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Opioid use in chronic non-cancer pain

Part 1: Known knowns and known unknowns

Background

Opioids have a critical, time-limited role in our management of acute and terminal pain and an open-ended role in our management of opioid dependency. They also have a use in the management of chronic non-cancer pain.

Objective

To provide an understanding of what is known, and what is not known, about the use of opioids in chronic non-cancer pain using an evidence-based approach.

Discussion

For chronic non-cancer pain, the evidence base for the long-term use of opiates is mediocre, with weak support for minimal improvements in pain measures and little or no evidence for functional restoration. Much research and professional education in this field has been underwritten by commercial interests. Escalating the prescribing of opioids has been repeatedly linked to a myriad of individual and public harms, including overdose deaths. Many patients on long-term opioids may never be able to taper off them, despite their associated toxicities and lack of efficacy. Prescribers need familiarity with good opioid care practices for evidence-based indications. Outside these areas, in chronic non-cancer pain, the general practitioner needs to use time and diligence to implement risk mitigation strategies. However, if a GP believes chronic non-cancer pain management requires opioids, prescribing must be both selective and cautious to allow patients to maintain, or regain, control of their pain management.

Keywords

opioids; chronic pain

CPD

Since antiquity, opium has played an important part in society and culture, weaving between medicine and commerce, pleasure and pain (*Figure 1* and *2*).[1] The 1960s Hospice Movement in the West fought oppressive regulations to make opioids accessible for symptomatic management of cancer pain following completion of active disease treatment.[2] Palliative care grew to take responsibility for symptom management in illnesses that were not immediately fatal but still required disease modifying treatment, such as HIV.[2] In the 1990s, palliative care specialists extended their guidelines to the general practice management of all chronic pain.[2,3] This was done without research, evaluation or meaningful input from general practitioners.[3] This shift has seen massive prescribing increases with the total number of Pharmaceutical Benefits Scheme opioid prescriptions increasing about 300% between 1992 and 2007.[4] Most opioids are being prescribed by GPs with only a minority being for cancer pain or for new problems (3.5% and 14.3% respectively).[5–7] This article reviews some of the controversies concerning the opioid management of chronic non-cancer pain (CNCP).

Indications and definitions

The main indications for prescribing opioids are for the management of opioid dependency, acute pain, terminal pain and for CNCP.

Opioid dependency has been treated with long term opioid substitutes for half a century. The risk mitigation strategies of opioid substitution therapy have found backing in over 30 randomised controlled trials (RCTs).[8]

Acute pain is a major perioperative focus of anaesthetists, but up to 41% of postoperative patients experience significant pain.[9] Moves to preference regional anaesthesia and multimodal analgesia rather than unimodal opioids aspire to improved pain relief with reduced opioid side effects.[9] These side effects include nausea, respiratory depression, acute tolerance and opioid induced hyperalgesia.[9] (Hyperalgesia being defined as an increased response to a stimulus which is normally painful.) Controversies as to the precise ending of the anaesthetist's responsibility

Figure 1. Mid-nineteenth century marketing saw the synthesis of opioids such as morphine, which was sold as a therapy for teething children

Figure 2. Diacetylmorphine ('heroin') was marketed as an over-the-counter 'non-addictive morphine substitute' for cough suppression from 1898 to 1913 and remains a prescription medicine today in the United Kingdom.

Cannabis, cocaine, nicotine and barbiturates have all variously been marketed as analgesics[1]

for analgesia[9] resemble the dilemmas faced by the GP, as acute pain becomes acute-on-chronic pain. A 10 year prospective study of acute back pain revealed a course of unpredictable recurrence in which recovery was often a temporary state, making it acute-on-chronic pain.[10]

Cancer pain used to be rapidly terminal, but this time-limiting boundary has blurred. Since 1982 in Australia, cancer 5 year survival rates have increased from 47% to 66%.[11] In the oncology community, opioids have been the cornerstone of management utilising a self titration model (liberal access, a months supply per prescription, minimal monitoring, take as much as you need).[12,13] The prevalence of abuse or addiction among cancer patients is unclear,[13] with 1980s surveys reporting rates of 0–4%.[14] However, in a cancer centre among a subgroup subject to urinary drug screening, the prevalence rate was 44.2%.[14,15] Hitherto, oncologists have regarded as foreign the risk mitigation strategies derived from opioid substitution therapy and more recently CNCP.[12,15] However, both acute and cancer pain services increasingly encounter problems such as hoarding, diversion (defined as any transfer via giving, borrowing, selling or theft), misuse (defined as use other than as directed, whether intentional or not) and addiction.[12,13]

Chronic non-cancer pain is usually defined as pain persistent beyond 3 months, deemed the duration of tissue healing.[16,17] Chronic non-cancer pain may be time-unlimited, although an annual recovery rate of 9.4% was reported in a Danish study.[2,18] Rather than treating the original acute cause, which may no longer exist, therapy serves to suppress the perceived pain.[17] The manner in which sensory stimuli become transformed into perception is complex and highly variable and involve genetic, environmental, cognitive and emotional processes.[19]

Chronic pain among Australian adults has a prevalence of almost 20%.[16,20] This prevalence is rising and the reason for this may be either apparent, from improved recording, or else real, from improved survival post-major trauma, cancer or heroic life-preserving treatments.[2,21] Pain's increasing prevalence is often equated to its undertreatment.[2,21] In 2010, the National Pain Summit agued that over 90% of Australians with chronic pain suffer undertreatment of pain making this 'the developed world's largest "undiscovered" health priority'. Most pain management advocacy has been funded by opioid manufacturers and, pharmacologically, tends to focus on improving access to opioids.[1,20–22]

Evidence about net benefits

The goals of CNCP treatment have been described as improved pain scores, function and quality of life.[23,24]

The watershed study supporting opioids for CNCP was a retrospective 1986 study of 38 patients treated in a cancer centre. Pain relief was reported by 24 and only two, both with a history of drug abuse, gave management problems.[25] Another oft cited follow up study tracked 233 selected patients on oxycodone for CNCP up to 3 years (mean duration of treatment 541 days).[26] The trial was sponsored by Purdue Pharmaceuticals and investigators were required to inform the sponsor whenever a patient showed drug seeking behaviours. Mean average pain intensity score out of 10 declined from 5.1 at commencement to 4.4 at 3 months. Average pain intensity worsened by three or more points in only 44%, permitting the conclusion that long term opioid therapy (LtOT) may provide sustained pain relief. The sponsor peremptorily terminated the study for 'administrative reasons' with only 39 patients completing 3 years.

A United States multidisciplinary expert panel identified 37 key questions requiring an answer to generate an evidence basis for the development of prescribing guidelines. A systematic evidence review was commissioned.[27] For virtually every key question, the findings identified important research gaps with critical weaknesses in the evidence.

A Cochrane review in 2009 of non-tramadol opioids in osteoarthritis identified 10 RCTs eligible for inclusion.[28] All trials claimed to be double-blind, but only three showed adequate randomisation and concealment. No study reported non-commercial funding sources. Median treatment duration was 4 weeks. Opioids gave better pain relief than placebo (2.7 cm vs 1.8 cm respectively on a 10 cm visual analogue scale). Function improved more than

placebo (1.9 units vs 1.2 units on a scale of 1 to 10). Side effects of opioids against placebo were more commonly enough to withdraw from the study (69 vs 17 per 1000 patient years: relative risk 4.05) and more commonly of a serious nature (13 vs 4 per 1000 patient years: relative risk 3.35). The Cochrane review concluded that the small to moderate beneficial effects were outweighed by large increases in the risk of adverse events.[28]

A 2010 Cochrane review found 26 studies of LtOT in CNCP eligible for inclusion that involved 4768 participants.[29] With few exceptions, they were open label case series, had commercial sponsors and excluded past substance abusers. The review found all studies were of low internal validity. For those able to remain on LtOT there was weak evidence that pain scores were lowered, although the effect on quality of life was inconclusive. Overall, the evidence for LtOT effectiveness was considered too sparse to draw firm conclusions.[29]

A 2011 Cochrane review of opioid use in rheumatoid arthritis included 11 RCTs.[30] None were considered at low risk of bias or lasted more than 6 weeks. A net benefit to harm calculation found no difference between opioids and placebo.

The most commonly prescribed pharmaceutical in the US is an opioid.[31] Yet compared to other medications, the evidence base for the effectiveness of LtOT is negligible.[22] A review noted there were about 1.8 million person years of observation in trials of medications for hypertension, three-quarters of a million person years for lipid lowering medications, but only 1500 person years in randomised trials of opioids for CNCP.[22]

Any evidence about efficacy from short term observational trials has not generalised to long term opioid use in less carefully selected and managed patient populations.[3] A Danish population wide epidemiologic study interviewed 1906 individuals with CNCP.[23] Those using opioids did not seem to be achieving the usual goals of pain management. Opioid use was significantly associated with: the reporting of severe pain, poor self rated health, inactivity during leisure, unemployment, higher healthcare utilisation, living alone and lower quality of life. In a prospective study of US workers with compensable back injuries, use of LtOT was associated with improved pain or function in only 27% and 16% respectively.[32] A Danish population study found the odds of recovery from chronic pain was decreased fourfold in individuals using opioids.[18]

The cessation of LtOT may actually improve outcomes. In 704 consecutive admissions to a US interdisciplinary chronic pain treatment program, all entrants on LtOT were tapered off. At admission those on LtOT had worse affect, sleep and mobility than non-opioid users. Both groups improved pain and function but those admitted on LtOT had similar or higher improvements.[33]

Overall, there does seem to be weak evidence of a short term improvement in pain levels with the use of opioids for CNCP in observational studies with no conclusive improvement in function or quality of life.[3] The studies had several risks for bias with one review noting 78% of the efficacy trials had pharmaceutical funding.[34] Conversely, in population studies, LtOT seems to be associated with worsening of outcomes, in terms of pain, function and recovery.

Evidence about adverse effects

Long term opioid therapy may cause adverse effects on the respiratory, gastrointestinal, musculoskeletal, cardiovascular, immune, endocrine and central nervous systems.[27,35] However, the evidence base on harms is limited being based on efficacy trials which have lacked the statistical power to detect uncommon problems or the duration to detect long term problems.[19,27] This precluded some meta-analyses from determining their incidence or significance.[19,27,29] However, a systematic review about older CNCP patients on LtOT reported constipation occurred with a median frequency of 30%, nausea 28%, dizziness 22% and somnolence 21%.[34] Long term opioid therapy is also associated with 1.4 increased relative risk of fractures in the elderly[35] and increased mortality;[18] in one review 87%.[35] Long term opioid therapy is related in a dose responsive pattern to sleep apnoeas (up to 75% vs 3–20% general population).[35,36] This may contribute to the high proportion of LtOT decedents being found in their beds.[36]

Overall, we have some evidence about the rates of the more common side effects of LtOT and emerging concerns about the adverse effects that are serious but uncommon or that are slow to develop. A useful guide for patients may be found in Baldini et al[35] (www.ncbi.nlm.nih.gov/pmc/articles/PMC3466038/table/tbl1).

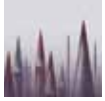
Evidence about discontinuation of opioids

Discontinuation rates are frequently higher in observational trials than in population studies, perhaps due to those ceasing treatment early not being picked up in population studies.[24] In a Swedish study 3 years after the commencement of opioids, only 51% of cancer and 27% of non-cancer patients continued LtOT.[17] However, as in many observational studies, it was unclear whether this was due to improvement in underlying condition, lack of benefit or adverse effects.

However, once established, LtOT is infrequently tapered or terminated.[24] A US healthcare data study of those prescribed opioids continuously over 90 days and then followed up for up to half a decade, showed about two-thirds remained on them.[37] It is emerging that patients who stay on opioids seem to be a self selected group who may be treating their existential suffering rather than more physically determined pain.[21,24,38] They include subgroups:

- with prior intermittent opioid prescriptions[37]
- initially risk stratified as possible misusers[37]
- with higher current rates of indicators of abuse[17,21,39]
- with higher rates of mental health and substance use disorders[17,38,40]
- who are on higher dosages or tend to dose escalate[21,37]
- who attend multiple prescribers and pharmacies.

Guidelines recommend the use of risk stratification whenever initiating LtOT, however there is often a gap between evidence and practice.[5,38] A recent New South Wales LtOT prescribing survey of 404 GPs found preliminary risk assessments were conducted with a mean reported frequency of 47%.[41] In a phenomenon described as 'adverse selection', those patients at higher risk for poor outcomes are more likely to be



initiated onto LtOT, be prescribed higher dose LtOT and avoid risk mitigation strategies.[38]

Many may never be able to come off LtOT, particularly those on higher doses.[3,37,42] They may not manifest any aberrant behaviours because they are effectively receiving opioid substitution therapy, suppressing their cravings.[42] If a clinical decision to taper the LtOT becomes necessary on risk management grounds then extreme pain, anhedonia, cravings or aberrant behaviours could emerge.[42] Some patients, unable or unwilling to taper, may need ongoing care titrated toward the structuring of a dependency program.[42]

Evidence about harms

Many of the harms from LtOT involve hoarding, diversion, abuse, overdoses and addiction.[19,39]

Hoarding was reported by over half the outpatients in a US pain clinic survey[40] and up to 42% in studies among elderly Australians.[43] Diversion is frequently quite careless and casual.[43] In a US survey of pharmaceutical opioid misusers, most sourced their drugs, not from dealers, but from friends or family.[44] These opioids were given freely (56%), purchased (9%) or stolen (5%). The friend or family member who diverted them usually (82%) had obtained them from just one doctor.[44] Of 352 US pain clinic patients, 45% experienced diversion of their LtOT at least once, most commonly loss through theft.[45] Similarly in Australia, borrowing or sharing medications is commonplace especially among certain ethnic groups.[43]

The past year prevalence rate of pharmaceutical opioid abuse in Australia is estimated to be 3.0%.[46] Opioid related deaths, which dropped after the heroin drought of 2001, have recommenced, returning to pre-drought levels among older Australians.[47] Overdoses occurred at a high rate (1.8% per annum) among those prescribed at least 100 mg morphine equivalents in one US study,[48] although the majority of overdoses occurred in the larger groups of people receiving lower doses. For every unintentional pharmaceutical opioid overdose death, US figures estimate nine are admitted for addiction treatment, 35 visit hospital emergency departments, 161 report drug abuse or dependence, and 461 report non-medical uses of opioid analgesics.[49] This latter is easily missed despite its frequency. Of 26 314 Americans on opioids in one study, a minority (19%) used the medication as prescribed, self medication was reported in 43% (significantly associated with psychoemotional issues), 27% used recreationally and 18% used chaotically, as seen with heroin dependency.[39]

The predominant opioids of misuse in Australia, New Zealand and North America, have now become the pharmaceuticals.[31,50]

Conclusion

The prescribing of opioids has escalated despite the evidence that the benefits of LtOT have been overstated and the individual and public health harms have been understated.[19,22,27] However, if a GP believes CNCP management requires opioids, prescribing must be both selective and cautious[3] to allow our patients to maintain, or regain, control of their pain management.

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Opioid use in chronic non-cancer pain

Part 2: Prescribing issues and alternatives

Background

Managing pain requires time and effort to attend to its biopsychosocial characteristics. This requires proper planning and a whole-of-practice approach.

Objective

This article describes how to prepare your practice for quality chronic pain care, and details a non-judgemental and effective management approach, including the minimisation of opioid harms.

Discussion

It is helpful to have a consistent, whole-of-practice approach when a patient new to the practice presents with a compelling case for opioids. Assessing patients with chronic pain includes a full medical history and detailed examination according to a biopsychosocial approach and applying 'universal precautions' to make a misuse risk assessment. A management plan should consider a range of non-opioid modalities, with a focus on active rather than passive strategies. Integrated multidisciplinary pain services have been shown to improve pain and function outcomes for patients with complex chronic pain issues, but access is often limited. Time-limited opioid use is recommended with initial and regular monitoring, including pain and function scores, urine toxicology, compliance with regulatory surveillance systems and assessment for adverse reactions and drug related aberrant behaviours. When ceasing prescribing, opioids should be weaned slowly, except in response to violence or criminal activity.

Keywords

opioids drugs; chronic pain

CPD

This article is not just about the availability and harms of opioid use; it concerns attitudes, professional identity and the business of healing. Despite our human tendency to be judgemental, no-one in pain comes to the doctor to be separated into 'genuine pain' patients or 'undeserving' drug addicts. People come for good care; which in this setting means good pain management, good dependency management or, when appropriate, a mixture of both.

Case study 1

Just before leaving work one Friday evening, your receptionist informs you that a short-acting oxycodone repeat prescription is required for a female patient, 74 years of age, who sees all the other doctors in the practice (who are absent). The receptionist says that she is a 'very nice lady', though always rushed and somewhat prone to missing appointments. The patient has rung from the next town where she is visiting her new great-grandchild. She had a total hip replacement 5 months previously and more recently has been diagnosed with complex regional pain syndrome in the foot. At her last presentation, a fortnight ago, the notes indicate that she told your colleague she had been discharged from the hospital emergency department the day before, having received an injection of morphine and a prescription for short-acting oxycodone tablets. Your colleague noted that she was in significant pain, staggering, and finding it difficult to talk and referred her back to the hospital to be admitted. You have no information about what happened subsequent to her presentation at the hospital.

You are in a terrible rush to get home as the babysitter has already arrived and your spouse has been expressing very clear displeasure about your lack of family focus. You hit the print button for the requested prescription. However, as you are signing the script you reflect on what you are about to do and consider the lack of continuity of care, her non-specific diagnosis and whether her last presentation could have been an overdose. You ring the Prescription Shopping Information Service (PSIS) to find that she has been positively identified. In the 3 months for which information is available, she has had Pharmaceutical

Benefits Scheme (PBS) prescriptions from 22 GPs, including 15 targeted medications. You discard the script and request the receptionist to telephone the patient to let her know you don't do scripts over the telephone and that she should book to see her usual doctor.

Developing a practice pain management protocol

You can prepare your practice for quality pain care in several ways. It can be helpful to put up a sign in the waiting room saying 'no drugs of addiction will be provided on the first appointment'. Work with colleagues to develop a consistent strategy for when you are faced with a patient new to the practice with a compelling case for opioids, or an urgent telephone request for a new prescription in established patients, including in time poor emergency situations similar to *Case study 1*. Here you might consider buying time for a detailed assessment by highly structured prescribing.

Before prescribing:

- check for injection sites
- order a urine drug screen
- confirm the patient's identity
- attempt to call the previous doctor
- consult the PSIS and fax (then post) to the pharmacy a 2-day prescription contingent on every dose being consumed at the pharmacy (this would need to be negotiated with the pharmacy).

Importantly, before the follow-up appointment, check that the patient is still coming, as they may only have wanted the script, not the supervision.

Case study 2

A couple moved to your area last week and have already seen your colleague. The husband presents requesting repeat pain killers for his wife who is 52 years of age. You look at the notes and find that she has attended the surgery twice for headaches and has been prescribed three prescriptions of 20 paracetamol/codeine 30 mg tablets. Unfortunately, your colleague has not completed the sections in the medical record on past history, medications or allergies. The husband says, 'We're getting desperate. Since moving here and unpacking the furniture she has had severe pain and has had no sleep at all. The tablets just aren't strong enough!' You politely refuse. 'At our practice we have a policy not to prescribe opioids without a thorough assessment of every patient to determine the best way to manage their pain.' He agrees to bring her in for an appointment later that day. She reports the pain is constant, worse at rest and 10/10 in severity. She had a breast lumpectomy and radiotherapy 6 months ago. Her neck is rigid with marked muscle spasm. You prescribe oral morphine and order a bone scan.

On review, they are delighted that she has finally been able to get some sleep, but unfortunately the scan shows bony metastases.

Clinical history and examination

Quality pain care requires a 'biopsychosocial' approach involving a careful positive diagnosis and exclusion of differential diagnoses.

A psychiatric history should consider diagnoses including depression and somatisation, as well as a history of trauma, and physical, emotional and sexual abuse in either childhood or adulthood. A suicide assessment should be performed. It is important to remember that depression and pain can trigger and perpetuate each other.

A drug and alcohol history should be routine, including licit and illicit drugs, synthetic cannabis ('Kronic') and 'designer' stimulants. This is not simply to allocate diagnoses such as abuse, addiction or dependency – which all may well change with the fifth version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V). Rather, explore individual substances along the dimensions of the amount and pattern of use, the social consequences of use, and the experience of compulsion/craving/loss of control.[1]

Ask specifically about pharmaceuticals including opioids or benzodiazepines. Has there ever been hoarding or diversion, eg. lending, giving, selling, bartering or stealing or vice-versa? Has there been use other than prescribed, eg. for stress or for escape. This may include over- or under-consumption, topping up with other drugs or pills, or tampering with tablets or patches. Tampering turns slow release formulations into immediate acting ones for smoking, swallowing or intranasal or intravenous consumption.

The physical examination should aim to clarify the pain diagnosis, monitor therapy effects and side effects, assess any opioid misuse risk and observe the behavioural responses to physical examination. Beware the tendency to over-rely on non-verbal indicators of pain (eg. limping or the wearing of a neck brace). Look for signs of intoxication or substance withdrawal. Respectfully but firmly explain you must inspect areas of potential intravenous access, including the upper limb, the femoral vein area, the feet and ankles and the neck (*Figure 1*).

Initial and regular assessments should employ measures such as the Brief Pain Inventory, which is freely available online (see *Resources*). This allows the quantification of both pain and function ('pain interference') including relationships, work, leisure, mood and sleep.

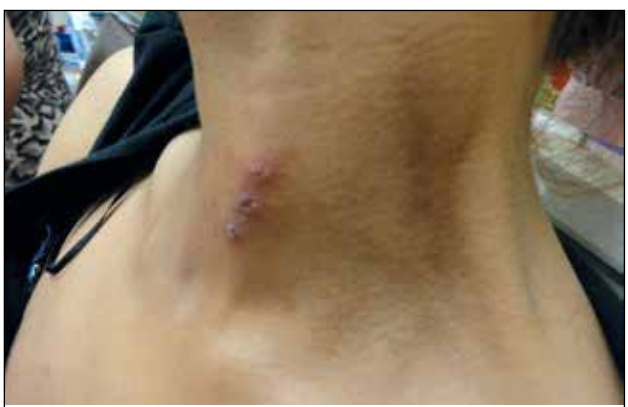


Figure 1. The neck of a patient who has been injecting the oxycodone her GP had been prescribing to her mother for cancer pain

Better documentation than that shown in *Case study 2* assists longitudinal diagnosis and continuity of care, and may minimise potential regulatory or medicolegal risks.

A full initial assessment and planning for holistic care for a patient with chronic pain (as described) can be time consuming. Importantly, reimbursement is available through the use of appropriate Medicare Benefits Schedule (MBS) item numbers. These could include a time-based item for each prescription, and where appropriate, accessing care plans, team care arrangements, mental health plans, medication reviews, health assessments and multidisciplinary case conferences.

Without sufficient clinical attention, complex pain patients will suffer from 'time poverty', so ensure they receive sufficient consultations and continuity of care.

Table 1. Non-pharmacological therapies for cancer pain or non-cancer pain based on Passik[25]

Passive therapy: biomedical[5]	Nerve blocks Neurodestructive surgical techniques Vertebroplasty Radiation therapy
Passive therapy: other	Acupuncture[5] Transcutaneous electrical nerve stimulation (TENS)[5] Topical therapy[5] Desensitisation Strapping Braces Splints Massage therapy Heat or cold application
Active therapy	Patient education Lifestyle and nutritional advice Social engagement Cognitive behavioural therapy[5,26] Acceptance and commitment therapy Distraction Goal setting and pacing strategies Psychotherapy for comorbid depression, anxiety or emotional contributors to pain[5,26] Positive psychology (enhancing positive emotions) Relaxation training[26] Mindfulness meditation Loving kindness meditation Exercise[5] Hydrotherapy Deep water running[27] Range-of-motion programs Yoga Mirror boxes (for phantom limb pain)[28]

Managing chronic pain with non-pharmaceutical strategies

As more information comes to light about brain and nervous system plasticity in chronic pain, there is a growing realisation that active rather than passive management strategies have a greater power to 'retrain the brain' with a view to reducing pain.[2] This does not mean that passive modalities, pharmacological or otherwise, cannot have an adjuvant role. However, the inherent limitations of such approaches need to be clearly discussed with the patient.

Some non-pharmacological therapies are listed in *Table 1* and many should be possible to implement in most general practice locations. One US study of primary care patients with both pain and depression, found psychotherapies compared to usual care increased the likelihood of significant pain improvement by 2.4-fold.[3] Integrated multidisciplinary pain services have been shown to be the best way to improve pain and function outcomes for those at the complex end of the chronic pain cohort.[4] Return-to-work rates after multidisciplinary input have been shown to exceed those after spinal surgery or spinal cord stimulators.[4,5] However in the real world, access is limited – specialised pain services are often geographically or financially inaccessible with long waiting lists.

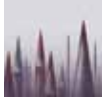
There is an increasing interest in the practice of yoga for chronic pain management. Yoga assists with flexibility, core stability, psychological training and spiritual development: a truly 'biopsychosocial' treatment.[6] Importantly, improvements in pain scores following spinal surgery or spinal cord stimulators are no better than those following non-invasive interventions such as psychotherapy, yoga and acupuncture.[4,6] Acupuncture has a role in osteoarthritis and headaches,[7] although when used in isolation, there is the potential to encourage a passive role for patients.

Managing chronic pain with non-opioid pharmaceutical strategies

Non-opioid pharmaceutical strategies may include omega-3 fish oil, paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), anticonvulsants, topical therapies and disease specific therapy such as sumatriptan for the treatment of migraines.[4,5] Antidepressants may be useful for analgesia (even in patients without depression), with tricyclics and duloxetine preferentially used. Doses tend to be lower than those used for depression (eg. amitriptyline 10 mg).[7]

Initiating an opioid trial

After a full assessment and initiation of non-pharmaceutical and non-opioid pharmaceutical strategies, the patient's pain may be manageable – or the patient may have sacked you to get their drugs from the reckless prescriber down the road! If not, the patient's management plan may need to include careful prescribing of opioids. The use of evidence based consensus guidelines can help GPs to manage patients according to current best practice. The Australian non-industry sponsored guideline *Opioid use in persistent pain: Information for health professionals*[8] is available free online (see *Resources*).



The 'universal precautions' approach is considered best practice and the original papers by Gourley et al[9,10] are well worth reading. The term hails from the time of HIV/AIDS, when it described applying a minimum standard of care to all patients, regardless of their perceived or confirmed infectious status, to reduce the risk of infection and stigmatisation. In analgesia, relying on ad hoc judgements reflects cultural stereotyping and is frequently inaccurate.[11] Chronic non-cancer pain is common and may last forever. For this reason, if analgesia is to include opioids, it cannot be just a simple matter of a prescription. Instruments such as the Opioid Risk Tool (ORT) may help to identify patients who are at risk of misusing opioids. The ORT is available online (see *Resources*). However, you still have to deal with misuse among genuine pain patients and pain among genuine drug addicts.

If analgesia is to include opioids, this requires negotiation, constant monitoring and dealing with the psycho-emotional effects of both the pain and the analgesics. 'We need to think … as if we were going to be marketing (or prescribing) heroin'.[12] Be frank about the addiction potential and lack of scientific evidence for ongoing use in your initial sales pitch. Intermittent prescribing for acute pain creates a subtle inertia to simply continue prescribing as the pain becomes chronic, despite a lack of scientific evidence for such ongoing use.

The current trend is to recommend time-limited rather than lifelong opioid use unless the opioid is used in terminal care. The aim of time-limited opioid use is to create breathing space in which the patient can develop active management approaches.

A urinary drug screen is a good tool to use initially and regularly. While some misusers may purchase a urine sample or even deliver it through a penile prosthesis, it may pick up a few surprises or reveal the absence of the drug that was prescribed. Be aware that oxycodone, fentanyl and buprenorphine are often omitted from routine immunoassay screens and analysis for these drugs with gas chromatography-mass spectrometry may need to be specifically requested, involving additional time and cost.

It is important to find out what is required to meet individual state regulations, such as obtaining a prescribing permit. A real-time online prescription surveillance system has been successfully piloted in Tasmania, and in the future should be rolled out across Bass Strait. Until this is available, for doctors on the mainland the PSIS (1800 631 181) remains a vital resource and GPs should register and routinely check it. Unfortunately, this limited and delayed service overlooks private prescriptions, prescriptions from specialists or dentists and identity fraud. You can also access a complete list of PBS prescriptions for an individual patient, albeit retrospectively, from Medicare (see *Resources*). This requires the patient's consent.

A patient centred care plan or contract, either written or verbal, educates about entry and exit strategies, informs consent and may cover boundaries and goals, benefits and harms (*Table 2* and *Resources*).[13,14] It spells out the considerable effort required of both patient and doctor.[15] However, it is important not to impose this type of contract coercively, as the patient may view it as a 'prelude to abandonment'.[13]

Monitoring and changing opioid therapy

Two-way communiation takes time and should improve pain assessment and decrease overprescribing: a risk factor for hoarding and diversion.[16,17] It is the basis for the routine '4As' of monitoring:[18]

- **A**nalgesia
- **A**ctivities of daily living
- **A**dverse reactions[19]
- **A**berrant behaviours ('red flag' behaviours or proxies for addiction) (*Table 3*).

Case study 3

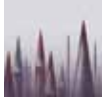
A distraught single mother presents for prescriptions for venlafaxine and oxycodone/naloxone prolonged release tablets, usually prescribed for endometriosis pain. You decline as last week she injected three of her pain tablets and required admission for 4 days for assessment and management of abdominal pain, hallucinations, agitation, aggression, incoherence and dyspnoea. Necessary sedation included midazolam, diazepam, morphine, clonazepam and haloperidol. She required airway management as her Glasgow Coma Score was 8. Her child has since been removed by the Department of Community Services.

She states: 'I can't cope with it all. I might as well be dead if you won't give me my pain killers.'

You answer: 'I can't imagine how awful you must feel. However, I am committed to give you the best care I can. This does not involve continuing chaotic use of pain killers.

Table 2. Components of an opioid contract

- Identification of the patient's functional goals
- Education about the side-effects and effects of co-ingestion with other medications or drugs
- Need for active engagement in management, including psychotherapies
- Therapy as a time-limited trial: Initially over 1–2 months and then on a rolling basis
- Only one prescriber and one dispenser
- No early repeats
- No replacements of lost or stolen scripts
- No telephone requests
- All appointments to be made in advance
- Secure storage of medications and their safe disposal
- No lending, giving or selling of medications
- Dispensing/structuring of plan for picking up medications will be according to risk assessment
- Escalating or higher doses will trigger a comprehensive review
- Option for random drug monitoring and pill counts
- Tapered termination or transfer to methadone or buprenorphine if:
  - treatment goals are not met
  - there are serious adverse outcomes
  - there is evidence of misuse
  - there are contract violations
  - review appointments are not kept



However, I can help you find stability and control with regular opioid doses like in a methadone program. Then together we can work on the broader issues of the pain and getting your life and family back together again.'

She states: 'I was on methadone before and no f***ing way will I go back on those liquid handcuffs.'

You answer: 'Okay, here is some information about buprenorphine, which works like methadone and goes under the tongue, have a read about it. Will you come back in tomorrow so we can meet to discuss it?'

Opioid rotation has been used to deal with tolerance and escalating doses. However, the evidence is poor unless one is rotating to an opioid substitution program.[4,7,20] Opioid equivalence tables are available online (see *Resources*) but were based on rapid multiple opioid changes for inpatients with cancer pain crises. As such, they should be used cautiously, as indiscriminate use in patients with chronic non-cancer pain may risk an overdose.[21]

Weaning patients off opioids

Case study 4

A panel beater, 42 years of age, fractured his pelvis and femur in a motorbike accident 3 months ago. He was discharged from hospital on 40 mg slow release oxycodone twice daily, 28 tablets of which have been prescribed regularly seven times. Today he presents requesting his next prescription. He still has a pain score of 8–9/10, enough to stop him sleeping or returning to work and there are no aberrant behaviours. You can see that he is neither getting on with his life, nor getting any relief from his pain. What could you say?

GP: 'How is our treatment going?'

Patient: 'Not great. I'm passing bricks and after I take the medication I can just manage to get out of bed for an hour or so. My fractures are real, Doc, and my pain is real and they said they may need to replace the hip. I just need to increase the dose until then.'

GP: 'I really want to help your pain. It would be magic if one medication could cure it. But you are already on a dose of opiates that would flatten most people and they clearly are not working. One of the problems of this class of drugs, such as oxycodone, morphine or heroin, is that once you have been on them a month or so you don't keep getting the same benefits without increasing the dose. There's lots of side effects, like your constipation, not to mention slower recovery, worsening pain, sexual problems and even a tendency for stopping breathing in your sleep. We need to look at some longer term options to manage your pain that are much safer than narcotics.'

Patient: 'No-one told me they could do that. But I don't think I can get off them.'

You negotiate a 10 week taper adding some non-opioid therapies. At review after cessation his pain remains severe, 5–6/10 at worst, but he says he has learned to get along with it with occasional use of weak opioids and is not so keen now on more surgery. He has lost some weight and reports more energy and a clearer head without the sweats or constipation. He has returned to selected work duties and is swimming more and walking.

Abrupt termination of long-term prescribing may be regarded as an abuse of power and should be avoided unless in response to violence

Table 3. Spectrum of aberrant drug taking behaviours among cancer pain patients[29]

Aberrant drug-related behaviours more suggestive of addiction	Aberrant drug-related behaviours somewhat suggestive of addiction	Differential diagnosis of aberrant drug-related behaviours
• Selling prescription drugs • Prescription forgery • Stealing or borrowing drugs from others • Obtaining prescription drugs from non-medical sources • Injecting oral formulations • Concurrent abuse of alcohol or illicit drugs • Multiple dose escalations or other non-compliance with therapy despite warnings • Repeatedly seeking scripts from other clinicians without informing the initial/ongoing prescriber • Evidence of deterioration in function related to drug use • Repeated resistance to a change in therapy, despite clear evidence of drug related diverse physical or psychological effects	• Aggressive complaining about the need for more drugs • Drug hoarding during periods of reduced symptoms • Requesting specific drugs • Openly acquiring similar drugs from other medical sources • Unsanctioned dose escalations or other non-compliance with therapy on one or two occasions • Unapproved use of the drug to treat another symptom • Reporting psychic effects not intended by the clinician • Resistance to a change in therapy associated with tolerable adverse effects accompanied by expressions of anxiety related to the return of severe symptoms	• Addiction/substance use disorder • Unrelieved cancer pain • Psychiatric disorder: – depression – anxiety – borderline personality disorder • Organic brain syndrome • Criminal intent

or criminal activity. Prescribers need to become as comfortable weaning patients off an opioid trial as they are at initiating one. There is no evidence-based recommended rate. A 5–10% per week reduction is reasonable, reducing the interval between prescriptions if required.

Training in pain management and addiction medicine

All opioid prescribers in California are required to do a 1 day course in pain management. Calls have been made for prescribers to spend similar time training in addiction medicine.[22] Such training has been associated with greater adherence to guidelines with more positive attitudes toward the identification, prevention and management of opioid disorders.[23,24] If you currently lack these skills, either seek training or consider referring patients to a pain or addiction medicine service. Contact your Medicare Local or state health department addiction services for details of training.

Key points

- A sign in the waiting room saying 'no drugs of addiction will be provided on the first appointment' can help prepare your practice for quality pain care.
- Apply a biopsychosocial approach to the assessment of patients with chronic pain, including a full medical history and detailed examination.
- Active rather than passive management strategies have a potentially greater power to 'retrain the brain' with a view to reducing pain.
- Non-pharmaceutical strategies and non-opioid pharmaceutical strategies should be trialled, if possible, before commencing an opioid trial.
- A 'universal precautions' approach helps avoid relying on ad hoc judgements that reflect cultural stereotyping and which are frequently inaccurate.
- The Opioid Risk Tool may help to identify patients who are at risk of misusing opioids.
- The aim of time-limited opioid use is to create breathing space in which the patient can develop active management approaches.
- Useful tools in management include contacting the PSIS, urinary drug screening and preparing a patient centred care plan or contract.
- When monitoring patients use the '4As' (**A**nalgesia, **A**ctivities of daily living, **A**dverse reactions, **A**berrant behaviours).
- When ceasing prescribing, opioids should be weaned slowly except in response to violence or criminal activity.

Resources

- The Brief Pain Inventory is available at www.hnehealth.nsw.gov.au/__data/assets/pdf_file/0003/28614/BPI.dec06.pdf
- Opioid use in persistent pain: Information for health professionals, including the Opioid Risk Tool and opioid equivalence tables, is available at www.hnehealth.nsw.gov.au/__data/assets/pdf_file/0007/76039/opioid_use_April_2012.pdf
- An excellent article by Cohen and Wodak is available at www.medicinetoday.com.au/cpd/files/articles/201201/MT2012-01-024-COHEN.pdf
- The recent article by Shand et al, 'Real-time monitoring of Schedule 8 medicines in Australia: evaluation is essential', has a most useful accompanying online appendix: 'Details of regulatory systems in Australia for S8 opioid analgesics for chronic non-cancer pain' is available from the Medical Journal of Australia at www.mja.com.au/journal/2013/198/2/real-time-monitoring-schedule-8-medicines-australia-evaluation-essential (access is limited to MJA subscribers)
- Opioid prescription guidelines by Drug and Alcohol Services South Australia are available at www.dassa.sa.gov.au/webdata/resources/files/Opioid_prescription_chronic_pain_guidelines_for_SA_GPs.pdf
- An example of an opioid contract is available at www.hnehealth.nsw.gov.au/__data/assets/pdf_file/0007/76039/opioid_use_April_2012.pdf
- A retrospective list of PBS prescriptions for individual patients is available from Medicare at www.medicareaustralia.gov.au/common/utils/files/authority-release-personal-pbs-claims-info-third-party.pdf
- The Australian Pain Society: www.apsoc.org.au
- ThinkGP education website for GPs: http://thinkgp.com.au/education/content/16040
- The University of Washington online CME course in opioid prescribing: http://depts.washington.edu/cme/online/course/EN0903
- The RACP free online CME modules on addiction medicine are available at www.racp.edu.au/page/australasian-chapter-of-addiction-medicine-acham-/addiction-medicine-online-education-modules.

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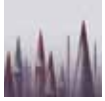

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