's supply of the painkiller and the pharmacist would not dispense her next authority prescription. She says she is feeling dizzy and she is clearly distressed from her chronic pain.

What would you do first?

Ask your receptionist to supervise the children in the waiting room so you can speak freely with Ms H.

First establish that Ms H has somewhere safe to stay with the children. If this is not the case, you must by law inform the police (given it is evening) or the Department of Community Services. The details of mandatory reporting requirements for domestic and family violence and child abuse vary between Australian states and territories. Are all the children with her now?

You then need to find out how Ms H is coping, especially with regard to her children. Could this ingestion of oxycodone be a cry for help, or even a failed suicide attempt? Is she significantly depressed? You need to explore her medical, psychiatric and drug and alcohol history, and then assess her chronic pain condition.

During the discussion you establish that Ms H's way of coping

is to misuse her painkillers. Although you may suspect that this is 'drug-dependent' behaviour and that her dizziness may indicate oversedation, it could also quite reasonably be a cry for help. This needs to be discussed openly and empathetically with her.

Assuming Ms H has somewhere safe to go and is coping, would you give her the script as requested?

Ms H is in a crisis situation. Saying 'no' to prescribing an opioid for a patient considered from their behaviour to be drug-dependent needs to be done with compassion and sensitivity and with an honest explanation. In such circumstances, saying 'yes' would be deemed unlawful. Unfortunately, compassion is no defence. In this situation you can explain to Ms H that you are concerned the opioids she has taken are making her dizzy and unwell and that she needs to be alert, given her home situation and the fact her young children depend on her. It is important to discuss with her other techniques for managing pain (e.g. heat, anti-inflammatories), as this emphasises that you understand her discomfort is genuine. If she insists on another prescription, you must tell her she needs to be assessed at the local hospital because it is not legal for you to prescribe opioids for her.

Ms H has many features that indicate problematic opioid use and there are multiple common factors associated with this, including concerns about domestic violence, possible homelessness, the welfare of her children and possible suicidality. A recent meta-analysis indicated that about one in four patients taking opioid analgesics long-term are misusers and one in 10 are addicted.¹ In the case of Ms H, there is clear misuse with her 'chemical coping' in the form of premature ingestion of her pills. Such behaviours would make it unlawful in all Australian states and territories to concede to her request for a prescription for oxycodone. Many doctors have been sanctioned for prescribing in such situations. You may feel more comfortable about refusing to prescribe opioids if a sign is placed in the waiting room stating no opioids are prescribed at a first consultation or without a comprehensive assessment.

This patient's need for an opioid prescription may seem compelling. However, it is safest for her and her children to see your colleague, who knows her well, as soon as possible. As this is an evening consultation there is little time for a detailed assessment and discussion about OST. Your colleague can also confirm Ms H's identity (if needed) and check for injection marks if you have not already done so, attempt to call any previous doctors and, if thought necessary, request a urine drug screen. He/she may also check the Prescription Shopping Information Service, although this is a delayed and limited service (<http://www.humanservices.gov.au/health-professionals/services/prescription-shopping-information-service/>). If you are in Tasmania, the Tasmanian Department of Health and Human Service's Electronic Recording and Reporting of Controlled Drugs service may be accessed.

Generally, it is not advisable to hand an opioid script to individuals at risk of dependency problems as some may forge an

TABLE 1. PHARMACEUTICAL SERVICES UNIT WEBSITES

State	Useful websites
Australian Capital Territory	ACT Health: www.health.act.gov.au/public-information/businesses/pharmaceutical-services
New South Wales	NSW Ministry of Health: www.health.nsw.gov.au/pharmaceutical/doctors/Pages/default.aspx
Northern Territory	NT Department of Health: www.health.nt.gov.au/Environmental_Health/Medicines_and_Poisons_Control/index.aspx
Queensland	Queensland Health: www.health.qld.gov.au/clinical-practice/guidelines-procedures/medicines/default.asp
South Australia	SA Health: www.sahealth.sa.gov.au/wps/wcm/connect/Public+Content/SA+Health+Internet/Clinical+resources
Tasmania	Tasmanian Department of Health and Human Services: www.dhhs.tas.gov.au/psbtas
Victoria	Victorian Department of Health & Human Services: www.health.vic.gov.au/dpcs/index.htm
Western Australia	Western Australia Department of Health: www.public.health.wa.gov.au/1/872/2/medicines_and_poisons.pm

increased amount of the medication. Instead, telephone and then fax the managing pharmacy a one- or two-day script, contingent on daily doses being consumed at the pharmacy. Arrange a follow-up appointment for the patient in a day or so, allowing time for more detailed care. However, ask your staff to confirm on the day that the patient is still coming as they may only have wanted the script and not the supervision.

18 months later

Ms H had a car accident six months after your first consultation and her opioid doses have all increased since then. She is now, a year after her accident, taking paracetamol/codeine 500 mg/30 mg two tablets three times daily, oxycodone immediate-release 5 mg three times daily and oxycodone slow-release 20 mg twice daily. She has seen a rehabilitation specialist, who approved her opioid analgesics, and a neurosurgeon, who placed her on a surgical waiting list of several years' duration.

Ms H has been seeing all the doctors and locums at your practice and offers an impressive range of narratives requiring early scripts and preventing her from

having blood tests, urine screens and routine health checks (including Pap smears) as requested. Today she sees you and states that all her Schedule 8 drugs were stolen from her house and so she needs the scripts repeated. You ask whether the crime has been reported to the police; she says she has done so and the police said they could do nothing as she had left a window open.

What would you do?

You tell Ms H you want to support her by phoning the police yourself to add weight to her story but she interjects, claiming she meant to say she was going to contact the police. You invite her to go and report the crime to the police now, before continuing the consultation.

After her return, you tell Ms H that you are concerned about her apparent loss of control with her opiates. You advise her that a drug treatment program would be helpful. You explain the treatment and offer her methadone or buprenorphine–naloxone and she chooses the latter. You contact your state or territory health department pharmaceutical services unit and seek an authority/permit to prescribe her OST (Table 1; see Case 2 for discussion of dependency).

The next few years

Over the next year, Ms H's presentations at the surgery decrease and become more orderly. Her care includes a Pap smear, serology for hepatitis B and C and vaccination for hepatitis B, and prescription of a range of coanalgesics. She is pleased to be more involved with her children.

After two and a half years of taking buprenorphine–naloxone, Ms H is generally stable and has no injection marks. Her pain and analgesia are now not dominating her life. This success is largely due to greater stability and support in her home life.

However, another year later Ms H reports increased domestic violence from her intermittently estranged de facto partner. On one occasion he accompanies her into the consulting room where he becomes demanding and belligerent before storming out of the surgery. You emphasise to him as he leaves that he is not to attend this surgery again, and that you will be forced to call the police if he does.

How would you manage this situation?

You need to determine again whether Ms H or her children are in danger. She denies this and you tell her how to access a refuge or organise Apprehended Violence Orders if necessary.

Missing appointments

At the next visit Ms H is very agitated about her oldest son who has been imprisoned recently. She is now repeatedly missing appointments, apparently to visit her son. You notice bruises on her left antecubital fossae, which she says are from being bitten by her pet lorikeet. You explain to her the bruises look as if the vein has been penetrated by a needle rather than by a bite from a bird, but she dismisses this. You now need to spend some time assessing her mental state and general coping skills. You need to ask her directly what medications (prescription and over-the-counter) and street drugs (if any) she is taking. You decrease the proportion of take-away doses of buprenorphine–naloxone she receives so she needs to

consume more under the supervision of the pharmacist.

The following month Ms H misses her appointment again. When she does present, she says her daughter's appendix had burst and while she was attending to this out of town she had to buy street buprenorphine-naloxone to stop withdrawal symptoms. You explain to her that, by law, she needs to obtain these medications only from you, as her registered prescriber, and that if she is ever again without these medications, she needs to present to a doctor or hospital and ask them to contact you. You remove all take-away privileges and shorten the duration of each script.

The pharmacist phones you a few days later to say Ms H refuses to dose correctly and keeps causing scenes, and that they believe she is doctor shopping again. A letter requesting a transfer of Ms H's notes then arrives from another practice. You notify your state's pharmaceutical services unit of her behaviour and of her transfer of care to the other practice.

Re-presentation two years later

Ms H presents to you two years later, asking to be put on the buprenorphine-naloxone program again. She says she has been getting fentanyl patches regularly from her GP for her chronic pain, and has been injecting fentanyl extracted from these patches up to 30 times a day, topping up with street fentanyl and using heroin if there is no fentanyl available. She says she finds withdrawal from fentanyl far worse than from heroin. You note that she has many injection marks (Figure 1).

You contact Ms H's GP, who says Ms H has been doing well and expresses surprise that you believe she is opioid-dependent and needs treatment for this. The GP is unaware that Ms H has received OST before. Furthermore, the GP had checked with the Prescription Shopping Information Service, registered Ms H with the state health authority and had been reducing her fentanyl dose. The GP had not referred her to the local drug and alcohol services because of the long waiting time.

Ms H is commenced on buprenorphine-naloxone again.

Case 2

Mr L, a 35-year-old chef, recently left a large city in the neighbouring state to be closer to his family after the breakdown of a long-term relationship. Seven years previously he had been sexually assaulted and had a lumbar disc prolapse. He has been taking 40 mg oxycodone twice daily since then. He has been trying to decrease this and has reduced the dose himself to 20 mg twice daily. He has now run out of tablets, has withdrawal symptoms and is distressed. He requests a script for more oxycodone.

Mr L has a history of childhood sexual abuse, depression and post-traumatic stress disorder following the assault. His drug and alcohol history includes cigarettes (tobacco), the consumption of 10 to 14 standard drinks over an evening approximately twice a month and the use, several years ago, of oral and intravenous amphetamines, 'ice' and ecstasy. Cessation of these stimulants has led to Mr L gaining weight. He has a family history of alcoholism and diabetes.

Mr L says that if he does not take oxycodone he has withdrawal symptoms of agitation, myalgia, cramps and diarrhoea. He used to rely on his ex-partner's buprenorphine-naloxone to treat his withdrawal symptoms. He denies injecting his painkillers apart from once about six years ago, and says otherwise he always uses the oxycodone as prescribed. His other medications are venlafaxine 300 mg daily and diazepam 5 mg half to one-tablet daily.

On examination, Mr L is overweight. He becomes teary when discussing the sexual assault. He is clammy with slightly dilated pupils, and has no injection marks. He moves slowly, maintaining a protective posture, and is mildly hypertensive.

What would your care involve over the next few visits?

You provide Mr L with some educational resources (e.g. those available on the Hunter Integrated Pain Service website, www.hnehealth.nsw.gov.au/pain).



Figure 1. Ms H's injection marks at presentation two years later.

Regarding his medications, you advise Mr L to cease the diazepam. You provide him with a prescription for 28 tablets of oxycodone 10 mg (dosage, one tablet three times daily), with the daily dose to be dispensed from the pharmacy, and negotiate to wean this down to zero over the next three months. You also commence him on ibuprofen and fish oil.

You tell Mr L that you will discuss with him the exclusion of sexually transmitted infections at the next visit. Depending on where you are practising, you need to consider if you have a legal requirement to phone your state or territory health regulatory body for authority to prescribe opioid analgesics for Mr L (Table 2).

Is Mr L opioid dependent, and what are the regulations on dependency?

Confusingly, the rules and definition of 'drug dependence' are different in each Australian state and territory; however, in each of these an authority (or permit) is required to prescribe opioids for drug-dependent patients. It is important to note that this requirement refers to the legal definition of dependence. This legal definition varies in its concordance to any clinical understanding of the meaning of dependence. As such, prescribers are obliged to practise in accordance with their local laws and regulations. These may change; the *NSW Poisons and Therapeutics Goods Act* for example is now undergoing review. More details are available at the

TABLE 2. A GUIDE TO THE REGULATORY REQUIREMENTS FOR PRESCRIBING SCHEDULE 8 DRUGS FOR NON-DRUG-DEPENDENT PATIENTS

State	Requirements
Australian Capital Territory	Authority required if prescribing for longer than two months
New South Wales	Specific drugs require authority if prescribed more than two months. These are: alprazolam, injectable drugs of addiction, buprenorphine (except transdermal preparations), flunitrazepam, hydromorphone and methadone
Northern Territory	Notification may be required – complex rules apply (see NT pharmaceutical services unit website)
Queensland	Notification and treatment report required if prescribing for longer than two months
South Australia	Authority required if prescribing for longer than two months
Tasmania	Authority is required if prescribing for longer than two months – note special requirements for alprazolam
Victoria	Permit required if prescribing for longer than two months
Western Australia	Authority is required if prescribing for longer than 60 days

various state and territory pharmaceutical services unit websites (Table 1). Regulatory requirements for prescribing for non-drug-dependent patients are listed in Table 2.

What would be the focus of Mr L's psychological care?

As Mr L initially presented distressed and in opioid withdrawal his mood requires reassessment after his opioid treatment is stabilised. You need to consider his current situation, past trauma, grief, depression, alcohol intake, benzodiazepine and opioid withdrawal symptoms and pain. Patients such as Mr L who have complex past histories often benefit from additional psychological or psychiatric care and may require medication for depression or anxiety.

How would you provide psychological management of Mr L's pain?

A Cochrane review indicated that cognitive behavioural therapy has small to moderate effects on several chronic pain outcomes.²

Psychological management of patients with chronic pain, which the GP may carry out or refer for, includes:³

- pain education
- identifying goals and dividing these into achievable, concrete and measurable subgoals
- teaching skills to achieve the subgoals, e.g. activity pacing or planning daily specific exercises or tasks
- teaching active self-management skills, e.g. dealing with barriers in reaching goals, dealing with flare-ups and problem-solving
- identifying and challenging unhelpful thoughts, e.g. black and white thinking, catastrophising and fear of movement.

Would you measure Mr L's pain outcomes?

You decide to measure Mr L's pain outcomes to assess his current pain and provide a benchmark for evaluating his therapy over time or with different providers. The simplest way to do this is by using the three-item PEG scale, which measures the pain outcomes of pain intensity, enjoyment of life and general activity (Figure 2).⁴ This, and other useful resources and links, are available on the website of the National Drug and Alcohol Research Centre (NDARC) at the University of New South Wales (<https://ndarc.med.unsw.edu.au/content/gp-toolkit>). It usually takes less than a minute to score this test the first time, and subsequent scoring is even quicker.

Would you address Mr L's smoking?

Mr L says smoking is his only vice and that it calms him down. You should discuss with him how he is coping overall and how he feels about continuing or ceasing smoking. Given that

smoking has been consistently linked to pain/opioid outcomes,^{5,6} you could discuss whether he would like to address his smoking. There have not been the neuropsychiatric adverse drug events reported with the use of nicotine replacement therapy as with the use of varenicline. However, a recent small trial indicated that varenicline may have a role in assisting with opioid analgesia detoxification independent of smoking status.⁸

Case 3

Ms W, aged 28 years, presents for antenatal care when she is nine weeks' pregnant. She had been on a methadone program following a jugular vein thrombosis from injecting fentanyl extracted from patches. She withdrew from the program six months previously. She says this was because she and her partner had been doctor-shopping for fentanyl patches again and she was worried this would be discovered.

How can you check what Ms W has been prescribed?

As well as the Prescription Shopping Information Service mentioned in Case 1, the PBS Third Party Information Service (<http://www.humanservices.gov.au/customer/forms/2690>) can also provide information on what has been prescribed to an individual. (A signed cover letter should be sent with the completed application form for this information request.)

How would you manage Ms W's dependence?

You offer OST to Ms W and she accepts, saying she hated doctor shopping because it was stressful to lie to doctors and she detested the withdrawal symptoms.

While you prepare the paperwork required for the OST, Ms W tells you how she accessed the fentanyl patches. She would book to see five or six GPs a day and then she would provide each with a referral letter from her GP to a specialist stating she had vertebral fractures from a car accident. She would explain that she was getting some physiotherapy and had too much pain to be able to care for her sick grandmother. Once she has asked for the script, she would distract the GP by discussing her epilepsy until the consultation time was finished. These presentations led to her being given fentanyl patch scripts from about 80 to 90 doctors; only about a dozen refused to provide her with a script. She injected part of a patch six times a day in her feet or arms. She says a couple of doctors checked her blood pressure and potentially would have seen the multiple punctures on her arms. However, none ever asked her about them.

Pain intensity, enjoyment of life, general activity (PEG) assessment tool

1. What number best describes your pain on average in the past week?

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

2. What number best describes how, during the past week, pain has interfered with your enjoyment of life?

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

3. What number best describes how, during the past week, pain has interfered with your general activity?

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

Figure 2. The PEG pain assessment scale, derived from the Brief Pain Inventory.⁴

What prevents doctors being more cautious and structured in their opioid prescribing?

Several studies have addressed the questions ‘What barriers prevent doctors using “Universal Precautions” when prescribing opioids?’ and ‘Why do doctors not actively offer structured opioid prescribing as per an OST program?’^{8,9}

The concept of Universal Precautions (UPs) was developed after the advent of HIV/AIDS to reduce the risk of the transmission of infection. It described minimum standards of care for all patients, regardless of their perceived or confirmed infectious status. Introducing UPs for chronic nonmalignant pain would systematise attention to the dimension of dependency when prescribing opioids. Rather than reserving harm minimisation strategies for those patients with confirmed dependency, doctors would systematically assess pain and addictive disorders along a continuum. They would manage the nuances of any behaviours suspicious of addiction as routinely as they currently manage cardiac risk factors. This would normalise flexibility in the degree of supervision and structuring for all opioid treatments.¹⁰

The barriers for GPs commencing OST for their patients involve stigma or fear about dealing with drug addicts. For opioid analgesia UPs, doctors struggle to determine the genuineness of a patient’s pain and the truthfulness of the patient.¹¹ They describe apprehension about performing ‘law enforcement’ activities. For both strategies (OST and UP), doctors blamed limited time and resources. An important facilitating factor promoting UPs for both doctors and patients was the concept of better protection of patients from the potential harms of high-risk opioid medications.

Many doctors feel uncomfortable being forced into the position of a police officer or a judge and the action of trying to assess the

genuineness of the pain or the truthfulness of the patient.¹² This approach can be contrasted with a patient-centred approach using a benefit-to-harm framework to make and communicate decisions about opioid treatments.¹²

Completing the training to become an authorised OST prescriber should increase comfort about opioid management as well as being associated with increased adherence to pain management guidelines.^{8,13} OST training, which is provided by state and territory governments, involves attending face-to-face metropolitan and regional courses, although on-line training is offered in New South Wales and Victoria.

What else would you do for Ms W?

For Ms W, given her partner is still injecting fentanyl, an additional harm minimisation strategy may be the prescribing of naloxone. This has been implemented systematically in some health systems in the USA and observational studies have described associations with reductions in fatal overdose rates.¹⁴

Ms W is referred to the local hospital for antenatal care. She is encouraged by the social worker to return to the addiction specialist who runs the methadone program and to discuss the best option for her and her baby.

Case 4

Mr K, aged 53 years, has a massive cirrhotic liver from hepatitis C and alcohol abuse. When he reached the palliative phase of his illness, he had ceased his methadone program and had been commenced on fentanyl patches. He describes severe pain, tiredness and breathlessness, and is hardly able to walk due to his

massive ascites. His estranged partner, still on methadone, and their 9-year-old son have returned to live with him to care for him during his terminal illness.

Mr K invariably requires his scripts early, stating the patches fall off because of his heavy sweating.

How would you manage Mr K's terminal care opioid analgesia?

With increasing numbers of people developing cancer and the palliative phases of illnesses becoming more prolonged, it is not surprising that doctors are seeing addictive-type behaviours among palliative care patients. Regardless of any concerns about Mr K's misuse, it would be unethical to suddenly terminate his opioid analgesia. However, the usual regulatory requirements of seeking authority would apply. As before, when concerned about aberrant opioid behaviours, prescribers can simply increase the opioid therapy structuring, as exemplified in an OST program. Due to the stigma associated with OST, there are particular barriers towards using this type of approach. Potentially, community nurses could be involved in the storage, application, removal and disposal of each patch. Another alternative that may be safe and effective in patients with hepatic failure is buprenorphine, as described in case reports.¹⁵

Mr K and his partner, incidentally, were widely known to be diverting most of the fentanyl patches onto the black market. A single 100 mcg patch may be cut into 10 portions and sold for the usual price of a cap of heroin (i.e. about \$50 each).

Whole-patient care

Opioids are essential medicines for acute and terminal analgesia and for dependency management, and may at times be prescribed for patients who have chronic pain resistant to other medications or treatments. However, the safety and efficacy of opioids for long-term use in chronic non-cancer pain lack the support of quality evidence of over 12 weeks' duration.¹⁶ For this reason, as GPs, we need to be comfortable providing quality care to such patients

without relying on opioid monotherapy. This care will involve active psychological management, encouraging active self-management and recognising the limitations of most medications in the treatment of patients with chronic nonmalignant pain.

Conclusion

GPs should be familiar with the strategies of UPs and OST. Further information about assessment and management of opioid dependence is provided in other articles in this supplement.

With training, all interested GPs can develop the skills, knowledge and expertise to be able to prescribe methadone or buprenorphine–naloxone as OST. Such expertise will enable GPs to better manage pain and/or opioid dependency independently and in a positive manner, with advice from the local drug and alcohol clinic or the regional addiction medicine specialist. It is certainly in the interest of most patients with chronic pain who have become opioid-dependent to maintain continuity of care with their GP over the long term. After all, their chronic pain may well be incurable and their potential for opioid misuse is also long-term. **MT**

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