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Evidence-Based Clinical Practice Guideline for Deprescribing Opioid Analgesics

Summary of Recommendations

THE UNIVERSITY OF SYDNEY

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Disclaimer: The recommendations in this guideline serve as a general guide to appropriate practice, to be followed subject to the health care professional's judgement and the person's values, preferences, circumstances and needs. The guideline is designed to provide information to assist shared decision-making and the recommendations are based on the best evidence available at the time of development.

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The guideline recommendations on pages 5-6 of this document were approved by the Chief Executive Officer of the National Health and Medical Research Council (NHMRC) on 14 September 2022 under section 14A of the National Health and Medical Research Council Act 1992. In approving the guideline recommendations, NHMRC considers that they meet the NHMRC standard for clinical practice guidelines. This approval is valid for a period of five years.

NHMRC is satisfied that the guideline recommendations are systematically derived, based on the identification and synthesis of the best available scientific evidence, and developed for health professionals practising in an Australian health care setting.

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PLAIN ENGLISH SUMMARY

Pain is an unpleasant experience linked with actual or potential damage to the body.[1] Pain conditions are a leading cause of disability and disease burden globally.[2] Opioid analgesics (opioids) are a group of medicines used to treat severe pain. In Australia, opioids include buprenorphine, codeine, fentanyl, hydromorphone, methadone, morphine, oxycodone, oxycodone with naloxone, pethidine, tapentadol and tramadol. Some opioids are also used to treat opioid dependency, however, this guideline focuses on opioids used for pain.

All medicines can cause both benefits and harms. The appropriate use of opioids means safely prescribing them for people who are likely to benefit from them. Appropriate use also means stopping or reducing opioids (deprescribing) when the risk of harm outweighs the benefits for the individual. This is particularly important when a person is taking opioids in the longer-term. There are harms of long-term opioid use, such as an increased risk of serious side effects (e.g. drowsiness, falls, breathing problems), dependence and death. The risk of harm can depend on a person, including their type of pain, whether they have other medical conditions or take other medicines, and for how long they have taken opioids. Changes in a person's situation, preferences and goals of care can alter the balance of benefits against harms over time.

When the risk of harm from opioids outweighs the benefits for a person, deprescribing should be considered. Some people who take opioids may be able to reduce or stop them with minimal negative consequences. Pain and function may improve or be unchanged, particularly if deprescribing occurs with the support of a multidisciplinary care team. In others, deprescribing may result in worse function or pain and some people experience side effects. People taking opioids may fear that deprescribing will result in worse pain and reduced quality of life. This is particularly the case when opioids are deprescribed without shared decision-making and without providing alternative pain management strategies. Healthcare professionals and the person taking opioids need to work together to create a deprescribing plan which takes into consideration the person's values, preferences and goals. This plan can also inform whether and when deprescribing is appropriate.

The purpose of this guideline is to assist healthcare professionals to determine: WHO should be considered for opioid deprescribing, WHEN to deprescribe opioids and HOW to deprescribe opioids. This document presents a Summary of Recommendations from the guideline. For additional information and accompanying practice points, please refer to the full guideline document.

EXECUTIVE SUMMARY

All medications have the potential to cause both benefits and harms. The appropriate use of opioid analgesics (opioids) involves safe prescription for people who are likely to benefit and deprescribing when the potential harms outweigh the benefits. Internationally, clinical practice guidelines recommend opioids for acute pain management, yet caution on the potential harms of chronic use.[3–5] This is due to a lack of evidence demonstrating a long-term benefit of opioids in improving pain and function when compared to no opioids or placebo for chronic pain.[6,7] Concerns regarding efficacy and iatrogenic morbidity and mortality are significant, with opioids increasing the risk of serious adverse events such as falls, respiratory depression and death.[5,8] The risk of harm associated with the use of opioids can depend on a person's characteristics such as the type of pain, whether they have other medical conditions or take other medicines, and how long they have used opioids. This risk-benefit profile may also change over time.

The purpose of this guideline is to assist healthcare professionals, particularly General Practitioners (also known as GPs, primary healthcare providers or family doctors) to determine for **whom** opioids should be deprescribed and **when** and **how** to do this in a safe and timely manner. Some opioids are used to treat opioid dependency, however, this guideline focuses on opioids used for pain management.

The process of developing class-specific deprescribing guidelines,[9] based on a comprehensive checklist for successful guideline development (Guideline 2.0),[10] the AGREE II criteria,[11] and the Australian National Health and Medical Research Council (NHMRC) 2016 Standards for Guidelines,[12] were followed for guideline development. Guideline development involved systematic evidence retrieval and synthesis and assessing the certainty of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. An evidence-to-decision framework was used to systematically consider the risks and benefits of opioid deprescribing compared to continuation, the certainty of the evidence, stakeholder values and preferences, acceptability, feasibility and resource requirements. Recommendations were developed and refined by a multidisciplinary Guideline Development Group (GDG).

How to use this guideline

The recommendations within this guideline apply to adults who have been prescribed one or more opioids. The recommendations relate to deprescribing. Deprescribing is the process for withdrawal of a medication (dose reduction or cessation), supervised by a healthcare professional, with the goal of improving outcomes and where relevant, managing polypharmacy.[13]

Each recommendation contained within this guideline has an accompanying 'certainty of evidence' rating in accordance with the GRADE approach. In the full guideline, a rationale is provided to describe how the GDG justified the recommendation direction and strength. To support each recommendation, a summary of the research evidence is also provided.

Additional considerations and practical information to support recommendations are presented as 'Practice Points'. Practice points are based on expert opinion and the evidence informing them are not directly derived from a systematic review of published evidence.

The recommendations contained within this guideline are classed as one of the following:

- Recommendation for
- Recommendation against
- Conditional Recommendation for
- Conditional Recommendation against
- Consensus Recommendation

Each recommendation type is explained in Table 1. The terminology "*we recommend*" is used for recommendations, and "*we suggest*" is used for conditional and consensus-based recommendations.[14]

To our knowledge, this is the first evidence-based guideline produced anywhere in the world to assist GPs with opioid deprescribing in general practice. Although we endeavoured to provide evidence-based recommendations to address each key clinical question in this guideline, for some questions we were unable to identify sufficient evidence. This guideline includes six evidence-based recommendations and five consensus-based recommendations, with accompanying practice points.

This summary document is intended to be used as a quick reference guide to aid in clinical decision making in practice. The full guideline provides additional information on the evidence informing each recommendation and practice points which may assist in implementing recommendations.

Table 1. Classification of Recommendations

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.

SUMMARY OF RECOMMENDATIONS

We present a summary of guideline recommendations for healthcare professionals to consider within the context of each person. Please refer to the full guideline document for additional information and accompanying practice points.

01

Consensus Recommendation

We suggest developing and implementing a deprescribing plan for persons being prescribed opioids at the point of opioid initiation.

02

Conditional Recommendation for (Very low certainty evidence)

We suggest initiating deprescribing for persons taking opioids for chronic non-cancer pain, if (any of the following):

a) there is a lack of overall and clinically meaningful improvement from baseline in function, quality of life or pain,

b) there is a lack of progress towards meeting agreed therapeutic goals, OR

c) the person is experiencing serious or intolerable opioid-related adverse effects in the physical, psychological or social domains.

03

Consensus Recommendation

We suggest initiating deprescribing for persons taking opioids for chronic cancer-survivor pain if, (any of the following):

a) there is a lack of overall and clinically meaningful improvement from baseline in function, quality of life or pain,

b) there is a lack of progress towards meeting agreed therapeutic goals, OR

c) the person is experiencing serious or intolerable opioid-related adverse effects in the physical, psychological or social domains.

04

Consensus Recommendation

We suggest considering deprescribing for persons taking opioids for chronic pain with one or more of the following clinical characteristics:

a) Co-morbidities which may increase risk of opioid related harms e.g. sleep-disordered breathing or sleep apnoea, chronic obstructive pulmonary disease (COPD).

b) Concomitant use of medicines or substances with sedating effects e.g. benzodiazepines, alcohol, gabapentinoids, antipsychotics and sedating antidepressants.

c) High doses of prescribed opioids.

05

Consensus Recommendation

We suggest avoiding deprescribing for persons taking opioids for pain or dyspnoea who are nearing the end-of-life.

06

Conditional Recommendation against (Moderate certainty evidence)

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.

07

Recommendation for (Low certainty evidence)

We recommend gradual tapering of opioids. Abrupt cessation of opioids without prior dose reduction may increase risks of harm.

08

Recommendation for (Very low certainty evidence)

We recommend tailoring the deprescribing plan based on the person's clinical characteristics, goals and preferences.

09

Consensus Recommendation

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.

10

Conditional Recommendation for (Low certainty evidence)

When available, we suggest the use of interdisciplinary or multidisciplinary care, or a multimodal approach which emphasises non-pharmacological and self-management strategies to deprescribe opioids.

11

Conditional Recommendation for (Very low certainty evidence)

We suggest the consideration of evidence-based co-interventions to support opioid deprescribing.

AREAS OF MAJOR DEBATE

The GDG extensively discussed the guideline scope. The main area of contention was whether individuals with opioid use disorders should be a target population group. A consensus was reached that individuals using opioids for maintenance therapy (e.g. methadone, buprenorphine-naloxone) were a distinct cohort when compared to those using opioids for pain and recommendations relating to opioid deprescribing would differ for these two distinct groups. The decision was made to focus the guideline on people using opioids for pain conditions, as it was agreed that opioid deprescribing was most relevant to this population. The GDG did however decide to make a recommendation (Recommendation 6) relating to individuals with chronic pain and an opioid use disorder. This decision was made after acknowledging that persons with an opioid use disorder may require different treatment plans compared to those without an opioid use disorder. As such, the GDG felt it was important to make a recommendation relating to this cohort in the context of opioid deprescribing. The GDG also acknowledged that opioid maintenance therapy may be a suitable treatment option for some individuals taking opioids for chronic pain conditions and that individuals using opioids for maintenance therapy may have initially been prescribed opioids for pain. There were significant discussions about whether to add qualifiers to recommendations to make them specific to the population groups which were examined in the evidence review. Although there was some reluctance to make broad statements that were not generalisable for persons with differing clinical characteristics, it was determined that healthcare professionals need to utilise clinical judgement when applying any guideline recommendations to individuals, and that recommendations should be clear and straightforward rather than overly specific to allow for ease of use by end-users.

Recent evidence suggested that opioid dose reduction, whether involuntary or voluntary, was not associated with changes in pain severity.[15] As such, there was some debate surrounding whether or not to promote the need for voluntary opioid deprescribing within the guideline. Some GDG members felt that due to the known cognitive, psychological, physical and social effects of long-term opioid use,[6,7] as well as unchanged or improved pain outcomes when opioids are tapered,[16–20] that opioid deprescribing should be the default position. Most GDG members felt that voluntary opioid deprescribing, whilst not always possible to achieve, should be encouraged. The majority of studies in the overview of systematic reviews which demonstrated effective deprescribing and positive clinical outcomes, were voluntary in nature.[19,20] Further, there are known benefits of shared decision-making in positive health outcomes.[21] Further, involuntary deprescribing was discouraged due to reported harms of involuntary deprescribing such as disengagement with care, increased hospitalisation due to depression/anxiety, overdose and suicide.[22–24] It was acknowledged that there may be the occasional necessity for involuntary prescribing where the risk of harm of continuing to prescribe the same dose is too great and the person is not agreeable to dose reduction. The GDG discussed whether to include recommendations within this guideline relating broadly to the pharmacological and non-pharmacological management of pain. It was decided that the purpose of this guideline was

to provide recommendations pertaining to opioid deprescribing and that existing prescribing and clinical practice guidelines focus on the management of pain. Where appropriate, we decided to provide links to existing resources regarding pain management within recommendation practice points. It was decided that it was outside the scope of this guideline to make evidence-based recommendations about pain management strategies and interventions beyond those used for opioid deprescribing.

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