A GUIDE TO

deprescribing

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CONSULTANT PHARMACY SERVICES

OPIOIDS

KEY POINTS

Due to poor efficacy and major side effects, opioid therapy is not indicated for the long-term management (>90 days) of non-cancer pain.

Opioids are playing a diminishing role in the management of chronic non-cancer pain.

Multidisciplinary pain management programs utilising psychology, exercise and functional-based outcomes result in better quality of life and better pain management than use of opioids.

Caution is warranted at oral morphine equivalent daily dose above 40 mg and doses above 100 mg should prompt reassessment and specialist advice.

Use of opioids for more than 90 days is associated with serious adverse effects (hormonal, psychological, immunological) and increased mortality.

Concurrent benzodiazepine or gabapentinoid use confers a higher risk of drug-related mortality from drug interactions.

Tolerance to the analgesic effects of opioids develops in almost all patients with long-term use.

Opioid reduction or cessation for chronic non-cancer pain patients is associated with reduced pain and improved function.

A phone or device-based application is available to assist in opioid conversion that has been prepared by the ANZCA (Free Opioid Calculator FPM ANZCA via app store).

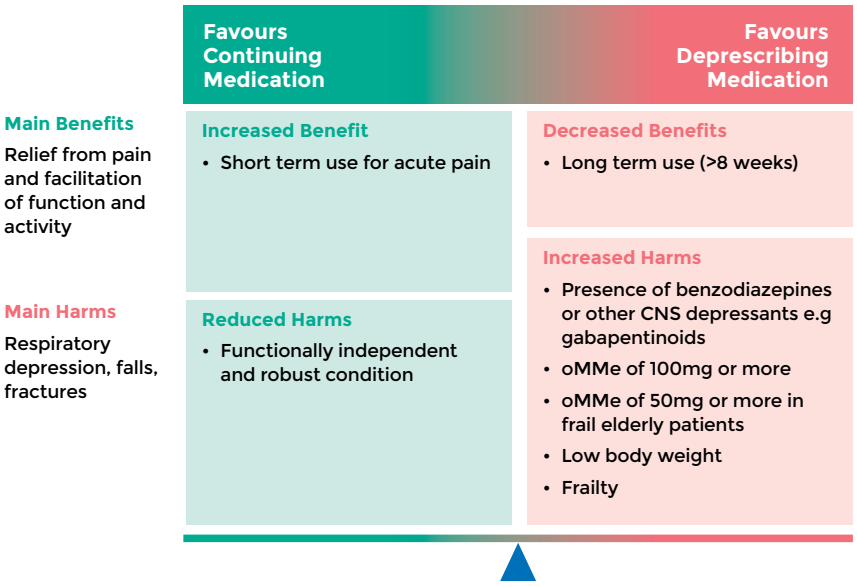
A number of consumer resources are available to assist with the management of chronic pain. NPS Pain Management Hub for Consumers (https://www.nps.org.au/pain-management-hub/consumers#consumer-pain-hub).

deprescribing
FOR BETTER HEALTH OUTCOMES

CONTEXT

Opioids are commonly used to treat acute pain, malignant pain and in palliative care. Certain opioids are used in the treatment of opioid addiction. This deprescribing guide applies to the use of opioids in chronic non-cancer pain.

BENEFIT VERSUS HARM



RECOMMENDED DEPRESCRIBING STRATEGY

An opioid deprescribing algorithm is shown in Figure 1, this should be considered in conjunction with the Faculty of Pain Medicine tapering strategies for particular situations below:[45]

Long term therapy: Where opioid therapy has been maintained for months or years without meaningful improvement in function. One practical strategy is to reduce the daily opioid dose each month by 10-25%.

Shorter period of therapy: If weaning is required after a shorter period of opioid therapy, such as after failure to achieve the goals of an opioid trial, or after a negotiated treatment phase for acute pain, then a faster rate of weaning is generally appropriate. One option is a step-wise reduction of the daily opioid dose each week by 10- 25%.

Significant adverse effects: If weaning is required in response to significant adverse effects or opioid misuse, then daily step-wise reduction may be appropriate. Alternatively, immediate opioid cessation and pharmacological treatment of withdrawal symptoms can be considered (which is preferably done in an inpatient setting).

Unsuccessful tapering: If an attempt at opioid weaning has proven unsuccessful, then the opioid tapering rate can be slowed. This can be achieved by reducing the proportion of the dose reduction and/or by increasing the time spent at each dose level (e.g. 2 or 3 months between reductions).

Opioid Use Disorder: In cases where it becomes apparent during weaning that the primary problem is opioid dependence rather than pain, involvement of an Addiction Medicine service is recommended.

BACKGROUND

Any substance that acts on the opioid receptors can be considered an opioid. Opioid receptors are distributed in the central and peripheral nervous system, gastrointestinal tract and immune cells. In addition to analgesia, the endogenous opioid system modulates a range of physiologic processes:

- hormonal secretion;
- motivation/reward;
- immune and stress responses;
- gastrointestinal transit and feeding.

Over the last couple of decades, the use of opioids for the management of chronic non-cancer pain has increased. This has been accompanied by increase in opioid overdoses and deaths, abuse, addiction and diversion, as well as uncertainty about long-term efficacy.[1,2,3,4,5] These alarming outcomes have been demonstrated both in Australia and worldwide.

Based on current evidence, opioid therapy is no longer recommended for the long-term management of chronic non-cancer pain (CNCP). Even in complex acute pain, opioids should be ceased within 90 days. If continued beyond this point, there is a 50% chance that patient will still be using opioids in 5 years-time.

The limited evidence supporting long term efficacy in CNCP is weak and is based on non-blinded, industry-sponsored trials with significant potential for bias. However, there is a consistent body of evidence demonstrating lack of long-term analgesic efficacy, lack of improvement in function or quality of life and greater risk of harm to both individuals and society than previously recognised.[6]

As a consequence, there is a consensus that opioids should play a diminishing role in the management of CNCP. Multidisciplinary pain management programs utilising psychology, exercise and functional-based outcomes result in better quality of life and better pain management than use of opioids.[7]

Opioid Use in Australia

A population analysis of opioid pharmaceutical claims in Australia examined the trends in community dispensing of opioids from 1990 to 2014.[8] The average amount of opioid consumption (from dispensing records) per person increased almost four-fold between 1990 and 2014, from 4.6 to 17.4 Defined Daily Dose equivalents (DDD, the Internationally accepted daily dose for the most common indication) per 1000 population per day.[8]

Recognising the harms associated with over the counter combination analgesics containing codeine (CACC), these were rescheduled to prescription only status in Australia in February 2018.

In February 2020, the Therapeutic Goods Administration made some regulatory changes to address prescription opioid use and misuse in Australia.[9] This includes smaller pack sizes, increased warnings on packs and increased restrictions on the prescribing of transdermal fentanyl.

Reason for Deprescribing	• No meaningful functional or pain improvements • Overt troublesome Adverse Effects • Use of the equivalent of 90mg oral morphine or more daily • Suspected hyperalgesia • Cause of pain resolved • Signs of misuse
Patient Engagement	• Determine readiness for tapering and set patient goals for function • Discuss potential harms of ongoing use and benefits of tapering • Provide information to address patient's beliefs and concerns regarding tapering of opioids • Advise patient that tapering may take several months • Reassure patient that monitoring and adjustment will take place as needed
Develop Tapering Plan	• Establish a tapering plan taking into account duration of use, dose of opioid, patient preferences (utilise the Faculty of Pain Medicine options)
Ongoing Review and Monitoring of Tapering	• Aim to taper to the lowest effective dose while monitoring function, pain intensity and side effects • If an attempt at opioid tapering is unsuccessful, then the opioid tapering rate can be slowed. (reduce the proportion of dose reduction and/or increase time spent at each dose level)

Figure 1: Opioid Deprescribing Algorithm

EFFICACY

In CNCP, systematic reviews of randomised controlled trials (RCTs) demonstrate modest, short-term analgesic benefit.[10,11,12] However, these research findings cannot be extrapolated into clinical practice given the short duration of therapy (average trial duration was 5 weeks with a range of 1 to 16 weeks). Tolerance, dependence and opioid-induced hyperalgesia are major limiting factors in regard to long-term use of these agents.

Ninety-six randomized clinical trials including 26169 patients were studied to assess the harms and benefits of opioids for chronic non-cancer pain.[13]

Compared with placebo, opioid use was associated with a statistical but clinically irrelevant reduction in pain scores (–0.69 cm on a 10-cm visual analogue pain scale, where 1cm is considered a clinically relevant change). A number of the studies reviewed assessed physical functioning using the 100-Point 36-Item Short Form Physical Component Score. Opioid use was associated with an improvement of 2 points on average, where 5 points is considered a clinically relevant change.[13] A summary of the findings is shown in **Table 1**.

Opioids were associated with less pain relief during longer trials, perhaps as a result of opioid tolerance or opioid-induced hyperalgesia. Long-term opioid therapy was also more likely to cause physical dependence and increased risk of addiction.

REAL WORLD OUTCOMES

Long-term opioids are often associated with loss of efficacy and overall worse outcomes, often due to the development of tolerance.[14] A Danish "real world" population study compared 228 patients with chronic pain that were using opioids to 1678 patients with chronic pain using non-opioid therapy.[14] They found that opioid use was significantly associated with

- higher level of reports of moderate, severe or very severe pain (~ 8 fold higher)
- more self-rated reports of poor health (~ 5 fold higher)
- a higher likelihood of not being engaged in employment (68% unemployed vs 45%)
- a higher use of the health care system (~2.5 fold more use)
- lower quality of life scores in all 8 domains of the Short Form 36 quality of life survey (more bodily pain, less general health, worse mental health, lower physical function, lower emotional, physical and social function and lower vitality)

Many specialist pain management services in Australia and New Zealand participate in the electronic Persistent Pain Outcomes Collaboration (ePPOC; https://www.uow.edu.au/ahsri/eppoc), an initiative for collecting standardised information about their patients. A recent review of some of this information showed that almost half of patients had their opioids either ceased or reduced by more than 50%.[15] These patients were more likely to have a significant reduction in their pain, than those who either had no change, an increase or a more modest reduction in their opioid dosage. See **Figure 2**.

Parameter	Number of Trials (participants)	% of patients achievening minimally significant difference		Number needed to treat or harm (statistical significance)
		Opioid	Placebo	
Pain Relief	42 trials (16617)	61	49	NNT=8 (significant)
Physical Functioning	51 trials (15754)	55	46	NNT=11 (significant)
Sleep quality	16 trials (6585)	53	47	NNT=16 (significant)
Emotional Functioning	23 trials (8962)	33	35	NNT=50 (NOT significant)
Vomiting	33 trials (11268)	9.4	2.3	NNT=14 (significant)

Table 1: Summary of significant differences in opioid vs placebo (from ref 13)

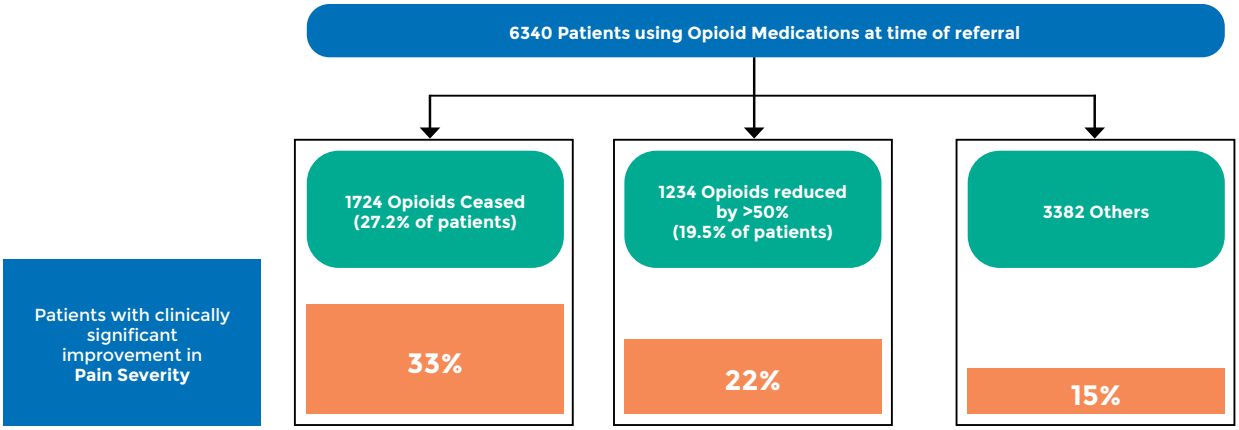


Figure 2: Proportion of patients with significant reduction in pain severity (from ref 15)

ADVERSE EFFECTS

Treatment with opioids for chronic non-cancer pain is associated with a 58% increase in the risk of all-cause mortality compared with other analgesic therapies (Hazard Ratio 1.58, 95% CI 1.38 to 1.82).[16] The absolute increase was 1.48% per person year, equating to an annual Number needed to harm of 67.[16]

Interactions that Increase Mortality

Most often the deaths were caused by combinations of agents (often other centrally acting agents) and the deaths were not intentional.[3]

The most commonly co-administered drugs in earlier studies were benzodiazepines, alcohol and other opioids. Coadministration of benzodiazepines, in particular, increases the risk of overdose mortality.[17] A history of benzodiazepine use more than doubled risk of mortality and current benzodiazepine use increased death from drug overdose almost four-fold.[17]

More recently, an increased risk of mortality with co-administration of opioids and gabapentinoids has been proposed.[18,19]

OPIOID DEPENDENCE, MISUSE AND ADDICTION

Prolonged use of opioids leads to many patients developing a physical dependence which can occur without an opioid use disorder. In these patients, cessation causes an unpleasant withdrawal syndrome, which may include both physical and psychological features. Opioid dependence may emerge at different times for different patients and withdrawal symptoms may occur if cessation is sudden.[27]

Problem use of prescription opioids ranges between overuse (occasionally or more often using more than prescribed), misuse (using for purpose not consistent with medical or legal guidelines, resulting in harmful or dangerous consequences) or opioid use disorder (addiction). Addiction is characterized by repeated compulsive drug seeking and continued use despite adverse social, psychological, or physical consequences.

FALLS AND FRACTURE RISK

A number of adverse opioid effects, such as sedation and dizziness, can increase the propensity to falls due to central nervous system effects. Opioids may also decrease bone mineral density by impairing the production of endogenous sex steroids, and the effect on bone metabolism may directly weaken bone structure.[20] As elderly persons are often at increased risk of osteoporosis and pain, opioid use in this population may further increase the risk of fractures.

A meta-analysis of eight studies found that opioids increase the risk of overall fractures by 88% and of hip fractures by 100%.[21]

ENDOCRINE/HORMONAL ADVERSE EFFECTS

Opioids may affect the hypothalamic-pituitary-adrenal axis, and lead to opioid-induced androgen deficiency (OPIAD) with reduced testosterone production. This may lead to osteoporosis and immune suppression in men, with recent data suggesting that up to five million men have OPIAD in the USA.[22] Among men with back pain, on a daily dose of at least 120 oral morphine milligram equivalents (oMMe) long term, 19% used drugs for erectile dysfunction or testosterone replacement, compared to only 7% of those with pain but no opioids.[23]

Chronic opioid use can lead to amenorrhea or oligomenorrhea in premenopausal women, due to a reduction in both testosterone and estradiol.[24]

LESS SERIOUS ADVERSE EFFECTS

Opioids are associated with a number of common, constitutional side effects. These are well known and include nausea and vomiting (particularly on initiation or with dose increases), sedation, dizziness, itching and dry mouth. Some of these effects may attenuate with ongoing use, although constipation often requires management for the duration of opioid therapy, further increasing medication burden and costs.

OPIOID TOLERANCE AND OPIOID-INDUCED HYPERALGESIA

Opioids are now understood to rapidly sensitise the nervous system and may result in the development of opioid tolerance and/or opioid-induced hyperalgesia.

OPIOID TOLERANCE

Opioid tolerance – a need for increased doses to achieve the desired effect – has been demonstrated in animal models and is seen in humans in both short term and long term studies of opioids in humans and is almost ubiquitous.[25,26,27,28] Factors strongly associated with continuation of opioids were intermittent prior opioid exposure, daily opioid dose over 120 oMMe and possible opioid misuse.

There is only limited cross-tolerance between opioids as a result of differing characteristics and responses of opioid receptors.[29] As a result, rotation of opioids, to a net lower dose, may be a useful short-term strategy for improving analgesia and reducing adverse effects.[30]

OPIOID-INDUCED HYPERALGESIA (OIH)

Excessive opioid exposure may also produce a paradoxical increase in pain sensitivity, manifested as hyperalgesia (exacerbated painful response to noxious stimulation) and/or allodynia (painful response to non-noxious stimulation).[31] This opioid-induced hyperalgesia has been demonstrated in both short term and long term use of opioids.[32,33] A common mechanism proposed for the development of OIH involves the central glutaminergic system with the excitatory NMDA neurotransmitter playing a major role while another proposed mechanism includes the activation of descending pain pathways from the rostral ventromedial medulla which causes certain neurons to respond uniquely to opioids.[34]

Opioid-induced hyperalgesia should be suspected when the treatment effect wanes in the absence of disease progression and in the context of increased pain. Often, hyperalgesia presents as a change in the nature or location of the pain, with neuropathic pain-like elements.

Opioid withdrawal, opioid dose reduction, opioid rotation and NMDA-receptor antagonists are suggested treatments.[33,35]

	Tolerance	Hyperalgesia
Clinical Features	Increased opioid dose requirements to achieve similar pain control level.	Increased opioid dose is associated with increased pain level.
	Occurs with all opioids in long-term use, particularly in non-elderly population.	Manifest as change in the nature of pain (hyperalgesia and allodynia) or the location of pain (wide spreading).
		May be less frequent with atypical opioids (Tramadol Tapentadol & Norspan Patch).
		More frequent with higher doses of opioids and long-term opioids use.
Potential Management Strategies	Rotation of opioid to an alternative opioid at a lower dose – often results in improved pain control with less risk of adverse effects.	Gradual opioid withdrawal with appropriate management of symptoms (note an initial increase in pain may occur as part of opioid withdrawal symptoms)
	Opioid withdrawal management.	Use of Gabapentinoids or NMDA antagonists (under specialist guidance- e.g Ketamine infusion).

Table 2: Clinical Features and Management of Opioid Tolerance and Hyperalgesia

OPIOID DISCONTINUATION

OPIOID-DISCONTINUATION (WITHDRAWAL) SYNDROME

Patient education is essential to successfully taper opioids. Clear written and verbal instructions should be given to patients and families to educate them about the tapering protocol that will minimise withdrawal symptoms

Opioid withdrawal can develop within hours of drug cessation. While the effects of withdrawal are unlikely to be life threatening in patients without significant comorbidities, it can be quite uncomfortable. Signs and symptoms of withdrawal may include

- gastrointestinal symptoms (e.g., abdominal cramping, nausea, vomiting, diarrhoea)
- musculoskeletal symptoms (e.g., myalgias, arthralgias, muscle spasms)
- anorexia, yawning, lacrimation, salivation, rhinorrhea, piloerection, insomnia, anxiety, irritability, dysphoria
- manifestations of sympathetic hyperactivity such as diaphoresis, tachycardia, fever, mydriasis or elevated blood pressure.

Opioid withdrawal is usually medically managed.

TAPERING STRATEGIES TO AVOID DISCONTINUATION SYNDROMES

The rate of tapering is dependent on the clinical context, the duration of opioid treatment and the reason for tapering. The aim is to limit withdrawal symptoms and avoid escalation of patient distress.

Patient education is essential to successfully taper opioids. Clear written and verbal instructions should be given to patients and families to educate them about the tapering protocol that will minimise withdrawal symptoms.

GENERAL APPROACH TO OPIOID TAPERING WITH PATIENTS

A motivational approach may be helpful as this elicits the patient's own reasons for change or intrinsic motivation and is likely to be much more effective.[36] A useful guide to assist patients to understand the possible benefits of lowering opioid doses (and the dangers of not lowering the dose) is available from the National Prescribing Service.[37]

The rate of tapering is dependent on the clinical context (duration of treatment and the reason for tapering) and the aim is to limit withdrawal symptoms and avoid escalation of patient distress.

The National Prescribing Service has published an opioid tapering algorithm that provides some detailed guidance for tapering of opioids, a modified version of this can be seen in **Figure 2**.[38]

FACTORS TO CONSIDER

A number of studies have shown that opioid tapering can result in improvement in pain management, improvement in physical and emotional functioning and a reduction in adverse effects.[39,40,41,42,43] These studies suggest that many patients with persistent pain can achieve favourable pain and function outcomes after stopping or reducing opioids in multidisciplinary interventions.

A phone or device-based application is also available to assist in opioid conversion that has been prepared by the ANZCA (Opioid Calculator FPM ANZCA).[50]

CAUTION WITH OPIOID ROTATION

Opioid rotation (switching to a different opioid) can be used to limit the impact of tolerance and to manage adverse effects. However, the main role of rotation is to reduce the total opioid dose to facilitate tapering and cessation. Opioid tolerance increases with duration of patient exposure to the opioid. Long-term high dose opioid use is usually associated with significant tolerance to the effects of that opioid. Conversion to an alternative opioid requires a greater level of dose reduction to account for this established tolerance. Reducing the dose by 25-50% of the calculated equianalgesic dose is usually required.

IN FAVOUR OF DEPRESCRIBING

Patients taking long term (greater than 6 months) opioid therapy for CNCP should be considered for dose reduction and/or cessation.

Patients with chronic non-cancer pain taking long term oMMe of 40mg or more daily should also be considered for opioid tapering, depending on individual circumstances (adverse effects, efficacy, risk of falls etc).

Patients with chronic non cancer pain taking any dose of opioids should be closely monitored and those whose pain control is stable should also be considered for dose reduction or cessation of opioids.

The following factors may be an indication for opioid dose tapering or cessation:

- Patients with a lack of demonstrable clinical effectiveness
- The existence of unmanageable adverse effects
- Patients who are stable and have a decreased level of pain
- Evidence of misuse, illegal or unsafe behaviours

If patients have a desire to discontinue their opioid therapy, then support and education will assist in achieving this goal.

AGAINST DEPRESCRIBING

Patients who require analgesia for serious exacerbations of pain (e.g. fractures, flares) may require short term opioid therapy for several weeks.

Opioid therapy can usually be ceased within one week of surgery or injury. In more complex cases, opioids should be weaned and ceased within (at the most) 90 days.[6]

REFERENCES

1. Roxburgh A, Bruno R, Larance B, Burns L. Prescription of opioid analgesics and related harms in Australia. Med J Aust 2011; 195: 280-284.
2. NPS Medicinewise. Unexpected deaths from legitimate opioid prescribing. Health News and Evidence 16 Dec 2014.
3. Pilgrim JL, et.al. An update on oxycodone: lessons for death investigators in Australia. Forensic Sci Med Pathol 2015 (11): 3-12.
4. Martins SS, Sampson L, Cerda M, Galea S. Worldwide prevalence and trends in unintentional drug overdose: A systematic review of the literature. Am J Public Health 2015; 105: e29-e49.
5. Rudd RA, Seth P, David F, Scholl L. Increases in drug and opioid-involved overdose deaths- United States 2010-2015. MMWR Morb Mortsal Wkly Rep. epub 16 Dec 2016 doi: 10.15585/mmwr.mm65505e1
6. Hunter Integrated Pain Service. Reconsidering Opioid Therapy: A Hunter New England Perspective. May 2014 Available at: http://www.hnehealth.nsw.gov.au/Pain/Documents/Reconsidering_opioid_therapy_May%202014.pdf accessed 20th Jul 2018.
7. Frank JW, et.al. Patient outcomes in dose reduction or discontinuation of long-term opioid therapy: A systematic review. Ann Intern Med 2017; 167(3): 181-191.
8. Karanges EA, et.al. Twenty-five years of prescription opioid use in Australia: a whole of population analysis using pharmaceutical claims. Br J Clin Pharmacol 2016:82: 255-267.
9. Australian Government Department of Health. Therapeutic Goods Administration. Addressing prescription opioid use and misuse in Australia: Regulatory Impact Self Assessment Report. Version1.0 November 2019.
10. daCosta BR, et.al. Oral or transdermal opioids for osteoarthritis of the knee or hip. Cochrane Database of Systematic Reviews 2014, Issue 9. Art. No.: CD003115. DOI: 10.1002/14651858.CD003115.pub4.
11. Noble M, et. al. Long-term opioid management for chronic noncancer pain. Cochrane Database of Systematic Reviews 2010; Issue 1. Art. No.: CD006605. DOI: 10.1002/14651858.CD006605.pub2.
12. Von Korff MR. Long-term use of opioids for complex chronic pain. Best Pract Res Clin Rheumatol 2013; 27(5): 663-672.
13. Busse JW et al Opioids for Chronic Noncancer Pain A Systematic Review and Meta-analysis. JAMA 2018;320;2448-2460
14. Eriksen J, Sjøgren P, Bruera E, Ekholm O, Rasmussen NK. Critical issues on opioids in chronic non-cancer pain: an epidemiological study. Pain 2006 Nov;125(1-2):172-9. Epub 2006 Jul 13.
15. Tardif H, Hayes C, Allingham SF. Opioid cessation is associated with reduced pain and improved function in people attending specialist chronic pain services. Med J Aust. 2021 May;214(9):430-432. doi: 10.5694/mja2.51031. Epub 2021 Apr 22. PMID: 33885163.
16. Häuser W, Schubert T, Vogelmann T, Maier C, Fitzcharles MA, Tölle T. All-cause mortality in patients with long-term opioid therapy compared with non-opioid analgesics for chronic non-cancer pain: a database study. BMC Med. 2020 Jul 15;18(1):162. doi: 10.1186/s12916-020-01644-4. PMID: 32664901; PMCID: PMC7362543.
17. Park TW, Saitz R,Ganoczy D, Ilgen MA,Bohnert ASB. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study BMJ 2015;350:h2698 doi: 10.1136/bmj.h2698.
18. Torrance N, Veluchamy A, Zhou Y, Fletcher EH, Moir E, Hebert HL, Donnan PT, Watson J, Colvin LA, Smith BH. Trends in gabapentinoid prescribing, co-prescribing of opioids and benzodiazepines, and associated deaths in Scotland. Br J Anaesth. 2020 Aug;125(2):159-167. doi: 10.1016/j.bja.2020.05.017. Epub 2020 Jun 19. PMID: 32571568.
19. Gomes T, Juurlink DN, Antoniou T, Mamdani MM, Paterson JM, van den Brink W. Gabapentin, opioids, and the risk of opioid-related death: A population-based nested case-control study. PLoS Med. 2017 Oct 3;14(10):e1002396. doi: 10.1371/journal.pmed.1002396. PMID: 28972983; PMCID: PMC5626029.
20. Vestergaard P, Rejnmark L, Mosekilde L. Fracture risk associated with the use of morphine and opiates. J Intern Med 2006;260:76-87.
21. Zhaowei Teng, et. al. Opioids contribute to fracture risk: A meta-analysis of 8 cohort studies. PLoS One. 2015; 10(6): e0128232. Published online 2015 June 1. doi: 10.1371/journal.pone.0128232
22. Elliot JA, Horton E, Fibuch EE. The endocrine effects of long-term oral opioid therapy: a case report and review of the literature. J Opioid Manag 2011;7:145-54.
23. Deyo RA, et. al. Prescription opioids for back pain and use of medications for erectile dysfunction. Spine 2013;38:909-15.
24. Daniell HW. Opioid endocrinopathy in women consuming prescribed sustained-action opioids for control of nonmalignant pain. J Pain 2008;9:28-36.
25. Chu LF, D'Arcy N, Brady C, Zamora AK, Young CA, Kim JE, et al. Analgesic tolerance without demonstrable opioid-induced hyperalgesia: a doubleblinded, randomized, placebo-controlled trial of sustained-release morphine for treatment of chronic nonradicular low back pain. Pain 2012;153:1583-92.
26. Ballantyne JC, Shin NS. Efficacy of opioids for chronic pain: a review of the evidence. Clin J Pain 2008;24:469-78.
27. McQuay H. Opioids in pain management. Lancet 1999;353:2229-32.
28. Paulozzi LJ, Zhang K, Jones CM, Mack KA. Risk of adverse health outcomes with increasing duration and regularity of opioid therapy. J Am Board Fam Med 2014;27:329-38.
29. Pasternak GW, Pan Y. Mu Opioids and Their Receptors: Evolution of a Concept.Pharmacol Rev 2013; 65:1257–1317.
30. Dale O, Moksnes K, Kaasa S. European Palliative Care Research Collaborative Pain Guidelines: Opioid switching to improve analgesia or reduce side effects. A systematic review. Palliative Medicine 2010; 25(5): 494-503.
31. Jamison RN, Mao J. Opioid analgesics. Mayo Clinic Proceedings Jul 2015; 90(7): 957-968.
32. Lee M, et. al. A comprehensive review of opioid-induced hyperalgesia. Pain Physician 2011; 14: 145-161.
33. Brush DE. Complications of long-term opioid therapy for management of chronic pain: The paradox of opioid-induced hyperalgesia. J. Med. Toxicol 2012; 8:387–392 .
34. Yi P, Pryzbylkowski P. Opioid Induced Hyperalgesia. Pain Medicine 2015; 16: S32–S36
35. Rogers E, Mehta S, Shengelia R, Reid MC. Four strategies for managing opioid-induced side effects in older adults. Clin Geriatr. 2013 April ; 21(4):
36. Murphy L et al. Guidance on opioid tapering in the context of chronic pain: Evidence, practical advice and frequently asked questions. CPJ/RPC_2018;151:114-120.
37. NPS Medicinewise. Lowering Your Opioid Dose. Available from https://www.nps.org.au/assets/NPS-MedicineWise-Lowering-your-opioid-dose.pdf accessed 21st March 2022.
38. NPS Medicinewise. Opioid Tapering Algorithm. Available at https://www.nps.org.au/assets/NPS-MedicineWise-opioid-tapering-algorithm.pdf accessed 21st March 2022.
39. Murphy JL, Clark ME, Banou E. Opioid cessation and multidimensional outcomes after interdisciplinary chronic pain treatment. Clin J Pain 2013;29:109-17.
40. Townsend CO, et. al. A longitudinal study of the efficacy of a comprehensive pain rehabilitation program with opioid withdrawal: comparison of treatment outcomes based on opioid use status at admission. Pain 2008;140:177-89.
41. Baron MJ, McDonald PW. Significant pain reduction in chronic pain patients after detoxification from high-dose opioids. J Opioid Manage 2006;2:277-82.
42. Crisostomo RA, et. al. Withdrawal of analgesic medication for chronic low-back pain patients: improvement in outcomes of multidisciplinary rehabilitation regardless of surgical history. Am J Phys Med Rehabil 2008;87:527-36.
43. Wright AP, Becker WC, Schiff GD. Strategies for flipping the script on opioid overprescribing. JAMA Intern Med 2016; 176(1): 7-8.

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