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CLINICAL PERSPECTIVES

Deprescribing long-term opioid therapy in patients with chronic pain

Paul Glare [1,2] Claire Ashton-James,[1] Esther Han[3] and Michael Nicholas[1,2]

[1]Pain Management Research Institute, Faculty of Medicine and Health, University of Sydney, and [2]Michael J Cousins Pain Management Research Centre, Royal North Shore Hospital St Leonards, and [3]Drug and Alcohol Services, Northern Sydney Local Health District, Royal North Shore Hospital, Sydney, New South Wales, Australia

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Correspondence
Paul Glare, Pain Management Research institute, Level 2, Douglas Building, RNSH, Reserve Road, St Leonards, NSW 2065, Australia.
Email: paul.glare@sydney.edu.au

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Abstract

Proposed regulatory changes will limit the access to opioids by Australian patients with chronic pain, many of whom are under the care of consultant physicians. This review summarises points of consensus on opioid deprescribing that emerged from the interaction of an expert panel and the audience at a symposium on the topic held in Sydney in 2019. Each of these consensus points speaks to the need for an individualised, patient-centred approach. In other words, 'treat the patient, not the pill count'.

Introduction

Chronic pain is a leading cause of years-lost-to-disability around the world.[1] In Australia, it affects approximately 5 million people, is disabling in approximately 1.5 million and costs the economy some $73 billion in direct medical costs annually, and a similar amount in lost productivity.[2]

Chronic pain is pain that persists well beyond the time expected for acute tissue damage to heal, typically 3–6 months. Chronic pain can indicate ongoing tissue damage but may also result from functional changes in the central nervous system that lead to pain being experienced in the absence of tissue damage, now referred to as nociplastic pain.[3] Chronic pain is a feature of many of the diseases treated by consultant physicians (e.g. arthritis, fibromyalgia, pancreatitis, migraine).

Opioid prescribing for chronic pain has increased rapidly in Australia over the past two decades.[4] It now appears, however, that the potential harms of long-term opioid therapy (LTOT) outweigh any benefits obtained.[5] Commonly referred to as 'the opioid epidemic', prescription opioids are now responsible for more deaths and poisoning hospitalisations in Australia than illegal opioids. Every day, nearly 150 hospitalisations and 14 emergency department admissions involve opioid harm and three Australians die from drug-induced deaths involving prescription opioid use.[6] These harms are dose related. North American surveys estimate the risk of accidental death doubles when the opioid dose exceeds 50 mg of oral morphine equivalents (OME) per day and increases fivefold above 100 mg OME daily.[7]

In response to this growing public health crisis, the Therapeutic Goods Administration has proposed regulatory changes to mitigate the risks of opioids. Most notably, modified release opioids will no longer be indicated for the treatment of chronic pain other than in 'exceptional circumstances' (yet to be defined).[8] As a result of these looming regulatory changes, physicians and other prescribers may find themselves having to deprescribe opioids for patients with chronic pain – many of whom have been on these medications at high doses for years without any apparent problems.

Opioid tapering is not always easy for patients or prescribers. Patients may be apprehensive about any changes to their pain management strategy, may be fearful of withdrawal symptoms and increased pain, may be angry that they have been prescribed a drug of dependence for many years or may feel like their doctor is abandoning them. Prescribers are often uncertain about

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how to respond to these concerns, whether the patient's circumstances are 'exceptional', what to offer as an alternative if not, how to taper opioids safely and how to support the patient through tapering.

To address some of these issues, The University of Sydney's Pain Management Research Institute convened a panel of 11 national and international experts from the fields of pain medicine, addiction medicine, primary care, psychology and pharmacy to present the latest evidence for best practices in chronic pain management and opioid tapering to an interdisciplinary audience of healthcare providers and researchers in Sydney in November 2019. Here, we summarise points of consensus on opioid-deprescribing for chronic pain that emerged from the interaction between the expert panel and audience. Each of these consensus points speaks to the need for an individualised, patient-centred approach to opioid deprescribing for chronic pain. In other words, 'treat the patient, not the pill count'.

The goal of opioid deprescribing is better pain management

First and foremost, the panel agreed that the goal of opioid deprescribing is to provide the patient with access to better pain management than opioids. Pain relief may be the stated goal of many patients with chronic pain, and they often believe their life will return to normal once they are given something that reduces the pain intensity. However, there is a lack of evidence for the long-term effectiveness of opioids to relieve chronic pain.[9]

Chronic pain has a devastating effect on people's quality of life. It affects their mood, physical functioning, participation in work and social activities, and social relationships.

Therefore, chronic pain management is not simply about managing pain levels. It is about helping patients to regain their quality of life. Opioids produce small but statistically significant improvements in pain and physical functioning in the short term,[10] with insufficient evidence to determine the effectiveness of LTOT for improving chronic pain and function.[5,10] The side-effects of LTOT include depressed mood, compromised physical and cognitive functioning, and further, reduced engagement in work and social activities.[11] Hence, in many ways, LTOT may worsen the impact of chronic pain on quality of life. Patient outcomes – including pain and disability – may even improve when opioid deprescribing is supported by multidisciplinary approaches to pain self-management.[12]

Better pain management: active pain self-management strategies

Most patients with chronic pain are unable to stop LTOT unless they are provided with an alternative pain management strategy. Non-pharmacological treatments that are active – involving the patient doing things to enable them to maintain activities of daily living and participate in social roles and relationships – are effective.[13] Patients usually learn the knowledge and skills to practise pain self-management (Box 1) by attending an interdisciplinary pain programme. These programmes provide intensive multimodal treatment, with coordinated contributions by physiotherapists, clinical psychologists, and medical practitioners, typically organised around a biopsychosocial model of chronic pain – or perhaps more appropriately, a socio-psycho-biomedical one.[14] Physicians who have a strong relationship with their patients are well positioned to introduce these skills to patients when recommending that they taper off opioids for chronic pain (Box 1). It is possible that these conversations take longer than the time taken to write a prescription, but it is also likely that patients will be rewarded for the physicians' time and effort. If the physician works in a coordinated way with a clinical psychologist and physiotherapist, these tasks can be less onerous for the physician. A recent systematic review on the outcomes of opioid tapering when it is offered as part of an interdisciplinary pain programme identified 31 studies presenting data from 19 distinct programmes.[12] Ten fair-quality studies described programmes that mandated discontinuation of LTOT: on average, 87% of participants discontinued opioids by programme completion (range, 74% to 100%).[12]

Box 1 Knowledge and skills that patients learn to practise active pain self-management

- Basic education about chronic pain, including differences between acute and chronic pain, the limits of treatment for chronic pain, and the importance of self-management
- Regular exercise – to maintain movement, flexibility, and strength and improve function (e.g. lifting and carrying)
- Goal setting – identifying self-relevant, personally valued ends to justify (or motivate) perseverance with active pain self-management strategies in the face of inevitable pain flare-ups
- Activity pacing – to encourage patients to 'start low and go slow' when making progress towards their goals
- Self-regulation strategies – to help patients to modulate stress (e.g. relaxation/meditation, problem-solving).

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Such multidisciplinary pain self-management programmes have been available in the pain clinics of public hospitals in Australia and New Zealand for decades and often achieve clinically significant improvements in pain intensity, disability and mood.[15] Opioid reduction, defined as 50% of patients reducing their dose by half and/or to less than 40 mg OME daily, is a goal of these programmes. One such programme has shown the outcomes – virtually no reliance on opioids, improved function and mood, pain no worse – are maintained at 12 months.[16] Hence, many patients who are currently taking LTOT for chronic pain can obtain improvements in quality of life and pain with opioid deprescribing in the context of learning active self-management strategies for managing their pain.

Adjuvant treatments to support opioid tapering

Patients on LTOT who are unwilling or unable to embrace active pain self-management techniques have various other alternatives to opioids available to them. Evaluating each was beyond the scope of the panel, but the systematic review mentioned earlier identified seven categories: interventional techniques (e.g. spinal cord stimulator implantation), detoxification, buprenorphine-assisted dose reduction, ketamine-assisted dose reduction, acupuncture, other types of outpatient programmes and other behavioural interventions.[12] The review concluded that there is evidence, albeit very low quality, for these approaches being effective substitutes for LTOT. Among the studies examining outcomes beyond just deprescribing, improvement was reported in pain severity (eight of eight fair-quality studies), function (five of five fair-quality studies) and quality of life (three of three fair-quality studies).

How to taper long-term opioid therapy

There is a plethora of information available on how to start opioids, but much less guidance is available on how to deprescribe them. In people with chronic pain who are on LTOT and in whom there is no medical reason to taper the dose rapidly, the typical approach is to reduce the dose slowly to prevent withdrawal or a sudden flare-up of pain.

International members of the panel related the American response to the opioid epidemic, and the introduction by the Centres for Disease Control (CDC) in 2016 of a guideline which required the dose of LTOT not to exceed 90 mg OME per day, and to wean the dose of patients on LTOT to less than 50 mg OME if not discontinuing it.[17] To begin weaning the dose, a decrease of 10% of the original dose in OME each week was proposed as the default starting point, individualised according to the patient's goals and concerns. Slower tapers (e.g. 10% per month) were recommended as more appropriate and better tolerated for patients who had been taking high doses of opioids for many years, with rapid tapers being indicated for patients who had overdosed on their LTOT. The CDC also recommended prescribers should access appropriate expertise if considering tapering opioids during pregnancy, and that primary care clinicians should collaborate with mental health clinicians and with other specialists as needed to optimise nonopioid pain management and provide psychosocial support for tapering-related anxiety.

In addition to tapering opioids, the CDC guideline recommends that patients remaining on LTOT should have a written opioid contract forbidding 'doctor shopping' and early prescription refills, undergo regular urine toxicology screening and have prescription monitoring. It is noted that these ancillary activities are not part of routine practice in Australia currently, and they are not found in the Therapeutics Goods Administration's recent changes to the regulation of opioid prescribing.

The US Veterans Health Administration (VA) issued their own guideline in 2017 due to the problem of prescription opioid abuse by their returned service personnel. It recommended a starting point of a 5–20% dose reduction, 5–20% per month for patients on very high doses (>300 mg OME per day) and rapid inpatient detoxification over 1–7 days for patients who overdose. More recently, there has been increased concern about the potential risks (e.g. self-harm) from rapid discontinuation of chronic opioid therapy.[18,19] The VA guideline has the same requirements as the CDC for opioid contracts and so on. To support implementation of guideline, the VA established the Opioid Safety Initiative, which featured an electronic dashboard of prescribing, monitored by a local 'champion' to address overprescribing at their hospital.[20]

Despite these regulatory changes, the evidence base for clinician-led opioid tapering is weak. A literature search of 'opioids', 'tapering' and 'pain' from 2016 (when the CDC guidelines were released) until the time of the symposium in November 2019 identified 14 studies evaluating clinician-led opioid tapering,[21–34] but with just one controlled study comparing different tapering schedules.[22] While it is therefore impossible to make strong recommendations about best practice currently, summarising the studies provides some relevant insights (Table 1). Seven studies followed the CDC or VA guidelines,[21,23–29] four used other sequential dose reduction schedules[22,29–31] and three took unstructured, individualised approaches.[32–34] Most were outpatient

Table 1 Studies of clinician-led opioid tapering in chronic pain patients, 2016–2019

Ref.	Study type	*n*	Mean base-line dose >100 mg OME per day	Tapering schedule	Alternative pain management strategy	Follow-up period (months)	% ceased	% reduced	% reduction in daily mg OME from baseline
[21,22]	UO	29	No	CDC	Cannabis	3	NR	NR	75%
[23]	RCT	985	No	CDC	NR	12	21%	33%	NR
[24]	UO	5	Yes	CDC	IPP	0	0%	100%	34%
[25]	UO	82	Yes	Modified CDC	Pain education	4	NR	NR	50%
[26]	RCT	75	Yes	Modified CDC	IPP	1	7%	NR	NR
[27]	CO	344	No	Modified CDC	IPP	6	100%	NA	NA
[28]	UO	43	Yes	VA	None	12	65%	16%	NR
[29]	UO	88	Yes	Other schedule	None	6	29%	25%	30%
[22]	CO	195	Yes	Other schedule	IPP + adjuvant drugs	0.25	87%	NR	NR
[30]	RCT	108	No	Other schedule	Acupuncture	6	NR	NR	21%
[31]	UO	70	Yes	Other schedule	Ketamine infusion	0	NR	NR	59%
[32]	UO	145	No	Individual	None	6	17%	18%	NR
[33]	UO	116	Yes	Individual	None	27	NR	37%	24%
[34]	UO	159	No	Individual	IPP	0	100%	NA	NA

CDC, Centres for Disease Control guideline; CM, complementary medicine; CO, controlled observational study; IPP, interdisciplinary pain programme; NA, not applicable; NR, not reported; OME, oral morphine equivalents; RCT, randomised controlled trial; Ref., reference number; UO, uncontrolled observational study; VA, Veterans Administration Guideline.

programmes but a few were inpatient. As a result, the time taken to taper varies greatly from a few days up to a year. The goal of the programme also varied, being complete discontinuation of LTOT goal in 4,[22,26,27,34] and reduction with or without discontinuation in the remainder. In 8 (57%) studies, the average starting dose was high (defined as greater than 100 mg OME daily). Clinician-led dose reduction was acceptable, with a median of 91% patients (range 40–100%) staying on study to the end point, although drop-out from the 8 studies, which included long-term follow up was high (median drop-out rate 59%, range 14–100%). An alternative approach to pain management was provided in 12 (75%) studies, interdisciplinary pain self-management programmes being the commonest.[22,24,26,27,34]

These methodologic limitations notwithstanding, clinician-led tapering achieved discontinuation of opioids in a median of 65% patients (range 7–100%) and dose reduction in another 26% (range 16–100%). In five studies that reported reduction of high-dose opioids (average dose >100 mg OME), a median of 81% (range 37–100%) participants reduced their dose. Where the size of the reduction was reported,[21,24,25,29–31,33] it was by a median of 30% from the baseline, which typically brought it down to a safer average level with low or moderate risk of accidental overdosage.[7] Only three of the studies reported adverse events of tapering.[22,26,29] Serious adverse events were reported by one but uncommon (less than 5% cases).[22] Most gradual dose reduction protocols did not offer medications such as clonidine to palliate the symptoms of withdrawal. Reduction in opioids was often associated with no change or improvement in pain scores, and improvement in function and quality of life. One programme with discontinuation as its goal reported a 6-month relapse rate of 10%.[27]

In summary, the available evidence, though mostly poor quality, suggests that most patients will adhere to a gradual, physician-led reduction of their opioid dose. Indeed, many patients can taper off altogether, or at least tapered to a safer dose, without adverse effects. Once the LTOT dose is reduced, most patients can be expected to report their pain is no worse and their function and quality of life is improved, especially when an alternative approach to pain management is provided.[12] Like patients on long-term corticosteroid therapy, the taper can take many months or even years to complete safely. It is currently unclear which subgroups of patients are most likely to be able to reduce their opioids, what is the best alternative pain management strategy, or what patient characteristics and other barriers make tapering more challenging. More well-designed studies of tapering LTOT are clearly needed, including studies of late adverse outcomes of tapering, for example, relapse of opioid use,[16,27,35] illicit drug use,[29] or depression and self-harm.[18,19,27,36]

Addressing patient barriers to opioid tapering

Despite the promising research data, significant barriers to tapering opioids may be encountered in the clinic. These should be addressed in conversations with patients in whom deprescribing is being proposed. The patient may feel that the risk of overdose does not apply to them and/or their present pain trumps any concerns about uncertain risks of opioid use.[37] Physicians can respond to these cognitive biases by pointing out that the majority of prescription opioid overdoses are accidental, and the risks of overdose are not uncertain – the longer patients take these medications and the higher the dose, the greater the risk.[7] Patients may also report pessimism about the value of non-pharmacological options for pain management. This highlights a need for clinicians to be confident when recommending evidence-based, non-opioid pain management strategies (Box 1).

Patient engagement with opioid tapering advice may be disrupted by emotions, including fear, anxiety, shame or anger. Negative emotions are almost inevitable in conversations about opioid tapering, even when patients are mostly positive about the change.[38] They may be anxious about increased pain or withdrawal symptoms, may be ashamed of their chemical dependence on prescribed medications and may express anger towards the clinician who has been responsible for their prescribing over the years. These emotions are understandable and need to be managed, since negative emotions are known to influence trust and acceptance of treatment advice. Evidence-based strategies for de-escalating negative emotions include acknowledgement, acceptance or validation, and reappraisal. There is work to be done here, as most physicians are not trained in these specific emotion-focussed communication skills.

Potential harms associated with standardised or 'forced' opioid deprescribing

International members of the panel spoke of the American experience in the first few years following introduction of the CDC and VA guidelines. The initial response was to get patients off opioids as quickly as possible. But the clinical experience of doing so pointed to the need to taper opioids in a patient-centred way – that means providing different tapering schedules for different people. Opioid tapering affects everyone differently.[37,39] Patients with chronic pain often have significant comorbidities, physical disability, mental illness and may have experience with substance use and opioid use disorder that requires management concomitantly.

Several panellists expressed deep concerns about the impact of pressures on prescribers to reduce opioids in certain chronic pain patients. Hard and fast rules proposed for opioid deprescribing may be harmful to some patients. So-called 'forced tapers' are associated with numerous iatrogenic risks including transition to illicit opioids, depression, suicidal ideation and suicide attempts.[40] When tapering, some patients do experience new pain, reduced function, mental health crises and withdrawal symptoms. Consistent with this, the US Department of Health and Human Services guidelines for opioid–tapering now state that 'reduction or discontinuation of long-term opioids has the potential to harm patients if not made in a thoughtful, deliberative, collaborative and measured manner'.[41]

Patients on LTOT with comorbid opioid use disorder (OUD) were noted to present a special challenge. OUD is difficult to diagnose in patients with chronic pain on LTOT because the current diagnostic criteria **(**Box 2**)** will often lead to a diagnosis of at least mild opioid use disorder in almost everyone.[42] Furthermore, it can be difficult to obtain the information to diagnose more moderate-

Box 2 Diagnostic criteria for opioid use disorder[43]

- Opioids are often taken in larger amounts or over a longer than intended.
- Persistent desire or unsuccessful efforts to cut down or control opioid use.
- Great deal of time is spent in activities necessary to obtain the opioid, use the opioid or recover from its effects.
- Craving or a strong desire to use opioids.
- Recurrent opioid use resulting in failure to fulfil major role obligations at work, school or home.
- Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
- Important social, occupational or recreational activities are given up or reduced because of opioid use.
- Recurrent opioid use in situations in which it is physically hazardous.
- Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids.
- Tolerance, as defined by either of the following: (a) a need for markedly increased amounts of opioids to achieve intoxication or desired effect; or (b) markedly diminished effect with continued use of the same amount of an opioid.
- Withdrawal, as manifested by either of the following: (a) the characteristic opioid withdrawal syndrome; or (b) the same (or a closely related) substance are taken to relieve or avoid withdrawal symptoms

Scoring of severity of OUD: mild, 2–3 criteria met; moderate, 4–5 criteria met; severe: 6 or more criteria met.

to-severe OUD as patients may not be forthcoming due to a variety of reasons including shame, and their own perceptions and understanding of how much their pain is contributing to their issues as opposed to their opioids. It can be useful to get a perspective of how the patient is functioning from someone close to them. The physician needs to be on alert for aberrant behaviours suggesting a more severe opioid use disorder, for example, taking family member's medications, seeing multiple prescribers, obtaining from the black market and taking medications in ways it was not intended. Services Australia now offers a Prescription Shopping Programme to help prescribers verify the patient's prescribing history and make more informed prescribing decisions. In some states, real-time prescription monitoring programmes are now available. Being attentive to physical signs of opioid withdrawal or intoxication is also helpful. If physicians are concerned about patients with moderate-to-severe OUD, referral to an addiction services (addiction medicine, addiction psychiatry) for consideration of opioid substitution therapy is an option.

Conclusion

Opioids have fallen out of favour for the management of chronic non-cancer pain. Patients who have been on them for many years will soon be expected to come off them, which will be distressing for some. Consultant physicians may become involved in this situation even if they are not the prescriber, so they should be familiar with the issues surrounding LTOT. Although the evidence base is currently weak, it suggests most patients can be weaned off opioids without their pain going out of control, and they often feel better as a result. The taper should be slow and may take months or even years if they have been on high doses for a long time. Providing patients with active cognitive and behavioural strategies when opioid tapering is commenced may help them to manage their pain during and after tapering is completed. These strategies are taught in pain clinics in public hospitals in Australia and New Zealand. Patients who have developed OUD are a special challenge and referral to addiction services is recommended if this is suspected.

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