Clinical practice guideline for deprescribing opioid analgesics: summary of recommendations

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Abstract

Introduction: Long term opioids are commonly prescribed to manage pain. Dose reduction or discontinuation (deprescribing) can be challenging, even when the potential harms of continuation outweigh the perceived benefits. The *Evidence-based clinical practice guideline for deprescribing opioid analgesics* was developed using robust guideline development processes and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology, and contains deprescribing recommendations for adults prescribed opioids for pain.

Main recommendations: Eleven recommendations provide advice about when, how and for whom opioid deprescribing should be considered, while noting the need to consider each person's goals, values and preferences. The recommendations aim to achieve:

- implementation of a deprescribing plan at the point of opioid initiation;
- initiation of opioid deprescribing for persons with chronic non-cancer or chronic cancer-survivor pain if there is a lack of overall and clinically meaningful improvement in function, quality of life or pain, a lack of progress towards meeting agreed therapeutic goals, or the person is experiencing serious or intolerable opioid-related adverse effects;
- gradual and individualised deprescribing, with regular monitoring and review;
- consideration of opioid deprescribing for individuals at high risk of opioid-related harms;
- avoidance of opioid deprescribing for persons nearing the end of life unless clinically indicated;
- avoidance of opioid deprescribing for persons with a severe opioid use disorder, with the initiation of evidence-based care, such as medication-assisted treatment of opioid use disorder; and
- use of evidence-based co-interventions to facilitate deprescribing, including interdisciplinary, multidisciplinary or multimodal care.

Changes in management as a result of these guidelines: To our knowledge, these are the first evidence-based guidelines for opioid deprescribing. The recommendations intend to facilitate safe and effective deprescribing to improve the quality of care for persons taking opioids for pain.

Pain and pain-related conditions are a leading cause of disability and disease burden globally,[1] with one in five adults aged 45 years and over reporting persistent, ongoing pain.[2] Opioids are commonly prescribed for the management of pain, and increases in the use of prescription opioids have been observed globally over recent decades, particularly in Organisation for Economic Co-operation and Development (OECD) countries.[3] In Australia, over 1.9 million adults initiate opioid therapies each year,[4] with the majority of prescriptions in primary care issued for maintenance therapy in chronic non-cancer pain.[5,6] Although shown to be an effective component of the management of acute pain, opioids may not provide longer term clinically important improvements in pain or function compared with placebo or non-opioid medications.[7,8] Further, opioid use presents a significant risk of harm, with about 80% of people who take opioids for three months or more experiencing adverse effects.[9]

Escalating opioid use and subsequent harm has been recognised as an international public health concern. The World Health Organization has set a global goal of reducing severe avoidable medication-related harm through its Medication Without Harm Global Patient Safety Challenge.[10] Australia's response to Medication Without Harm, published in 2020, identifies opioids as one of the four medicines of focus for the Australian context.[11] Health care professionals across a range of disciplines acknowledge that opioid deprescribing is a complex and challenging practice, with continued prescribing the default behaviour.[12] Deprescribing is the process for medication dose reduction or cessation, supervised by a health care professional, with the goal of improving outcomes and, where relevant, managing polypharmacy.[13] In Australia, existing clinical guidance focuses primarily on pain management and the prescription of analgesia.[14] However, there is a need for evidence-based guidelines that focus on the safe and effective reduction and cessation of prescribed opioids in primary care. Emerging evidence of an association between precipitous opioid tapering and overdose, suicide, and mental health crises[15,16] further highlights that additional advice on deprescribing is required.

These guidelines aim to provide evidence-based recommendations on when and how to deprescribe opioids for adults prescribed opioids for pain in primary care settings. To our knowledge, these are the first evidence-based opioid deprescribing guidelines, offering recommendations based on the most recent scientific evidence, informed by expert opinion and stakeholder and public input.

Methods

We followed the process of developing class-specific medication deprescribing guidelines,[17] and the Appraisal of Guidelines for Research and Evaluation (AGREE) II criteria.[18] We complied with the Australian 2016 National Health and Medical Research Council (NHMRC) standards for guidelines,[19] and the procedures and requirements for meeting the 2011 NHMRC standard for clinical practice guidelines.[20] The guideline methods are summarised hereafter (Supporting Information), with complete guideline methods available online.[21,22]

The Guideline Development Group was composed of 17 members who were health care professionals (general practitioners, pain specialists, addiction specialists, registered nurses,

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pharmacists, physiotherapists) with experience in caring for persons taking opioids and with research expertise in the field of deprescribing in Australia and internationally; methodologists with expertise in the areas of guideline development, conducting systematic reviews, and the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach; implementation experts; and organisational (NPS MedicineWise) and consumer representatives.

Two qualitative studies were conducted with health care professionals[12] and with persons taking opioids[23] to elucidate their beliefs and attitudes towards opioid deprescribing and identify perceived facilitators and barriers to achieving successful outcomes. The guideline development group then defined three key clinical questions for the guideline:

- Does deprescribing of opioids result in benefits or harms compared with continuation?
- What is the evidence on how to deprescribe opioids?
- Which interventions are effective to facilitate opioid deprescribing?

Systematic evidence retrieval and synthesis was conducted via an overview of systematic reviews (containing both randomised clinical trials and observational studies).[24] Five databases — Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Library, Excerpta Medica Database (EMBASE), Medical Literature Analysis and Retrieval System Online (MEDLINE) and PsycINFO — were searched for systematic reviews published in the past ten years examining one or more interventions for deprescribing opioids in adult populations (aged ≥ 18 years). The search strategy was intentionally broad, placing no restrictions on the type of pain, characteristics of participants, dose or duration of opioid use, or intervention setting. A supplemental search of guidelines was conducted to inform the benefits and harms of opioid deprescribing for individuals with opioid use disorders, and a supplemental search of primary literature was conducted to locate additional evidence on how to deprescribe opioids.[22] The GRADE approach was applied to assess the certainty of the evidence.[25] Before guideline meetings, evidence summaries with GRADE certainty of evidence ratings were circulated to the guideline development group members. The evidence was reviewed by all group members and during meetings, the group collaboratively and iteratively refined the GRADE Evidence to Decision frameworks,[26] systematically considering the certainty of the evidence, the risks and benefits of deprescribing, stakeholder values and preferences, acceptability, feasibility, equity, and resource requirements. The direction (for or against) and strength of the recommendation (recommendation or conditional recommendation) were determined by consensus, and the wording of the recommendations was formulated. Where there was insufficient direct evidence to generate an evidence-based recommendation but the guideline development group still considered it important to provide a recommendation, a consensus recommendation was formulated by the expert panel.

Box 1 provides an overview of each recommendation type contained within this guideline. The terminology "we recommend" is used for recommendations, and "we suggest" is used for conditional and consensus-based recommendations.[26]

Three independent expert reviewers appraised the draft guideline using the AGREE II approach before its release for public consultation. Given the importance of the guideline to a wide variety of stakeholders, public consultation was undertaken for a period of 60 days from 2 February to 3 April 2022 to optimise the recommendations' specificity, applicability, and ease of implementation. Following public consultation and externally commissioned expert and methodological review, the guideline was refined, and the final guideline recommendations were approved by the NHMRC in September 2022.

1 Classification of recommendations, adapted from the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) handbook[25]

Recommendation for

A "recommendation for" is given when the guideline development group is confident that the desirable effects of an intervention outweigh its undesirable effects. This implies that most or all individuals will be best served by the recommended course of action.

Recommendation against

A "recommendation against" is given when the guideline development group is confident that the undesirable effects of an intervention outweigh its desirable effects. This implies that most or all individuals will be best served by the recommended course of action.

Conditional recommendation for

A "conditional recommendation for" is given when the guideline development group considers that the intervention's desirable effects probably outweigh the undesirable effects but appreciable uncertainty exists. A conditional recommendation implies that not all individuals will be best served by the recommended course of action. There is a need to consider the individual person's circumstances, preferences and values more carefully than usual.

Conditional recommendation against

A "conditional recommendation against" is given when the guideline development group considers that the intervention's undesirable effects outweigh the desirable effects but appreciable uncertainty exists. A conditional recommendation implies that not all individuals will be best served by the recommended course of action. There is a need to consider the individual person's circumstances, preferences and values more carefully than usual.

Consensus recommendation

A consensus recommendation can be given for or against an intervention. This type of recommendation is used when there is not enough evidence to give an evidence-based recommendation but the guideline development group still considers it important to give a recommendation. These recommendations are made based on expert opinion and were formulated by a consensus process.

Recommendations

The eleven recommendations and accompanying practice points (Box 2) provide advice about when, how and for whom opioid deprescribing may be appropriate, while noting the need to consider the recommendations within the context of the person and their goals, values and preferences. The guideline target population is adults (≥ 18 years old) prescribed one or more opioids for any type of pain (eg, acute, chronic, cancer-related, end-of-life). Persons with opioid use disorders, those with prescribed opioid substitution therapy, or people taking illicit opioids (eg, heroin) are not the target population, although there may be overlap of clinical characteristics between the identified populations. The target care setting is community primary care; however, the recommendations may be relevant to other care settings (residential care, inpatient and outpatient). Overall, the certainty of evidence informing recommendations was rated as predominantly very low to low.[21,24] The full guideline[28] and

2 Summary of guideline recommendations and practice points

Recommendation	Recommendation classification (certainty of evidence)[22,24]	Key practice points
1. We suggest developing and implementing a deprescribing plan for persons being prescribed opioids at the point of opioid initiation.	Consensus recommendation	• An opioid deprescribing plan should form part of an agreed pain management plan which incorporates non-opioid treatment modalities and/or non-pharmacological pain management strategies. • Optimisation of appropriate non-opioid pharmacotherapy may improve pain management and may have an opioid-sparing effect. Consider the use of evidence-based non-opioid pharmacotherapy where appropriate. Avoid sole reliance on opioids. • Optimisation of appropriate non-pharmacological therapy may improve pain management and may have an opioid-sparing effect. Consider the use of evidence-based non-pharmacological strategies for pain management and referral to allied health care professionals where appropriate. • When initiating opioids, assess and discuss the expected duration of therapy. Advise the person that it will be a time-limited course of therapy, generally limited from days to weeks. Provide relevant information to the person regarding the safe use, safe storage, and safe discarding of opioids. Avoid repeat prescribing for acute, or acute-on-chronic, pain conditions. • Discuss naloxone when prescribing opioids.
2. We suggest initiating deprescribing for persons taking opioids for chronic non-cancer pain if (any of the following): • there is a lack of overall and clinically meaningful improvement from baseline in function, quality of life, or pain; • there is a lack of progress towards meeting agreed therapeutic goals; or • the person is experiencing serious or intolerable opioid-related adverse effects in the physical, psychological or social domains.	Conditional recommendation for (very low certainty evidence)	• The use of an opioid deprescribing conversation guide (eg, *Communication techniques for opioid analgesic tapering conversations*[27]) may assist in assessing the willingness and readiness of a person taking opioids to engage in deprescribing. The guide may be used to structure conversations relating to the potential benefits and harms of deprescribing in the context of the person's values, goals and preferences. • A deprescribing plan, agreed upon by the person taking opioids and their health care professional, may facilitate person-centred medication dose reduction or cessation. • Baseline function can be determined by both the person taking opioids and their health care professional. This may be aided by the use of validated tools (see Recommendation 9).
3. We suggest initiating deprescribing for persons taking opioids for chronic cancer-survivor pain if (any of the following): • there is a lack of overall and clinically meaningful improvement from baseline in function, quality of life, or pain; • there is a lack of progress towards meeting agreed therapeutic goals; or • the person is experiencing serious or intolerable opioid-related adverse effects in the physical, psychological or social domains.	Consensus recommendation	• Cancer-survivor populations may be at risk for recurrent disease or second malignancies and, therefore, new or worsening pain should be carefully evaluated. • The use of an opioid deprescribing conversation guide (eg, *Communication techniques for opioid analgesic tapering conversations*[27]) may assist in assessing the willingness and readiness of a person taking opioids to engage in deprescribing. The guide may be used to structure conversations relating to the potential benefits and harms of deprescribing in the context of the person's values, goals and preferences. • A deprescribing plan, agreed upon by the person taking opioids and their health care professional, may facilitate person-centred medication dose reduction or cessation. • Baseline function can be determined by both the person taking opioids and their health care professional. This may be aided by the use of validated tools (see Recommendation 9).
4. We suggest considering deprescribing for persons taking opioids for chronic pain with one or more of the following clinical characteristics: • comorbidities that may increase risk of opioid-related harms (eg, sleep-disordered breathing or sleep apnoea, chronic obstructive pulmonary disease); • concomitant use of medicines or substances with sedating effects (eg, benzodiazepines, alcohol, gabapentinoids, antipsychotics, and sedating antidepressants); • high doses of prescribed opioids.	Consensus recommendation	• Health care professionals need to consider clinical outcomes when making decisions about the appropriateness of opioid deprescribing in populations at increased risk of opioid-related harms. This includes considering the person's response to opioids in terms of their function, quality of life, pain, and adverse effects (see Recommendation 2). Optimisation of medical management of comorbid conditions and the overall medication regimen is required. This may involve reducing or stopping other substances such as benzodiazepines or alcohol in addition to, or instead of, opioid deprescribing. • Liaising with other health care professionals, particularly those trained in mental health conditions, may assist in deducing the reasoning behind the use of concomitant medications and any other concerns worth noting. • When deprescribing opioids for a person taking concomitant medicines, ensure that opioid deprescribing does not result in increased use of other substances with detrimental effect. • Consider generating a referral for a pharmacist to conduct a Home Medicines Review (HMR). HMRs may improve the person's understanding of their medicines and inform the development of a medication management plan and/or deprescribing plan.
5. We suggest avoiding deprescribing for persons taking opioids for pain or dyspnoea who are nearing the end of life.	Consensus recommendation	• Persons taking opioids and their carers should be educated about opioid safety and how to monitor for opioid-related harms. • There may be specific circumstances where prescribers identify reasons to deprescribe opioids for people who are nearing the end of life. These may include unwanted confusion, opioid hyperalgesia, unmanageable constipation, dry mouth, sweating and itching, and/or organ deterioration. This approach to deprescribing should be discussed with the person taking opioids and/or their family/carer and monitored over time.

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Recommendation	Recommendation classification (certainty of evidence)[22,24]	Key practice points
6. We suggest avoiding opioid deprescribing for persons taking opioids with a severe opioid use disorder and suggest that evidence-based care, such as transition to, or referral for, medication-assisted treatment of opioid use disorder is provided.	Conditional recommendation against (moderate certainty evidence)	• General practitioners can offer, or arrange, evidence-based treatments for people with an opioid use disorder. This may include medication-assisted treatment with buprenorphine or methadone and associated strategies in combination with behavioural therapies. Depending on the skills and experience of the health care professional, this may occur in the general practice setting in collaboration with a pharmacist, through an addiction medicine specialist or psychiatrist, a tertiary drug treatment service, or a combination. • Specialist advice or referral may be appropriate for people with chronic pain and opioid dependence or an opioid use disorder. This is due to the potential complexity of managing both conditions. Health care professionals should continue to use non-pharmacological and non-opioid pharmacological pain treatments, as appropriate, and consider consulting a pain or addiction specialist if required. • In some Australian states and territories, Schedule 8 medications cannot be prescribed for persons who meet specified criteria related to drug dependence, without a permit or an appropriate approval from the relevant state or territory medicines regulatory area. Please refer to specific state and territory regulations and guidelines for more information. Many states and territories in Australia have a Drug and Alcohol Specialist Advisory Service that prescribers can contact for advice.
7. We recommend gradual tapering of opioids. Abrupt cessation of opioids without prior dose reduction may increase risks of harm.	Recommendation for (low certainty evidence)	• A deprescribing plan agreed upon by the person taking opioids and the health care professional may facilitate person-centred medication dose reduction or cessation. • There is limited evidence to inform a preferred protocol for opioid deprescribing. Local guidance for gradual dose reduction strategies may be used. • For people who have been receiving long term opioid therapy (ie, for years) or taking high doses, the rate of reduction may need to be slower to prevent withdrawal symptoms. Alternatively, more rapid tapers or cessation might be needed for patient safety under certain circumstances (eg, for people who have experienced overdose on their current dosage). In these circumstances, consider the provision of naloxone. • If a person has been using opioids short term (eg, less than one week) or has been using opioids infrequently, opioids may be discontinued without gradual tapering. • Instructions should be provided to the individual and/or carer/family on what to look out for and what to do if symptoms occur during deprescribing, particularly the possible risk of withdrawal effects (see Recommendation 9).
8. We recommend tailoring the deprescribing plan based on the person's clinical characteristics, goals, and preferences.	Recommendation for (very low certainty evidence)	• The use of an opioid deprescribing conversation guide (eg, *Communication techniques for opioid analgesic tapering conversations*[27]) may assist in assessing the willingness and readiness of a person taking opioids to engage in deprescribing. The guide may be used to structure conversations relating to the potential benefits and harms of deprescribing in the context of the person's values, goals and preferences. • A deprescribing plan, agreed upon by the person taking opioids and their health care professional may facilitate person-centred medication dose reduction or cessation. • Where possible, opioid deprescribing should be voluntary in nature, with the deprescribing plan mutually agreed upon by the person taking the medication and the health care professional to facilitate person-centred deprescribing. This may involve discussions around which medications will be decreased first, the rate of taper, and timing of doses. The plan may be adjusted over time to meet the person's ongoing needs. • Opioid deprescribing should involve consideration of a person's starting dose and the available opioid dosage forms (eg, immediate release or modified release formulations, oral or transdermal opioids), the total daily dose in 24 hours, and the pharmacokinetic profile (absorption and elimination) of the opioid. Based on these factors, plans may involve gradually reducing the total daily dose of the medication to the next available dose through to the smallest available unit dosage. • Small reductions in doses initially may help to cultivate trust between the health care professional and the person taking opioids, minimise fears about withdrawals, and enhance self-efficacy to engage in opioid deprescribing. • Characteristics of the person may influence the deprescribing approach, such as previous response to opioids, previous deprescribing attempts and experiences, age, body mass index, liver and renal function, comorbidities and mental health conditions, concomitant medications, and psychosocial factors. • Individualisation of the rate and approach of opioid deprescribing may require additional monitoring and input from health care professionals. At times, deprescribing might have to be slowed (eg, once a person reaches a low dosage) or may have to be paused and restarted again when the person is ready. See Recommendation 9 for further details on monitoring. • If a person has noticeable decline in function, quality of life or pain control after dose reduction/cessation (after exclusion of other causes), then the medication should be restarted at the previous minimum effective dose. • Where opioid deprescribing results in significant withdrawal symptoms or a noticeable decline in function, quality of life, or pain control, consider pausing the taper to stabilise and re-evaluate the person's pain status, diagnosis, overall clinical status, coping mechanisms, and psychosocial factors before resuming deprescribing. When resuming deprescribing, consider slowing down both the amount and frequency of the opioid reduction. Opioid deprescribing may not always be unidirectional and opioid dose increases may be necessary.

Continues

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Recommendation	Recommendation classification (certainty of evidence)[22,24]	Key practice points
9. We suggest conducting regular monitoring and review of a person taking opioids throughout the opioid deprescribing process. Response against agreed therapeutic goals contained in a deprescribing plan should be regularly assessed.	Consensus recommendation	• The success of opioid deprescribing may be measured by assessing progress in relation to goals contained within the deprescribing plan. The benefits of opioid deprescribing may not be observed immediately, and assessing response against set goals in the deprescribing plan may be useful. Monitor and document cognitive and functional status, behavioural and psychological symptoms, and how these have changed over the follow-up period. • Health care professionals should monitor parameters including function, pain, sleep, mood, withdrawal effects, and dependence. Validated tools to assist monitoring are linked in the full guideline. • The person engaging in opioid deprescribing should be provided with information and support to ensure they are aware of common opioid withdrawal symptoms, the likely severity and duration of the symptoms they may experience with each dose reduction, and who to contact if additional advice or support is required. Education and support may assist the person to self-monitor and implement strategies to manage the emergence of these symptoms as their dose is reduced. Consider providing both verbal and written communication that considers the person's health literacy. • Establish and document a plan for when and how follow-up is going to occur. Monitoring should be conducted by the prescriber during each clinical review (at a minimum), but a person may receive support from other health care professionals such as pharmacists in between reviews. Practically, monthly reviews may be appropriate, but more frequent monitoring may be required at the beginning and end of the deprescribing process, or if there is concern about managing a person's health condition. • Where opioid deprescribing results in significant withdrawal symptoms or a noticeable decline in function, quality of life or pain control, consider pausing the taper to stabilise and re-evaluate the person's overall clinical status, diagnosis, coping mechanisms and psychosocial factors before resuming deprescribing. When resuming deprescribing, consider slowing down both the amount and frequency of the opioid reduction. Opioid deprescribing may not always be unidirectional and opioid dose increases may be necessary in the short term. • If complicated withdrawal symptoms are experienced, we suggest discussion with or referral to a pain or addiction medicine specialist. • Health care professionals should consider the potential harms of opioid continuation or deprescribing for people receiving high dose chronic opioid treatment and monitor specifically for suicidal thoughts, mental health issues, and illicit opioid use. We suggest discussion with or referral to a psychiatrist where appropriate. • Health care professionals should discuss the increased risk for overdose on abrupt return to a previously prescribed higher dose after deprescribing and may consider the provision of naloxone.
10. When available, we suggest the use of interdisciplinary or multidisciplinary care, or a multimodal approach that emphasises non-pharmacological and self-management strategies to deprescribe opioids.	Conditional recommendation for (low certainty evidence)	• Interdisciplinary or multidisciplinary care programs provide multimodal treatment, with coordinated contributions by health care professionals from different disciplines typically organised around a biopsychosocial model of chronic pain. • While recognising the cost of formal interdisciplinary opioid reduction programs and their current limited availability/capacity, an alternative is a coordinated multidisciplinary collaboration that includes several individual health care professionals whom the person taking opioids can access (eg, nurse, pharmacist, occupational therapist, physiotherapist, addiction medicine specialist, psychiatrist, psychologist). Another alternative is for prescribers to implement a multimodal approach.
11. We suggest the consideration of evidence-based co-interventions to support opioid deprescribing.	Conditional recommendation for (very low certainty evidence)	• The appropriateness of co-interventions for opioid deprescribing must be discussed between the health care professional and the person taking opioids, taking into consideration the person's clinical status, preferences, lived experience, values and costs of alternative treatments for the person.

supporting documents are available online at www.opioiddeprescribingguideline.com/guideline.

Summary of evidence informing recommendations

The evidence informing recommendations is predominantly very low to low certainty. In the absence of high certainty evidence, guideline development groups should not fail to make a recommendation; rather, the benefits and harms of interventions, as well as patients' values, acceptability, feasibility, equity and resource considerations, should be considered to recommend a course of action.[29] Recognising the low certainty evidence informing recommendations, further research on the effectiveness and outcomes of opioid deprescribing is required.

Key clinical question 1: benefits and harms of opioid deprescribing

About 5% of opioid-naïve patients who fill an opioid prescription transition to long term use.[30] When initiating opioids, prescribing less than seven days of medication could mitigate the chance of unintentional chronic use,[31] highlighting the importance of planning for deprescribing (Recommendation 1). A systematic review of opioid treatment agreements found weak evidence to support the effectiveness of patient–prescriber agreements in the reduction and mitigation of opioid misuse.[32] However, there is

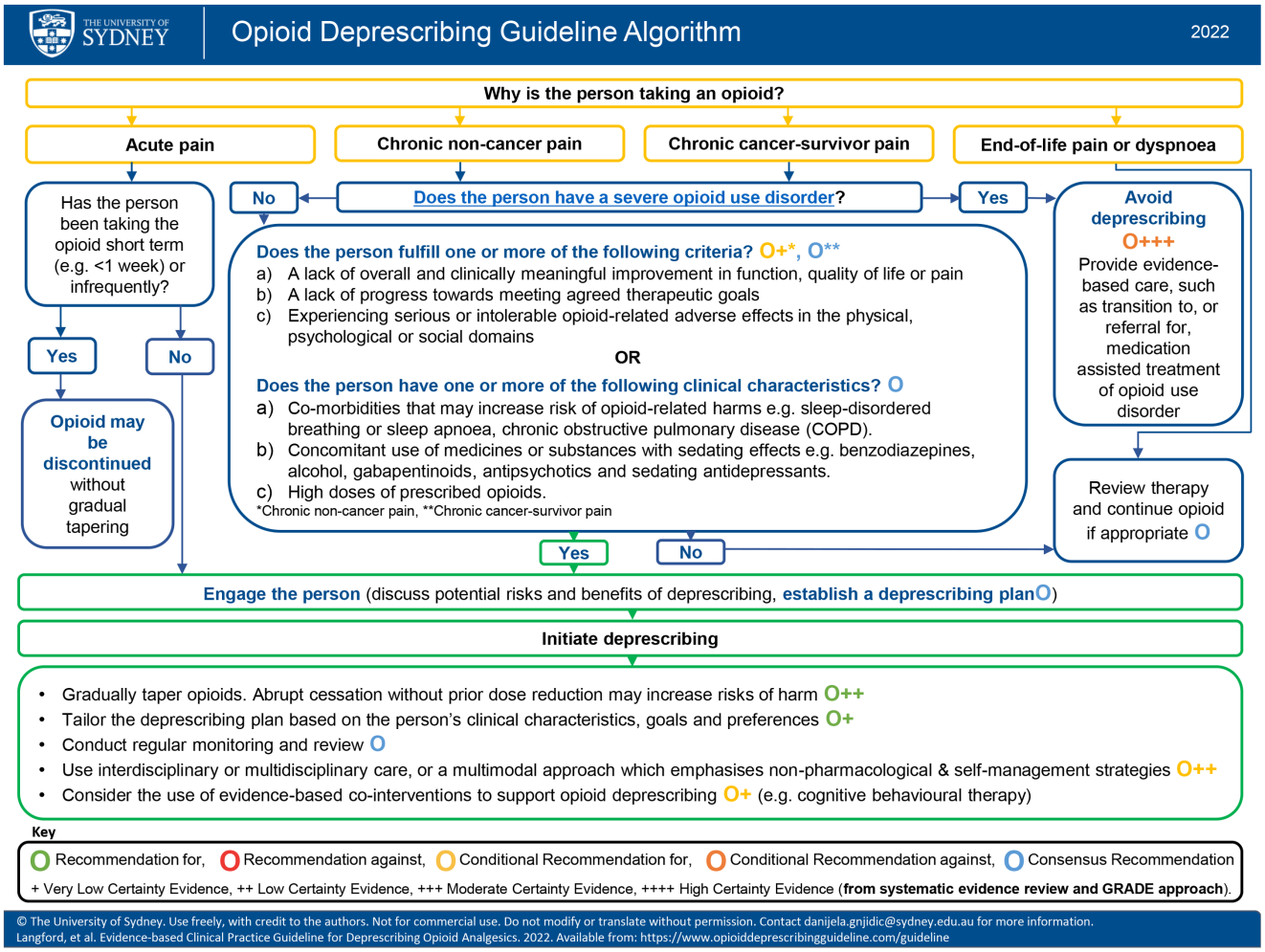
insufficient evidence to determine whether the implementation of a deprescribing plan at the point of opioid initiation reduces use or opioid-related harms.

Consistent low certainty evidence suggests that mean pain scores and functional measures improved, or did not significantly change, for most persons with chronic non-cancer pain who reduced or discontinued opioids.[33-38] Pain reduction following opioid deprescribing was greater for those taking higher baseline opioid doses compared with those with lower baseline doses.[35] Reporting of quality of life measures was heterogeneous across reviews, but very low certainty evidence suggests that quality of life may improve with opioid deprescribing (Recommendation 2).[33,35,39] Some reviews reported decreased opioid-related adverse effects such as dry mouth for intervention groups compared with control groups,[37] but serious harms relating to opioid deprescribing remain uncertain. There is emerging evidence that opioid tapering, particularly when precipitous or involuntary in nature, may increase the risk of substance use, emotional dysregulation, opioid overdose, and suicide.[15,16,35]

Relevant literature on opioid use in cancer-survivor populations (those with a history of cancer who are beyond the acute diagnosis and treatment phase) provided limited evidence to support the safety and efficacy of long term opioid use.[40] Adverse effects from long term opioid use, including sexual dysfunction, immune system effects, fatigue and osteoporosis have been identified in this population,[41] as well as similar rates of prescription opioid misuse when compared with individuals without cancer (Recommendation 3).[42] Although there is a paucity of evidence regarding the benefits and harms of opioid deprescribing in specific populations (eg, individuals with comorbid conditions that may increase the risk of opioid-related harms, such as chronic obstructive pulmonary disease; concomitant use of medicines or substances with sedating effects; high doses of prescribed opioids), there is evidence of increased risk of opioid-related harms in each of the identified populations (Recommendation 4).[43,45]

Opioids are used to relieve pain and/or breathlessness for persons nearing the end of life, and there is insufficient evidence to inform the benefits and harms of opioid deprescribing for this population (Recommendation 5).[24] Existing clinical practice guidelines recommend against opioid deprescribing as a stand-alone strategy for individuals with opioid use disorders.[46-48] Moderate certainty evidence indicates that for

3 Opioid deprescribing guideline algorithm[60]



Source: Figure adapted and reproduced with permission from the Faculty of Pain Medicine, Australian and New Zealand College of Anaesthetists — Opioid Calculator (http://www.opioidcalculator.com.au/).

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Opioid dose equivalence

	Oral (swallowed)							Rectal	Sublingual	Transdermal	
Current opioid	Morphine (mg/day)	Oxycodone (mg/day)	Hydromorph-one (mg/day)	Codeine (mg/day)	Dextroprop-oxyphene (mg/day)	Tramadol (mg/day)	Tapentadol (mg/day)	Oxycodone (mg/day)	Buprenor-phine (mg/day)	Buprenor-phine (mcg/hr)	Fentanyl (mcg/hr)
Conversion factor	1	1.5	5	0.13	0.1	0.2	0.3	1.5	40	2	3

To calculate an oral Morphine Equivalent Daily Dose (oMEDD), **multiply the daily dose of opioid by the listed conversion value**. Oral morphine equivalents of different opioids can be calculated using The Faculty of Pain Medicine of the Australian New Zealand College of Anaesthetists (ANZCA) online opioid equianalgesic calculator.

Engaging the person

The use of an opioid deprescribing conversation guide may assist healthcare professionals to initiate and continue conversations about opioid deprescribing.
- Discuss treatment goals.
- Ask about side effects.
- Tailor discussion about benefits and harms to the individual.
- Explore fears and concerns about deprescribing.

Tapering advice

Tailor the deprescribing plan based on the person's clinical characteristics, goals and preferences. Consider:
- **<3 months use**: reduce the dose by 10 to 25% every week
- **>3 months use**: reduce the dose by 10 to 25% every 4 weeks
- **Long-term opioid use (e.g., >1 year) or on high doses:** slower tapering and frequent monitoring

Monitoring advice

The success of opioid deprescribing may be measured by assessing progress in relation to goals achieved over time.
Monitor and document:
- Cognitive and functional status, behavioural and psychological symptoms, and how these have changed over time.
- Monitor and manage parameters including function, pain, sleep, mood, withdrawal effects and dependence.
- Discuss the increased risk for overdose on abrupt return to a previously prescribed higher dose after deprescribing.
- Consider the provision of **naloxone** for persons taking opioids at risk of opioid overdose when prescribing or deprescribing opioids.

Symptomatic medications for use in opioid withdrawal

(adapted from the 2018 Alcohol and other Drug Withdrawal: Practice Guidelines, 3rd ed.)

Symptoms	Symptomatic Medication(s)
Nausea and vomiting	Antiemetics such as metoclopramide 10 mg three times a day as required for up to three to four days or prochlorperazine 5 mg three times a day for 4–7 days, best 30 minutes before food or as required, ondansetron 4–8 mg, every 12 hours as required. Note: Also encourage fluids and a simple diet
Diarrhoea	Anti-diarrhoeals such as loperamide
Abdominal cramps	Antispasmodics such as hyoscine butylbromide
Muscles and joint pains	Non-steroidal anti-inflammatory agents such as ibuprofen (avoid if contraindications are present) or paracetamol

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Langford, et al. Evidence-based Clinical Practice Guideline for Deprescribing Opioid Analgesics. 2022. Available from: https://www.opioiddeprescribingguideline.com/guideline

people with severe opioid use disorders, opioid deprescribing, when performed without providing access to long term opioid maintenance treatment and care, is associated with elevated risk of harm and death from drug overdose.[46] Further, opioid agonist or partial agonist treatment with methadone or buprenorphine maintenance therapy has been shown to be more effective in preventing relapse than opioid withdrawal and cessation (Recommendation 6).[49,50]

Key clinical question 2: how to deprescribe opioids

Withdrawal signs and symptoms (eg, craving, anxiety, insomnia, abdominal pain, vomiting, diarrhoea, diaphoresis, mydriasis, tremor, tachycardia) are likely to occur when opioids are withdrawn abruptly.[51] The adverse physical, psychological and social outcomes of abrupt reduction or discontinuation of opioids include withdrawal effects, pain exacerbation, related loss of function and quality of life, psychological distress, hospitalisation, accidental overdose, and suicide.[52-54] One cohort study of people prescribed 120 mg oral morphine equivalent daily dose or more of long term opioid therapy found each additional week of gradual tapering to discontinuation was associated with a 7% reduction in risk of an opioid-related emergency department visit or hospitalisation (Recommendation 7).[53]

There is insufficient evidence to determine which individual or tapering characteristics are associated with greater success of opioid deprescribing.[24] Given the heterogeneity of studies examining opioid deprescribing and the limited reporting of deprescribing protocols and participant baseline characteristics, we were unable to assess the comparative effectiveness of different opioid tapering approaches. Many of the tapering schedules were not well defined,[34] with some studies and reviews reporting that the tapering approach was tailored to the specific participant's needs (Recommendation 8).[35,55] There was limited evidence regarding the management of individuals who experienced unsuccessful opioid deprescribing attempts or did not complete tapers, as these populations were often excluded from study analysis.

The evidence informing the benefits and harms of opioid deprescribing, which demonstrated improvements in pain, function and quality of life, were largely derived from studies involving voluntary opioid deprescribing.[33,35] Evidence of increased harms (suicide, overdose, illicit opioid use) in the context of involuntary opioid deprescribing informed the need for voluntary opioid deprescribing where possible.[56] There is emerging evidence of an association between opioid deprescribing and overdose, suicide and mental health crises due to cognitive and psychological withdrawal effects.[15,16,52] Therefore, frequent and close monitoring throughout the opioid deprescribing process is warranted to prevent or minimise potential harms (Recommendation 9).

Key clinical question 3: interventions to facilitate opioid deprescribing

Interdisciplinary, multidisciplinary and multimodal care that emphasised non-pharmacological and self-management strategies showed the greatest evidence for effective opioid deprescribing.[33,35] Non-pharmacological interventions in these programs included cognitive behavioural therapy and physical and occupational therapy. People receiving long term opioid therapy who voluntarily participated in intensive multidisciplinary pain management interventions that incorporated opioid tapering experienced improvements in pain severity and function.[33-38] In contrast, those who tapered opioids with less intensive co-interventions were more likely to experience unchanged pain and function (Recommendation 10).[33,35]

Evidence for the effectiveness of different co-interventions to achieve opioid deprescribing for the management of chronic pain was inconclusive and varied substantially across the interventions examined.[24] Consistent low certainty evidence suggests that regardless of intervention, mean pain scores and functional measures improved or did not significantly change for most persons who reduced or discontinued opioids.[33-39,57-59] Improved quality of life may accompany opioid dose reduction when using deprescribing co-interventions, but the evidence is very low certainty (Recommendation 11).[24,33,35,39]

Additional considerations

The full guideline[28] addresses a range of additional relevant considerations, including how to engage a person in deprescribing, stakeholder values and preferences, cost and resources, opioid-related stigma, characteristics of opioids, equivalent and equianalgesic opioid doses, opioid withdrawal symptoms and management, opioid-induced hyperalgesia, legal and ethical considerations, opioid-related harm minimisation strategies, and specific population considerations.

Implementation

We are working to translate the guideline into user-friendly materials for distribution and use by health care professionals, health service users, professional and health service user organisations, and public health departments. An implementation toolkit is under development, and, to date, we have created a health provider-directed conversation guide[27] and a one-page (double-sided) guideline algorithm (Box 3).[60] A health service user-directed information leaflet is under development.

At the system level, a lack of accessible pain management services for end-users in the face of a fragmented health system and limited resources is an ongoing barrier for the guideline recommendations to be implemented. Initiatives that may assist their implementation include increased funding and coverage for non-pharmacological pain management treatments, improved access to medication-assisted treatment for individuals with opioid use disorder, reimbursable time for patient counselling and payment models that improve geographical and financial access to multidisciplinary, interdisciplinary or multimodal coordinated care.

Conclusion

To our knowledge, the *Evidence-based clinical practice guideline for deprescribing opioid analgesics* is the first international guideline focused on opioid deprescribing and contains NHMRC-approved recommendations to assist general practitioners with deprescribing opioids for adults with pain. This guideline's recommendations and supporting information contribute to existing literature and guidelines on the quality use of opioids by providing explicit and evidence-based recommendations, developed by a multidisciplinary team through a systematic and rigorous development process. Very low to low certainty evidence suggests that in specific populations, it is possible to reduce opioid use and harms without worsening pain, while maintaining or improving function and quality of life. Additional high certainty evidence is needed to strengthen existing recommendations and inform future recommendations on when, how and for whom opioid deprescribing is appropriate.

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Supporting Information

Additional Supporting Information is included with the online version of this article.