THE UNIVERSITY OF SYDNEY

Evidence-Based Clinical Practice Guideline for Deprescribing Opioid Analgesics

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Disclaimer: This guideline is 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. This guideline is designed to provide information to assist decision-making and the recommendations included within are based on the best evidence available at the time of development.

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Glossary

Aberrant Behaviour	Any behaviour on the part of the person taking opioids that suggest the presence of a substance use disorder.
Acute Pain	Pain of recent onset and probable limited duration (less than three months); it usually has an identifiable temporal and causal relationship to injury or disease.[1]
Adverse Effect	An undesired harmful effect resulting from a medication or other intervention. In relation to opioids, adverse effects may be: **Physical** e.g. sedation, dizziness, nausea, vomiting, constipation, physical dependence, tolerance, respiratory depression, increased sensitivity to feeling pain (hyperalgesia), hormonal effects. **Psychological** e.g. impacts on mood, cognitive function, motivation, sleep. **Social** e.g. negative impacts on ability to engage in activities of daily living and participate in social activities. Aberrant prescription opioid behaviours and recurring emergency department visits for chronic pain management can be considered adverse events.
AGREE II	An international tool that is used to assess and report the quality and transparency of a clinical practice guideline. It evaluates the development of the guideline and can be used to inform the methodological strategy for development of guidelines and how the information ought to be and is reported.[2]
Carer	Individuals, typically a family member or friend, who provide informal and ongoing care for a person. A carer provides their support in a non-professional and unpaid manner. Also known as a caregiver.
Care Staff	People employed to provide personal, physical and emotional support to individuals in need of this assistance (such as older adults) often in the community or in a long-term care facility. Care staff are different from carers because they are paid for their services.
Cancer-related Pain	Pain caused by cancer (by the primary tumor or by metastases) or by its treatment (surgery, chemotherapy, and radiotherapy).[3]

Cancer-survivor	A person with a history of cancer who is beyond the acute diagnosis and treatment phase.
Chronic Pain	Pain in one or more anatomical regions that persists or recurs for longer than three months and is associated with significant emotional distress or functional disability (interference with activities of daily life and participation in social roles).[3]
Co-intervention	An intervention which aims to reduce opioid use through modifying a person's physical condition or behaviour, or providing them with an alternate treatment approach.
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.[4] It refers to slowly reducing the medication, with monitoring throughout the process. The purpose of 'deprescribing' is to improve the overall risk-benefit profile of medication use in individuals through withdrawal of inappropriate medications in a safe and effective manner. Deprescribing should be considered as part of a good prescribing continuum. It is ideally undertaken with the assistance of a multidisciplinary care team that may involve general practitioners (GPs), pharmacists, residential aged care facility (RACF) staff, registered nurses, nurse practitioners, psychologists and psychiatrists, other specialist medical practitioners and allied health professionals.
Deprescribing Plan	A deprescribing plan is a plan agreed upon by the person taking the medication and their health care professional to facilitate person-centred medication dose reduction or cessation. This plan is ideally developed when medicines are initiated but can be instituted at any point in time. A deprescribing plan should specify realistic and relevant goals of treatment, detail the intended process of dose reduction and identify potential supports that may be required during deprescribing. Progress should be evaluated at regular intervals against mutually agreed upon outcomes and goals. The plan may be adjusted to meet the ongoing needs of the person. A deprescribing plan is ideally a written document,[5] but may be a verbal agreement between the person and the healthcare professional. A deprescribing plan is a component of an overall pain management plan.
Drug-disease Interaction	Where administration of a medication may lead to

	exacerbation of a medical condition in that individual.
Drug-drug Interaction	Where co-administration of two or more medications leads to an alteration in the activity of one or more of those medications. Drug-drug interactions may lead to clinically significant results (reduced efficacy of the medication or increased risk of harm).
Disability	An umbrella term for impairments, activity limitations or participation restrictions.[6]
End-of-life	End-of-life typically refers to the 12 months prior to death. There are two different stages of the end-of-life definition: i) likely to die in the next 12 months (involving periods of illness exacerbation that may be reversible); and ii) likely to die in the near term (within days to weeks), where clinical deterioration is likely to be irreversible.[7]
Evidence to Decision (EtD) Framework	The GRADE Evidence to Decision (EtD) framework provides a structured way to combine research findings with other key factors to develop guidelines and make clinical recommendations. It helps to guide decision-makers through a set of criteria, ensuring that each criterion is considered equally, and decisions are transparently reported.[8]
Function	What a person with a health condition can do in a standard environment (their level of capacity), as well as what they actually do in their usual environment (their level of performance). Function can be measured by activities and participation.[6]
General Practitioner (GP)	A medical practitioner who works in primary care and has the skills and experience to provide whole person, comprehensive, coordinated and continuing medical care. GPs typically assess and treat a wide variety of medical conditions, rather than specialising in one specific area of medicine. Also known as a Primary Care Physician or Family Physician.
Generic Medication	A medication that is therapeutically equivalent to a brand name medication. It must be similar in strength, dosage form, route of administration and intended use.
GRADE	The Grading of Recommendations, Assessment, Development and Evaluation is a comprehensive and explicit approach used to rate the quality of evidence and strength of recommendations that are made.[9]

Inappropriate Medication	A medication with potential harms that outweigh the potential benefits for the individual, is no longer indicated for the treatment of a condition, or is not in alignment with their treatment goals.
Indigenous	Ethnic groups who have historical ties to a territory and identify with the culture of the original inhabitants. In Australia, this refers to Aboriginal and Torres Strait Islander Australians.
Interdisciplinary Treatment	Multimodal treatment provided by a multidisciplinary team collaborating in assessment and treatment using a shared biopsychosocial model and goals. For example: the prescription of an anti-depressant by a physician alongside exercise treatment from a physiotherapist, and cognitive-behavioural treatment by a psychologist, all working closely together with regular team meetings (face to face or online), agreement on diagnosis, therapeutic aims and plans for treatment and review.[10]
Meta-analysis	A statistical analysis that is used to combine the results of multiple studies to identify common effect or variation in findings.
Multidisciplinary Treatment	Multimodal treatment provided by practitioners from different disciplines (such as general practitioners (GPs), pharmacists, residential aged care facility (RACF) staff, registered nurses, other specialist medical practitioners, allied health professionals, health educators, and specialists). For example: the prescription of an anti-depressant by a physician alongside exercise treatment from a physiotherapist, and cognitive-behavioural treatment by a psychologist, all the professions working separately with their own therapeutic aim for the patient and not necessarily communicating with each other.[10]
Multimodal Treatment	The concurrent use of separate therapeutic interventions with different mechanisms of action within one discipline aimed at different pain mechanisms. For example: the use of pregabalin and opioids for pain control by a physician; the use of NSAID and orthosis for pain control by a physician.[10] A healthcare professional may use a multimodal approach based on input from different disciplines.
Multimorbidity	The presence of two or more medical conditions (diseases or disorders) in a single individual. Also known as comorbidity.

Nurse Practitioner	A Registered Nurse (RN) experienced in their clinical specialty, educated at Masters Level, and who is endorsed by the Nurses and Midwives Board of Australia to provide patient care in an advanced and extended clinical role. This may include diagnosing health problems and prescribing medications.
Opioid	A scientific term that refers to both natural and synthetic morphine-like drugs whose effects are mediated by opioid receptors in the central and peripheral nervous systems. Opioids include buprenorphine, codeine, fentanyl, hydromorphone, methadone, morphine, oxycodone, pethidine, tapentadol and tramadol.
Opioid Dependence	Opioid dependence is a disorder of regulation of opioid use arising from repeated or continuous use of opioids. There are many classifications and many focus on a strong internal drive to use opioids, which is manifested by impaired ability to control use, increasing priority given to use over other activities and persistence of use despite harm or negative consequences. These experiences are often accompanied by a subjective sensation of urge or craving to use opioids. Physiological features of dependence may also be present, including tolerance to the effects of opioids, withdrawal symptoms following cessation or reduction in use of opioids, or repeated use of opioids or pharmacologically similar substances to prevent or alleviate withdrawal symptoms. The features of dependence are usually evident over a period of at least 12 months but the diagnosis may be made if opioid use is continuous (daily or almost daily) for at least one month.[11]
Opioid Use Disorder (Mild, Moderate, Severe)	A problematic pattern of opioid use leading to clinically significant impairment or distress, manifested by at least two of the following defined criteria occurring within a 12-month period: • Taking larger amounts or taking drugs over a longer period than intended. • Persistent desire or unsuccessful efforts to cut down or control opioid use. • Spending a great deal of time obtaining or using the opioid or recovering from its effects. • Craving or a strong desire or urge to use opioids. • Problems fulfilling obligations at work, school or home. • Continued opioid use despite having recurring social or interpersonal problems.

- Giving up or reducing activities because of opioid use.
- Using opioids in physically hazardous situations.
- Continued opioid use despite ongoing physical or psychological problems likely to have been caused or worsened by opioids.
- Tolerance* (i.e., need for increased amounts or diminished effect with continued use of the same amount).
- Experiencing withdrawal* (opioid withdrawal syndrome) or taking opioids (or a closely related substance) to relieve or avoid withdrawal symptoms.

Severity: Mild: 2-3 symptoms. Moderate: 4-5 symptoms. Severe: 6 or more symptoms.[12]

Note: This criterion is not considered to be met for those individuals taking opioids solely under appropriate medical supervision.

Oral Morphine Equivalent Daily Dose (OMEDD)	A marker of analgesic potency which allows for comparisons between different opioids in terms of their ability to produce the same analgesia as would be expected from a given dose of morphine.[13]
Pain	An unpleasant sensory and emotional experience that is associated with, or resembling that associated with, actual or potential tissue damage.[14]
Pain Management Plan	A written document agreed upon by the person taking opioids, their prescribing healthcare professional, (e.g. general practitioner) and relevant others where indicated (e.g. pharmacist, pain management team). A pain management plan should specify the goals of treatment and a timeframe for reaching each goal. The goals should be patient-centred, realistic and relevant. The plan should outline all treatments or strategies to be used, when they are to be used and any possible side effects. Progress should be evaluated at regular intervals. The treatments or strategies may need adjustment when progress is less than satisfactory. The person's compliance with the plan may also need evaluation.[15]
Person	We have adopted the term 'person' when referring to the individual who is taking opioids. This term has been used in preference to 'patient' or 'consumer'.

Physical Dependence	A state of adaptation that is manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, reducing blood level of the drug or administration of an antagonist.[16]
Polypharmacy	The concurrent use many medicines. Often described as the use of five or more medicines.[17]
Person-centred Care	Care that is respectful of, and responsive to an individual's preferences, needs and values.[18]
Pharmaceutical Benefits Scheme (PBS)	A program implemented by the Australian government that aims to provide greater access to necessary medications by offering financial aid in the form of subsidies.
PICO Framework	A framework used in evidence-based medicine to formulate a clinical question. It ensures that the clinical question is directly related to the individual or population, involves the interventions and comparators in question and examines the outcome of interest.
Placebo	A substance that is pharmaceutically inactive. Placebos are often given to participants in clinical research trials as a control, to observe if a perceived improvement is due to the participant's expectations rather than the treatment.
Psychological Dependence	A subjective sense of need for a specific psychoactive substance, either for its positive effects or to avoid negative effects associated with its abstinence.[16]
Quality of Life (QoL)	A subjective measure of the well-being of a person and the degree to which a person is healthy, comfortable and able to participate in or enjoy life events. QoL measurements consider factors such as life circumstances, the burden of illnesses and the person's level of functioning.
Randomised Controlled Trial (RCT)	A study design in which participants are randomly assigned to either an intervention or control group. The intervention group receives the intervention that is being studied and the control group receives the standard or placebo treatment. This is done to examine the effect of specific interventions on a specific outcome. Aside from the intervention they receive, participants should be similar in all other aspects.
Shared Decision Making	Discussion and collaboration between a person and their healthcare professional to bring together the person's values, goals and preferences with the best available evidence about benefits, risks and uncertainties of treatment, to reach the most appropriate healthcare decisions for that person. If a person experiences cognitive impairment, shared decision

	making may not be feasible and supported decision making should be used.
Supported Decision Making	The process of enabling a person who requires decision-making support to make and/or communicate decisions about their own life. The decision-making is supported, but the decision is theirs.[19]
Stakeholder	A person who has an interest or role in a specific organisation or service.
Systematic Review	An explicit and predefined methodology to identify, critically appraise, and summarise relevant research studies for the purpose of answering a specific clinical question.
Taper	The gradual dose reduction of a medication.
Therapeutic Goals	Relevant and realistic targets for condition management. Examples of therapeutic goals include; reducing the severity of pain, improving physical function, increasing activity at home or work, increasing participation in social activities, reducing medication use, increasing self-management of pain and related problems, improving mood, improving sleep patterns.
Tolerance	A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time. Requiring more of the substance to obtain an effect previously obtained with a smaller amount.[20]
Withdrawal	A characteristic pattern of signs and symptoms (psycho-behavioural and physical) that occur when a drug is stopped after a period of chronic administration or an antagonist is given. Opioid withdrawal signs and symptoms reflect sympathetic stimulation and may include anxiety, hypertension, tachycardia, restlessness, mydriasis, diaphoresis, tremor, piloerection, nausea, abdominal cramps, diarrhoea, anorexia, dizziness, hot flashes, shivering, myalgias or arthralgias, rhinorrhoea, sneezing, lacrimation, insomnia, and yawning.
5-year Survival Rate	The percentage of people who are alive five years after they were diagnosed with, or started treatment for a disease, compared with the overall population.

Acronyms

CALD	Culturally and Linguistically Diverse
CBT	Cognitive Behavioural Therapy
CI	Confidence Interval
COI	Conflict of Interest
COPD	Chronic Obstructive Pulmonary Disease
COWS	Clinical Opiate Withdrawal Scale
ED	Emergency Department
EtD	Evidence-to-decision
GDG	Guideline Development Group
GP	General Practitioner
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HR	Hazard Ratio
IM	Intramuscular
IV	Intravenous
MID	Minimally Important Difference
NHMRC	National Health and Medical Research Council
NSAID	Non-steroidal Anti-inflammatory Drug
OIH	Opioid Induced Hyperalgesia
OMEDD	Oral Morphine Equivalent Daily Dose
OOWS	Objective Opioid Withdrawal Scale
OR	Odds Ratio
ORCC	Opioid Regulatory Communications Committee
OUD	Opioid Use Disorder
PBS	Pharmaceutical Benefits Scheme
PDMP	Prescription Drug Monitoring Programs
PICO	Population, Intervention, Comparison, Outcome
QoL	Quality of Life
RCT	Randomised Controlled Trial
RACGP	The Royal Australian College of General Practitioners
ROOM	Routine Opioid Outcomes Monitoring
SOWS	Subjective Opiate Withdrawal Scale
SC	Subcutaneous
SMD	Standardised Mean Difference
TGA	Therapeutic Goods Administration
UK	United Kingdom
USA	United States of America
WHO	World Health Organization
WMD	Weighted Mean Difference

Plain English Summary

Pain is an unpleasant experience linked with actual or potential damage to the body.[10] Pain conditions are a leading cause of disability and disease burden globally.[21] 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 harms outweigh 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 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 harms of opioids outweigh the benefits for a person, deprescribing should be considered. Some people who take opioids may be able to reduce or stop opioids with minimal negative consequences. Pain and function may be improved or 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 a 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. A Summary of Recommendations contained within this guideline has been provided in the Executive Summary. For additional information and accompanying practice points, please see Recommendations.

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.[22-24] 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.[25,26] Concerns regarding efficacy, abuse liability and iatrogenic morbidity and mortality are significant, with opioids increasing the risk of serious adverse events such as falls, respiratory depression and death.[24,27] 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 for. 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,[28] based on a comprehensive checklist for successful guideline development (Guideline 2.0),[29] the AGREE II criteria,[2] and the Australian National Health and Medical Research Council (NHMRC) 2016 Standards for Guidelines,[30] 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.[4]

Each recommendation contained within this guideline has an accompanying 'certainty of evidence' rating in accordance with the GRADE approach. 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 provided. Additional considerations and practical information to support recommendations are presented as 'Practice Points'.

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

i)	Recommendation for
ii)	Recommendation against
iii)	Conditional Recommendation for
iv)	Conditional Recommendation against
v)	Consensus Recommendation

Further details of each recommendation type can be found in Table 4.

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 recommendation and five consensus-based recommendations, with accompanying practice points. Recommendations are presented in two formats:

    i)   The Summary of Recommendations.
    ii)   A detailed discussion of the Recommendations.

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

The terminology "we recommend" is used for recommendations, and "we suggest" is used for conditional and consensus-based recommendations.[31] 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.

Summary of Recommendations

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

1. Consensus Recommendation

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

2. 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.

3. 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.

4. 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.

5.   Consensus Recommendation

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

6.   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.

7.   Recommendation for (Low certainty evidence)

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

8.   Recommendation for (Very low certainty evidence)

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

9.   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.

Background

Pain is an unpleasant and potentially challenging sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.[10] Pain and pain-related conditions are a leading cause of disability and disease burden globally,[21] with one in five adults reporting persistent, ongoing pain.[32,33] The impact of chronic pain is clinical, psychological, social and economic in nature. At an individual level, pain can contribute to limitations in activities, impact on work, sleep and relationships and result in reduced quality of life.[34] At a societal level, pain is associated with significant productivity losses and increased healthcare utilisation.[35] Australia's National Pain Strategy and the National Strategic Action Plan for Pain Management, developed by Painaustralia and endorsed by the Australian Government Department of Health, aims to minimise the burden of pain for people with pain, their families and communities.[36,37] To achieve this, it is essential that pain management strategies are safe, effective, appropriate, accessible and affordable, with careful consideration of the benefits and harms of treatment options.

Opioids, including buprenorphine, codeine, fentanyl, hydromorphone, methadone, morphine, oxycodone, oxycodone with naloxone, pethidine, tapentadol and tramadol, are commonly prescribed for the management of severe pain. Some opioids are also used to treat opioid dependency, however, this guideline focuses on opioids used for pain. Over the last three decades, increases in the use of prescription opioids have been observed globally,[38,39] particularly in Organisation for Economic Co-operation and Development (OECD) countries.[40] In Australia, over 1.9 million adults initiate opioid therapies each year,[41] with the vast majority of prescriptions issued for maintenance therapy in chronic non-cancer pain.[42] Opioids, whilst shown to be an effective component of the management of acute pain, may not provide longer-term clinically important improvements in pain or function compared with placebo.[25] Opioid use presents a significant risk of harm, with approximately 80% of people taking opioids for 3 months or more experiencing adverse effects.[43] Adverse outcomes appear to be dose-dependent and range from mild (nausea, constipation, somnolence) through to severe (respiratory depression, central or obstructive sleep apnoea, impaired cognition, dependence) and fatal.[43] Utilisation of opioids for acute pain is associated with increased risk of chronic use,[44,45] further amplifying the potential for opioid-related morbidity and mortality.

Escalating opioid use and subsequent harm has been recognised as an international public health concern and there is impetus for action to reduce opioid prevalence and to re-evaluate prescribing practices. The World Health Organisation (WHO) has set a global goal of reducing severe avoidable medication-related harm through its Medication Without Harm Global Patient Safety Challenge.[46] Australia's response to Medication Without Harm, published in 2020, identifies opioids as one of the four medicines of focus in the Australian context.[47] As part of a National response, multiple organisations have called for action and advocated for legislative reform, additional training for healthcare professionals and greater patient education and support.[46,48-50] Similarly, the formulation of practice-specific guidelines has

been suggested as a mechanism to curb current prescribing trends.[36] In Australia, existing clinical guidance from the Royal Australian College of General Practitioners,[51] the Therapeutic Guidelines (Pain and Analgesia)[52] and the Faculty of Pain Medicine, Australian and New Zealand College of Anaesthetists (ANZCA),[53] focus primarily on pain management and the prescription of analgesia. However, there is a need for evidence-based guidelines which focus on opioid 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.[4] This guideline aims to provide evidence-based recommendations on when and how to deprescribe opioids, for adults prescribed opioids for pain in primary care settings.

Objective

The 'Evidence-based Clinical Practice Guideline for Deprescribing Opioid Analgesics' was developed to address the need for a systematic, evidence-based approach to opioid deprescribing in adults taking opioids for pain. It aims to promote evidence-based practice and assist healthcare professionals to identify individuals who are suitable to trial opioid deprescribing and provide advice on when and how to conduct deprescribing. The intended outcome of this guideline is to improve outcomes for persons prescribed/taking opioids through the translation of research evidence, along with clinical and consumer expertise, into recommendations that will guide improvements in the quality of care for people taking opioids for pain in Australia and internationally.

Rationale

Healthcare professionals across a range of disciplines acknowledge that opioid deprescribing is a complex and challenging practice, with continued prescribing the default behaviour.[42,54] Evidence-based opioid deprescribing guidelines have been identified as a valuable resource for healthcare professionals to support clinical decision-making and reduce suboptimal opioid use.[54] There are however currently no evidence-based guidelines internationally that specifically focus on the deprescribing of opioids. Australian Institute of Health and Welfare data shows that most Australians seek medical management in primary care.[55] GPs are well-positioned to conduct opioid deprescribing due to their ongoing relationship with patients, opportunities for shared-decision making and ongoing monitoring and management.[56] Uncertainty of research evidence has been identified by GPs as a key barrier to deprescribing.[57] Clinical practice guidelines focused on opioid deprescribing may improve healthcare professional knowledge and empower healthcare professionals and persons taking opioids to engage in deprescribing. Emerging evidence of an association between opioid tapering and overdose, suicide and mental health crisis[58,59] provides further evidence to suggest that additional advice on safe and effective opioid deprescribing is required. This guideline offers recommendations based on the most recent scientific evidence, informed by expert opinion and public input. Providing guidelines to healthcare professionals to support opioid deprescribing has the potential to optimise care through evidence-based practice.

Scope

The Evidence-based Clinical Practice Guideline for Deprescribing Opioid Analgesics aims to provide recommendations on when, how and for whom opioid deprescribing should be considered. Local treatment guidelines should be used to determine if it is appropriate to start an opioid. This guideline does not provide comprehensive advice about pain management and healthcare professionals should refer to relevant clinical practice guidelines for further advice on this topic. Healthcare professional's judgement and the values, preferences and goals of the person taking opioids should be considered when enacting guideline recommendations.

Target population

The target population of this guideline is adults (aged ≥ 18 years old) prescribed one or more opioids for any type of pain (e.g. acute, chronic, cancer-related (including cancer survivors), end-of-life). This includes single-ingredient and combination opioid preparations of any dose, formulation (immediate release, modified release, capsule, tablet, oral suspension, intravenous solution, patch, suppository) and route of administration (intravenous, oral, transdermal, rectal). Where applicable, indications (such as the type and duration of pain) are specified. Persons with opioid use disorders, prescribed opioids for opioid substitution therapy or people taking illicit opioids (e.g. heroin) are not the target population of this guideline, although there may be considerable overlap. The target care setting is community primary care; however, recommendations may be relevant to other care settings (residential care, inpatient and outpatient).

Target audience

The target audience for this guideline is healthcare professionals involved in the care of persons prescribed opioids in primary care. This is primarily GPs. The guideline is to be used alongside healthcare professional judgement and person preferences and values. Additional audiences that may find this guideline useful include specialist physicians (e.g. general physicians, geriatricians, pain specialists, addiction specialists, rheumatologists, psychiatrists), nurses (including nurse practitioners, registered nurses and enrolled nurses), psychologists and pharmacists. The guideline may be applied in other care settings (e.g. acute care, across care transitions). The recommendations contained within this guideline may also be of use to policymakers when implementing policy or developing health service user resources.

Key Clinical Questions

    i)   Does deprescribing of opioids result in benefits or harms compared to continuation?

    ii)   What is the evidence on how to deprescribe opioids?

    iii)   Which interventions are effective to facilitate opioid deprescribing?

What this guideline does not address

This guideline does not provide advice to healthcare professionals on when or how to prescribe or initiate opioid therapies. It does not provide comprehensive advice about pain management and healthcare professionals should refer to relevant clinical practice guidelines for further advice on this topic.

Guiding Principles

Principles of Care

A person's identity and self-image are closely linked to the words used to describe them.[60] We have chosen to use person-centred language in this guideline and have adopted the term 'person' when referring to the individual who is taking opioids. This has been used in preference to 'patient' or 'consumer'.

The principles of person-centred care and shared decision making are understood to be essential for effective healthcare. This entails providing care that is respectful of, and responsive to an individual's preferences, needs and values, and ensuring that these values guide clinical decisions.[18] Clinical interactions between healthcare professionals and individuals provide an opportunity for a person to become engaged in their own healthcare and develop a collaborative relationship on which to base shared decision making. Person-centred care emphasises the importance of improving the understanding of the experience of illness and addressing a person's specific needs. This approach uses the expertise of the healthcare professional in appropriately explaining the features of conditions and treatments, as well as their potential impact, benefits and risks. Providing a supportive environment within which a person can explore their values and preferences regarding treatment options (including deprescribing), emphasises the therapeutic relationship between healthcare professionals and the person. The treatment plan and goals, including time frame, are ideally individualised according to the needs of the person. When impaired decision-making is a feature of the presentation, the person's family, carer, or other support people should be consulted where possible to assist with supported decision making.[19]

Principles of 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.[4] Deprescribing is a dynamic process which involves the gradual reduction of medication (where appropriate), with monitoring throughout the process. The purpose of deprescribing is to improve the overall benefit-harm profile of medication use in individuals through withdrawal (with tapering where appropriate) of medications in a safe and effective manner. Decisions surrounding deprescribing should be conducted through shared decision making with the person taking opioids, ensuring that they are informed of the likely benefits and potential harms of both continuation and discontinuation of medications. The risk-benefit profile of deprescribing may change over time and should be re-assessed regularly. Similarly, the clinical characteristics (such as pain severity, duration, symptom profile and aetiology), overall health state (such as comorbidities, psychological risk factors, polypharmacy, life expectancy), values, preferences and treatment of the person engaging in deprescribing may change over time and shift the benefit-harm profile accordingly. It is important to consider a person's previous response to the medication

or other treatments. Improvement or stabilisation of pain, function and quality of life can all be considered benefits of opioid treatment and may influence decisions about medication continuation or deprescribing. As such, deprescribing should be considered as part of a good prescribing continuum including the reduction of iatrogenic harms. If a person has a noticeable decline in condition after dose reduction/cessation (after exclusion of other causes), then the medication should be restarted at the previous minimum effective dose. Deprescribing is ideally undertaken with the assistance of a multidisciplinary care team as various healthcare professionals may need to be consulted to determine the appropriateness of deprescribing, assist in the delivery of interventions, and ensure monitoring is conducted throughout the process. The multidisciplinary care team may comprise of GPs, pharmacists, residential aged care facility (RACF) staff, nurse practitioners, registered nurses, psychologists, psychiatrists, other specialist medical practitioners and allied health professionals.

A deprescribing plan is a plan agreed upon by the person taking the medication and their healthcare professional, to facilitate person-centred medication dose reduction or cessation. This plan is ideally developed when medicines are initiated, but can be instituted at any time point. A deprescribing plan should specify realistic and relevant goals of treatment, detail the intended process of dose reduction and identify potential supports that may be required throughout the deprescribing process. This may include involvement of other relevant healthcare professionals (e.g. psychologist and/or psychiatrist if a person exhibits clear psychological risks). Progress should be evaluated against mutually agreed upon outcomes and goals at regular intervals. The plan may be adjusted to meet the ongoing needs of the person. A deprescribing plan is ideally a written document,[5] but may also be a verbal agreement between the person and the healthcare professional, if appropriate.

Methods

The University of Sydney is the organisation responsible for developing and publishing this guideline. We followed the process of developing class-specific medication deprescribing guidelines,[28] based on a comprehensive checklist for successful guideline development (Guideline 2.0)[29] and the AGREE II criteria.[2] We complied with the Australian National Health and Medical Research Council (NHMRC) 2016 Standards for Guidelines,[30] and Procedures and Requirements for Meeting the 2011 NHMRC Standard for Clinical Practice Guidelines.[61] Guideline development involved systematic evidence retrieval and synthesis, and the use of the GRADE process to assess the certainty of the evidence. Development of evidence-based recommendations involved the utilisation of an evidence-to-decision framework to systematically consider the certainty of the evidence, the risks and benefits of deprescribing and opioid continuation, stakeholder values and preferences, acceptability, feasibility and resources requirements. See the Technical Report for further details.

Funding

Guideline development, publication and dissemination were funded through a University of Sydney Research Training Program Scholarship ($38,464.92 per annum, 76.7% of total funding) and Internal Supplementary Scholarship ($10,000 per annum, 20% of total funding) awarded to Ms AV Langford and a 2019 Sydney Pharmacy School, Faculty of Medicine and Health, University of Sydney Research Support Grant ($5000, 3.3% of total funding). The funding bodies were not involved in guideline development and the views or interests of the funding body have not influenced the guideline recommendations. Individual guideline development group members received funding from the NHMRC during guideline development, however these grants did not directly fund guideline development activities.

Guideline Development Group Composition

The Guideline Development Group (GDG) was composed of 17 members who were:
- Healthcare professionals (general practitioners, pain specialists, addiction specialists, registered nurses, pharmacists, physiotherapists) with experience in caring for persons taking opioids and research expertise in the field of deprescribing in Australia and internationally.
- Methodologists with expertise in the areas of deprescribing guideline development, conducting systematic reviews and the GRADE approach.
- Implementation experts.
- Organisational representative.
- Consumer representative.

All members of the GDG along with their affiliations and roles are listed in Table 1. The core guideline group consisted of guideline development group members AV Langford, CR Schneider, CWC Lin and D Gnjidic.

Process and criteria for selecting members

We recruited GDG members who were either content experts, end-users, methodology experts, implementation experts or consumers. We sought to include healthcare professionals who are involved in the prescription, monitoring or management of prescription opioids (end-users). At a minimum, we intended for our GDG to have at least one member from the following groups: GPs (family physicians, primary care physicians), pain specialists, addiction specialists, pharmacists and registered nurses. To recruit potential content experts, end-users and methodology experts, we contacted local and international experts in relevant fields. All potential members were invited via an email which briefly explained the aim of the guideline and the process of guideline development. If a potential member declined, they were asked to suggest another person in their place. If they expressed an interest in participating, they were provided with more information (via email or in-person) and were asked to complete the conflict of interest (COI) form. The consumer representative was remunerated for her time. Other GDG members received no reimbursement for their involvement in guideline development.

Consumer involvement in the Guideline Development Group

We sought to recruit a person who currently/previously uses/used opioid(s) for the management of pain as a guideline consumer representative. The consumer was recruited through The Consumers Health Forum. They have lived experience with chronic pain and opioid use. As a GDG member, they attended each GDG meeting and provided input throughout the entire development process.

Group interaction and processes

We conducted five GDG meetings over video-conference in May, August and November 2020 and two in April 2021. The initial meeting was conducted to introduce members and discuss the scope and content of the prospective guideline and to propose key clinical questions. Follow-up meetings were conducted to discuss evidence synthesis and draft recommendations. Meeting minutes were circulated to the GDG following each meeting. Refinement of recommendations and revision of the draft guideline occurred via email correspondence and video-conference meetings between the core guideline group and individual GDG members.

Declaration and management of competing interests

All GDG members were required to declare any potential or perceived COIs. Where possible, potential COIs were reviewed prior to inviting members (for example, recent publications reviewed for COIs). After the invitation to join the GDG was accepted, each GDG member was asked to complete the COI form. The procedure for declaring and managing COIs was conducted as per the NHMRC Guideline Development and COI Policy. The purpose of disclosure of interests was to provide information on financial, business/professional, and intellectual competing interests related to the topic addressed. Each member completed the

[International Committee of Medical Journal Editors (ICMJE) Disclosure of Interest Form](#). GDG members were asked at all meetings and prior to the public consultation period and submission to the NHMRC for approval if they had any new interests to declare, and their forms were updated accordingly. If a COI was declared, it was documented, and if required, a management plan was discussed with the group member. Individual guideline members' COIs are documented in the Administrative Report.

Guideline development group members

All GDG members and other individuals involved in the development of the guideline are listed in [Table 1](#) and [Table 2](#). Please see the Administrative Report for a full explanation of individual guideline group member's roles and responsibilities.

Table 1: Guideline Development Group members, affiliations and expertise

Name	Organisational affiliation(s)	Profession/discipline/expertise
Ms Aili V Langford	Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney, NSW, Australia	Pharmacist PhD candidate
Associate Professor Danijela Gnjidic	Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney, NSW, Australia	Deprescribing Expert Pharmacologist
Dr Carl R Schneider	Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney, NSW, Australia	Registered Nurse Pharmacist
Professor Chung-Wei Christine Lin	Institute of Musculoskeletal Health, School of Public Health, The University of Sydney, NSW, Australia	Physiotherapist Methodologist
Professor Lisa Bero	University of Colorado Anschutz Medical Center, Schools of Medicine and Public Health, Colorado, USA	Methodologist Systematic Review Expert
Professor Fiona M Blyth	School of Public Health, Faculty of Medicine and Health, The University of Sydney, NSW, Australia	Public Health Physician Pain Epidemiologist
Professor Jason N Doctor	Sol Price School of Public Policy, University of Southern California, California, USA	Behavioural Scientist Implementation Expert

Dr Simon Holliday	School of Medicine and Public Health, University of Newcastle, NSW, Australia; HealthHub Taree	General Practitioner Addiction Physician
Professor Yun-Hee Jeon	Sydney Nursing School, Faculty of Medicine and Health, University of Sydney, NSW, Australia	Registered Nurse Nurse Gerontologist Methodologist
Dr Joanna C Moullin	School of Population Health, Faculty of Health Sciences, Curtin University, WA, Australia	Implementation Scientist Pharmacist
Associate Professor Bridin Murnion	Discipline of Addiction Medicine, Faculty of Medicine and Health, The University of Sydney, NSW, Australia	Clinical Pharmacologist Addiction Medicine Pain Medicine
Associate Professor Suzanne Nielsen	Monash Addiction Research Centre, Faculty of Medicine, Nursing and Health Sciences, Monash University, VIC, Australia	Content Expert Pharmacist
Ms Rawa Osman	NPS MedicineWise, NSW, Australia	Organisational Representative Pharmacist
Dr Jonathan Penm	Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney, NSW, Australia	Pharmacist Content Expert
Dr Emily Reeve	Centre for Medicine Use and Safety, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, VIC, Australia	Pharmacist Deprescribing Expert Deprescribing Guidelines Expert
Dr Sharon Reid	Royal Australian College of General Practitioners; Specialty of Addiction Medicine, Central Clinical School, Faculty of Medicine and Health, University of Sydney, NSW, Australia; Drug Health Services, Sydney Local Health District, NSW, Australia.	General Practitioner Senior Lecturer, Specialty of Addiction Medicine Medical Officer, Drug Health Services, Sydney Local Health District
Dr Janney Wale	Independent consumer representative	Community Engagement Lived Experience

Table 2: Non-Guideline Development Group members and role in guideline development

Name	Organisational affiliation(s)	Profession/discipline *Role in guideline development*
Ms Benita Suckling	Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney, NSW, Australia; Metro North Health, Queensland Health, QLD, Australia	Pharmacist MPhil Candidate *Reviewer for overview of systematic review (title/abstract screening, full text screening and eligibility assessment)*
Dr Jack Collins	Sydney Pharmacy School, Faculty of Medicine and Health, The University of Sydney, NSW, Australia	Pharmacist Post-doctoral Research Associate *Reviewer for overview of systematic reviews (Risk of Bias Assessment, GRADE Assessment)*

Guideline development methods

Figure 1: Recommendation Generation Process

A detailed report outlining the search strategies, search outcomes and review methods used for the literature review is included in the Technical Report that accompanies this guideline; however, a summary is provided here. Guideline development (summarised in Figure 1) involved:

i)   Qualitative stakeholder perspective research with healthcare professionals and persons taking opioids.

ii)   Systematic evidence retrieval and synthesis, and the use of the GRADE process to assess the certainty of the evidence.

iii)   Utilisation of an evidence-to-decision framework to systematically consider the certainty of the evidence, the risks and benefits of deprescribing and opioid continuation, stakeholder values and preferences, acceptability, feasibility and resources requirements.

iv)   Development and refinement of recommendations.

Stakeholder Perspective Research

Two qualitative studies were conducted with i) healthcare professionals[54] and ii) persons taking opioids[62] to elucidate their beliefs and attitudes towards opioid deprescribing and identify perceived facilitators and barriers to achieving successful outcomes.

i)   Healthcare professionals

A purposive sampling technique was used to recruit healthcare professionals with an interest and/or expertise in deprescribing. Two focus groups were used to identify areas of importance to healthcare professionals. Subsequent individual interviews were conducted with pain and addiction specialists, general practitioners, geriatricians, registered nurses and pharmacists who met the inclusion criteria of being a registered healthcare professional and having experience in the treatment of patients using opioid analgesics to enable in-depth exploration of themes. Data collection was undertaken by four pharmacy academics with experience in qualitative research. A semi-structured interview guide was developed from a review of the literature and discussion with experienced multidisciplinary healthcare professionals and academic co-investigators to ensure face and content validity. Open-ended questions focused on beliefs, attitudes and behaviours surrounding opioid deprescribing and the content and utility of prospective opioid deprescribing guidelines. All transcripts were audio-recorded, transcribed verbatim and de-identified to maintain participant confidentiality. A phenomenological approach was adopted for data analysis.[63] Multiple phases of inductive thematic analysis[64] were conducted, using NVivo V.12 software as the data management tool. Initial analysis involved a discussion among researchers of major themes, followed by independent open coding by AV Langford and CR Schneider. A coding index was developed and applied to subsequent transcripts, regularly assessing coding consistency across transcripts. The coding index was refined throughout the analysis to ensure that the derived themes adequately represented the obtained data.

ii)   Persons taking opioids

A purposive sample of people taking one or more opioids for the management of pain was recruited. Participants with both acute and chronic pain conditions were sought. Study advertisements were distributed through Painaustralia, community pharmacies, and Facebook. An interview guide was developed from a review of the literature and discussion with experienced healthcare professionals and researchers. Interview questions related to the management of opioids, interactions with healthcare professionals and resources to support the development of opioid deprescribing guidelines. Interviews were conducted

either face-to-face or over the telephone and were audio-recorded, transcribed verbatim, and de-identified. Initial data analysis was conducted in parallel with ongoing recruitment to allow for evaluation of sample size requirements in relation to thematic saturation. Inductive thematic analysis[64] preceded a deductive framework analysis.[65] Open coding was initially performed, whereby transcripts were coded descriptively using QSR International NVivo-12 software. AV Langford and CR Schneider developed the initial coding index by independently coding transcripts and comparing consistency in the themes observed. Coding categories were refined throughout the study with input from all members of the research team. Bandura's Social Cognitive Theory[66] was applied to the findings using a framework analysis approach.[65]

Evidence retrieval and synthesis

Three key clinical questions were generated:

i) Does deprescribing of opioids result in benefits or harms compared to continuation?

ii) What is the evidence on how to deprescribe opioids?

iii) Which interventions are effective to facilitate opioid deprescribing?

Key clinical questions were structured using the Population Intervention Comparator Outcome (PICO) approach as shown in Box 1 and Box 2. We conducted a single overview of systematic reviews, examining interventions to deprescribe opioids, their effectiveness and outcomes. The review protocol was registered on The International Prospective Register of Systematic Reviews (PROSPERO). The full review methodology is detailed in the Technical Report and is summarised hereafter.

Box 1: Key clinical question 1 and 2 PICO

Population	People (aged ≥ 18 years old) who are currently prescribed an opioid (buprenorphine, codeine, fentanyl, hydromorphone, methadone, morphine, oxycodone, oxycodone with naloxone, pethidine, tapentadol and tramadol) for pain relief / management.
Intervention	Opioid deprescribing (attempted discontinuation with or without dose reduction)
Control	Opioid continuation
Outcome	Reduction in opioid use in oral morphine milligram equivalent daily dose (OMEDD), Function, Pain, Quality of life, Adverse events

Box 2: Key clinical question 3 PICO

Population	People (aged ≥ 18 years old) who are currently prescribed an opioid (buprenorphine, codeine, fentanyl, hydromorphone, methadone, morphine, oxycodone, oxycodone with naloxone, pethidine, tapentadol and tramadol) for pain relief / management.
Intervention	Any patient-focused intervention to facilitate opioid deprescribing (attempted discontinuation with or without dose reduction)
Control	Continuation of opioid or alternative intervention
Outcome	Reduction in opioid use in oral morphine milligram equivalent daily dose (OMEDD), Function, Pain, Quality of life, Adverse events

We searched five databases (Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Library, Excerpta Medical Database (EMBASE), Medical Literature Analysis and Retrieval System Online (MEDLINE) and PsycINFO) from date of inception through to August 2021, with English language restrictions. The search terms used related to opioids (such as narcotics) and pain and related conditions. Systematic reviews published in the last 10 years (with or without meta-analyses) were included if they examined one or more intervention(s) that aimed to deprescribe opioids in adult populations (aged ≥18 years) and reported on opioid use. Supplementary searches were carried out for key clinical questions one and two in August 2021. We intentionally kept the search strategy broad, placing no restrictions on the type of pain (acute, chronic non-cancer, cancer-survivor, end-of-life), characteristics of participants (co-morbidities, concomitant use of medicines) dose or duration of opioid use or intervention setting. Key clinical question 1 addressed outcomes of opioid deprescribing regardless of approach, whereas key clinical question 3 focussed on patient-focussed deprescribing interventions, which aim to reduce opioid use through modifying the person's physical condition or behaviour, or providing them with an alternate treatment approach. Participants utilising opioids as opioid substitution therapy were excluded from the overview of systematic reviews. We used a broad and inclusive approach in the design of the search criteria and anticipated that published studies pertaining to vulnerable and minority groups such as Aboriginal and Torres Strait Islander communities and culturally and linguistically diverse populations would be identified using this approach.

The primary outcomes of interest were: i) reduction in opioid use, which was converted into the oral morphine milligram equivalent daily dose (OMEDD) if necessary using accepted conversion formulas to standardise for comparison[24] and ii) the success of opioid deprescribing, reported as the proportion of the sample for which opioid use declined. Secondary outcomes were pain, physical function, quality of life and adverse events. The results of the overview were presented at two meetings to GDG members.

iii)   Evidence-to-decision

The evidence's certainty was determined by critically appraising the evidence using the GRADE

approach.[9] Table 3 contains a summary of the GRADE certainty of evidence ratings. The GRADE evidence-to-decision framework provided a systematic approach to consider the body of evidence, certainty of evidence (as determined by the GRADE approach), benefits and harms of opioid deprescribing, stakeholder preferences (informed by qualitative studies), acceptability, feasibility, equity and cost and resource implications.[67] The Technical Report contains the evidence-to-decision (EtD) frameworks for each key clinical question.

Table 3: GRADE Certainty of Evidence Ratings[9]

Grade	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Development of recommendations

Recommendations were drafted by the core GDG team, through reviewing the summary of the evidence, stakeholder perspective research and populated EtD framework. After drafting, the recommendations were refined through group discussion with all GDG members via teleconference, followed by discussion with individual group members and email until unanimous consensus was reached. The recommendations contained within this guideline may be classed as one of the following:

i)   Recommendation for
ii)   Recommendation against
iii)   Conditional Recommendation for
iv)   Conditional Recommendation against, OR
v)   Consensus Recommendation.

Evidence-based practice (EBP) is an approach to care that integrates the best available research evidence with clinical expertise and patient values.[68] When implementing recommendations, clinicians should consider the strength of the recommendation as defined in Table 4, and use clinical judgement to inform the appropriateness of implementing both evidence-based and consensus-based recommendations. The terminology "we recommend" is used for recommendations, and "we suggest" is used for conditional and consensus-based recommendations.[31] For each recommendation, a supporting discussion is included to provide details about the certainty of evidence that informed the recommendation and the GDG's rationale when developing the recommendation.

Development of evidence-based recommendations

GDG members used GRADE to review the evidence base and assign a strength to each recommendation. The body of evidence for each question was assessed first by the project team and given a preliminary certainty of evidence (High, Moderate, Low or Very Low) rating following the GRADE criteria. The GDG reviewed the evidence and adjusted the rating. The GDG also confirmed the wording of each recommendation and assigned a strength to the recommendation. The strength assigned to each recommendation reflects the GDGs confidence in the evidence, as well as the desirable and undesirable consequences of implementing each recommendation, as determined by the EtD framework.

Development of consensus-based recommendations

Where the evidence synthesis produced no direct evidence relating to the key clinical questions, the GDG devised a consensus-based recommendation based on their clinical, consumer, policy and content expertise. This was done in accordance with NHMRC guidance which states that "recommendations formulated in the absence of quality evidence (where a systematic review of the evidence was conducted as part of the search strategy) are clearly labelled as such. The preferred term for this type of recommendation is a consensus-based recommendation."

Development of practice points

Where the GDG felt that additional advice on a topic outside the scope of the search strategy was warranted, practice points were devised. Practice points are additional considerations and practical information to support recommendations, based on expert opinion rather than being derived directly from a systematic review of evidence.

Method to achieve group consensus in the development of the recommendations

Two guideline group meetings were held for review of guideline recommendations in April 2021, to ensure input was received from each GDG member. Where a GDG member could not attend the group meeting, individual meetings with the guideline leads were conducted. After the two group meetings, a revised version of the recommendations was sent out electronically, which GDG members provided further feedback on. This was repeated until group consensus was reached. No formal voting on recommendations was performed. Any GDG member who had comments on the final recommendations that were not fully resolved, was provided the opportunity to report their concerns in the guideline section entitled 'Areas of major debate'.

Table 4: 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.

External clinical review and public consultation

We are seeking NHMRC approval of the guideline under section 14A of the National Health and Medical Research Council Act 1992. As part of the approval process, public consultation is required. In preparation for public consultation, the Australian Department of Health Chief Medical Officer was informed of the development of evidence-based opioid deprescribing guidelines. The draft guideline was reviewed by three expert reviewers for external clinical review. Changes were made (where appropriate) in response to the reviewers' comments. Given the importance of the guideline for a wide variety of stakeholders, public consultation was undertaken for a period of 60 days from February 2nd to April 3rd 2022 to improve the recommendations' specificity, applicability and ease of implementation. The draft guideline and supporting documents were publicly available during this period.

The Therapeutic Goods Administration (TGA) Opioid Regulatory Communications Committee was consulted to develop the public consultation strategy. We approached representatives from professional organisations that represent specialties that commonly prescribe opioids (e.g., general practitioners, pain medicine physicians, physical medicine and rehabilitation physicians), delivery systems within which opioid prescribing occurs (e.g., hospitals) and representation from community organisations with interests in pain management and opioid prescribing. We asked each organisation to review the full draft guideline and provide written comments. The core guideline group reviewed comments and revised the draft guideline accordingly with input from the whole GDG. Public consultation feedback and subsequent changes to the guideline are detailed in the Public Consultation Submission Summary.

Organisations endorsing the guideline will be listed in the final published Guideline and Administrative Report. Organisations who will be approached to consider endorsement of the final published guideline once the recommendations are NHMRC approved include:

- Australian and New Zealand College of Anaesthetists (ANZCA) and Faculty of Pain Medicine
- Australian Deprescribing Network (ADeN)
- Australian Pain Society (APS)
- Australian Physiotherapy Association (APA)
- Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT)
- Chronic Pain Australia
- Dementia Australia
- National Aboriginal Community Controlled Health Organisation (NACCHO)
- National Prescribing Service MedicineWise (NPS)
- NSW Agency for Clinical Innovation (ACI)
- Painaustralia
- Palliative Care Australia (PCA)
- Pharmaceutical Society of Australia (PSA)
- Royal Australasian College of Physicians (RACP)
- Royal Australian & New Zealand College of Psychiatrists (RANZCP)
- Royal Australian College of General Practitioners (RACGP)
- Society of Hospital Pharmacists of Australia (SHPA)
- State and Federal Departments of Health
- The Australian College of Nurse Practitioners (ACNP)

Recommendations

The recommendations in this guideline provide advice about when, how and for whom opioid deprescribing may be appropriate, whilst noting the need to consider the recommendations within the context of the person and their goals, values and preferences. A brief evidence summary accompanies each recommendation. Please refer to the Summary of Findings and the Technical Report for full details of the overview of reviews and the evidence informing guideline recommendations.

Recommendation 1

1. Consensus recommendation

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

Practice points:

- 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.
    - The NSW Agency for Clinical Innovation and Pain Management Network provides a Chronic Disease Management - Chronic Pain Management Plan template.[69]
    - The NPS MedicineWise tapering plan[70] may be a useful resource to use when developing a deprescribing plan.
- 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. Resources to inform the prescription of analgesia include:
    - Acute Pain Management: Scientific Evidence 5th edition. [71]
    - Faculty of Pain Medicine, Australian and New Zealand College of Anaesthetists Better Pain Management educational series.[72]
    - Faculty of Pain Medicine, Australian and New Zealand College of Anaesthetists: Position statement regarding the use of opioid analgesics in patients with chronic non-cancer pain.[73]
    - Cancer Pain Management in Adults - Australian guidelines for cancer pain assessment and management in adults.[74]
    - Centres for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain.[24]
    - Prescribing wellness: comprehensive pain management outside specialist services.[75]
    - Therapeutic Guidelines – Pain and Analgesia.[52]
    - Australian Commission on Safety and Quality in Health Care Opioid Analgesic Stewardship in Acute Pain Clinical Care Standard.[76]
- 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 healthcare professionals where appropriate. Resources to inform non-pharmacological pain management strategies include:
    - Therapeutic Guidelines – Pain and Analgesia.[52]
    - Agency for Clinical Innovation Network – Management of Chronic Pain.[77]

- 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 pain conditions.
- Consider the provision of naloxone if indicated when prescribing opioids for the management of pain. See Naloxone for further information.

Rationale: If initiating opioid treatment, we suggest that the prescriber and person taking opioids should agree on the goals of therapy and the criteria for treatment success and/or failure. A clear plan for opioid reduction and discontinuation should be established through the development and use of a deprescribing plan. Developing and implementing a deprescribing plan at the point of opioid initiation may limit opioid dose and duration to attenuate opioid-related harms. Further, it may assist in setting appropriate expectations about the role of opioids in the management of pain. A pain management plan which emphasises appropriate alternate pain management strategies (pharmacological and/or non-pharmacological) at the point of opioid initiation may reduce reliance on opioids for pain management. See EtD Framework Table 1 for further factors considered when developing this recommendation.

Research Evidence Summary: There is insufficient evidence to determine whether the development and implementation of a deprescribing plan at the point of opioid initiation reduces long-term opioid use or opioid-related harms, as no studies were identified on this topic. The use of a pain management plan is recommended in pain management clinical practice guidelines;[78,79] however, we did not find any direct evidence for the impact of pain management plans on opioid use or clinical outcomes. A systematic review on opioid treatment agreements found weak evidence to support the effectiveness of patient-prescriber agreements in the reduction and mitigation of opioid misuse and abuse, however it is unknown if these agreements are beneficial as an opioid management strategy.[5] This recommendation is informed by evidence of persistent opioid use following initial opioid prescription. Data from the United States revealed that one in seven people who filled a repeat opioid prescription, or had a second opioid prescription authorised, remained on opioids one year later.[44] This study found that prescribing less than seven days of medication when initiating opioids could mitigate the chances of unintentional chronic use.[44] Another retrospective cohort study suggested that 5% of opioid-naïve patients who filled an opioid prescription, were taking opioids long-term.[45] This highlights the importance of discussions surrounding the intended duration of use and deprescribing early in the opioid prescribing process.

Recommendation 2

<div style="background-color:orange">

2. Conditional recommendation for (Certainty of Evidence: Very low)

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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

Practice points:

- The use of an opioid deprescribing conversation guide (Communication techniques for opioid analgesic tapering conversations)[80] 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.

  - NPS MedicineWise has a series of educational videos to support effective conversations about the use of opioids for the management of chronic non-cancer pain and opioid deprescribing.[81]

  - Other resources include: Safer management of opioids for chronic pain: Principles and language suggestions for talking with patients,[82] and The Department of Human Services - Difficult conversations: Tapering Opioid Dose.[83]

- A deprescribing plan, agreed upon by the person taking opioids and their healthcare professional may facilitate person-centred medication dose reduction or cessation.

  - The NPS MedicineWise tapering plan[70] may be a useful resource when developing a deprescribing plan.

- Baseline function and subsequent improvements or declines can be determined by both the person taking opioids and their healthcare professional. This may be aided by the use of validated tools (See Recommendation 9).

Rationale: We acknowledge that there is individual variability in response to opioid treatment. However, under the following conditions, the risks associated with opioid continuation likely outweigh the benefits and deprescribing is suggested. If there is a lack of overall and clinically meaningful improvement in function, quality of life or pain, or if there is a lack of progress toward meeting therapeutic goals, this is suggestive of a lack of opioid efficacy in treating the pain condition and a trial of opioid deprescribing is suggested. Function, pain and quality of life may improve when opioids are deprescribed. Due to a dose-related risk of opioid-related harms, dose reduction or discontinuation is anticipated to reduce opioid-related adverse effects. Experience of a non-fatal opioid overdose is a serious opioid-related adverse event which may prompt deprescribing. The aim of opioid therapy in chronic pain should extend

beyond pain reduction to encompass improvements in function, coping skills and quality of life. We acknowledge that not everyone will benefit from opioid cessation and persons taking opioids with improved function, adequate pain relief and low risk for opioid-related harms may be considered suitable to continue opioid therapy. Additionally, there may be circumstances where chronic pain overlaps with end-of-life or acute analgesia care, with terminal dyspnoea or dependency treatment. The opioid deprescribing approach may influence clinical outcomes. Please see recommendations 7-11 for further information on the deprescribing approach. See EtD Framework Table 1 for further factors considered when developing this recommendation.

Research Evidence Summary: 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.[84-89] The benefits of deprescribing on pain reduction were greater for those on higher baseline opioid doses (OMEDD) compared to those with lower baseline doses.[86] Reporting of quality of life measures were heterogeneous across reviews; however, very low certainty evidence suggests that quality of life may improve with opioid deprescribing.[84,86,90] Some reviews reported decreased opioid-related adverse effects such as dry mouth for intervention groups compared to control groups.[88] Across reviews, a smaller proportion of participants withdrew from the deprescribing cohorts than the continuation cohorts due to worsening symptoms/lack of efficacy.[86,90] Serious harms of opioid deprescribing remain uncertain, including substance use, opioid overdose, and suicide.[84-89,91]

Recommendation 3

3. 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.

Practice points:

- 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 (Communication techniques for opioid analgesic tapering conversations)[80] 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.
  - NPS MedicineWise has a series of educational videos to support effective conversations about the use of opioids for the management of chronic non-cancer pain and opioid deprescribing.[81]
  - Other resources include: Safer management of opioids for chronic pain: Principles and language suggestions for talking with patients,[82] and The Department of Human Services - Difficult conversations: Tapering Opioid Dose.[83]
- A deprescribing plan, agreed upon by the person taking opioids and their healthcare professional may facilitate person-centred medication dose reduction or cessation.
  - The NPS MedicineWise tapering plan[70] may be a useful resource when developing a deprescribing plan.
- Baseline function and subsequent improvements or declines can be determined by both the person taking opioids and their healthcare professional. This may be aided by the use of validated tools (See Recommendation 9).

Rationale: There is a lack of evidence on the benefits and harms of deprescribing in the cancer-survivor population. Due to the known harms of long-term opioid use and increasing cancer survivorship, we expect a similar benefit-harm profile for opioid deprescribing in this population when compared to populations with chronic non-cancer pain. We have extrapolated evidence from the chronic non-cancer pain population (See Recommendation 2) to provide a consensus-based recommendation relevant to those with chronic cancer-survivor pain. The GDG acknowledge that there is individual variability in response to opioid treatment. However, the risks associated with opioid continuation likely outweigh the benefits and

deprescribing is suggested under the following conditions. If there is a lack of overall and clinically meaningful improvement in function, quality of life or pain, or if there is a lack of progress toward meeting therapeutic goals, this is suggestive of a lack of opioid efficacy in treating the pain condition and a trial of opioid deprescribing is suggested. Function, pain and quality of life may improve when opioids are deprescribed. Due to a dose-related risk of opioid-related harms, dose reduction or discontinuation is anticipated to reduce opioid-related adverse effects. The aim of opioid therapy in chronic pain should extend beyond pain reduction to encompass improvements in function, coping skills and quality of life. We acknowledge that not everyone will benefit from opioid cessation and persons taking opioids with improved function, adequate pain relief, and low risk for opioid-related harms may be considered suitable to continue opioid therapy. Additionally, there may be circumstances where chronic pain overlaps with end-of-life or acute analgesia care, with terminal dyspnoea or dependency treatment. The deprescribing approach may influence clinical outcomes associated with opioid deprescribing. Please see recommendations 7-11 for further information on the deprescribing approach. See EtD Framework Table 1 for further factors considered when developing this recommendation.

Research Evidence Summary: Opioids remain the main treatment for cancer pain, as recommended by the World Health Organization.[92] However, there is limited evidence to inform the benefits and harms of long-term opioid use in cancer-survivors (those with a history of cancer who are beyond the acute diagnosis and treatment phase). Cancer survival rates in Australia continue to increase with a 5-year survival rate of 69% for all cancers combined.[93] Estimates of chronic pain in cancer survivors range from 20-40%,[37] with recent data from the United States reporting that 35% of cancer survivors have chronic pain.[94] The average prevalence rate of long-term opioid use in cancer survivors ranges widely in the literature (2%–45%),[95] with higher reported opioid use compared to populations without a history of cancer.[96] There was insufficient evidence to inform an evidence-based recommendation for deprescribing opioids in persons with chronic cancer-survivor pain due to a lack of information on the benefits and harms of opioid deprescribing in this population. However, relevant literature on opioid use in cancer-survivor populations has provided limited evidence to support the safety and efficacy of long-term opioid use.[97] Adverse effects from long-term opioid use, including sexual dysfunction, immune system effects, fatigue, and osteoporosis have been identified in this population,[98] as well as similar rates of prescription opioid misuse when compared to individuals without cancer.[96] There is also concern about the potential adverse effects of prolonged use of opioids in cancer survivors that may complicate recovery, such as sedation, cognitive impairment, tolerance, potential immunomodulation and endocrine dysfunction.[99]

Recommendation 4

4. 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.

Practice points:

- Healthcare 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 for further information). Optimisation of medical management of comorbidities 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.
    - An [evidence-based clinical practice guideline for deprescribing benzodiazepine receptor agonists](#) has been developed.[100]
- Liaising with other healthcare 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 and/or deprescribing plan, particularly for people taking multiple medicines.

Rationale: We would expect to see additional benefits from opioid deprescribing through opioid-related harm risk-reduction for persons with the identified clinical characteristics. Healthcare professional discretion is required to assess the potential benefits and harms of opioid deprescribing in the context of the individual and their comorbidities, concomitant medication use and clinical status. Persons taking opioids with improved function and/or quality of life, adequate pain relief and low risk for opioid-related harms may be considered suitable to continue opioid therapy. Note: We have not presented an upper limit or dose

threshold which indicates when opioid deprescribing should be considered. 'High doses' of prescribed opioids is variably defined. Evidence presented on cautionary dosages should not result in rapid tapers or abrupt discontinuation of opioids. See EtD Framework Table 1 for further factors considered when developing this recommendation.

Research Evidence Summary: We did not find any studies within our overview of reviews which linked the identified demographics or clinical characteristics to the benefits and harms of opioid deprescribing. Although there is a paucity of evidence regarding the benefits and harms of opioid deprescribing in the specified populations, there is evidence of increased risk of opioid-related harms in every identified populations.[101-109] The findings from the overview of systematic reviews, suggested that the benefits of deprescribing on pain reduction, were greater for those on higher baseline opioid doses compared to those with lower baseline doses. Among studies reporting mean pain scores at baseline and endpoint, improvements were greatest (19-47%) in studies of participants on higher baseline OMEDD (99-177mg) and more modest (8-10%) among studies of participants with lower baseline OMEDD (47-61mg), suggesting those on higher doses may see the greatest benefit from deprescribing.[86] There are differing estimates of the dose-dependent nature of overdose risk, however one study has demonstrated an almost 9-fold increase among persons prescribed >100mg OMEDD and a 4-fold increase among participants prescribed >50mg OMEDD (relative to participants on opioid regimens of less than 20mg OMEDD).[110] An Australian cohort study found that participants receiving daily opioid doses greater than 90mg OMEDD experienced less pain relief and were more likely to develop complications such as aberrant behaviour and opioid dependence.[108]

Recommendation 5

5.   Consensus recommendation

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

Practice Points:

- Resources which provide guidance on end-of-life care pain and symptom management include:
  - Therapeutic Guidelines: Palliative Care.[111]
  - Palliative Care Australia: Learn more about pain management.[112]
  - Facts about morphine and other opioid medicines in palliative care - Palliative Care Australia.[113]
- 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.[114] This approach to deprescribing should be discussed with the person taking opioids and/or their family/carer and monitored over time.

Rationale: We have placed an emphasis on symptom management and the prevention of suffering for populations with limited life expectancy. We recognise that the goals of therapy at end-of-life are different from the goals of care for chronic pain management and that there are different ethical and moral issues involved in providing opioids for end-of-life analgesia or dyspnoea. Therefore, we suggest that opioid deprescribing should be avoided in this population, unless deemed appropriate by the treating healthcare professional. See EtD Framework Table 1 for further considerations relating to this recommendation.

Research Evidence Summary: There is insufficient evidence to inform the benefits and harms of opioid deprescribing for people with pain who are nearing the end-of-life. We did not find any studies that reported on opioid deprescribing in this population group. Opioids are used to relieve pain and/or breathlessness for persons nearing end-of-life. Up to 25% of persons in palliative care report severe pain,[115] and up to 60% experience pain that causes them distress in the last 4 months of life.[116] Chronic breathlessness is also recognised as a distressing symptom in advanced disease, with reports of prevalence of up to 70% in advanced cancer and 60-100% in non-malignant life-limiting illness.[117,118]

Recommendation 6

6. Conditional recommendation against (Certainty of evidence: Moderate)

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.

Practice points:

- The Diagnostic and Statistical Manual of Mental Disorders (DSM–5) 5th edition[12] provides guidance on the diagnosis and severity of opioid use disorders.

- 'The OWLS' is a screening tool validated to screen for opioid use disorder in people with chronic pain who are prescribed opioids.[119]

- GPs 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 healthcare professional, this may occur in the general practice setting in collaboration with a pharmacist, through an addiction medicine specialist or psychiatrist, 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. Healthcare professionals should continue to use non-pharmacologic and non-opioid pharmacologic pain treatments, as appropriate, and consider consulting a pain or addiction specialist if required.

- A 'warm referral' describes a process of the healthcare professional arranging an appointment and taking care to ensure that the specialist is contacted, and the person is provided with correspondence explaining the person's medical history and the reason for referral.[120] A warm referral may be more likely to ensure that transition of care for a patient with opioid use disorder for appropriate treatment than if the patient themselves have to make arrangements without assistance.[120]

- In some Australian states and territories, Schedule 8 medications cannot be prescribed for persons who are known or suspected to be drug dependent, without a permit or an appropriate approval from the relevant state or territory medicines regulatory area.[121] 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.

- Additional resources to assist in the management of individuals with opioid use disorders may include:
  - National guidelines for medication-assisted treatment of opioid dependence.[122]
  - Headspace Substance Use Assessment & Treatment.[123]

- The Michigan Department of Health and Human Services and the University of Michigan Injury Prevention Centre, provides a fact-sheet on [Words Matter: Using people-first, non-stigmatizing language](#) for opioid use disorders.[124]

Rationale: The boundary between chronic pain and opioid use disorder management is complex, with a continuum of presentations. Although persons with opioid use disorders were not the target population of this guideline, we felt it was important to provide a recommendation pertaining to opioid deprescribing in individuals with opioid use disorders. The purpose is to minimise the risks of unintended harms from opioid deprescribing. Efforts to reduce opioid-related harm through opioid deprescribing must be carefully balanced against considerations of harms that may result from discontinuation or tapering such as seeking other, at times more dangerous, sources of opioids. If a severe opioid use disorder is suspected or diagnosed, alternative supports and management strategies are likely required and we advise against using deprescribing as a sole management strategy. See [EtD Framework Table 1](#) for further considerations relating to this recommendation.

Research Evidence Summary: The prevalence of opioid dependence (using DSM-IV diagnosis criteria) varies widely in primary care settings among people with chronic pain on opioid therapy, ranging from 3%–26%.[125] Reported rates of problematic use in chronic pain are also broad, ranging from <1-81%.[126] Up to 18% of persons commenced on opioid treatment develop an opioid use disorder,[127] with reported rates of addiction averaging between 8-12% of the population.[126] People with diagnosed opioid use disorders are routinely excluded from studies of opioid deprescribing, including those contained within the overview of systematic reviews. As such, we sought additional evidence to inform recommendations for this population. Existing clinical practice guidelines recommend against opioid deprescribing as a stand-alone strategy for individuals with opioid use disorders.[122,128-135] Moderate certainty evidence indicates that 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.[129] Further, moderate certainty evidence demonstrates 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.[24,136] We found limited evidence pertaining to persons with opioid use disorders, stratified by opioid use disorder severity (i.e. mild, moderate or severe). The conditional recommendation against using deprescribing as a sole strategy due to evidence of increased harms has been applied to individuals with a suspected or diagnosed severe opioid use disorder.

Recommendation 7

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7. Recommendation for (Certainty of evidence: Low)

</div>

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

Practice points:

- A deprescribing plan agreed upon by the person taking opioids and the healthcare professional may facilitate person-centred medication dose reduction or cessation.
    - The NPS MedicineWise tapering plan[70] may be a useful resource when developing a deprescribing plan.
- There is limited evidence to inform a preferred protocol for opioid deprescribing. Local guidance for gradual dose reduction strategies may be utilised.
    - The Therapeutic Guidelines – Pain and Analgesia[52] and NPS MedicineWise opioid tapering algorithm[137] provide a standard approach to opioid deprescribing for chronic non-cancer pain:
        - If the person has been taking the opioid for less than 3 months, reduce the dose by 10 to 25% every week
        - If the person has been taking the opioid for longer than 3 months, reduce the dose by 10 to 25% every 4 weeks
    - A summary of other published opioid tapering protocols is provided in Appendix 1 and Other Guidelines and Guides for Opioid Deprescribing.
- For people who have been on long-term opioid therapy (i.e. for years), or on 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 (e.g. for people who have experienced overdose on their current dosage). In these circumstances, consider the provision of naloxone. See Naloxone for further information.
- If a person has been using opioids short term (e.g. <1 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). Please see Recommendation 9 for further information.
- Additional resources to assist in determining a deprescribing protocol include:
    - Therapeutic Goods Administration: Clinician information sheet on opioid analgesic tapering[138]
    - NSW Therapeutic Advisory Group: Deprescribing guide for regular long-term opioid analgesic use (>3 months) in older adults[139]
    - Agency for Clinical Innovation, Pain Management Network: How to de-prescribe and wean opioids in general practice[140]
    - Primary Health Tasmania: A guide to deprescribing opioids[141]

- [NPS MedicineWise: Recommendations for deprescribing or tapering opioids Information for health professionals](#)[142]

Rationale: We present a 'Recommendation for' in spite of low certainty evidence, due to evidence of certain harms of abrupt opioid withdrawal or cessation. We recommend that deprescribing be performed at a slow enough rate to minimise withdrawal effects, thereby reducing the risk of harm to the patient and disruptions to the therapeutic relationship between the healthcare professional and person taking opioids. Qualitative work highlighted that persons who experienced negative consequences of abrupt opioid withdrawal spoke of mistrust of healthcare professionals and expressed trepidation in reattempting deprescribing. In contrast, gradual reduction allows for the deprescribing plan to be adjusted based on the person's history, use of opioids/dose, experience of deprescribing, and their acquisition of self-management skills. See [EtD Framework Table 2](#) for further factors considered when developing this recommendation.

Research Evidence Summary: Withdrawal signs and symptoms are likely to occur when opioids are withdrawn abruptly (e.g. craving, anxiety, insomnia, abdominal pain, vomiting, diarrhoea, diaphoresis, mydriasis, tremor, tachycardia).[143] The adverse physical and psychological outcomes of abrupt reduction or discontinuation of opioids include withdrawal effects, pain exacerbation, related loss of function and quality of life, psychological distress, hospitilisation, accidental overdose and suicide.[144,145][146] We identified insufficient evidence to enable a recommendation for or against a specific opioid tapering approach. To our knowledge, there is no trial that directly compares rapid opioid deprescribing protocols with slower deprescribing protocols in persons with pain. One cohort study of people prescribed 120mg OMEDD or more of long-term opioid therapy found each additional week to discontinuation was associated with a 7% reduction in risk of an opioid-related emergency department visits or hospitalisation, supporting the benefit of gradual tapering.[145]

Recommendation 8

<div style="background-color:green">**8.   Recommendation for (Certainty of evidence: Very low)**</div>

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

Practice points:

- The use of an opioid deprescribing conversation guide (Communication techniques for opioid analgesic tapering conversations)[80] 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.
    - NPS MedicineWise has a series of educational videos to support effective conversations about the use of opioids for the management of chronic non-cancer pain and opioid deprescribing.[81]
    - Other resources include: Safer management of opioids for chronic pain: Principles and language suggestions for talking with patients,[82] and The Department of Human Services - Difficult conversations: Tapering Opioid Dose.[83]
- A deprescribing plan, agreed upon by the person taking opioids and their healthcare professional may facilitate person-centred medication dose reduction or cessation.
    - The NPS MedicineWise tapering plan[70] may be a useful resource when developing a deprescribing plan.
- Opioid deprescribing should, where possible, be voluntary in nature with the deprescribing plan mutually agreed upon by the person taking the medication and the healthcare 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 (e.g. 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 healthcare 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, liver and renal function, comorbidities and mental health conditions, concomitant medications and psychosocial factors.
- Transition from one opioid to another may be required to facilitate deprescribing. Oral morphine equivalent daily dose (OMEDD) of different opioids can be calculated to

standardise the dose based on the knowledge that different opioids with varying potency may produce a similar analgesic effects.[13] The Faculty of Pain Medicine, Australian and New Zealand College of Anaesthetists (ANZCA) has released an online opioid equianalgesic calculator[147] (also available in table format)[148] which may assist when transitioning between different opioids or developing a tailored opioid deprescribing plan. See Clinical Considerations for additional information and considerations when using this calculator.

- Individualisation of the rate and approach of opioid deprescribing may require additional monitoring and input from healthcare professionals. At times, deprescribing might have to be slowed (e.g. once patients reach low dosages) 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 condition 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.

Rationale: Due to the diversity of clinical situations and varying needs, goals and personal preferences of people who may engage in opioid deprescribing, there is a need for a tailored and individualised deprescribing approach. We present a 'Recommendation for' in spite of very low certainty evidence, due to evidence harms from abrupt, forced deprescribing. We emphasise the importance of shared decision making between the person taking opioids and the healthcare professional when determining the deprescribing approach and the importance of voluntary opioid deprescribing where possible. Our qualitative work has found that deprescribing of opioids, if guided by an explicit and mutually agreed management plan, may be acceptable to both persons taking opioids and healthcare professionals. There may be acceptability concerns if opioid deprescribing is rigid in approach, involuntary or occurs without the consent of the person taking opioids. See EtD Framework Table 2 for further factors considered when developing this recommendation.

Research Evidence Summary: There is insufficient evidence to determine which individual or tapering characteristics are associated with greater success of opioid deprescribing. 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. Further we were unable

to ascertain differences in clinical outcomes based on tapering schedule. Many of the tapering schedules were not well defined;[85] however, some studies and reviews reported that the tapering approach was tailored to the specific participant's needs.[86,149] 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. Some evidence suggests that pain may remain unchanged in these populations.[150] 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.[84,86] 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.[151]

Recommendation 9

9. 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.

Practice points:

- 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.
- The Pain Self-Efficacy Questionnaire (PSEQ) may be a useful tool when developing a pain management plan and assessing progress over time.[152,153]
- Healthcare professionals may wish to monitor parameters including function, pain, sleep, mood, withdrawal effects, aberrant behaviours and dependence. Validated tools to assist monitoring include:
    - The PEG pain intensity scale[154]
    - The Brief Pain Inventory (BPI)[155]
    - Abbey Pain Scale[156] for those who can't communicate their pain and needs.
    - PainCheck is an App which can be used by registered users to calculate a pain severity score based on the Abbey Pain Scale.
    - The Pain Assessment in Advanced Dementia (PAINAD)[157]
    - The Clinical Opiate Withdrawal Scale (COWS)[158]
    - The Subjective Opiate Withdrawal Scale (SOWS)[159]
    - The Objective Opioid Withdrawal Scale (OOWS)[159]
    - The Routine Opioid Outcomes Monitoring (ROOM)[160]
- 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 which 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 healthcare professionals such as pharmacists in between reviews. Practically, one-monthly review 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.

- During the deprescribing period only prescribe enough opioid until the next scheduled clinical review date.
- 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.
- If complicated withdrawal symptoms are experienced, we suggest discussion with, or referral to a pain or addiction medicine specialist.
- Healthcare professionals should consider the potential harms of opioid continuation or deprescribing for people on 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.
- Healthcare 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. See Naloxone for further information.
- Real time prescription drug monitoring programs (PDMPs) can provide real-time information about the supply of opioids. Australian states and territories have been introducing real-time prescription monitoring. See Prescription Drug Monitoring Programs for further information.

Rationale: Regular monitoring for effect and adverse effects, along with education and support may mitigate potential harms associated with opioid deprescribing. Measuring success over time in accordance with a deprescribing plan can examine and/or address multiple measures of success such as dose reduction, effects on quality of life, function, adverse effects, and pain. Regular monitoring may allow for early detection of decline in clinical condition or withdrawal effects which may necessitate a readjustment of the deprescribing approach. The guideline development group acknowledges that the frequency of follow-up in research studies may be higher than what is feasible in clinical practice. We therefore recommend monitoring at each clinical review (at a minimum one-monthly), however, more frequent monitoring may be required at the start and end of the deprescribing process, or if challenges in opioid deprescribing are anticipated or experienced. See EtD Framework Table 2 for further factors considered when developing this recommendation.

Research Evidence Summary: Adverse effects when deprescribing opioids have the potential to cause significant harm, and have been identified as a key reason for disengagement with

deprescribing.[62] There is emerging evidence of an association between opioid deprescribing and overdose, suicide and mental health crises due to cognitive and psychological withdrawal effects.[58,59,144,161] Frequent and close monitoring throughout the opioid deprescribing process is warranted to prevent or minimise potential harms.

Recommendation 10

10. Conditional recommendation for (Certainty of evidence: Low)

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

Practice Points:

- Interdisciplinary or multidisciplinary care programmes provide multimodal treatment, with coordinated contributions by healthcare professionals from different disciplines, typically organised around a biopsychosocial model of chronic pain.
- The integrated primary health care model adopted by Aboriginal Community Controlled Health Organisations is in keeping with the philosophy of Aboriginal community control and the holistic view of health.
- Whilst 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 healthcare professionals whom the person taking opioids can access (e.g. nurse, pharmacist, occupational therapist, physiotherapist, substance use disorder specialist, psychiatrist, psychologist). Another alternative is for prescribers to implement a multimodal approach.
- The National Pain Services Directory[162] has a comprehensive list of available services to help manage pain conditions.

Rationale: Interdisciplinary and multidisciplinary care programmes have demonstrated effective opioid deprescribing, resulting in reductions in opioid dose and improvements in pain severity and function. Such care is consistent with expert guidelines for the management of long-term opioid therapy and chronic pain. We acknowledge that interdisciplinary and multidisciplinary pain management services may be difficult to access or implement, particularly in rural or remote areas, among socially-disadvantaged communities, or in primary care settings where resources or access to specialist services are limited. In such cases, this recommendation may be difficult to implement without additional resources, and hence we present it as a conditional recommendation. Note: The integrated primary health care model adopted by Aboriginal Community Controlled Health Organisations is in keeping with the philosophy of Aboriginal community control and the holistic view of health. Addressing the ill health of Aboriginal people is best achieved by local Aboriginal people controlling health care delivery, this has demonstrated improved health outcomes.[163] See EtD Framework Table 3 for further factors considered when developing this recommendation.

Research Evidence Summary: Interdisciplinary, multidisciplinary and multimodal care which emphasised non-pharmacologic and self-management strategies showed the greatest evidence for effective opioid deprescribing.[84,86] Non-drug interventions in these programs included cognitive behavioural therapy, physiotherapy and occupational therapy. The direct evidence for the effect of interdisciplinary or multidisciplinary care on the outcome of opioid

dose reduction is of low certainty. People on long-term opioid therapy who voluntarily participated in intensive multidisciplinary pain management interventions which incorporated opioid tapering experienced improvements in pain severity and function. [84-89] In contrast, those who tapered opioids with less intensive co-interventions were more likely to experience unchanged pain and function.[84,86] Addressing the ill health of Aboriginal people is best achieved by local Aboriginal people controlling health care delivery, this has demonstrated improved health outcomes.[163]

Recommendation 11

11. Conditional recommendation for (Certainty of evidence: Very Low – Low)

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

Practice points:

- The appropriateness of co-interventions for opioid deprescribing must be discussed between the healthcare 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.
- Refer to Table 5 for further information about the types of co-interventions utilised to facilitate opioid deprescribing.
  Note: *Interventions have not been directly compared against each-other and the GDG does not recommend any intervention over another.*

Rationale: Opioid deprescribing is clinically challenging and may be difficult to initiate and maintain. Evidence-based co-interventions may assist in achieving opioid reduction and managing pain when deprescribing opioids. Co-interventions have been defined as interventions which aims to reduce opioid use through modifying a person's physical condition or behaviour, or providing them with an alternate treatment approach. It is likely that the use of appropriate co-interventions to facilitate deprescribing of opioids, may be acceptable to both patients and healthcare professionals, however difficulties in accessing care and significant costs associated with co-interventions were described by participants in our qualitative studies. Further, co-interventions for opioid deprescribing may take substantial time and effort to engage in (e.g. cognitive behavioural therapy) and some proposed co-interventions may be invasive such as spinal cord stimulation or acupuncture, impacting on the acceptability of the intervention. As such, we present a 'conditional recommendation'. See EtD Framework Table 3 for further factors considered when developing this recommendation.

Research Evidence Summary: Evidence for the effectiveness of different co-interventions to achieve opioid reduction or cessation for the management of chronic pain was inconclusive and varied substantially across the interventions examined. Our overview identified reviews examining pharmacological, physical, interventional, psychological and behavioural, or mixed interventions. Opioid reduction varied widely across reviews and the interventions that were examined throughout the study periods. 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.[84-90,164-166] Quality of life may accompany opioid dose reduction when using deprescribing co-interventions.[84,86,90] The evidence to inform this recommendation relates to the role of co-interventions in opioid deprescribing rather than the benefit of co-interventions for chronic

pain management. We were unable to make recommendations regarding specific interventions due to the heterogeneity of interventions, populations and their types of pain, disparity in outcomes selected, and other limitations of the included studies and reviews.

Summary of Findings

The following section contains a narrative summary of findings from the overview of systematic reviews and supplementary searches where relevant, stratified by key clinical question. Full details of the overview of systematic review methodology, evidence synthesis, GRADE ratings and evidence-to-decision frameworks can be found in the Technical Report.

Key Clinical Question 1: Does deprescribing of opioids result in benefits or harms compared to continuation?

Summary of benefits and harms of long-term opioid use

There is a lack of evidence that demonstrates a long-term benefit of opioids in improving pain and function when compared to no opioids or placebo for managing chronic pain.[25,26] Most placebo-controlled randomised clinical trials (RCTs) have been limited to six weeks or less in duration, with a lack of evidence for long-term (>1 year) outcomes related to pain, function and quality of life.[26] Compared with placebo, opioids have been shown to be associated with small improvements in pain (weighted mean difference [WMD], −0.69 cm [95% CI, −0.82 to −0.56 cm] on a 10-cm visual analogue scale for pain; modelled risk difference for achieving the minimally important difference [MID], 11.9% [95% CI, 9.7% to 14.1%]), physical functioning (WMD, 2.04 points [95% CI, 1.41 to 2.68 points] on the 100-point SF-36 PCS; modelled risk difference for achieving the MID, 8.5% [95% CI, 5.9% to 11.2%]), and sleep quality; no significant improvements in social functioning; and no improvements in emotional functioning or role functioning.[25] Compared with placebo, opioids are associated with increased vomiting (5.9% with opioids vs 2.3% with placebo for trials that excluded patients with adverse events during a run-in period), drowsiness, constipation, dizziness, nausea, dry mouth, and pruritus.[25] Evidence supports a dose-dependent risk for serious harms associated with long-term opioid therapy, including overdose, opioid abuse, fractures, myocardial infarction and markers of sexual dysfunction.[26] 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 Ration [HR] 1.58, 95% CI 1.38 to 1.82), equivalent to 148 excess deaths per 10,000 person-years of treatment.[167]

Summary of benefits and harms of opioid deprescribing

Our overview of systematic reviews found consistent low certainty evidence of improved or unchanged mean pain scores and functional measures for most participants with chronic non-cancer pain who reduced or discontinued opioids. Very low certainty evidence suggested quality of life was unchanged or improved following opioid deprescribing. The certainty of evidence for adverse effects relating to opioid deprescribing was graded as very low. Reductions in opioid-related adverse effects such as dry mouth were observed.[88] Evidence of serious harms resulting from opioid deprescribing such as suicide and overdose were inconclusive. Evidence relating to Key Clinical Question 1 informed Recommendations 1-6.

The main findings in relation to Key Clinical Question 1 are presented below and are stratified by outcome of interest.

Pain

We found consistent low certainty evidence of improved or unchanged mean pain scores when opioids were deprescribed for persons with chronic non-cancer pain.[84-89] Fishbain et al.[85] found that opioid reduction was associated with improved or unchanged pain outcomes in persons with chronic non-cancer pain. In this review of 20 non-RCTs (pre-and post-cohort studies, group comparison), 80% of studies showed improved pain after opioid tapering and 15% of studies showed pain was the same by taper completion.[85] In 81.2% of studies, the reduction in pain was statistically significant. The 15% of studies that showed no pain change represented 1.9% of participants. One study reported that 97% of participants' pain dropped or was unchanged by the end of taper. Pain was worse in 3% of participants in this study, which represents 0.09% of all participants across the 20 studies.[85] The certainty of evidence for the outcome of pain was low, due to limitations in the study design of the included studies (retrospective non-randomised studies), lack of controls for non-treatment arms and variability in the opioid deprescribing approaches used across studies.

Mackey et al.[86] examined 5 RCTs, 6 controlled observational studies and 33 uncontrolled observational studies and found consistent low certainty evidence that opioid deprescribing resulted in improved or unchanged pain scores for persons with chronic non-cancer pain. Among studies reporting mean pain scores at baseline and endpoint, improvements were greatest (19-47%) in studies of patients on higher baseline OMEDD (99-177mg) and more modest (8-10%) among studies of patients with lower baseline OMEDD (47-61mg).[86] In one observational study of tapering included in the review, 50 participants with high baseline OMEDD (64% >200mg) who tapered opioids with usual care, had less pain (40%) or unchanged pain (28%) at 6– 12 months.[86] The body of evidence had several limitations including a high proportion of uncontrolled observational studies, unclear fidelity to interventions and inadequate reporting and handling of missing data. Further, most studies did not define clinically important changes on pain scales that were used.[86] The findings of reduced or unchanged pain following opioid deprescribing for persons with chronic non-cancer pain were mirrored in the review by Frank et al.[84] When stratifying based on the quality of studies, eight fair quality studies included in the review reported improvements in pain severity after opioid dose reduction, however the GRADE certainty of evidence was rated as very low.[84]

Mathieson et al.[90] examined RCTs of opioid deprescribing interventions for persons with chronic non-cancer pain. Pain outcomes were reported in seven studies and only two studies reported a greater reduction in pain in the intervention group compared to the control group. Overall, the interventions examined in this review did not reduce opioid dose in the intermediate term, nor did they increase the number of participants who ceased their dose.[90]

Therefore, the influence of opioid deprescribing on pain outcomes was unclear. Other reviews examining the effectiveness of interventions which facilitate opioid deprescribing are reported under Key Clinical Question 3, however, many of these reviews reported modest improvements in pain outcomes for persons with chronic non-cancer pain following an opioid deprescribing intervention.[87,88] Inconsistency and heterogeneity in the interventions and the reporting of outcomes, study design limitations and small sample sizes makes it difficult to draw firm conclusions about the impact of opioid deprescribing on pain from these reviews. Further, there is uncertainty whether opioid deprescribing resulted in the observed outcomes, or whether the co-intervention was primarily responsible for improvements in pain scores.

There was limited evidence to inform the influence of opioid deprescribing on pain outcomes in persons with acute pain, cancer-related pain or chronic cancer-survivor pain. Garland et al.[87] did not restrict their search strategy to one type of pain and from the 60 RCTs examined, 5 studies examined cancer pain and 40 examined burn pain or acute pain conditions. The results were not stratified by pain type so no conclusions about the impact of opioid deprescribing on specific pain types can be drawn from this review. He Y, et al.[164] conducted a systematic review and meta-analysis on acupuncture and/or acupressure for cancer pain and found that the intervention was significantly associated with reduced cancer pain.[164] A favourable association was also seen when acupuncture and acupressure were combined with analgesic therapy in 6 RCTs for reducing pain intensity (MD, −1.44 points; 95% CI, −1.98 to −0.89; I 2 = 92%) but only in 2 RCTs for reducing opioid dose (MD, −30.00 mg morphine equivalent daily dose; 95% CI, −37.5 mg to −22.5 mg).[164] Ferrer-Mileo et al.[168] reported that Cryoablation which resulted in opioid deprescribing decreased mean pain scores by 62.5% at 24 hours post-cryoablation, by 70% at 3 months and by 80.9% at 6 months.[168] Nabal et al.[169] investigated the additive effect of NSAIDs and paracetamol when combined with opioids in adult patients with chronic cancer pain. Three of seven studies examining NSAIDs showed an improvement in analgesia, however there was is insufficient evidence to support the use of paracetamol in combination with opioids for this purpose.[169] There is uncertainty whether opioid deprescribing resulted in the observed outcomes, or whether the co-intervention was primarily responsible for improvements in pain scores.

Physical Function

Low certainty evidence suggests that physical function may improve or remain unchanged when opioids are deprescribed for persons with chronic non-cancer pain. Mackey et al.[86] found that the greatest improvements in function were observed in a group of 1457 patients (baseline OMEDD 117mg) who participated in an intensive outpatient multimodal pain management program at the Cleveland Clinic.[86,170] The mean score on the pain disability index decreased from 42.95 at baseline to 18.29 at discharge (− 57.4%) and was 23.7 after 6–12 months of follow-up (− 44.8%). In a study of an intensive intervention in which 705 participants (baseline OMEDD 61mg) voluntarily participated in a 3-week interdisciplinary

pain program incorporating opioid cessation, scores on the Pain Outcomes Questionnaire-interference in Activities of Daily Living (POQ-ADL) decreased from 16 at baseline to 13 at 3-week discharge (− 18.8%).[86] Although the findings were consistent across the studies examined, the GRADE certainty of evidence rating was Low due to several limitations in the body of evidence including study designs (predominantly observational studies) and unclear fidelity to the interventions.[86] Frank et al.[84] also examined the effect of opioid deprescribing on function for persons with chronic non-cancer pain. Five of the 17 studies examining function were deemed to be fair-quality and were observational studies of interdisciplinary pain programs.[84] Each of the five studies reported improved function after opioid dose reduction, however the overall certainty rating for this outcome was 'very low'.[84]

Mathieson et al.[90] examined 22 RCTs of opioid deprescribing interventions for persons with chronic non-cancer pain. Disability outcomes were reported in six studies, with two studies demonstrating a greater reduction in disability compared to controls.[90] Overall, the interventions examined in this review did not reduce opioid dose in the intermediate term or increase the number of participants who ceased their dose, therefore we are uncertain of the influence of opioid deprescribing on the outcome of physical function. Some other reviews examining the effectiveness of interventions for opioid deprescribing, reported improved or unchanged physical function outcomes for persons with chronic non-cancer pain. Hassan et al.[88] reported that integrative medicine approaches were associated with overall improvements in function, particularly in studies assessing CBT and acupuncture.[88] Inconsistency and heterogeneity in the interventions and the reporting of outcomes and sample size concerns makes it difficult to draw firm conclusions about the impact of opioid deprescribing on physical function. Ratnayake, et al.[166] explored the effectiveness of spinal cord stimulation for pain associated with chronic pancreatitis in seven studies. Function was reported in two studies; one study reported an improvement in the pain disability index from a score of 62 to 15 and the other reported an improvement in the Korean Brief Pain Inventory score from 45 to 42. There were considerable concerns relating to the study design of included articles (case reports, case series, cohort study), sample sizes and quality of studies which limited the confidence in findings. Further, the applicability of the findings to other population groups outside those with chronic pancreatitis are unknown.

Quality of Life (QoL)

The outcome of QoL was not consistently reported across reviews and where reported, measures were heterogeneous. Very low certainty evidence suggests that opioid deprescribing may result in improved or unchanged QoL. Both the review by Mackey et al.[86] and Frank et al [84] rated the certainty of evidence for the outcome of QoL as very low. In the review by Frank et al.[84] the effect of opioid deprescribing on quality of life was assessed in 12 studies. Three fair-quality studies were uncontrolled observational studies of interdisciplinary pain programs and all reported improved quality of life.[84]

In Mathieson's review of 22 RCTs,[90] QoL outcomes were reported in three studies and one study had a small effect on quality-of-life mental and physical composite scores.[90] Overall, the interventions examined in this review did not reduce opioid dose in the intermediate term or increase the number of participants who ceased their dose, therefore the influence of opioid deprescribing on QoL was unclear. Hassan et al.[88] reported that integrative medicine approaches were associated with overall improvements in QoL, specifically in studies assessing acupuncture and Ferrer-Mileo et al.[168] reported that Cryoablation was associated with a 44.2% improvement in quality of life after 4 weeks and a 59.6% improvement at 8 weeks.[168] Inconsistency and heterogeneity in the interventions and the reporting of outcomes, as well as potential confounders makes it difficult to draw firm conclusions about the impact of opioid deprescribing on QoL in these studies.

Adverse events

The certainty of evidence for adverse effects relating to opioid deprescribing was graded as very low. Many reviews contained studies which did not report on adverse events,[85,87,89,165] or reported limited adverse events resulting from deprescribing.[88,90,164,166] Some reviews reported decreased opioid-related adverse effects such as dry mouth for intervention groups compared to control groups.[88] Across reviews, a small proportion of participants withdrew from the deprescribing cohorts than the continuation cohorts due to worsening symptoms/lack of efficacy.[86,90] Serious harms of opioid deprescribing were not routinely examined in reviews contained within the overview.

Mackey et al.[86] sought to assess rates of serious harms including substance use, opioid overdose and suicide resulting from opioid deprescribing. The evidence of serious harms was unclear due to insufficient outcome data in primary studies.[86] In a retrospective study of 572 participants in a primary care clinic on long-term opioid therapy over a 5-year period, 17 (4.9%) participants who discontinued opioids died of an overdose and 4 (1.75%) who continued prescription opioids died of an overdose. Opioid discontinuation was associated with a hazard ratio for overdose death of 2.94 (1.01 to 8.61) after adjusting for age and race. In another retrospective study included in Mackey's review,[86] of 43 participants who stopped opioids due to opioid agreement violations, no patients overdosed. The association between opioid dose reduction or discontinuation and retention in healthcare remains unclear. One study found that opioid taper was significantly associated with termination of care (AOR 4.3, 95% CI 2.2 to 8.5) compared to continuing opioids.[171]

Eighteen of the 67 studies included in the Frank et al.[84] review, examined opioid withdrawal symptoms, with reported incidence ranging widely (0-100%). The evidence relating to adverse events, including opioid withdrawal symptoms and substance use was very low certainty. Five studies assessed mortality outcomes and one study reported a single opioid related overdose death.[84] Mathieson et al.[90] assessed adverse events and serious adverse events in RCTs of interventions for opioid deprescribing and found they were infrequent (in the short term, one

event in 93 participants in the intervention group and zero events in 77 participants in the control group. In the intermediate term, one event in 18 participants in the intervention group and zero events in 17 participants in the control group). There was no risk difference between intervention and control groups for serious adverse events.

Although not included in the overview of systematic reviews, recent observational studies have reported increased incidence of suicide, overdose, illicit opioid use and mental health crises for some populations after stopping opioids, particularly for those on high doses.[58,59,91,144]

Opioid Use Disorders

Our overview of systematic reviews found limited evidence to inform the benefits and harms of opioid deprescribing in populations with opioid use disorders. This correlates with the guideline target audience and the overview search strategy which focussed on persons taking opioids for pain rather than for opioid maintenance therapy. Mackey et al.[86] included a 2019 retrospective study of Medicaid claims data in Vermont, USA. Among a cohort of 694 Medicaid recipients who had a high prevalence of substance use disorders (60%) on ≥ 120mg OMEDD, almost half (49%) of participants who discontinued opioids subsequently had an ED visit or hospitalisation due to opioid poisoning or substance use disorder.[86] In this study, opioids were most often discontinued without a gradual taper (median length of time to discontinuation was 1 day) and < 1% of participants were prescribed medication to treat substance use disorders.[86]

Supplementary searches provided moderate certainty evidence which indicated that 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.[129] 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.[24,136] Methadone and buprenorphine for opioid dependence have been found to increase retention in treatment and to decrease illicit opioid use among persons with an opioid use disorders, however the evidence base primarily relates to the use of heroin rather than prescription opioids.[24] [129]Some evidence suggests that evidence-based psychosocial treatments used in conjunction with medication-assisted therapy may reduce opioid misuse and increasing retention during maintenance therapy. [24]

Key Clinical Question 1 - Evidence-based Recommendations

Recommendation 2 (Conditional, Very Low Certainty): 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.

Consistent low certainty evidence suggested 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. Reporting of quality of life measures were heterogeneous across reviews, however, very low certainty evidence suggests that quality of life may improve with opioid deprescribing. Opioid deprescribing may be associated with a reduction in opioid-related adverse effects. Serious harms of opioid deprescribing remain uncertain, including substance use, opioid overdose, and suicide.

Recommendation 6 (Conditional, Moderate Certainty): 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.

The prevalence of opioid dependence (using DSM-IV diagnosis criteria) varies widely in primary care settings among people with chronic pain on opioid therapy, ranging from 3%–26%.[125] Reported rates of problematic use in chronic pain are also broad, ranging from <1-81%.[126] Up to 18% of persons commenced on opioid treatment develop an opioid use disorder,[127] with reported rates of addiction averaging between 8-12% of the population.[126] People with diagnosed opioid use disorders are routinely excluded from studies of opioid deprescribing, including those contained within the overview of systematic reviews. As such, we sought additional evidence to inform recommendations for this population. Existing clinical practice guidelines recommend against opioid deprescribing as a stand-alone strategy for individuals with opioid use disorders.[122,128-135] Moderate certainty evidence indicates that 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.[129] Further, moderate certainty evidence demonstrates 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.[24,136] We found limited evidence pertaining to persons with opioid use disorders, stratified by opioid use disorder severity (i.e. mild, moderate or severe). The recommendation against using deprescribing as a sole strategy due to evidence of increased harms has been applied to individuals with a suspected or diagnosed severe opioid use disorder. The GDG suggested that many individuals taking opioids for pain conditions may fulfil the criteria of a mild opioid use disorder in accordance with DSM-IV diagnostic criteria. This recommendation should not deter healthcare professionals or persons taking opioids from trialling opioid deprescribing if a mild opioid use disorder was diagnosed but a trial of opioid deprescribing was deemed appropriate. Furthermore, the evidence informing this recommendation was largely in the

context of individuals using illicit opioid use such as heroin rather than prescription opioids and individuals with severe opioid use disorders.[24,129,136] This recommendation was categorised as a conditional recommendation. Some persons taking opioids for pain may wish to attempt deprescribing or undertake withdrawal management without transition to opioid maintenance therapy. As such, not all individuals may be best served by the recommended course of action and there is a need to consider the individual person's circumstances, preferences and values more carefully than usual.

Key Clinical Question 1 - Consensus Recommendations

Recommendation 1 (Consensus): We suggest developing and implementing a deprescribing plan for persons being prescribed opioids at the point of opioid initiation.

Recommendation 1 is informed by the known harms of long-term opioid use as summarised above. There is insufficient evidence to determine whether the development and implementation of a deprescribing plan at the point of opioid initiation reduces long-term opioid use or opioid-related harms, as no studies were identified on this topic. The use of a pain management plan is recommended in pain management clinical practice guidelines;[78,79] however, we did not find any direct evidence for the impact of pain management plans on opioid use or clinical outcomes. A systematic review on opioid treatment agreements found weak evidence to support the effectiveness of patient-prescriber agreements in the reduction and mitigation of opioid misuse and abuse, however it is unknown if these agreements are beneficial as an opioid management strategy.[5] This recommendation is informed by evidence of persistent opioid use following initial opioid prescription. Data from the United States revealed that one in seven people who filled a repeat opioid prescription, or had a second opioid prescription authorised, remained on opioids one year later.[44] This study found that prescribing less than seven days of medication when initiating opioids could mitigate the chances of unintentional chronic use.[44] Another retrospective cohort study suggested that 5% of opioid-naïve persons who filled an opioid prescription, were taking opioids long-term.[45] This highlights the importance of discussions surrounding the intended duration of use and deprescribing early in the opioid prescribing process.

A growing body of literature which suggests that persons who are prescribed opioids postoperatively are at an increased risk of chronic opioid use.[172-175] In a systematic review and meta-analysis of 33 observational studies including more than 1.9 million participants, 6.7% of people continued to fill opioid prescriptions more than 3 months after surgery, with 1.2% of opioid-naïve participants transitioning to long-term opioid use.[176] Similarly, a recent review of 12 studies examining persistent opioid use after surgery in Europe reported the rate of opioid use 3 months after total hip or total knee arthroplasties as 7.9-41%.[177] In the Australian context, studies have shown that a small percentage of the population who initiate opioids post-surgically transition to chronic use (1.3-10.5%).[178-181] However, given the frequency at

which surgical procedures occur, a large number of people may be affected. More than 1.9 million Australian adults initiate opioids use each year. About half are initiated by general practitioners, with 25% initiated by surgeons (6.6%), interns (8.3%) or anaesthetists (10.1%), suggesting that a substantial proportion of opioids are initiated in hospital, and a large proportion following postoperative discharge.[41]

Greater initial opioid exposure (i.e. higher total dose, longer duration prescription) has been shown to be associated with greater risks of long-term use,[45,182,183] adverse healthcare events,[184] and overdose.[183] Further, the use of low-potency or low-dose opioids can escalate to high-dose therapy, often without improvements in pain,[185] increasing the risk of opioid-related morbidity and mortality.[186,187] Initiating therapy with long-acting opioids has been shown to pose a higher risk of long-term use than initiating with short-acting opioids.[45]

Analgesics that act by different mechanisms and at different receptor sites can be combined to produce additive or synergistic pain relief and may reduce opioid use.[188] Similarly, non-pharmacological therapies (e.g. electrostimulation, cognitive behavioural therapy, physical therapy) have been employed to improve both acute and chronic pain management and reduce the need for opioid-containing medication.[189] [75]

As such, the GDG suggests if initiating opioid treatment, that the prescriber and person taking opioids should agree on the goals of therapy and the criteria for treatment success and/or failure. A clear plan for opioid reduction and discontinuation should be established through the development and use of a deprescribing plan. Developing and implementing a deprescribing plan at the point of opioid initiation may limit opioid dose and duration to attenuate opioid-related harms. Further, it may assist in setting appropriate expectations about the role of opioids in the management of pain. A pain management plan which emphasises appropriate alternate pain management strategies (pharmacological and/or non-pharmacological) at the point of opioid initiation may reduce reliance on opioids for pain management.

Recommendation 3 (Consensus): 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.

Opioids remain the main treatment for cancer pain, as recommended by the World Health Organization.[92] However, there is limited evidence to inform the benefits and harms of long-term opioid use in cancer-survivors (those with a history of cancer who are beyond the acute

diagnosis and treatment phase). Cancer survival rates in Australia continue to increase with a 5-year survival rate of 69% for all cancers combined.[93] Estimates of chronic pain in cancer survivors range from 20-40%,[37] with recent data from the United States reporting that 35% of cancer survivors have chronic pain.[94] The average prevalence rate of long-term opioid use in cancer survivors ranges widely in the literature (2%–45%),[95] with higher reported opioid use compared to populations without a history of cancer.[96] There was insufficient evidence to inform an evidence-based recommendation for deprescribing opioids in persons with chronic cancer-survivor pain due to a lack of data on the benefits and harms of opioid deprescribing in this population. However, relevant literature on opioid use in cancer-survivor populations has provided limited evidence to support the safety and efficacy of long-term opioid use.[97] Adverse effects from long-term opioid use, including sexual dysfunction, immune system effects, fatigue, and osteoporosis have been identified in this population,[98] as well as similar rates of prescription opioid misuse when compared to individuals without cancer.[96]

Recommendation 4 (Consensus): 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.

We did not find any studies within our overview of reviews which linked the identified demographics or clinical characteristics to the benefits and harms of opioid deprescribing. Although there is a paucity of evidence regarding the benefits and harms of opioid deprescribing in the specified populations, there is evidence of increased risk of opioid-related harms in each of the identified populations.[101-108]

Chronic opioid use is associated with multiple features of sleep-disordered breathing, including central sleep apnoea, ataxic breathing, hypoxemia, and carbon dioxide retention.[102,190] For persons on regular opioid therapy, the prevalence of central sleep apnoea is 24%,[104] and the prevalence of sleep-disordered breathing is as high as 75%.[191] Chronic opioid use is a risk factor for the development of central sleep apnoea and ataxic breathing, with the adverse respiratory effects of opioids occurring in a dose-dependent fashion.[102] Ataxic breathing has been observed in up to 92% of individuals taking 200mg OMEDD, 61% of individuals taking under 200mg OMEDD, and just 5% of individuals not taking opioids.[102] The deleterious effect of opioids on sleep-disordered breathing and sleep apnoea, can increase the risk of unintentional opioid-related overdoses,[103] with an OMEDD of greater than 200mg being a threshold of particular concern.[104] An analysis examining root causes and risk factors

for opioid-related poisoning deaths, determined that sleep-disordered breathing was a likely contributor to a proportion of deaths.[105]

Opioids can decrease respiratory drive, leading to oxygen desaturation in people with COPD. COPD has been identified as a prominent risk factor for life-threatening respiratory central nervous system depression or overdose among individuals prescribed opioids.[105] Incident opioid use, particularly with more potent opioids, has been associated with increased risk of adverse respiratory outcomes, including respiratory-related mortality, among older adults with COPD.[106] When examining risk factors for opioid-related events in hospital, COPD is shown to be a significant risk-factor, even when accounting for OMEED and coadministration of other sedative agents.[192,193] Australian data suggests that COPD had a similar increased odds ratio (OR=1.43) as being on >100mg OMEDD (OR=1.57) or being on a benzodiazepine and opioids (OR=1.53).[192,193]Some clinical practice guidelines do recommend opioids for individuals with COPD who experience refractory dyspnoea despite otherwise optimal therapy.[194]

Medications with sedative properties can potentiate opioid-induced respiratory and sedative effects, thereby elevating the risk for adverse events among those receiving long-term opioid therapy, such as falls, fractures, opioid-induced ventilatory impairment (OIVI) and fatal overdose.[195,196] The combination of opioids and benzodiazepines is of particular concern as co-administration increases the risk of mortality.[197] Other contributors to opioid-related deaths are the presence of additional central nervous system-depressant drugs (e.g. alcohol and antidepressants).[107]

High-dose opioids are associated with worse functional outcomes and an increased risk of death.[186,198,199] Many persons do not experience benefit in pain or function from opioid dosages ≥50mg OMEDD but are exposed to progressive increases in risk as dosage increases. Additional dosages beyond 50mg OMEDD are progressively more likely to yield diminishing returns in benefits relative to risks."[24] The findings from the overview of systematic reviews, suggested that the benefits of deprescribing on pain reduction, were greater for those on higher baseline opioid doses compared to those with lower baseline doses. Among studies reporting mean pain scores at baseline and endpoint, improvements were greatest (19-47%) in studies of participants on higher baseline OMEDD (99-177mg) and more modest (8-10%) among studies of participants with lower baseline OMEDD (47-61mg), suggesting those on higher doses may see the greatest benefit from deprescribing.[86] There are differing estimates of the dose-dependent nature of overdose risk, however one study has demonstrated an almost 9-fold increase among persons prescribed >100mg OMEDD and a 4-fold increase among participants prescribed >50mg OMEDD (relative to participants on opioid regimens of less than 20mg OMEDD).[110] An Australian cohort study found that participants receiving daily opioid doses greater than 90mg OMEDD experienced less pain relief and were more likely to develop complications such as aberrant behaviour and opioid dependence.[108]

Recommendation 5 (Consensus): We suggest avoiding deprescribing for persons taking opioids for pain or dyspnoea who are nearing the end-of-life.

There is insufficient evidence to inform the benefits and harms of opioid deprescribing for people with pain who are nearing the end-of-life. We did not find any studies that reported on opioid deprescribing in this population group. Opioids are used to relieve pain and/or breathlessness for persons nearing end-of-life. Up to 25% of persons in palliative care report severe pain,[115] and up to 60% experience pain that causes them distress in the last 4 months of life.[116] Chronic breathlessness is also recognised as a distressing symptom in advanced disease, with reports of prevalence of up to 70% in advanced cancer and 60-100% in non-malignant life-limiting illness.[117,118] We have placed an emphasis on symptom management and the prevention of suffering for populations with limited life expectancy. We recognise that the goals of therapy at end-of-life are different from the goals of care for chronic pain management and that there are different ethical and moral issues involved in providing opioids for end-of-life analgesia or dyspnoea.[113] Therefore, we suggest that opioid deprescribing should be avoided in this population, unless deemed appropriate by the treating healthcare professional.

Key Clinical Question 2: What is the evidence on how to deprescribe opioids?

There was limited evidence derived from our overview of systematic reviews on the benefits and harms of different opioid reduction or discontinuation approaches. Although we were unable to evaluate which tapering characteristics were associated with the greatest benefits and harms, some information could be gleaned about the rate and nature of successful opioid deprescribing approaches. This evidence on how to deprescribe opioids has informed Recommendations 7-9.

Tapering Schedules

Participant baseline characteristics were not sufficiently described in the studies examined and interventions were too nonspecific to draw conclusions about the comparative effectiveness of different deprescribing protocols or approaches. Fishbain et al.[85] reported that 60% of studies included in their review did not report the tapering protocol. When a tapering protocol was documented in studies contained within the overview of reviews, they were often general, describing gradual or individualised opioid reductions rather than specific schedules. Some reviews reported that the tapering approach was tailored to the specific participant's needs.[86,149]

In the overview of systematic review, most studies examined gradual opioid tapering approaches prior to discontinuation, with the duration of tapers reported in the Fishbain, et al. review ranging from 2 to 180 days, with an average of 45 days.[85] Characteristics from studies included in the evidence synthesis which showed positive outcomes included gradual reductions (over 22 weeks in one study).[86] Mackey et al.[86] included a 2019 retrospective study

of Medicaid claims data in Vermont, USA which found that almost half (49%) of a cohort of 694 participants who had a high prevalence of substance use disorders (60%) on ≥ 120mg OMEDD who discontinued opioids subsequently had an ED visit or hospitalisation due to opioid poisoning or substance use disorder.[86] In this study, opioids were most often discontinued without a gradual taper (median length of time to discontinuation was 1 day) and < 1% of participants were prescribed medication to treat substance use disorders.[86] Gradual opioid tapers (>3 weeks) were associated with lower rates of ED visits and hospitalizations due to opioid-related adverse events than abrupt discontinuation and rapid tapers (<3 weeks). After controlling for sociodemographic and clinical factors, each additional week of discontinuation time was associated with a 7% reduction in the probability of having opioid related adverse event (p < 0.01).[145]

Due to the limited evidence from the overview of systematic reviews to inform key clinical question 2, we conducted a supplementary search of primary studies to obtain additional evidence about how best to deprescribe opioids for persons taking prescribed opioids for pain. There were very few relevant studies identified and evidence on the comparative effectiveness of opioid deprescribing approaches was largely limited to small, observational studies, or examined populations using opioid maintenance therapies.[149,200-204] Furthermore, qualitative studies provide insight into the barriers to opioid deprescribing through reporting patient-specific factors such as medical history, personal motivations and rapport between the healthcare professionals and the person taking opioids, which may influence the deprescribing process and outcomes.[54,205,206]

Appendix 1 presents the findings of a systematic review examining the deprescribing schedules recommended in existing clinical practice guidelines. In this guideline, we have recommended individualising the deprescribing approach to meet the needs of the individuals, however the protocols listed in Appendix 1 and Other Guidelines and Guides for Opioid Deprescribing may be used as a starting point or can be adapted for use. The CDC guideline suggests that tapering opioid doses by 10% of the initial dose each week is reasonable to avoid withdrawal symptoms.[24] However, newer data indicates that successful tapers in persons with chronic pain may require smaller dose reductions over longer periods.[207] As such, we recommend a gradual taper and individually tailoring the deprescribing plan based on the person's clinical characteristics, goals and preferences.

Voluntary Opioid Deprescribing

Patient engagement has been shown to impact the success of opiod deprescribing.[208] The demonstrated clinical benefits of opioid deprescribing in the overview of systematic reviews, relate predominantly to studies in which participants voluntarily engaged in opioid deprescribing.[84,86] Although there is emerging evidence that involuntary opioid reduction may also result in improved or unchanged pain outcomes,[209] increased harms (suicide, overdose, illicit opioid use) have been associated with involuntary tapers.[59] Mackey et al.[86] was one of

the only reviews which compared outcomes of patient-initiated tapers and healthcare professional-initiated tapers. In a retrospective study of 551 participants with a baseline OMEDD of 76mg, the majority of participants (85%) underwent healthcare professional-initiated tapers and pain scores improved by 3.8%. Another retrospective study had 509 participants who underwent healthcare professional-initiated tapers, 47 (9.2%) participants had new-onset suicidal ideation and 12 participants (2.4%) had suicidal self-directed violence in the year following opioid discontinuation.

Key Clinical Question 2 - Evidence-based Recommendations

Although the certainty of evidence for Recommendation 7 was rated as 'Low' and 'Very Low' for Recommendation 8, a 'Recommendation For' has been presented. The GDG was confident that the desirable effects of the proposed interventions outweigh the undesirable effects and that most or all individuals will be best served by the recommended course of action.

Recommendation 7 (Recommendation For, Low Certainty of Evidence): We recommend gradual tapering of opioids. Abrupt cessation of opioids without prior dose reduction may increase risks of harm.

Withdrawal signs and symptoms are likely to occur when opioids are withdrawn abruptly (e.g. craving, anxiety, insomnia, abdominal pain, vomiting, diarrhoea, diaphoresis, mydriasis, tremor, tachycardia).[143] The adverse physical and psychological outcomes of abrupt reduction or discontinuation of opioids include withdrawal effects, pain exacerbation, related loss of function and quality of life, psychological distress, hospitilisation, accidental overdose and suicide.[144-146] To our knowledge, there is no trial that directly compares rapid opioid deprescribing protocols with slower deprescribing protocols in persons with pain. We identified insufficient evidence to enable a recommendation for or against a specific opioid tapering approach. One cohort study contained within the overview of systematic reviews found that for people prescribed 120 mg OMEDD or more of long-term opioid therapies, each additional week to discontinuation was associated with a 7% reduction in risk of an opioid-related emergency department visit or hospitalisation, supporting the benefit of gradual tapering.[134] Characteristics from studies included in the evidence synthesis which showed benefit included gradual reductions (over 22 weeks in 1 study).[86]

Recommendation 8 (Recommendation For, Very Low Certainty of Evidence): We recommend tailoring the deprescribing plan based on the person's clinical characteristics, goals and preferences.

There is insufficient evidence to determine which individual or tapering characteristics are associated with greater success of opioid deprescribing. 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 on clinical outcomes such as pain and function. 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.[84,86] 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.[86,151]

Key Clinical Question 2 - Consensus Recommendations

Recommendation 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.

There was insufficient evidence to inform an evidence-based recommendation on monitoring associated with opioid deprescribing. Adverse effects when deprescribing opioids have the potential to cause significant harm, and have been identified as a key reason for disengagement with deprescribing.[62] There is emerging evidence of an association between opioid deprescribing and overdose, suicide and mental health crises due to cognitive and psychological withdrawal effects.[58,59,144,161] The association between opioid dose reduction or discontinuation and retention in healthcare remains unclear, however one study found that opioid taper was significantly associated with termination of care compared to continuing opioids.[171] Frequent and close monitoring throughout the opioid deprescribing process, along with education and support, is warranted to prevent or minimise potential harms. Measuring success over time in accordance with a deprescribing plan can examine and/or address multiple measures of success such as dose reduction, effects on quality of life, function, adverse effects and pain. Regular monitoring may allow for early detection of decline in clinical condition or withdrawal effects which may necessitate a readjustment of the deprescribing approach. The guideline development group acknowledges that the frequency of follow-up in research studies (sometimes daily or weekly) may be higher than what is feasible in clinical practice. We therefore recommend monitoring at each clinical review (at a minimum one-monthly), however, more frequent monitoring may be required at the start and end of the deprescribing process, or if challenges in opioid deprescribing are anticipated or experienced.

Key Clinical Question 3: Which interventions are effective to facilitate opioid deprescribing?

Accumulating evidence on the harms of prescription opioids, particularly in the context of long-term use for chronic non-cancer pain[26,210,211] has resulted in a substantial body of literature examining alternate pain management strategies and interventions to facilitate opioid deprescribing. This section aims to summarise the available evidence on the

effectiveness and outcomes of opioid deprescribing interventions. Please see the Technical Report for further information about the reviews examining each intervention. Evidence relating to Key Clinical Question 3 has informed Recommendations 10 and 11 and is summarised below, stratified by outcome.

Opioid Reduction

Multiple interventions showed evidence of opioid reduction, ranging from -5.00 to -160.00 OMEDD over the study periods. We were unable to make recommendations regarding specific interventions due to the heterogeneity of interventions, populations and their types of pain, disparity in outcomes selected, and other limitations of the included studies and reviews. We did not identify any studies directly comparing different interventions and their effectiveness. Psychological and behavioural, physical and interventional and mixed interventions resulted in variable opioid reduction and discontinuation, demonstrating feasibility of the deprescribing interventions. Table 5 summarises information on the success of co-interventions utilised to facilitate opioid deprescribing. The Technical Report contains the GRADE tables pertaining to key clinical question 3.

Pharmacological interventions

Pharmacological interventions, namely cannabinoids, showed insufficient evidence of effect in reducing opioids. Two reviews examined cannabanoids with mixed findings relating to the effect of cannabinoids on opioid use.[88,165] Reviews comprised of studies where participants self-reported opioid intake and did not specify the types of cannabis used or the method of administration. There were no overlapping studies in these two reviews and overall there was no clear evidence for the association between cannabinoid use and reduction in opioids.

Physical and interventional interventions

A range of physical interventions were examined including acupuncture and/or acupressure,[164] and physical therapy.[88] Interventional interventions included spinal cord stimulation,[89,166] and cryoablation.[168] He et al.[164] synthesized RCTs relating to the impact of acupuncture and acupressure on cancer pain. Two RCTs found that acupuncture or acupressure reduced OMEDD by a mean difference of -30.00 whilst also resulting in reduced cancer pain. Similarly, Frank et al.[84] linked acupuncture with opioid discontinuation rates of 66%-86%. Hassan et al.[88] reported improvements in pain and function and reductions in opioid use associated with acupuncture, however these findings were not quantified. In the same review, physical therapy was not found to result in decreased opioid usage.[88] Ratnayake et al.[166] examined the impact of spinal cord stimulation on pain and opioid use in participants with chronic pancreatitis. A 69% reduction in opioid usage was observed post spinal cord stimulation (-101.00 OMEDD) and an accompanying 61% reduction in pain scores. Small participant numbers and variable quality limited the confidence of these findings. Pollard et al.[89] also synthesized evidence on the effect of spinal cord stimulation for participants with intractable spine or limb pain. High frequency spinal cord stimulation decreased OMEDD by -

7.30 to -24.80 and overall was associated with increased odds of reducing opioid consumption, with pooled data reaching statistical significance (OR 8.60, CI [1.93-38.30]). Ferrer-Mileo et al.[168] reported decreased pain scores and opioid consumption (-24.00 OMEDD) after cryoablation in people with cancer pain. These findings were observed both immediately after the intervention and 3 and 6 months' post-procedure with the need for opioids decreasing by 61% at 3 months.

Psychological and behavioural interventions

Psychological interventions which were examined in the included systematic reviews include, mindfulness, cognitive behavioural therapy (CBT), meditation, hypnosis, relaxation, guided imagery. Garland et al.[87] examined the effect of mind-body therapies on opioid dose reduction for persons with pain. Mind-body therapies were associated with improved pain and small reductions in opioid dose (Cohen d = -0.26; 95% CI, -0.44 to -0.08). Meditation, CBT and hypnosis had the greatest evidence of effect out of the interventions examined. Frank et al.[84] reported on behavioural interventions including CBT and meditation. Across five studies, opioid discontinuation rates ranged from 6-55%, with modest reductions in OMEDD observed (-10.10). One clinician-targeted intervention of education plus decision tools versus decision tools alone reduced the number of opioid prescriptions (risk difference (RD) −0.1, 95% CI −0.2 to −0.1), dose (MD−5.3 OMEDD, 95% CI −6.2 to −4.5) and use (RD−0.1, 95% CI −0.1 to −0.0) in the long term, however no other studies in that review showed effective opioid deprescribing.[90]

Mixed Interventions

The two most common mixed interventions that were examined were i) multidisciplinary pain programs and ii) multimodal taper support interventions. Multidisciplinary pain programs provided consistent evidence of reduced opioid use and improved or unchanged pain and quality of life outcomes and provided the greatest evidence for effective opioid deprescribing.[84,86] Mackey et al.[86] found that participants on long term opioid therapy who voluntarily participated in intensive pain management interventions experienced improvements in pain severity and pain-related function, whilst those who tapered with less intensive co-interventions had unchanged pain and function. Among studies reporting mean pain scores, improvements were greatest in studies where participants had higher baseline OMEDD (99-177mg) and more modest among studies of participants with lower baseline OMEDD (47-61mg).

Mathieson et al.[90] demonstrated a -27.9 OMEDD difference in opioid use after a dose-tapering protocol intervention in the short term, however this effect was not sustained. Overall, this review concluded that patient-focussed interventions did not reduce opioid dose at the intermediate term or increase the number of individuals who were able to cease their opioids. Frank et al.[84] included 32 studies examining interdisciplinary pain programs which had a range of program components, resulting in a mean opioid discontinuation rate of 87%

(range 29%-100%). Hassan et al.[22] found that taper support interventions comprising of psychiatric consultation, motivational meetings for tapering and learning pain management skills resulted in 95.23 OMEDD reduction at 22 weeks and 107.66 OMEDD total reduction from baseline dose at 34 weeks. In this review, the greatest evidence for opioid reduction came from multidisciplinary pain programs. It is difficult for programs with multiple features to show causality between one component of the intervention and the outcomes observed. Further, many primary studies included in the reviews were cross-sectional, preventing inference of causality between variables.

Adverse effects of co-interventions

The general trend of opioid reduction resulting from physical, interventional, psychological and behavioural and mixed interventions may be favourable, based on the assumption that removing a treatment without proven benefit and known harms would result in harm risk reduction and improve outcomes. However, the risks of deprescribing co-interventions must be considered. Psychological therapies and multidisciplinary care may be considered low risk when compared to opioid continuation, yet reports of significant complications were reported in some reviews, including subdural haematoma resulting in death following spinal cord stimulation.[89] To guide future recommendations about safe and appropriate opioid deprescribing co-interventions, additional research into the harms of opioid deprescribing and co-interventions is warranted.

Table 5: Effectiveness of co-interventions for opioid deprescribing

Intervention Category	Intervention	Pain Type	Proportion of population who ceased opioids
Pharmacological	Cannabinoids[88,165]	Chronic non-cancer	0-44%
	Buprenorphine[84]	Chronic non-cancer	33-100%
	Ketamine[84]	Chronic non-cancer	18-27%
	Clonidine and benzodiazepines for opioid detoxification[84]	Chronic non-cancer	91-100%
	Nonsteroidal anti-inflammatory drugs (NSAIDs)[169]	Cancer	Not reported
	Acetaminophen (Paracetamol)[169]	Cancer	Not reported
Physical	Acupuncture / acupressure[84,164]	Chronic non-cancer	66%-86%

	Physical therapy[88]	Chronic non-cancer	Not reported
Interventional	Cryoablation[168]	Chronic non-cancer	40-97%
	Spinal cord stimulation[89,166]	Chronic non-cancer	26-34%
Psychological and/or behavioural	Cognitive behavioural therapy[84,87]	Chronic non-cancer	6-55%
	Mindfulness / meditation[84,87]	Chronic non-cancer	Not reported
	Therapeutic Interactive Voice Response (TIVR)[87]	Chronic non-cancer	21%
	Therapeutic suggestion[87]	Chronic non-cancer	Not reported
	Hypnosis[87]	Chronic non-cancer	Not reported
	Guided imagery[87]	Chronic non-cancer	Not reported
Mixed interventions	Multidisciplinary pain programs[84,88]	Chronic non-cancer pain	19%-100%
	Multi-component tapering support[84,85,88]	Chronic non-cancer pain	45%-72.2%

Table 5 provides information on the success rates of co-interventions utilised to facilitate opioid deprescribing, determined by the proportion of population who ceased opioids. We note that this data may not provide a true indication of the 'success' of deprescribing. This is due to significant variabilities in study designs, time points of measurements and follow-up (i.e. short- or long-term outcomes of deprescribing) and contextual factors which may have influenced the outcomes. As such, this table provides a numeric overview of the proportion of the population who may be able to cease opioids with each intervention category. This summary does not indicate which populations the interventions were successful for. In accordance with the guiding principles of this guideline, opioid deprescribing plans are ideally individualised according to the needs, values, preferences and goals of the person. Therefore, success may be defined differently for different individuals. 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 or deprescribing interventions. This further highlights how context is integral to the success of opioid deprescribing and that success may be measured differently depending on the individual and their values, preferences, clinical characteristics and goals.

Key Clinical Question 3 - Evidence-based Recommendations

Recommendation 10: When available, we recommend the use of interdisciplinary or multidisciplinary care which emphasises non-pharmacological and self-management strategies to deprescribe opioids.

Interdisciplinary, multidisciplinary and multimodal care which emphasised non-pharmacologic and self-management strategies showed the greatest evidence for effective opioid deprescribing.[84,86] Non-drug interventions in these programs included cognitive behavioural therapy, physiotherapy and occupational therapy. The direct evidence for the effect of interdisciplinary or multidisciplinary care on the outcome of opioid dose reduction is of low certainty. People on long-term opioid therapy who voluntarily participated in intensive multidisciplinary pain management interventions which incorporated opioid tapering experienced improvements in pain severity and function. [84-89] In contrast, those who tapered opioids with less intensive co-interventions were more likely to experience unchanged pain and function.[84,86]

Recommendation 11: We recommend the consideration of evidence-based co-interventions to support opioid deprescribing.

Evidence for the effectiveness of different co-interventions to achieve opioid reduction or cessation for the management of chronic pain was inconclusive and varied substantially across the interventions examined. Our overview identified reviews examining pharmacological, physical, interventional, psychological and behavioural, or mixed interventions. Opioid reduction varied widely across reviews and the interventions that were examined throughout the study periods. 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.[84-90,164-166] Quality of life may accompany opioid dose reduction when using deprescribing co-interventions.[84,86,90] The evidence to inform this recommendation relates to the role of co-interventions in opioid deprescribing rather than the benefit of co-interventions for chronic pain management.

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.[209] As such, there was some debate surrounding whether or not to promote the need for voluntary opioid deprescribing within the guideline. Some group members felt that due to the known cognitive, psychological, physical and social effects of long-term opioid use,[25,26,125] as well as unchanged or improved pain outcomes when opioids are tapered,[84,86,212-214] 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.[84,86] Further, there are known benefits of shared decision making in positive health outcomes.[215] 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.[58 59,144] 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.

Stakeholder Values and Preferences

Stakeholder Values and Preferences were primarily informed by two qualitative studies conducted with i) healthcare professionals and ii) people taking opioids. A summary of the findings, alongside other relevant stakeholder perspective research, is presented below.

Deprescribing

The decision to stop a medication by an individual is influenced by multiple competing barriers and enablers,[216] and existing literature suggests that prescribers face significant challenges when considering minimisation of potentially inappropriate medicines.[217] A systematic review identified the following main barriers and facilitators to deprescribing in primary care:[218]

- **Cultural and organisational barriers**: a culture of diagnosing and prescribing; evidence-based guidance focused on single diseases; a lack of evidence-based guidance for the care of older people with multimorbidities; and a lack of shared communication, decision-making systems, tools, and resources.
- **Interpersonal and individual-level barriers**: professional etiquette; fragmented care; prescribers' and persons' uncertainties; and gaps in tailored support.
- **Facilitators**: prudent prescribing; greater availability and acceptability of non-pharmacological alternatives; resources; improved communication, collaboration, knowledge, and understanding; person-centred care; and shared decision-making.

Opioids for chronic pain

A systematic review was conducted on values and preferences regarding opioids for chronic non-cancer pain.[219] The main findings of this review were that pain relief and nausea and vomiting were ranked as highly significant outcomes for persons taking opioids. The adverse effect of personality changes was rated as equally important. Constipation was assessed in most studies and was an important outcome, secondary to pain relief and nausea and vomiting. Of only two studies that evaluated addiction, both found it less important to participants than pain relief. No studies examined opioid overdose, death, or diversion. These findings suggest that the adverse effects of opioids, especially nausea and vomiting, may reduce or eliminate any net benefit of opioid therapy unless pain relief is significant (>2 points on a 10-point scale).[219]

Opioid Deprescribing

Perspectives of healthcare professionals[54]

Note: The term 'patient' has been used in this section as this is the terminology used by healthcare professional participants during this study.

Two main themes were identified from an inductive thematic analysis; i) *The 'too hard' basket*: challenges of deprescribing and ii) *'Even if I want to, I don't know how'*: development of opioid deprescribing guidelines. The first theme related to the range of reported challenges which influence health professionals' willingness and ability to deprescribe opioids.

Subthemes explored medication, patient, prescriber and health system-related challenges. The second theme acknowledged that participants feel current practices surrounding opioid management are suboptimal and that opioid deprescribing guidelines are required to direct and support clinical practice. A summary of the main findings is presented below.

Medication-related challenges

Participants' perceived limited clinical utility in the continuation of opioids in chronic non-cancer pain and identified an array of side effects warranting cautious use. Despite this, opioid deprescribing was not regarded as routine practice. Opioid deprescribing was considered by participants to be more complex than the deprescribing of other medication classes. 'Dependence' was perceived as a key barrier to the withdrawal of opioids due to intrinsic addictive drug properties. It was suggested that some individuals consume opioids for euphoric effects rather than for physical analgesia and would therefore be less receptive to deprescribing. A lack of alternative pharmacotherapy options was deemed a contributing factor for opioid continuation. Paracetamol and non-steroidal anti-inflammatory agents were identified as possible alternative analgesics. However, participants saw limited clinical utility of these agents as opioid substitutes due to a perceived lack of efficacy, clinical contraindications in specific patient cohorts and concerns about long-term use.

Patient-related challenges

Specific vulnerable patient populations were identified by participants as being at higher risk of opioid related harms. These included persons with mental health issues, chronic pain and those with existing or previous substance use disorders. Healthcare professionals felt most concerned about continuing opioids for these populations but also felt that they would be the most difficult groups to engage in deprescribing. Individual patient psychosocial factors were emphasised as being integral to the deprescribing approach. Due to the variability of patients and their individual circumstances, participants highlighted that prospective opioid deprescribing guidelines would need to address patient psychosocial factors whilst allowing healthcare professionals to tailor care to patients' personal circumstances.

Individual patients' perceptions of pain and analgesics was thought to influence opioid taking behaviours. Opioid-related stigma was thought to prevent patients from initiating conversations with healthcare professionals about deprescribing, potentially limiting the opportunity for intervention, engagement and education. It was highlighted by multiple health care professionals that some patients refuse to trial opioid medications due to 'opioid phobia', limiting healthcare professionals' pain management options. Participants emphasised that a balance was required between curtailing opioid misuse and adequately managing patients' pain.

Prescriber-related challenges

Participants believed that many prescribers refrain from opioid deprescribing as it may disrupt the prescriber-patient therapeutic relationship. Similarly, fear that a patient may experience an adverse outcome from opioid deprescribing such as withdrawal symptoms, pain exacerbations, reductions in physical function or a decreased quality of life was a perceived barrier. It was acknowledged that healthcare professionals would be more willing to deprescribe opioids if the patient actively raised the topic with them. Other commonly suggested catalysts for prescriber initiated opioid deprescribing included medication-related side effects or treatment failure. Alternatively, one participant suggested that discussing deprescribing with patients may in fact be beneficial for the therapeutic relationship and considered it a form of patient advocacy. Some physicians expressed that they felt an obligation to provide pain relief and often opted to continue therapies if patients were deemed 'stable'. Many hospital prescribers did not view opioid deprescribing as their responsibility and often prioritised management of acute pain rather than modification of existing opioid therapies in an inpatient setting.

Health System-related challenges

Workload pressures, inadequate remuneration for health professionals and insufficient resources for healthcare professionals and patients were viewed as barriers to opioid deprescribing. Specialist and multidisciplinary care were largely seen as enablers to opioid deprescribing, however, the effectiveness of a multidisciplinary approach was thought to be limited by accessibility and lengthy wait times for referrals to pain clinics. Some participants expressed concern that specialised and multidisciplinary services, once engaged, decrease general practitioner agency to deprescribe opioids. Significant costs associated with alternate pain management strategies such as pain psychoeducation and physiotherapy, which were thought to accompany successful opioid deprescribing, limited their applicability.

Transitions of care were identified as critical points in determining if opioids would be continued or deprescribed. Many participants suggested that opioids initiated in hospital for acute pain were then continued in the community setting. Targeting of routine opioid prescribing practices in acute surgical and emergency care settings was suggested to prevent pre-emptive opioid prescribing without adequate assessment of appropriateness and need. Many participants highlighted discontinuity in the health system and a need for improved communication between hospitals and community prescribers at the point of care transfer. Community based practitioners requested clearer guidance on anticipated weaning of analgesics after hospital discharge. Within the community setting, it was suggested that prescribers need to be more proactive in initiating opioid deprescribing when they "inherit" a patient from another prescriber. It was thought that opioid deprescribing guidelines could be utilised to improve consistency in opioid management across various care settings.

Other relevant Australian studies

Recent Australian studies on opioid deprescribing have identified similar barriers and facilitatiors to opioid deprescribing, focusing on general practice and exploring resrouces available to assist deprescribing in primary care. [205]

Perspectives of persons taking opioids[62]

Twenty people using opioids were recruited and included in the analysis. Thematic framework analysis utilising Bandura's Social Cognitive Theory provided three overarching constructs; i) behavioural, ii) cognitive and iii) environmental factors, governing health behaviors.[220] Inductively derived subthemes reflect specific barriers and enablers to opioid deprescribing as identified by participants. People taking opioids expressed a general desire to reduce or cease opioid therapies, however, they felt engaging and persevering with opioid deprescribing was difficult. Opioid deprescribing guidelines were viewed as an enabler to opioid deprescribing.

Behavioural factors

Previous attempts at opioid deprescribing were revealed as a significant influence on future attempts. Failed or difficult deprescribing attempts, either self-initiated or under the supervision of a healthcare professional, undermined participants' beliefs in being able to discontinue opioids. Some participants spoke of severe withdrawal effects or pain exacerbations when attempting deprescribing. Participants who experienced negative consequences of abrupt opioid withdrawal spoke of mistrust of healthcare professionals and expressed trepidation in re-attempting deprescribing. Many participants had trialled other medications for pain without significant improvement in symptoms and therefore opted to continue opioids. In contrast, previous successful dose reduction attempts positively influenced participants' self-efficacy. Observed improvements in opioid related side effects and decreased pill burdens encouraged continuation of deprescribing.

Cognitive factors

Many participants expressed a desire to deprescribe opioids due to negative physiological feedback in the form of opioid-induced side effects. Constipation, fatigue, nausea and impaired cognition were reported. Similarly, concerns about long term use and the development of physical dependence were voiced. Most participants explained that despite these concerns, opioids were continued in the interest of alleviating pain. Some participants reported negative withdrawal symptoms when missing doses of opioids or attempting de-escalation. Others spoke of building tolerance to opioid therapies, requiring increased doses to achieve equivalent analgesic effects. Affective feedback in the form of fear and anxiety were influential, with participants expressing significant worries about the possibility of experiencing pain exacerbations or withdrawal effects.

Individual participant's self-efficacy and motivation to attempt or persevere with opioid deprescribing varied. Despite wanting to stop or reduce opioids, many participants had reservations about being able to achieve dose reductions or cessation and therefore did not engage in deprescribing. Alternatively, some participants who had experienced negative outcomes when attempting dose reductions, maintained a strong desire to reduce opioids and persisted with deprescribing efforts, demonstrating that self-efficacy could modify previous experience.

Significant emotional distress was caused by the perceived stigma associated with opioid use. Many participants wished they didn't take opioids to avoid judgement from family, friends, and particularly healthcare professionals. Expressing a desire to initiate or continue opioids made participants feel type-cast as 'addicts' by prescribers. As such, some individuals felt unable to speak candidly about their pain and medication requirements as they did not want to be perceived as opioid seeking. Many participants specifically spoke of this judgement with new or unknown healthcare professionals, suggesting that rapport between persons taking opioids and healthcare professionals is essential for optimum pain and medication management.

Persons taking opioids requested increased communication between healthcare professionals and themselves about the deprescribing process including potential benefits, expectations surrounding tapering, and assurance regarding continued support throughout deprescribing. Participants advocated for additional resources and information to inform decision making about opioid use, and deprescribing guidelines were largely viewed as an enabler to opioid deprescribing. Many participants commented that deprescribing guidelines which considered the person and provided directives about safe and effective opioid tapering would assist prescribers to make informed decisions. It was also highlighted that information needs to be effectively communicated with person taking opioids.

Environmental factors

The desire to deprescribe opioids and one's belief in the ability to achieve opioid reduction was significantly influenced by relationships with healthcare professionals. Some participants described difficult interactions with prescribers regarding ongoing opioid provision and suggested that healthcare professionals lacked empathy regarding pain management. Participants felt that prescribers were predominately concerned about misuse and protecting themselves in a medico-legal context, rather than the person's pain. Many participants felt confused by their physicians' reluctance to continue opioids as they felt they were taking their medications as prescribed. A consideration for individual circumstances was believed to be beneficial when broaching the topic of opioid deprescribing and participants suggested this would be required in prospective guidelines. Tailoring recommendations to individuals was requested, rather than reiterating population-level benefits of opioid deprescribing. Further,

it was reinforced that guidelines would need to be flexible to account for individual circumstances and only be utilised if the person was willing to have opioids deprescribed.

Despite many participants expressing a desire to deprescribe opioids, most stated that they had not actively raised the topic with their prescriber. Many participants felt that if they agreed to deprescribing, their prescriber would be reluctant to allow re-initiation or dose increases in future. Participants felt that the power lay with the prescriber and that they were not equal partners in decision making. Some participants expressed fears that the implementation of deprescribing guidelines may encourage unsolicited opioid deprescribing.

The perceived self-efficacy and behaviour of people taking opioids was influenced by the experiences of others. Individuals known to participants who had either successfully or unsuccessfully reduced opioids, provided an indication of the difficulty of deprescribing. Those who had not attempted deprescribing themselves relied heavily on reported experiences of others. Aspirational modelling of those who had successfully deprescribed opioids served as an effective tool for promoting self-efficacy, whereas reported negative experiences were used as a justification against deprescribing.

Perceived failures of the healthcare system undermined beliefs about the feasibility of opioid deprescribing. Difficulties in accessing care, limited appointment times, travel and significant costs associated with alternative pain management therapies such as physiotherapy, hydrotherapy and psychotherapy were described. Waiting times to see specialists, pain clinics or undergo surgeries were described as significant and many participants spoke of a need to continue opioids due to a lack of alternative supports.

Other relevant Australian studies

McNeilage et al.[206] conducted a qualitative trajectory analysis of persons' experiences of opioid tapering for chronic pain and identified four distinct opioid-tapering trajectories; i) thriving, ii) resilient, iii) surviving, and iv) distressed. The authors identified readiness to taper, life adversity and supportive relationships as factors which characterise different trajectories. This study provides insight into patient characteristics which may influence the trajectory of deprescribing and enable healthcare professionals to better prepare for and support people with chronic pain who are undertaking opioid deprescribing.[206]

Public Consultation Feedback

The Australian Pain Management Association Limited (APMA) conducted an anonymous survey over a period of 20 days, commencing 3 March 2022, with 111 respondents completing the survey. The survey summary was submitted as a public consultation response and is presented below in Figure 2 and Figure 3.
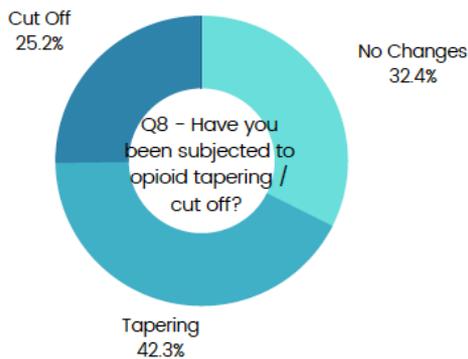
Survey Responses

Q7 – Were you of the understanding that taking this opioid medication would be a long term option to help manage your pain> (i.e > 3 months)

Yes 81.1%   No 18.9%

Q8 – Have you been subjected to opioid tapering / cut off?

Cut Off 25.2%
No Changes 32.4%
Tapering 42.3%

Q9 – Did you feel you & your doctor discussed the reasons why you were not going to continue taking the opioid?

Not in a way where I got to explain my perspective 41%
No 30.5%   Yes 28.6%

Q10 – Did your doctor prescribe something else?

No 62.3%   Yes 37.7%

Q11 – Has your pharmacist completed a medicine review in the last year?

No 22.9%   Yes 77.1%

Figure 2: Survey Responses (Page 1)

Survey Responses

Q1 – Do you feel your GP understands persistent pain?

No 56.8%   Yes 43.25%

Q2 – Have you seen this GP for pain management treatment more than 3 times in the last year?

No 10.8%   Yes 89.2%

Q3 – Was your opioid medication prescribed by a GP?

Yes 64.9%   No 35.1%

Q4 – When you first commenced taking an opioid, did you & your doctor discuss the objective of taking it? For example, by taking this medication I hope to have enough pain relief to be able to hang up my washing by myself / walk my dog / sleep through the night?

Yes 69.4%
No 30.6%

Q5 – Was a timeframe set to review whether you had gained this functionality?

No 58.6%   Yes 41.4%

Q6– Did you discuss other treatment options that were not related to medication?

Yes 76.4%
No 23.6%

Figure 3: Survey Responses (Page 2)

Cost and Resource Considerations

A comprehensive review of the resource requirements and cost implications of opioid deprescribing was outside of the scope of this guideline, however, below we present some general resource and cost considerations relating to opioid deprescribing in Australia.

The Cost of Pain in Australia Report, conducted by Deloitte Access Economics in collaboration with Painaustralia, estimated that the total financial cost of chronic pain in Australia in 2018 was $73.2 billion, comprising of $12.2 billion in health system costs, $48.3 billion in productivity losses, and $12.7 billion in other financial costs, such as informal care, aids and modifications and deadweight losses.[221] Additionally, people with chronic pain also experience a substantial reduction in their quality of life, valued at an additional $66.1 billion, demonstrating the large burden of pain on Australian society.[221]

Opioid use and subsequent harms and costs have increased over recent decades in Australia.[222] Between 1992 and 2012, opioid dispensing episodes increased 15-fold (500 000 to 7.5 million) and the corresponding cost to the Australian government increased 32-fold ($8.5 million to $271 million).[27] The 'extra-medical' use of opioids (both illicit and pharmaceutical) is estimated to result in more than 2200 deaths and cost Australia approximately $15.7 billion a year.[223] As of June 2020 there have been changes to the Pharmaceutical Benefits Scheme (PBS) listings of opioids which are summarized in the [PBS opioid listings for the treatment of pain](#).[224] These changes may result in individuals incurring larger out-of-pocket costs for continuation of opioid therapies.

The GDG has postulated that opioid deprescribing may reduce costs associated with opioid-related adverse events, hospitilisations and deaths. Conversely, there may be increased costs associated with the implementation of guideline recommendations which may result in increased frequency of follow-up with healthcare professionals for regular monitoring and accessing additional co-interventions to support deprescribing. The cost of implementing alternative pain management strategies or accessing multidisciplinary or interdisciplinary care programs may result in additional upfront costs, however, the Cost of Pain in Australia Report provides insight into the potential cost savings of multidisciplinary care programs.[221] The report found that doubling current levels of access to multidisciplinary care could reduce health system costs by $3.7 million (net of the $70 million in intervention costs), with a benefit cost ratio of 4.9 to 1 from the perspective of society.[221] The report suggests that multidisciplinary pain management interventions are cheaper and more effective than standard treatment and may lead to reduced health expenditure in the long-term.[221] As such opioid deprescribing interventions may result in reduced healthcare system expenditure, however an economic evaluation has not been conducted and this remains an area for future research.

Clinical Considerations

This section provides additional practical information which may assist healthcare professionals to plan and execute opioid deprescribing in collaboration with the person taking opioids.

Engaging the person

It is extremely important to engage the person taking opioids (and/or their family or carer) in the conversation about deprescribing.[208] This conversation is required to determine if it is suitable to deprescribe. Discussions on the potential benefits and harms of deprescribing for the individual person will be required. Deprescribing conversations may not occur in a single appointment; instead, the dialogue may be continued over multiple appointments. The use of an opioid deprescribing conversation guide (Communication techniques for opioid analgesic tapering conversations)[80] may assist healthcare professionals to initiate and continue conversations about opioid deprescribing.

Psychosocial considerations

Once the decision to trial deprescribing is agreed upon by the person taking opioids and the healthcare professional, a deprescribing plan should be developed. It is important to consider the person's individual circumstances and needs when making this plan, and acknowledge that the plan may need to be modified over time. Planning for deprescribing will involve discussing the person's beliefs and goals, assessing the person's support network and inquiring about whether additional support will be required. This may involve liaising with other healthcare professionals who are involved in the care of the person (e.g. psychologist, psychiatrist, etc). Individuals may or may not want family members or support networks involved in the planning and decisions about opioid deprescribing. Identifying stressors or potential barriers for a particular person may assist to tailor the plan to their needs and circumstances. For example, if a person has had a recent change in employment or has experienced another major life event, it may make sense to commence deprescribing after this, or pause or slow the taper to give time to re-evaluate or put alternate supports in place before continuing the deprescribing process.

Stigma

Stigma is a powerful social process that is characterised by labelling, stereotyping, and separation, leading to status loss and discrimination, all occurring in the context of power.[225] Stigma can result in a range of negative outcomes including exclusion from, and denial of, health services.[226] Many people experience stigma from family, friends, the community and healthcare professionals in regard to their opioid use.[62] These in turn can create substantial barriers when accessing psychological and other treatments,[227] impair treatment outcomes and overall quality of life.[226] The language used by health professionals can perpetuate stigma.[228] Language guides may be referred to by healthcare professionals for non-stigmatising terminology. Terms that are prejudicial such as "addict" should instead be

replaced with person-centred language.[124] The Michigan Department of Health and Human Services and the University of Michigan Injury Prevention Centre, provides a fact-sheet on [Words Matter: Using people-first, non-stigmatizing language](#) for opioid use disorders.[124]

Characteristics of Opioids

Opioids are available in a range of formulations and can be administered via a range of routes (oral, buccal, sublingual, rectal, Intravenous (IV), Subcutaneous (SC), Intramuscular (IM), transdermal, epidural and intrathecal). [Table 6](#) outlines available opioid formulations in Australia currently. Please refer to the PBS A-Z Medicine Listing for up to date information about available opioid formulations.

Table 6: Available Opioid Formulations[229]

Drug	Oral			Injection	Other
	conventional	**controlled release**	**buccal or sublingual**		
buprenorphine			tablet	IV, IM	patch
codeine	tablet, liquid				
fentanyl			lozenge, tablet	IV, SC, epidural, intrathecal	intranasal solution, patch
hydromorphone	tablet, liquid	tablet		IV, SC, IM	
methadone	tablet, liquid			SC, IM	
morphine	tablet, liquid	tablet, capsule, liquid		IV, SC, IM, epidural, intrathecal	
oxycodone	tablet, capsule, liquid	tablet		IV, SC	suppository
pethidine				IV, SC, IM, epidural	
tapentadol	tablet	tablet			
tramadol	capsule, liquid	tablet		IV, IM	

Atypical opioids (buprenorphine, tapentadol, tramadol) are opioids which achieve analgesic effects by additional mechanisms or via alternate interactions with opioid receptors, as opposed to conventional opioids (codeine, fentanyl, hydromorphone, methadone, morphine, oxycodone, oxycodone with naloxone, pethidine) which achieve analgesia solely through *mu* agonism.[71,230] This is important when interpreting OMEDD and when switching/transitioning from conventional opioids to atypical opioids or vice versa. Care must be taken to avoid potential opioid withdrawal or overdose when switch/transitioning.[52,147,231,232]

Equivalent and equianalgesic opioid doses

Transition from one opioid to another may be required to facilitate deprescribing. Different opioids are not equianalgesic, however oral morphine equivalents daily doses (OMEDD) of different opioids can be calculated. The Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists (ANZCA) has released an [online opioid equianalgesic](#)

[calculator](#)[147] (also available in [table format](#))[148] which may assist when transitioning between different opioids or developing a tailored opioid deprescribing plan. Note:

- Caution is required if opioid dose equivalence tables are used to guide opioid switching, as the administration of a calculated 'equivalent' dose of the replacement opioid may lead to overdosage.[148]
- The equianalgesic dose expressed as OMEDD does not reflect equivalent opioid activity of atypical opioids due to differences in pharmacology compared to conventional opioids.[4] If transition from a conventional opioid to an atypical opioid such as tapentadol is considered, take an individualised approach and consider cross-tapering to avoid opioid withdrawal.[52,227,228] E.g. the calculated equianalgesic doses of tapentadol does not reflect equivalent opioid activity as efficacy is partly due to noradrenaline reuptake inhibition. [52,147,231,232]
- There is considerable variability in pharmacokinetics and pharmacodynamics of the different opioids, within and between individual patients. In addition interactions with non-opioid drugs can strongly influence opioid pharmacokinetics.[148]

Opioid withdrawal

Individuals may experience withdrawal symptoms when opioids are deprescribed. Efforts should be made to prevent the emergence of opioid withdrawal through gradual opioid tapering (in accordance with Recommendation 7). However, each person may respond differently to opioid deprescribing and may experience none, some, or all of the following symptoms: lacrimation or rhinorrhea, piloerection (goosebumps), myalgia, diarrhea, nausea/vomiting, pupillary dilation, photophobia, insomnia, autonomic hyperactivity (tachypnea, hyperreflexia, tachycardia, sweating, hypertension, hyperthermia), and yawning.[12]

Assessment scales for determining the severity of opioid withdrawal include the Clinical Opioid Withdrawal Scale (COWS),[158] The Objective Opioid Withdrawal Scale (OOWS)[159] and The Subjective Opiate Withdrawal Scale (SOWS).[159] Opioid withdrawal symptoms can be very unpleasant but are generally not life threatening. [Healthdirect's Opioid Withdrawal Symptoms website](#)[233] provides information and resources about opioid withdrawal symptoms for persons taking opioids. If significant withdrawal symptoms are experienced when deprescribing opioids, the taper may be paused to allow time for the person to overcome symptoms before the next dose reduction. More gradual dose reductions may be warranted when re-starting deprescribing. If a person is experiencing severe or intolerable withdrawal symptoms, seek specialist advice.

Medications for opioid withdrawal

Medications may be used to manage some symptoms of opioid withdrawal. [Table 7](#) details common withdrawal symptoms and medications which may be recommended or prescribed. Some guidelines recommend Alpha$_2$ adrenoreceptor agonists such as clonidine for excessive

sympathetic nervous system activity during withdrawal, such as sweating, agitation and restlessness.[79,234] Much of the evidence pertaining to the use of clonidine for opioid withdrawal is derived from studies examining abrupt withdrawal or detoxification rather than gradual opioid deprescribing,[84] and the evidence is predominantly of low certainty.[79,84,234] In most cases, clonidine should only be used where intense observation and medical assistance is readily available, such as inpatient settings due to the potential adverse effects such as hypotension, bradycardia and drowsiness.[235] It is not advisable to treat withdrawal symptoms with more opioids or benzodiazepines.[121] If a person is experiencing severe or intolerable withdrawal symptoms, seek specialist advice.

Table 7: Symptomatic medications for use in opioid withdrawal
(adapted from the 2018 Alcohol and other Drug Withdrawal: Practice Guidelines, 3rd ed.)[235]

Symptom(s) Of Opioid Withdrawal	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	Non-opioid 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) or paracetamol

Opioid deprescribing may trigger a 'deprescribing cascade' whereby other medicines may also need to be reviewed and adjusted following opioid reduction or cessation. For example, if a person takes regular laxatives to combat opioid-induced constipation, this medication may also need to be reduced or stopped. Refer to individual drug monographs for a full list of drug-drug interactions for each opioid or consult a pharmacist if there are concerns about reversal of drug–drug interactions, suspicion of a prescribing cascade, non-adherence, complex medication regimen or polypharmacy requiring a medication review.

Opioid-induced Hyperalgesia (OIH)

There is a growing body of evidence suggesting chronic opioid use may unexpectedly worsen the perception of pain in some individuals due to a central nervous system response termed 'opioid-induced hyperalgesia' (OIH).[236] The prevalence of OIH is unknown,[236] however if pain increases and becomes more widespread particularly in the absence of disease progression, OIH may be suspected.[23,236] Improved pain relief following a dose reduction can confirm opioid-induced hyperalgesia. [25,236]

Legal and Ethical Considerations

The key bioethical principles of; beneficence, non-maleficence, justice and autonomy, should be considered when making healthcare decisions.[237] Deprescribing is a key component of the overall prescribing process[238] and as such, healthcare professionals should consider the potential outcomes of the decision to deprescribe opioids equally against the potential outcomes of the decision to continue opioids. This will require an assessment of the benefits and harms of treatment in the context of the individual person and their values, preferences and needs and ensuring that the principles of informed consent and shared decision making are employed.

Barnett and Kelly outlined that the potential legal ramifications surrounding deprescribing are the same as those surrounding initiation and continuation of medications.[239] They state "*When deprescribing is undertaken in partnership with patients, supported by the knowledge, skills and experience of both patient and clinicians and the patient's values and preferences based on clinical skill, judgement and evidence-based medicine, law presents no barriers to deprescribing.*" This highlights that prescribing should not be considered the default and appropriate deprescribing is integral to optimal care.

Healthcare professionals may be faced with circumstances where the person taking opioids is not agreeable to deprescribing, yet they feel it is not safe to continue to prescribe. This may present a conflict between ethical principles (especially between beneficence and autonomy). Non-consensual deprescribing (when opioids are deprescribed despite the person taking opioids being not agreeable to reduce or cease opioids) has potential ethical concerns which have been discussed by Rieder, in an article entitled 'Is Nonconsensual Tapering of High-Dose Opioid Therapy Justifiable?'[240] In such instances, refusal of treatment without providing alternative supports, or abandonment of the person taking opioids due to suspected opioid misuse or an opioid use disorders without providing access to ongoing care, may contravene the principle of non-maleficence. A recent consensus panel has provided further information and recommendations pertaining to patient protections when tapering opioids.[241]

As highlighted in Recommendation 6, in some Australian states and territories, Schedule 8 medications cannot be prescribed for persons who are known or suspected to be drug dependent, without a permit or an appropriate approval from the relevant state or territory medicines regulatory area.[121] Many states and territories in Australia have a Drug and Alcohol Specialist Advisory Service that GPs can contact for advice. Resources such as 'Laws and Regulation' in the Royal Australian College of General Practitioners Prescribing drugs of dependence in general practice, Part A – Clinical governance framework[121] provides further information. Please refer to specific state and territory regulations for more information.

Opioid related harm risk minimisation strategies

Naloxone

Naloxone is an opioid antagonist that can reverse severe respiratory depression and prevent death from opioid overdose.[242] Administration of naloxone by laypersons, such as friends and family of persons who experience opioid overdose has been shown to save lives.[243] Provision of naloxone through community-based distribution, also known as 'take-home naloxone' has been shown to be effective in reducing opioid overdoses and has become a key response to rising opioid-related mortality in many countries.[244] Since 2016, naloxone has been accessible in Australia from pharmacies without a prescription, as well as on a prescription, subsidised through the Pharmaceutical Benefits Scheme (PBS).[245] Naloxone supply may be warranted for many individuals who are prescribed opioids for pain. In Australia most overdose deaths involve prescription opioids and approximately half of prescription opioid deaths involve people with chronic pain.[246] It is estimated that four in five people receiving long-term opioids meet the Centre for Disease Prevention and Control criteria for overdose risk, such as being prescribed 50mg OMEDD or more, having a history of substance use disorder, being prescribed concurrent benzodiazepines or having a history of opioid overdose.[247,248] Further, recent studies have demonstrated unintended negative consequences following prescribing changes including dose reduction, such as individuals seeking illicitly obtained opioids, resulting in overdose.[58,59] If rotating opioids, difficulties in understanding different potencies may result in individuals taking more than their prescribed dose. Therefore, provision of naloxone may be considered for those having opioids prescribed or deprescribed. A recent study in Australia has estimated that scaling up take-home naloxone by 2030 to reach 90% of people prescribed daily doses of ≥ 50 mg of oral morphine equivalents would be cost-effective and save more than 650 lives.[249] A pilot program of take home naloxone suggests that the program is estimated to save three lives per day.[250] Accessible health information resources on naloxone[251] have been developed for healthcare professionals and people who are prescribed opioids, including the Pharmaceutical Society of Australia's Non-prescription medicine treatment guideline: Naloxone for opioid overdose[113] and The Penington Institute Community Overdose Prevention Education (COPE) program.[252]

Prescription Drug Monitoring Programs (PDMP)

In Australia, all states and territories have committed to implementing PDMPs in cooperation with the Australian Government. At present Victoria, Tasmania, Queensland, South Australia and Australian Capital Territory have implemented real-time prescription monitoring programs. Australian PDMPs are accessible to prescribers, including medical practitioners, nurse practitioners and dentists, as well as pharmacists. PDMPs allow access to information about the prescribing and dispensing of a range of medicines, including opioids and benzodiazepines.

Many opioid-related deaths involve people obtaining multiple prescriptions from multiple healthcare providers. PDMPs are a public health initiative and regulatory mechanism designed to reduce harms associated with increased opioid prescribing by providing healthcare professionals with additional information about the supply of opioids at the time of prescribing or dispensing.[253] They also identify more liberal prescribers. Healthcare professionals can review a person's history of opioid prescriptions using state prescription drug monitoring program data to determine whether the person is receiving high opioid dosages, has multiple prescribers, or is being prescribed dangerous combinations of medicines that put them at high risk for overdose. It is recommended that healthcare professionals review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months. Recent systematic reviews have found limited evidence to support overall associations between PDMPs and reductions in opioid-related consequences such as opioid dependence, opioid related adverse events opioid-related legal and crime outcomes.[254] However, unintended consequences from PDMPs such as their influence on healthcare professional decision making, resulting in a reluctance to manage individuals with suspected opioid use disorders, refusal of treatment, abrupt cessation of opioids and significant impacts on continuity of care have been reported.[253,255] Information provided by PDMPs to prescribers and pharmacists about the supply of opioids and other monitored medicines may fail to identify individuals who may be at risk, allowing continued prescribing. The links below contain state and territory specific PDMP information.

- Australian Capital Territory
- New South Wales
- Northern Territory
- Queensland
- South Australia
- Tasmania
- Victoria
- Western Australia

Non-initiation and Judicious Opioid Prescribing

Non-initiation of opioids and judicious opioid prescribing can prevent long-term opioid use and mitigate the associated risks. A retrospective cohort study suggested that 5% of opioid-naïve participants who filled an opioid prescription, were taking opioids long-term.[45] Data from the United States revealed that one in seven people who filled a repeat opioid prescription, or had a second opioid prescription authorised, remained on opioids one year later.[44] This study found that prescribing less than seven days of medication when initiating opioids could mitigate the chances of unintentional chronic use.[44] If initiating opioid treatment, a clear plan for opioid reduction and discontinuation should be established. Developing and implementing a deprescribing plan at the point of opioid initiation may limit opioid dose and duration to attenuate opioid-related harms. Further, it may assist in setting appropriate expectations about the role of opioids in the management of pain.

Population considerations

Healthcare professionals should work to provide clinically and culturally appropriate care when deprescribing opioids. Although there was limited evidence to inform the benefits and harms of opioid deprescribing for specific population groups, this section of the guideline aims to highlight some population specific considerations.

Aboriginal and Torres Strait Islander peoples

It is important to focus on ways to optimise the care of Aboriginal and Torres Strait Islander populations in the context of opioid deprescribing and ensure that care is culturally suitable and tailored to the individual. Culturally appropriate care involves building on the strengths of Aboriginal and Torres Strait Islander peoples to determine their own health priorities, through protective factors such as strength of family, community and culture. Aboriginal and Torres Strait Islander peoples experience substantially higher rates of mortality and morbidity than the general population. [256] The incidence of long-term opioid use in Aboriginal or Torres Strait Islander populations is 1.7–1.9 higher than non-Aboriginal and Torres Strait Islander populations, [257] increasing the risk of opioid-related harm. To address these inequities will require an understanding of the historical and ongoing social and emotional determinants of health. Healthcare professionals are required to consider language barriers and cultural differences and how this may impact communication and treatment. It is important to discuss the recommendations within this guideline in a culturally suitable manner, with trusted Aboriginal and/or Torres Strait Islander Health Workers or Practitioners and trained interpreters if necessary. A range of resources that have been designed for clinical use are available at the [Australian Indigenous HealthInfoNet website.](#)[258]

Culturally and linguistically diverse (CALD) populations

In Australia, one in three people are born overseas and one in five households speak languages other than English.[259] Most chronic, high-dose opioid treatment episodes that ended in 2017 or 2018 were discontinued more rapidly than recommended by clinical guidelines and rapid discontinuation was more likely among residents of areas with higher percentages of racial/ethnic minority residents.[260] As such, it is important to focus on ways to optimise the care of CALD populations in the context of opioid deprescribing. CALD communities can experience significant barriers to accessing and engaging in treatment programs due to language difficulties, health literacy, lack of cultural relevance and appropriateness, concerns about trustworthiness and inclusivity of services, fear of consequences of service involvement or confidentiality breaches. As such, it is important to discuss the recommendations within this guideline in a culturally suitable manner, with a trained interpreter if necessary.

Rurality

Some pain conditions are more prevalent in rural communities, with people outside major cities reported to be 23% more likely to have back pain.[261] The incidence of long-term opioid use is 37%-52% higher among practices located in rural Australia or lower socioeconomic areas.[257] The Australian Institute of Health and Welfare report that the highest (population-adjusted) rates of opioid dispensing is in inner- and outer- regional areas.[222] Rurality may impact on pain management health service utilisation and should be considered when recommending interventions to accompany or facilitate opioid deprescribing. Barriers to pain management in a rural setting include limited infrastructure and recreation opportunities, larger geographic distances, limited transportation and reduced access to health services.[262] Accessibility to pain management services has been exacerbated by the COVID-19 pandemic.[263] Although Recommendation 10 encourages the use of multidisciplinary, interdisciplinary or pain management programs, they may have limited applicability to specific populations given that many individuals lack access to or means to participate in such programs. Consider options for remote assessment and management (e.g. Telehealth) in the context of individuals with impaired access to treatment and services.

Older adults and persons with cognitive impairment

Long-term opioid use prevalence is 4.8 times higher among those aged 80 years and older compared to those aged 18-34.[257] Pain management for older persons can be challenging given increased risks of both non-opioid and opioid pharmacologic therapies in this population.[264] Factors such as reduced renal function and medication clearance in older adults, polypharmacy, and multimorbidity can lead to increased susceptibility of accumulation of opioids, increased risk of drug and disease state interactions and a smaller therapeutic window between safe dosages and dosages associated with adverse effects and overdose.[264,265] Many older adults experience cognitive impairment or dementia, which can increase the risk for medication errors and make opioid-related confusion more dangerous. Conversely, pain is often undertreated in people living with dementia and individuals may be more likely to have difficulties in communicating their pain, or may display pain in different ways.[266] Many older people, especially those with significant cognitive impairment and more advanced dementia, receive funded aged care either at home or in residential care. For those receiving aged care, it is important to involve formal carers and nursing staff, and informal carers (e.g. relatives and significant others) in overall pain management and when considering deprescribing. These people will know the person, their preferences and how signs of pain may be manifested. When deprescribing opioids in persons with cognitive impairment, consider the need for robust pain assessment and management. In those with advanced dementia who may be unable to communicate verbally about their pain, their condition (and their response to treatment) may need to be evaluated by facial expressions, verbalisations, body movements, changes in interactions, activity patterns and routines such as sleep disruption and appetite suppression.[267] Multiple tools have been developed for eliciting pain levels in persons with dementia, including the Abbey Pain Scale[156] and PainChek™.[268]

Pregnant women

Opioid withdrawal in the first trimester of pregnancy is thought to be associated with an increased risk of miscarriage, and opioid withdrawal in the third trimester of pregnancy may be associated with foetal distress and death.[269,270] Consult with a specialist in pain or addiction medicine about managing opioid use in pregnancy.

Individuals with mental health conditions

Major depression is the most common mental illness associated with chronic pain, whilst high rates of generalised anxiety disorder, post-traumatic stress disorder and substance misuse have also been described.[271] In person's with chronic pain presenting for treatment, the prevalence of major depression is 30%–40%.[272] Recent evidence indicates pain medication beliefs and pain catastrophising is linked with opioid use[10]. Importantly, this research suggests that early psychological co-intervention may help to improve opioid use outcomes.[273] In terms of opioid deprescribing, depressive symptoms have been shown to be predictive of disengagement with opioid tapering.[207,274] Treating comorbid mental disorders can improve the likelihood of success. The expertise of psychiatrists and addiction psychiatrists may be of particular use when deprescribing opioids for people with mental health comorbidities.

Other Guidelines and Guides for Opioid Deprescribing

The following guidance relates directly to opioid deprescribing in clinical practice and may be useful for healthcare professionals.

- Therapeutic Goods Administration: Clinician information sheet on opioid analgesic tapering[138]
- Agency for Clinical Innovation, Pain Management Network: How to de-prescribe and wean opioids in general practice[140]
- Primary Health Tasmania: A guide to deprescribing opioids[141]
- NSW Therapeutic Advisory Group: Deprescribing guide for regular long-term opioid analgesic use (>3 months) in older adults[139]
- NPS MedicineWise: Recommendations for deprescribing or tapering opioids Information for health professionals[142]
- NPS MedicineWise: Opioid tapering algorithm[137]
- National Health Service Nottinghamshire Area Prescribing Committee: Opioid deprescribing for persistent non-cancer pain[275]
- United States Department of Health and Human Services (HHS): HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics[276]

No other evidence-based guidelines were identified that focused solely or primarily on the deprescribing of opioids. International treatment guidelines which provide information on when or how to deprescribe opioids are presented in Appendix 1. The recommendations provided in this guideline do not conflict with existing recommendations in clinical practice guidelines. Rather the recommendations contained within this guideline address similar topics, including when and how to deprescribe opioids. The deprescribing recommendations contained in this guideline are more comprehensive and detailed when compared to existing treatment guidelines, providing additional clinical and implementation considerations. The Recommendations in this guideline are also tailored to the Australian context with strength and nature of recommendations directly influenced by the available interventions, resources and healthcare system.

The proposed Centers for Disease Control and Prevention (CDC) guideline for Prescribing Opioids, United States, 2022 has recently been released for public consultation. This draft guideline provides considered and evidence-based recommendations for deprescribing opioids, mirroring much of the content contained in this guideline. Of note, the draft CDC guideline suggests that "*patients for whom risks of continued high-dose opioid use outweigh benefits but who are unable to taper and who do not meet criteria for opioid use disorder might benefit from transition to buprenorphine.*"[277] Specific recommendations about transition to buprenorphine for people who not have an opioid use disorder has not been included in this guideline and as such, should be considered in future guideline updates.

Gaps in knowledge and future guidance

This guideline provides recommendations that are based on the best available evidence that was interpreted and informed by expert opinion. The evidence informing the recommendations is predominantly low certainty and for some key clinical questions, no reliable evidence was identified. More research is necessary to inform future guideline development, fill critical evidence gaps and increase certainty relating to the effectiveness, safety and outcomes of opioid deprescribing. There is limited information to guide how to conduct deprescribing (the process of tapering), what to monitor for and how often to monitor during the deprescribing process. It is also important to obtain data to inform the cost feasibility and cost-effectiveness of recommendations, such as the use of interdisciplinary or multidisciplinary care programs.

Specific guidance is required for opioid deprescribing in specific conditions and populations (e.g., persons with chronic cancer-survivor pain). We acknowledge that an overview of systematic reviews approach may have omitted relevant primary studies evaluating the outcomes of opioid deprescribing in these populations. Therefore, future guidance should be informed via systematic review and synthesis of relevant primary research evidence, and may even require the conduct of primary research where such evidence is lacking. Additional populations which require further guidance include; Aboriginal and Torres Strait Islander people (with research led by Aboriginal and Torres Strait Islander peoples in a culturally appropriate model), CALD populations, older adults and people living in rural and remote Australia. Additionally, there is a need for evidence on the impact of pre-operative opioid deprescribing on post-surgical outcomes.[278] This guideline did not examine opioid deprescribing in paediatric or adolescent populations and further research in this area may be warranted. Research to improve pain management, including the validation of pain education evaluation instruments for multidisciplinary or multimodal pain management strategies, would inform recommendations relating to opioid deprescribing. Examining ways to stop the initiation of opioids or prevent the transition from short-term opioid use to long-term opioid use would also be valuable, particularly at transitions of care. Finally, there is a need to conduct further assessment of the safety and efficacy of the guideline recommendations in clinical practice.

Plans for updating guidelines

We will revisit this guideline as new evidence becomes available to determine when an update is warranted. We have identified trials currently in progress that may lead to changes in recommendations (See Table 8). We recommend that this guideline be updated when new evidence to inform the strength and direction of recommendations is ascertained, no longer than five years from the date of the NHMRC approval of recommendations, in 2027.

Table 8: Ongoing Studies on Opioid Deprescribing

Identifier	Status	Title	Outcomes Reported
NCT03521960	Completed	Buspirone for opioid tapering	Number participants ceased/reduced
NCT03743402	Active, not recruiting	Strategies to improve pain and enjoy life (STRIPE)	Dose reduction, pain
NCT03889418	Enrolling by invitation	Opioid treatment and recovery through a safe pain management programme	Dose reduction, pain, quality of life
NCT03916276	Recruiting	Living in Full Even (LIFE) with pain study	Dose reduction, pain
NCT03950791	Recruiting	Single session class to reduce opioid use in chronic pain	Dose reduction, pain
NCT04013529	Completed	Connected health to decrease opioid use in participants with chronic pain	Dose reduction, pain
NCT04097743	Recruiting	Pain catastrophising and prescription opioid craving	Dose reduction, pain
ISRCTN49470934	Ongoing	Improving the Wellbeing of people with Opioid Treated CHronic pain; I-WOTCH	Dose reduction, number participants ceased/reduced, pain, quality of life and adverse events
NCT03445988	Recruiting	Cognitive Behavioral Therapy and Chronic Pain Self-Management Within the Context of Opioid Reduction: The EMPOWER Study	Dose reduction, pain
NCT03400384	Completed	Trial Applying Policy to Eliminate or Reduce Inappropriate Narcotics in the General-population (TAPERING)	Cessation, dose reduction
NCT03890263	Completed	Evaluating Chronic Pain Self-Management Support With an Opioid De-prescribing Intervention	Dose reduction, pain, adverse events, mood, quality of life, function, satisfaction with care

Conclusions

Chronic pain remains a significant public health problem. It is important that efforts are maintained to address and improve pain management, as well as prevent and mitigate harms resulting from prescription opioid use. 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 development process. Evidence suggests that it is possible to reduce opioid use and associated harms whilst reducing or maintaining pain, function and quality of life. Additional high certainty evidence is needed to strengthen existing recommendations and inform future recommendations on when, how and for who opioid deprescribing is appropriate. In addition to opioid deprescribing, it is necessary to strengthen the evidence base for pain prevention and treatment strategies, reduce disparities in pain treatment, improve access to services and provide effective professional and public education and training to ensure appropriate access to pain relief for those in pain.

Appendices

Appendix 1: Other relevant guidelines

Guidelines were included if they were less than 5 years old, were reported to follow a guideline development process, were national (not based on a single institution) and were the most current from the developing organisation.

Appendix 1 – Table 1: Opioid deprescribing in patients with chronic non-cancer pain: A systematic review of international guidelines [279]

Guideline Author, Country (Year)	Developing Organisation	When to deprescribe	How to deprescribe	Managing withdrawal symptoms	Additional support	How to monitor	Deprescribing in patients with co-prescription of sedatives
Busse J. et al, Canada. (2017)[280] Used the GRADE approach** to classify the guidelines.		<u>Weak recommendations</u> Patients on ≥90 OMEDD with lack of improvement in pain and/or function. Non-adherence to treatment plan. Signs of substance misuse. Serious opioid-related adverse event.	<u>Weak recommendations</u> A gradual reduction of 5-10% of the original OMEDD dose every 2-4 weeks Rapid dose reduction should be carried out in a medically supervised centre. Clinicians should collaborate with	<u>Weak recommendations</u> Have a plan in place to manage withdrawal symptoms and emerging pain. In patients struggling with the tapering plan, pause the taper and re-evaluate the patient's clinical status.	<u>Strong recommendations</u> Coordinated multidisciplinary collaboration. <u>Weak recommendation</u> Patients/physicians may wish to consult a pharmacist to assist with scheduling dose reductions.	<u>Weak recommendations</u> Clinicians should monitor their patients using opioid therapy for their response to treatment and adjust accordingly. Creating a schedule for dose reductions and follow-up visits.	Nil

		Patient request Conflicting evidence, agreed upon by expert opinion To possibly improve opioid-induced central sleep apnoea or correct hypogonadism	patients on a tapering plan. Optimise non-opioid strategies and psychosocial support. Set realistic functional goals. Taper to the lowest dose without an increase in pain or a loss of function. Tapering may be paused in patients who have an increase in pain or decrease in function.		Consult experts for significant mental health symptoms and /or drug-related behaviours		
Dowell D. et al, USA (2016)[24] Within the ACIP GRADE framework, the quality of A body of evidence was	Centres for Disease Control and Prevention (CDC)	Recommendation category: A; evidence type: 3 If patients do not experience improvement in pain and/or function at ≥90 OMEDD or if there are escalating	Recommendation category: A; evidence type: 4 A gradual dose reduction of 10% of the original OMEDD dose every week.	Recommendation category: A; evidence type: 4 Clinicians should consider urine drug testing to help determine whether opioids can be discontinued	Recommendation category: A; evidence type: 3) Utilise a multidisciplinary collaborative team-based approach.	(Recommendation category: A; evidence type: 4) Clinicians may use validated instruments or progress towards patient centred	(Recommendation category: A; evidence type: 3) Taper opioids before tapering benzodiazepine to reduce risk of fatal respiratory depression.

graded, and there recommendations were developed and placed into categories***		dosage requirements\n\nRecommendation category: A; evidence type: 4\n\nIf benefits do not outweigh harms or serious opioid-related adverse events.\n\nPatient request.\n\nIf clinicians suspect their patients are sharing or selling opioids and not taking them.\n\nNot meeting treatment goals	Tapering plans should be individualised. Slower tapers might be more tolerated and minimise withdrawal symptoms. Opioids can be stopped when taken less frequently than once a day.\n\nMore rapid tapers may be required under certain circumstances e.g. patients who have experienced overdose\n\nRecommendation category: A; evidence type: 3\n\nClinicians should collaborate with patients on a tapering plan.	without causing withdrawal.	Optimise non-opioid strategies.\n\nRecommendation category: A; evidence type: 4\n\nAccess appropriate expertise if considering tapering opioids during pregnancy.	goals to track patients' outcomes.\n\nClinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently.	
Manchikanti L et al, USA (2017)[79]	American Society of Interventional	Evidence: Level III; Moderate recommendations:	Evidence: Level I-II; Moderate recommendations:	No strength of recommendation	The patient may be referred to	Evidence: Level I; Strong recommendations:	Nil

National Guideline Clearinghouse Extent Adherence to Trustworthy Standards (NEATS) instrument was used to rate the strength of the guidelines****	Pain Physicians (ASIPP)	Lack of improvement in pain or function, adverse consequences, or abuse with rehabilitation. Evidence: Level I; Strong Recommendations: Strong) Minimal requirements for continued opioid therapy are analgesia of at least 30%, and/or activity improvement of 30% without misuse/abuse, or major adverse effects. Opioid related adverse events. If there is any indication of abuse, misuse or aberrant behavior.	A gradual reduction of 10% of the original OMEDD dose every week or monthly in some patients. Some patients can be tapered more rapidly over a 6-8-week period. Discontinuation may be carried out in patients who have been on opioids short-term. Clinicians should collaborate with patients on a tapering plan.	The physician may consider using adjuvant agents, such as clonidine or antidepressants to treat withdrawal symptoms However, physicians should not treat withdrawal symptoms with opioids or benzodiazepines.	counsellors, chemical dependency centres, pain management specialists, addiction specialists or detoxification facilities for complicated withdrawal symptoms.	Patients should be monitored often for side effects such as significant hypotension and anticholinergic side effects.

| Rosenberg J et al. USA (2017)[281]

Used GRADE approach** in the creation of these guidelines | US Department of Veterans Affairs and US Department of Defense (VaDOD) | <u>Strong</u>
Patients on ≥90 OMEDD with lack of improvement in pain or function.

When risks exceed benefits.
Patient preference

Co-occurring use of medications or comorbidities that increase risk.

Patient adherence with opioid safety measures and opioid risk mitigation strategies.

If there is any indication of abuse or misuse

Patient non-participation in a comprehensive pain care plan. | <u>Strong</u>
Individualise opioid tapering

Complete a biopsychosocial assessment prior to tapering.

A gradual taper of 5-20% every four weeks is better tolerated and is necessary for patients on a higher dose and longer duration of opioid therapy. A rapid taper of 5-20% per week is used for patients who are non-adherent to the treatment plan and with escalating high-risk medication-related behaviors.
The rate of taper should be determined through a specialty | <u>Strong</u>

Educate the patient/family about opioid withdrawal symptoms and provide treatment strategies to mitigate these symptoms as appropriate.

Clear written and verbal instructions should be given to the patient/family regarding the strategies to mitigate withdrawal symptoms, and additional non-opioid treatments for the patient's pain condition.

The clinician may need to frequently assess for withdrawal | <u>Strong</u>

Utilise a multidisciplinary collaborative team-based approach including psychological and physical support.
The treatment approach should incorporate patient preferences.

If necessary, recommend substance use disorder assessment and appropriate treatment

The care team should maintain frequent contact and clear communication with the patient during the opioid taper.

Overdose education for patients at risk | <u>Strong</u>

Periodic re-evaluation of risks and benefits and a biopsychosocial assessment, at a frequency determined by risk assessment (from one week to one month after any dosage change). Each follow-up is an opportunity to provide self-management strategies and the risks associated with opioid therapy while optimizing whole person approaches to pain care and treatment of co-occurring medical and mental health conditions.

We recommend close monitoring for; Patients with | <u>Strong</u>

For patients on long-term opioid therapy and benzodiazepines, consider tapering one or both when risks exceed benefits and obtaining specialty consultation as appropriate. |

		Prescribed dose higher than the maximal recommended dose Pain condition improved or not effectively treated with opioids Patient preference	consultation and reevaluated at each follow-up and after each dose change. Consider tapering long-acting opioids before short-acting or if suitable both simultaneously. Abrupt discontinuation should be avoided unless required for safety concerns. Patient preference.	symptoms, and offer necessary support for withdrawal symptoms.	for an overdose during tapering. The clinician may consider providing urgent or emergent psychiatric referral and medical care for the management of opioid withdrawal when a patient exhibits dangerous behaviours.	untreated substance use disorder. Engage in substance use disorder treatment and patients less than 30 years of age. Ongoing assessment of suicide risk	
Ackermann E. et al, Australia (2017)[234] Each body of evidence as high, moderate, low, or very low are based on the GRADE approach**	The Royal Australian College of General Practitioners (RACGP)	<u>Strong recommendation, very low quality of evidence</u> If benefits do not outweigh harms <u>Weak recommendation, very low quality evidence</u>	A faster rate of tapering of 10–25% of the daily starting dose each week is generally appropriate after short-term opioid therapy. If tapering is required in response to significant adverse effects or opioid misuse, then daily	Manage symptoms with clonidine or simple supportive therapy. Symptoms of mild opioid withdrawal may persist for six months after discontinuation. Do not treat withdrawal symptoms with opioids or	If the patient has an opioid use disorder, opioids should be discontinued and the addiction treated. Seek authority from the state regulatory authorities when treating these patients.	Schedule frequent visits and ask about and emphasise the benefits of taper at each appointment.	Consider tapering benzodiazepines and seeking specialist opinion or a specialised pain management facility in the management of patients with polydrug use or comorbid alcohol or substance use disorders.

		For patients on >100 OMEDD with lack of improvement in pain or function,	tapering may be more appropriate. Alternatively, immediate opioid discontinuation and pharmacological treatment of withdrawal symptoms can be considered.	benzodiazepines after discontinuation.	Referral for counselling or other support during the taper is recommended, especially if there are significant behavioral issues. If a patient is not successfully reducing their dose, or there is an escalation in dose beyond prescription, involve other practitioners.		
		When planned care fails, or aberrant behaviors become apparent.					
		For pregnant women already on opioids, opioid therapy should be tapered slowly enough to avoid withdrawal symptoms and then discontinued if possible.	Otherwise, a decrease of 10% of the original dose every 5–7 days until 30% of the original dose is reached, followed by a weekly decrease by 10% of the remaining dose.				
		Patients suffering from opioid tapering relapse (who are also at higher risk of opioid-related adverse events)	If a previous attempt at opioid tapering has proven unsuccessful, the rate of tapering can be slowed, by reducing the size of the dose reduction and/or by increasing the time				

			spent at each dose level				
Reib L. et al, Canada (2020)[282] **The GRADE approach was utilized in the creation of these guidelines	The Canadian Coalition for Seniors' Mental Health **(CCSMH)**	GRADE Quality: Moderate; Strength: Strong Discontinue if function does not improve or if adverse events arise. In older adults with polypharmacy or comorbidities that increase the risk of opioid overdose (e.g., benzodiazepine use, renal failure, sleep apnoea).	GRADE: Quality: Low; Strength: Weak A slow outpatient tapering schedule (e.g., 5% drop every 2–8 weeks with rest periods) is preferable to more rapid tapering. Faster taper schedules can be employed if the patient is in a residential or hospital care setting under medical supervision and there is a medical indication for faster lowering of the opioid. GRADE Quality: Low; Strength: Strong	GRADE Quality: Moderate; Strength: Strong Opioid withdrawal management should only be offered in the context of connection to long-term addiction treatment. The threshold to admit an older adult with social, psychological, or physical comorbidities to either residential or hospital care for opioid withdrawal management should be lower than for a younger adult. GRADE Quality: Moderate; Strength: Weak	GRADE Quality: Moderate; Strength: Strong If experienced, clinicians may manage older adults with a mild-to-moderate OUD; however, for patients with more severe or complex disorders, it is recommended that personnel with advanced substance use disorder management skills support clinicians. Working group consensus For those in care facilities, detoxification alone may be a viable option, when	Nil	GRADE Quality: Moderate Strength: Strong Advise patients that the use of alcohol and sedatives is hazardous when combined with opioid agonist treatment. Slow tapering of the substance(s) (to elimination if possible) rather than abrupt cessation is recommended. If the patient is in hospital, residential treatment, detoxification can progress more rapidly.

			Reduce initial doses of medications for treatment of an OUD (e.g., by 25–50%).	For symptom control during opioid withdrawal management, adjuvant medications can be used, use the lowest effective dose to suppress cravings and withdrawal symptoms but with caution due to medical comorbidities, side effect risk, and other concerns related to older age.	combined with general supportive counselling		
Häuser W. et al, Germany (2020)[283]	German Pain Society	<u>Strong Consensus</u> Discontinue if effectiveness of opioids does not improve or is not achieving functional goals or if adverse events arise within the first 12 weeks. If the same effect can be reached by other medical	<u>Strong Consensus</u> In cases of long-term use of opioids, it should be ceased gradually and replaced with other therapies, including self-management programmes and self-help If opioid reduction was not successful	<u>Strong Consensus</u> When a patient experiences opioid associated psychological disturbance, options for management include reduction of dosage, change the opioid,	Nil	Nil	Nil

		treatments (e.g. operations, physiotherapy or psychotherapy). If a patient abuses/ misuses opioid medications. Pause after 6 months, clinicians should talk to the patient about the reduction of the dosage/ or a break and options for non-medical treatments. In pregnant women, it is urgently recommended to cease ongoing use of opioids.	as part of an outpatient multimodal therapy programme an in-patient opioid reduction should be considered.	stopping the treatment of the opioid. Gradually reduce the daily dose and supplement with doxepin (antidepressant) to avoid withdrawal symptoms.			

OMEDD = Oral Morphine Equivalent Daily Dose

** **GRADE approach** classifies recommendations as strong or weak with the strength of recommendation being determined by the balance between desirable and undesirable consequences of alternative management strategies, quality of evidence, variability in values and preferences, and resource use.
Strong recommendations mean that most informed patients would choose the recommended management and that clinicians can structure their interactions with patients accordingly.
Weak recommendations mean that patients' choices will vary according to their values and preferences, and clinicians must ensure that patients' care is in keeping with their values and preferences.

*** **Recommendation categories** are based on evidence type, balance between desirable and undesirable effects, values and preferences, and resource allocation (cost).
Category A recommendation: Applies to all persons; most patients should receive the recommended course of action.

Category B recommendation: Individual decision making needed; different choices will be appropriate for different patients. Clinician's help patients arrive at a decision consistent with patient values and preferences and specific clinical situations.

Evidence type is based on study design as well as a function of limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and constellation of plausible biases that could change effects.

Type 1 evidence: Randomized clinical trials or overwhelming evidence from observational studies.

Type 2 evidence: Randomized clinical trials with important limitations or exceptionally strong evidence from observational studies.

Type 3 evidence: Observational studies or randomized clinical trials with notable limitations.

Type 4 evidence: Clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations.

**** NEATS Rating for Strength of Recommendation

Strong There is high confidence that the recommendation reflects best practice. This is based on: a) strong evidence for a true net effect (e.g., benefits exceed harms); b) consistent results, with no or minor exceptions; c) minor or no concerns about study quality; and/or d) the extent the panellists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.

Moderate There is moderate confidence that the recommendation reflects best practice. This is based on: a) good evidence for a true net effect (e.g. benefits exceed harms); b) consistent results, with minor and/or few exceptions; c) minor and/or few concerns about study quality; and/or d) the extent of panellists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.

Weak There is some confidence that the recommendation offers the best current guidance for practice. This is based on: a) limited evidence for a true net effect (e.g., benefits exceed harms); b) consistent results, but with important exceptions; c) concerns about study quality; and/or d) the extent of panellists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Appendix 2: Evidence-to-decision Frameworks

Appendix 2 – Table 1: Evidence-to-decision Framework for Key Clinical Question 1

Question	Does deprescribing of opioids result in benefits or harms compared to continuation?
Population	Adult (>18) taking opioids for any duration and for any pain condition
Intervention	Opioid Deprescribing
Comparison	Opioid Continuation
Main Outcomes	Pain Physical Function Quality of life Adverse events
Settings	No setting restrictions

Assessment

Criteria	Judgement	Summary of evidence	Additional considerations
Does the balance between desirable and undesirable effects favour the intervention (opioid deprescribing) or the comparison (opioid continuation)?	☐ Favour comparator ☐ Probably favours comparator ☒ Probably favours the intervention ☐ Favour the intervention ☐ Varies ☐ Don't know	**Summary**: The evidence of benefits and harms of opioid deprescribing primarily relates to persons with chronic non-cancer pain. Important harms of opioid continuation were identified, including opioid-related adverse effects such as constipation and nausea. Serious and intolerable adverse effects such as opioid use disorders, respiratory depression and overdose were also of concern. There was a lack of evidence for the benefit of long term opioids in reducing pain and improving function for persons with chronic non-cancer pain. **Benefits of opioid deprescribing vs continuation**: Consistent low quality evidence suggests that mean pain scores and functional measures improved or did not significantly change for most patients who reduced or discontinued opioids. Reporting of quality	Is the baseline risk for benefit and harms of deprescribing similar across subgroups? Yes☐ No☒ There is a difference in baseline risk for benefit and harms of deprescribing for those with/without an opioid use disorder. There may also be differences based on clinical characteristics including the indication for opioid use, dose, co-morbidities and concomitant medication use. Should there be separate recommendations for subgroups?

of life measures were heterogeneous across reviews, however, many studies reported improved quality of life after opioid dose reduction. Reduced opioid-related adverse effects such as nausea and constipation were associated with opioid deprescribing. The benefits of deprescribing on pain scores were greater for those on higher baseline opioid doses (measured in daily morphine milligram equivalents) compared to those with lower baseline doses.

Harms of deprescribing vs continuation: Across reviews, a small number of participants withdrew from the deprescribing cohorts due to worsening symptoms/lack of efficacy. Serious adverse events resulting from opioid deprescribing were infrequently reported but included suicidal self-directed violence and overdose. Evidence regarding the impact of deprescribing on serious harms including substance use, opioid overdose, and suicide was lacking.

Based on this evidence, the panel has identified specific conditions under which the risks associated with opioid continuation are believed to outweigh the benefits and therefore recommend deprescribing:

a) there is a lack of overall improvement in function, quality of life and/or pain,
b) there is a lack of progress toward meeting established therapeutic goals, OR
c) the person is experiencing serious or intolerable opioid-related adverse effects in physical, psychological or social domains

Subgroups:
There was a relative lack of evidence pertaining to the benefits and harms of opioid deprescribing in persons with cancer-related or

Yes☒ No☐

Subgroups for consideration:
- End-of-life care pain
- Chronic cancer-survivor pain
- Individuals with opioid use disorders

Additionally, clinical characteristics may increase the risk of opioid-related harms. Baseline risk of adverse events with continued opioid use may be higher for persons with:

a) Sleep disordered breathing or sleep apnoea
b) Chronic Obstructive Pulmonary disease
c) Concomitant use of medicines or substances with sedating effects. For example; benzodiazepines, alcohol, pregabalin.
d) Polypharmacy or multiple medication use
e) Prescribed higher doses of opioids

cancer-survivor pain. There was a small body of evidence which showed reduced pain and improved quality of life accompanying opioid deprescribing interventions for cancer patients. Due to the known harms of long-term opioid use, and increasing cancer survivorship, the panel expects to see similar benefit and harms in the population of cancer-survivors as those with chronic non-cancer pain.

We do not have evidence for benefits or harms of opioid deprescribing for persons with end-of-life care pain. The panel has placed an emphasis on symptom management for populations with limited life expectancy and therefore, recommended against opioid deprescribing in this population unless deemed appropriate by the treating clinician.

Persons with opioid use disorder were often excluded from the reviews which were examined in our overview of reviews. This population group is not routinely examined in the opioid deprescribing literature. We sought additional evidence to inform recommendations for this population. Moderate-quality evidence indicates that opioid deprescribing, when performed without providing access to long-term addiction treatment and care, is associated with elevated risk of harms and death from drug overdose. There was limited evidence pertaining to persons with mild-moderate opioid use disorders. As such, in the case of individuals with a suspected or diagnosed severe opioid use disorder, we recommend against using deprescribing as a sole strategy due to evidence of increased harms.

| What is the overall certainty of the evidence of effects? | ☒ Very low ☒ Low ☒ Moderate | The certainty of evidence for the benefits of deprescribing is **very low to low**. | **Key reasons for downgrading**: Study design, risk of bias, indirectness. |

	☐ High	The certainty of evidence for the harms of deprescribing is **very low**.	**Certainty of evidence for benefits:** Very low to low from overview of systematic reviews containing both randomized controlled trials (RCTs) and non-randomised studies.

☐ High
☐ Very high

The certainty of evidence for the harms of deprescribing is **very low**.

The certainty of evidence for harms of deprescribing in the population of persons with severe opioid use disorders is **moderate**.

Certainty of evidence was downgraded due to study design with systematic reviews including both RCTs and non-randomised studies. The panel had concerns about attrition bias in the intervention groups and the selective reporting of outcomes, particularly relating to adverse effects. Strict inclusion and exclusion criteria across studies limited generalisability. Populations examined in reviews and primary studies were relatively homogenous (predominantly middle aged, Caucasian women) with limited co-morbidities which may not be reflective of the general population using opioids. Outcomes were often measured in the short term and maintenance was not assessed.

Certainty of evidence for benefits: Very low to low from overview of systematic reviews containing both randomized controlled trials (RCTs) and non-randomised studies.

Certainty of evidence for harms: Very low from overview of systematic reviews containing both randomized controlled trials (RCTs) and non-randomised studies. Certainty of evidence of harms from additional systematic review sought which examines persons with opioid use disorders is moderate.

Given the benefits and harms, what choice do you expect patients to make?

☐ Favour comparator
☒ Probably favours comparator
☐ Probably favours the intervention
☐ Favour the intervention
☒ Varies
☐ Don't know

Both healthcare professionals and persons taking opioids expressed resistance to change. Opioid continuation, rather than deprescribing, was identified as the current default behaviour.

Persons taking opioids: Persons taking opioids expressed a general desire to reduce or cease opioid therapies, however they believed engaging and persevering with opioid deprescribing was difficult. Persons taking opioids placed a high value on achieving pain relief and maintaining quality of life, but also on avoiding the adverse events related to opioid use such as nausea, vomiting, fatigue, impaired cognition and constipation. Other adverse effects, including risk of addiction, were of lesser importance to the interviewed population. Persons taking opioids were also

Perspective taken: Evidence suggests there are persons who wish to discontinue opioids to avoid side effects and the harms of long terms use. There are others who may be hesitant or may have failed or difficult deprescribing attempts due to increased pain and/or decreased function and quality of life after dose reduction or cessation.

Source of values and preferences: Two qualitative studies were conducted with key stakeholder groups (healthcare professionals and persons taking opioids) regarding opioid deprescribing and the development of opioid deprescribing guidelines.

concerned about the negative effects of opioid deprescribing such as withdrawal effects, increased pain, and functional limitations.

Significant emotional distress was caused by the perceived stigma associated with opioid use and persons taking opioids described judgement from family, friends, and healthcare professionals. Expressing a desire to initiate or continue opioids made some people feel type cast as "addicts" by healthcare professionals.

Healthcare professionals: Deprescribing of opioids was thought to be more challenging than continuation, requiring more time and effort. Opioids were considered more challenging to deprescribe than other medication classes due to medication related factors such as dependence and euphoria. Concerns about opioid continuation contributing to misuse, dependence, opioid-related overdoses and mortality were expressed by healthcare professionals. Conversely, there were concerns expressed about the potential harms of opioid deprescribing such as withdrawal symptoms and pain exacerbations. A lack of appropriate alternative analgesia available for pain management were viewed as a barrier to opioid deprescribing.

Healthcare professionals also expressed concerns about potential disruptions to patient-provider relationships if opioid deprescribing is not desired by the person taking opioids. This may be further exacerbated if there is difficult or failed deprescribing attempts.

Source of variability, if any: There was substantial variability in values and preferences. Sources of variability may include pain category (e.g. acute pain, chronic pain), pain and function scores, duration of opioid use, opioid dose, education levels and health literacy.

Method for determining values satisfactory for this recommendation?
Yes☒ No☐

All critical outcomes measured?
Yes☒ No☐

| Is the intervention acceptable to patients, their caregivers and | ☐ No
☐ Probably no
☒ Probably yes
☐ Yes | It is likely that the deprescribing of opioids, if guided by an explicit and mutually agreed management plan, may be acceptable to both persons taking opioids and healthcare professionals. | **Perspective taken**: Evidence suggests there are persons who wish to discontinue opioids to avoid side effects and the harms of long terms use. There are others who may be hesitant or may have failed or difficult deprescribing attempts due |

| healthcare providers? | ☐ Varies
☐ Don't know | | |

Persons taking opioids: There may be acceptability concerns if opioid deprescribing is involuntary or occurs without the consent of the person taking opioids. In our qualitative study, persons taking opioids requested increased communication between healthcare professionals and consumers about the deprescribing process, including potential benefits, expectations surrounding tapering, and assurance regarding continued support throughout deprescribing. Addressing these factors may increase the acceptability of opioid deprescribing.

The societal stigma toward opioid use disorders and opioid substitution therapy, coupled with the regulatory framework in Australia relating to the prescribing of opioid substitution therapy, may impact the acceptability of opioid deprescribing or alternative management options.

Healthcare professionals: Healthcare professionals may not find it acceptable to continue to prescribe opioids due to the nature of Australia's current regulatory framework. Opioid deprescribing may be more acceptable to healthcare professionals than ongoing opioid prescribing.

Planned opioid reduction at the point of prescribing was thought to create an expectation to deprescribe, minimising potential disruptions to therapeutic relationships during therapy withdrawal.

Opioid deprescribing may require close monitoring and engagement between the person taking opioids and the healthcare professional. As such, this may have implications for acceptability for primary healthcare professionals (general

to increased pain and/or decreased function and quality of life after dose reduction or cessation. Several factors may influence the acceptability of opioid deprescribing for persons taking opioids and healthcare professionals.

Source of acceptability: Two qualitative studies were conducted with key stakeholder groups (healthcare professionals and persons taking opioids) regarding opioid deprescribing and the development of opioid deprescribing guidelines. Additional acceptability considerations have been proposed by guideline development group members.

Source of variability, if any: There is some variability between acceptability of opioid deprescribing between persons taking opioids and healthcare professionals.

Method for determining acceptability satisfactory for this recommendation?
Yes☒ No☐

All critical outcomes measured?
Yes☒ No☐

practitioners) due to increased workload in the form of additional time and effort spent engaging in opioid deprescribing.

Policymakers: Given the potential net harms of opioids use at the population level, widespread use and continuation of opioids for chronic non-cancer pain may not be acceptable to policy-makers.

Is the intervention feasible for patients, their caregivers and healthcare providers?

☐ No
☐ Probably no
☒ Probably yes
☐ Yes
☒ Varies
☐ Don't know

Opioid deprescribing: Opioid deprescribing may involve multidisciplinary and multimodal pain management strategies and services and therefore may be difficult to access or implement. This may particularly be the case in rural or remote areas, among socially-disadvantaged individuals, or in primary care settings where resources or access to multidisciplinary or specialist services are limited. In such cases the barriers to opioid deprescribing may make a recommendation difficult to implement without additional resources. Further detail relating to opioid deprescribing interventions can be found in evidence-to-decision (EtD) question 3.

Is opioid deprescribing generally available?
Yes☒ No ☐

Yes, however co-interventions to support opioid deprescribing may be less readily available (See EtD Question 3 for further detail).

How large are the resource requirements (costs)?

☐ Large
☒ Moderate
☐ Neutral
☐ Moderate savings
☐ Large savings
☐ Varies
☐ Don't know

Opioid continuation: Opioids are a widely-available and feasible treatment option. Direct costs of prescription opioid analgesics to individuals are generally relatively low, although prescribing rules in Australia require frequent visits to healthcare providers for ongoing prescriptions which may result in higher out-of-pocket costs.

Opportunity cost: Is this intervention and its effects worth withdrawing or not allocating resources from other interventions?
Yes☒ No ☐

Economic and preventive benefits for harms at an individual and societal level.

Is there lots of variability in resource requirements across settings?
Yes☒ No ☐

The societal costs of chronic non-cancer pain are significant. Potential costs to society of widespread use of opioids for chronic non-cancer pain include direct and indirect costs relating to overdose, misuse, dependence and altered productivity. The societal costs of opioid misuse and abuse and are also considerable. Indirect costs include the economic burden of

Deprescribing in isolation is a low resource intervention, feasible for primary and long term care. Additional monitoring required during deprescribing may increase resource requirements.

untreated opioid dependence, drug-related crime, illicit opioid use and loss of productivity.

The addition of co-interventions to support deprescribing would increase the cost but may provide benefits in terms of efficacy, and clinical outcomes. (See EtD Question 3 for further detail).

| What would be the impact on health equity? | ☐ Large
☒ Moderate
☐ Negligible
☐ Varies
☐ Don't know | | |

Socioeconomic factors are important determinants of chronic pain, opioid use and opioid-related adverse outcomes. Populations which are disproportionally impacted by opioid related harms may be expected to derive the greatest benefit from opioid deprescribing.

Populations which may require additional support or consideration when implementing opioid deprescribing and related co-interventions include: culturally and linguistically diverse populations, Aboriginal and Torres Strait Islander populations, Aged Care Facility residents, individuals with co-morbidities such as dementia, those in the justice system and those with a severe opioid use disorder.

Perspective taken: Opioid deprescribing may have moderate impacts on health equity.

Source of equity:
Equity implications discussed amongst guideline development group.

Source of variability, if any: We anticipate substantial variability in equity implications across population groups.

Method for determining equity satisfactory for this recommendation?
 Yes☒ No☐

All critical outcomes measured?
Yes☒ No☐

Appendix 2 – Table 2: Evidence-to-decision Framework for Key Clinical Question 2

Question	What is the evidence on how to deprescribe opioids?
Population	Adult (>18) taking opioids for any duration and for any pain condition
Intervention	Opioid Deprescribing
Comparison	Opioid Continuation
Main Outcomes	Pain Physical Function Quality of life Adverse events
Settings	No setting restrictions

Assessment

Criteria	Judgement	Summary of evidence	Additional considerations
Does the balance between desirable and undesirable effects favour the intervention or the comparison?	☐ Favour comparator ☐ Probably favours comparator ☒ Probably favours the intervention ☐ Favour the intervention ☐ Varies ☐ Don't know	**Rate of tapering**: Abrupt opioid cessation can precipitate severe withdrawal effects. There is existing literature which demonstrates harms of abrupt opioid withdrawal such as serious withdrawal symptoms, uncontrolled pain, psychological distress and suicide. To our knowledge, there is no review or trial that directly compares rapid vs slower opioid deprescribing protocols in persons with chronic non-cancer pain. One primary study suggested that more gradual tapers reduced the risk of serious harms. In the cohort study of persons prescribed 120 mg OMEDD or more of long-term opioid therapy, each additional week to discontinuation	Is the baseline risk for benefit of deprescribing similar across subgroups? Yes☒ No☐ There is no evidence to suggest different subgroups would benefit or harm from different mechanisms of opioid deprescribing at this time. Should there be separate recommendations for subgroups based on risk levels? Yes☐ No☒ Insufficient evidence to guide differences in recommendations for subgroups.

associated with a 7% reduction in risk of an opioid-related emergency department visit or hospitalization.

In our overview of reviews, we were not able to evaluate which patient or tapering characteristics were associated with greater success of deprescribing or ascertain differences in clinical outcomes based on tapering schedule. This was largely due to the heterogeneity across patient baseline characteristics, interventions, and the lack of adequate reporting of tapering schedules used. When a tapering protocol was documented, it was often general and described gradual or individualised opioid reductions rather than specific schedules. Whether to taper the short-acting opioid first or the long-acting opioid first in sequence is not known nor has been compared.

Many of the tapering schedules were reported as being individualised to the specific participant and their needs. We acknowledge that individuals will have different starting doses and formulations of opioids. As such, the panel recommends individualised and person-centred opioid deprescribing. Individualisation of the rate and nature of deprescribing may require additional monitoring and input from healthcare professionals.

The evidence base for benefits and harms of opioid deprescribing derived from the overview of systematic reviews is largely from studies involving voluntary opioid deprescribing. We also note there is evidence relating to increased harms (suicide, overdose, illicit opioid use) in the context of involuntary opioid deprescribing.

What is the overall certainty of the evidence of effects?	☒ Very low ☐ Low ☐ Moderate ☐ High ☐ Very high	The certainty of evidence relating to the rate and nature of deprescribing is **very low**. There are a lack of studies or reviews comparing opioid deprescribing schedules and their outcomes, as well as lack of evidence regarding the management of individuals who experience unsuccessful opioid deprescribing attempts or do not complete tapers. These populations are often excluded from analysis.	**Key reasons for downgrading**: Study design, risk of bias, indirectness, missing data. **Certainty of evidence:** Very low from overview of systematic reviews containing both randomized controlled trials (RCTs) and non-randomised studies, as well as primary studies.
Given the benefits and harms, what choice do you expect patients to make?	☐ Favour comparator ☐ Probably favours comparator ☐ Probably favours the intervention ☐ Favour the intervention ☐ Varies ☒ Don't know	**Persons taking opioids**: Failed or difficult deprescribing attempts, either self-initiated or under the supervision of a healthcare professional, undermined beliefs in being able to discontinue opioids. Some participants spoke of severe withdrawal effects, pain exacerbations, or reduction in function when attempting deprescribing. Participants who experienced negative consequences of abrupt opioid withdrawal spoke of mistrust of healthcare professionals and expressed trepidation in reattempting deprescribing. Many participants had trialled other medications for pain without significant improvement in symptoms and opted to continue opioids. By contrast, previous successful dose reduction attempts positively influenced self-efficacy. Observed improvements in opioid-related side effects and decreased pill burdens encouraged continuation of deprescribing. Persons taking opioids requested increased communication between healthcare professionals and themselves about the deprescribing process, including potential benefits, expectations surrounding tapering, and assurance regarding continued support throughout deprescribing. Opioid consumers advocated for	**Perspective taken**: Persons engaging in opioid deprescribing would want to minimise adverse outcomes and maximise the chance of successful deprescribing. **Source of values and preferences**: Two qualitative studies were conducted with key stakeholder groups (healthcare professionals and persons taking opioids) regarding opioid deprescribing and the development of opioid deprescribing guidelines. **Source of variability, if any**: There was variability in values and preferences. Sources of variability may include pain category (e.g. acute pain, chronic pain), pain and function scores, duration of opioid use, opioid dose, education levels and health literacy, previous attempts at deprescribing and relationships with healthcare professionals. **Method for determining values satisfactory for this recommendation?**

additional resources and information to inform decision making about opioid use.

Yes☒ No☐

All critical outcomes measured?

Yes☒ No☐

The desire to deprescribe opioids and one's belief in the ability to achieve opioid reduction was significantly influenced by relationships with healthcare professionals. A consideration for individual circumstances was believed to be beneficial when broaching the topic of opioid deprescribing. Tailoring recommendations to individuals was requested, rather than reiterating population-level benefits of opioid deprescribing. Furthermore, it was reinforced that guidelines would need to be flexible to account for individual circumstances and only be used if the person taking opioids was willing to have opioids deprescribed.

Most persons taking opioids stated that they had not actively raised the topic of deprescribing with their prescriber and felt that if they agreed to deprescribing, their prescriber would be reluctant to allow re-initiation or dose increases in the future. Consumers felt that the power lay with the prescriber and that they were not equal partners in decision making.

Healthcare professionals:
Some participants saw deprescribing as an essential component of prescribing and advocated for a treatment agreement to be made between each patient and prescriber at the point of initiation regarding how opioids are going to be used, when to assess efficacy and when to withdraw. Planned opioid reduction at the point of prescribing was thought to create an expectation to

deprescribe, minimising potential disruptions to therapeutic relationships during therapy withdrawal. A structured and holistic approach to deprescribing was considered optimal, with adjunct or alternate analgesic agents, non-pharmacological pain management strategies and involvement of multidisciplinary healthcare members. There was some concern about guidelines and their ability to be applicable to the heterogeneous group of individuals who consume opioids. As such, it was thought that opioid deprescribing guidelines would require a multi-target, multimodal intervention strategy. Healthcare professionals suggested that functional measures, quality of life measures and overall risk reduction should be considered when assessing the effectiveness of opioid deprescribing in addition to pain outcome measures.

Is the intervention acceptable to patients, their caregivers and healthcare providers?	☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☒ Varies ☐ Don't know	It is likely that the deprescribing of opioids, if guided by an explicit and mutually agreed management plan, may be acceptable to both patients and healthcare professionals.	**Perspective taken**: Persons engaging in opioid deprescribing would want to minimise adverse outcomes and maximise the chance of successful deprescribing.

Persons taking opioids: It is likely that a gradual and individualised deprescribing approach which is modified based on an individual's clinical progress and needs would be acceptable to persons taking opioids. There may be acceptability concerns if opioid deprescribing is involuntary or occurs without the consent of the person taking opioids. In our qualitative study, persons taking opioids requested increased communication between healthcare professionals and consumers about the deprescribing process, including potential benefits, expectations surrounding tapering, and assurance

Source of values and preferences: Two qualitative studies were conducted with key stakeholder groups (healthcare professionals and persons taking opioids) regarding opioid deprescribing and the development of opioid deprescribing guidelines.

Source of variability, if any: There may be variability in acceptability. Sources of variability may include pain category (e.g. acute pain, chronic pain), pain and function scores, duration

regarding continued support throughout deprescribing. Addressing these factors may increase the acceptability of opioid deprescribing.

The association between opioid deprescribing and retention in healthcare is unclear and as such our overview of reviews does not provide significant insight into the acceptability of opioid deprescribing.

Healthcare professionals:
Planned opioid reduction at the point of prescribing was thought to create an expectation to deprescribe, minimising potential disruptions to therapeutic relationships during therapy withdrawal and may increase healthcare professional's acceptability.

Gradual opioid deprescribing may require close monitoring and engagement with between person and healthcare professional. As such, this may have implications for acceptability for primary healthcare professionals (general practitioners) due to increased workload in the form of additional time and effort spent engaging in opioid deprescribing.

Opioid deprescribing: Opioid deprescribing may involve regular clinician follow up which may be difficult for persons to access. This may particularly be the case in rural or remote areas, among socially-disadvantaged individuals, or in primary care settings where appointment times and bookings are limited. In such cases the barriers to opioid deprescribing may make a recommendation difficult to implement without additional resources.

of opioid use, education levels and health literacy.

Method for determining values satisfactory for this recommendation?
 Yes☒ No☐

All critical outcomes measured?
Yes☒ No☐

Is the intervention feasible for patients, their caregivers and healthcare providers?

☐ No
☐ Probably no
☐ Probably yes
☐ Yes
☒ Varies
☐ Don't know

How large are the resource requirements (costs)?

Is opioid deprescribing generally available?
Yes☒ No ☐

Yes, however regular monitoring and follow-up with clinicians may impact upon intervention feasibility.

☐ Large
☒ Moderate
☐ Neutral
☐ Moderate savings
☐ Large savings
☒ Varies
☐ Don't know

Medicare and the public hospital system provide free or low-cost access for all Australians to many healthcare services. Private health insurance provides choice outside the public system and requires individuals to contribute toward the cost of healthcare. Approximately 53% of the Australian population has some form of private health insurance. People living in major cities are the most likely to have private health insurance. Those with private health insurance may still incur out-of-pocket costs for 'medical gaps'.

Transitions of care have been identified as a target area to implement a deprescribing plan (E.g. when persons are discharged from hospital on opioids). Targeting of transitions of care may be a feasible intervention strategy.

Opioid continuation: Direct costs of prescription opioid analgesics to individuals are generally relatively low, although prescribing rules in Australia require frequent visits to healthcare providers for ongoing prescriptions which may result in higher out-of-pocket costs or may have an impact on work.

The societal costs of chronic non-cancer pain are significant. Potential costs to society of widespread use of opioids for chronic non-cancer pain include direct and indirect costs relating to overdose, misuse, dependence and altered productivity. The societal costs of opioid misuse and abuse and are also considerable. Indirect costs include the economic burden of untreated opioid

Opportunity cost: Is this intervention and its effects worth withdrawing or not allocating resources from other interventions?
Yes☒ No ☐

Gradual and individualised deprescribing may increase resource requirements but may also improve patient outcomes and minimise withdrawal effects and harms of abrupt opioid cessation.

Is there lots of variability in resource requirements across settings?
Yes☒ No ☐

Deprescribing in isolation is a low resource intervention, feasible for primary and long term care. Additional monitoring required during deprescribing may increase resource requirements.
The addition of co-interventions to support deprescribing would increase the cost but may provide benefits in terms of efficacy, and clinical outcomes. (See EtD Question 3 for further detail).

		dependence, drug-related crime, illicit opioid use and loss of productivity.	
What would be the impact on health equity?	☐ Large ☒ Moderate ☐ Negligible ☐ Varies ☐ Don't know	It is possible that gradual opioid tapering which requires regular follow up with healthcare professionals may not be as accessible for individuals who have limited access to healthcare. This may be the case for those who live in rural or remote areas or are socioeconomically disadvantaged.	**Perspective taken**: Gradual opioid deprescribing with regular clinician follow up may have moderate impacts on health equity. **Source of equity**: Equity implications discussed amongst guideline development group. **Source of variability, if any**: We anticipate substantial variability in equity implications across population groups. **Method for determining equity satisfactory for this recommendation?** Yes☒ No☐ **All critical outcomes measured?** Yes☒ No☐

Appendix 2 – Table 3: Evidence-to-decision Framework for Key Clinical Question 3

Question	Which interventions are effective to facilitate opioid deprescribing?
Population	Adult (>18) taking opioids for any duration and for any pain condition
Intervention	Opioid Deprescribing
Comparison	Opioid Continuation
Main Outcomes	Pain Physical Function Quality of life Adverse events
Settings	No setting restrictions

Assessment

Criteria	Judgement	Summary of evidence	Additional considerations
Does the balance between desirable and undesirable effects favour the intervention or the comparison?	☐ Favour comparator ☐ Probably favours comparator ☒ Probably favours the intervention ☐ Favour the intervention ☐ Varies ☐ Don't know	Opioid deprescribing is clinically challenging, and may be difficult to achieve and maintain. Co-interventions may assist in opioid reduction and pain management when deprescribing. Evidence for the effectiveness of different methods designed to achieve reduction or cessation of prescribed opioids for the management of chronic non-cancer pain is inconclusive and varies substantially across interventions and reviews examined. Our overview of reviews identified pharmacological, physical, interventional and psychological or behavioural interventions. Additional reviews examined multiple intervention types. Across interventions rates of opioid reduction varied widely across reviews and examined interventions (12.43 – 101.00 OMEDD) Persons on long term opioid therapy who voluntarily participate in intensive pain management interventions that incorporate opioid tapering may experience improvements in pain severity and pain-related function, while those who taper opioids with less intensive	Is the baseline risk for benefit of deprescribing interventions similar across subgroups? Yes☒ No☐ There is no evidence to suggest different subgroups would benefit from specific deprescribing interventions at this time. Should there be separate recommendations for subgroups based on risk levels? Yes☐ No☒ No – no evidence of benefit for any risk level.

co-interventions may have unchanged pain and function. Although the best evidence for opioid deprescribing effectiveness relates to multidisciplinary interventions, the direct evidence for the effect of multidisciplinary care on the outcome of opioid dose reduction is generally low certainty. Consistent low quality evidence suggests that regardless of intervention used, mean pain scores and functional measures improved or did not significantly change for most persons who reduced or discontinued opioids. Intensive outpatient multimodal pain management programs saw greater improvements in pain related function compared to less intensive interventions.

| What is the overall certainty of the evidence of effects? | ☒ Very low
☒ Low
☐ Moderate
☐ High
☐ Very high | The certainty of evidence for the effectiveness of opioid deprescribing interventions ranged from **very low** to **low**.

Certainty of evidence was downgraded due to study design with systematic reviews including both RCTs and non-randomised studies. The panel had concerns about attrition bias in the intervention groups and the selective reporting of outcomes. Many studies examined pain as the primary outcome rather than opioid reduction and as such, this secondary outcome was poorly reported. Strict inclusion and exclusion criteria across studies limited generalisability. Populations examined in reviews and primary studies were relatively homogenous (predominantly middle aged, Caucasian women) with limited co-morbidities which may not be reflective of the general population using opioids. Outcomes were often measured in the short term and maintenance was not assessed. | **Key reasons for downgrading**: Study design, risk of bias, indirectness.

Certainty of evidence: Very low to low from overview of systematic reviews containing both randomized controlled trials (RCTs) and non-randomised studies. |
| Given the benefits and harms, what choice do you | ☐ Favour comparator
☐ Probably favours comparator | **Persons taking opioids**: Persons taking opioids expressed a desire to deprescribe opioids because of negative physiological feedback in the form of opioid-induced side effects. Constipation, fatigue, | **Perspective taken**: Evidence suggests there are patients who wish to discontinue opioids to avoid the harms of long terms use. There are others who may be hesitant and may fail due to increased pain |

expect patients to make?	☐ Probably favours the intervention ☐ Favour the intervention ☒ Varies ☐ Don't know

nausea, and impaired cognition were reported. Similarly, concerns about long-term use and the development of physical dependence were voiced. Perceived failures of the healthcare system undermined beliefs about the feasibility of opioid deprescribing. Difficulties in accessing care, limited appointment times, travel, and significant costs associated with co-interventions and alternative pain management therapies such as physiotherapy, hydrotherapy and psychotherapy were described. Waiting times to see specialists, pain clinics, or undergo surgeries were described as significant and many participants spoke of a need to continue opioids due to a lack of alternative supports.

Persons taking opioids advocated for additional resources, interventions and information to inform decision making about opioid use.

Healthcare professionals: A structured and holistic approach to deprescribing was considered optimal, with adjunct or alternate analgesic agents, non-pharmacological pain management strategies and involvement of multidisciplinary healthcare members. There was some concern about guidelines and their ability to be applicable to the heterogeneous group of individuals who consume opioids. As such, it was thought that prospective opioid deprescribing guidelines would require a multitarget, multimodal intervention strategy.

A lack of alternative pharmacotherapy options was deemed a contributing factor for opioid continuation. Paracetamol and non-steroidal anti-inflammatory agents were identified as possible alternative analgesics; however, participants saw limited clinical

and/or decreased function after dose reduction or cessation. Co-interventions may help to facilitate opioid deprescribing,

Source of values and preferences: Two qualitative studies were conducted with key stakeholder groups (healthcare professionals and persons taking opioids) regarding opioid deprescribing and the development of opioid deprescribing guidelines.

Source of variability, if any: There was substantial variability in values and preferences. Sources of variability may include pain category (e.g. acute pain, chronic pain), pain and function scores, duration of opioid use, education levels and health literacy and access to care.

Method for determining values satisfactory for this recommendation?
Yes☒ No☐

All critical outcomes measured?
Yes☒ No☐

utility of these agents as opioid substitutes due to a perceived lack of efficacy, clinical contraindications in specific patient cohorts and concerns about long-term use. As such healthcare professionals requested further information about additional co-interventions to support opioid deprescribing.

Workload pressures, inadequate remuneration for healthcare professionals and insufficient resources for clinicians and patients were viewed as barriers to opioid deprescribing. Specialist and multidisciplinary care were largely seen as enablers to opioid deprescribing; however, effectiveness of a multidisciplinary approach was thought to be limited by accessibility and lengthy wait times for referrals to pain clinics. Significant costs associated with alternate pain management strategies such as pain psychoeducation and physiotherapy which were thought to accompany successful opioid deprescribing, limited their applicability.

| Is the intervention acceptable to patients, their caregivers and healthcare providers? | ☐ No ☐ Probably no ☒ Probably yes ☐ Yes ☒ Varies ☐ Don't know | **Persons taking opioids**: It is likely that the use of appropriate co-interventions to facilitate deprescribing of opioids, may be acceptable to both patients and healthcare professionals.

Co-interventions for opioid deprescribing may take substantial time and effort to engage in (e.g. cognitive behavioural therapy) and may come with higher costs to individuals, limiting acceptability. Further, some proposed co-interventions may be invasive such as spinal cord stimulation or acupuncture which may not be acceptable.

Healthcare professionals:

It may not be acceptable for healthcare professionals to continue to prescribe opioids due to the nature of Australia's current regulatory | **Perspective taken**: Persons taking opioids may require additional support and interventions to engage and persevere with opioid deprescribing. The effectiveness of opioid deprescribing and clinical outcomes may improve using co-interventions.

Source of acceptability: Two qualitative studies were conducted with key stakeholder groups (healthcare professionals and persons taking opioids) regarding opioid deprescribing and the development of opioid deprescribing guidelines. Additional acceptability considerations have been proposed by guideline development group members. |

framework. Opioid deprescribing may be more acceptable to healthcare professionals than ongoing opioid prescribing.

Some healthcare professionals expressed concern that specialised and multidisciplinary services, once engaged, decrease general practitioner agency to deprescribe opioids. As such, recommendation of co-interventions for opioid deprescribing may not be acceptable to all healthcare professionals.

Source of variability, if any: There is likely some variability between acceptability of opioid deprescribing interventions across the cohorts of persons taking opioids and healthcare professionals.

Method for determining acceptability satisfactory for this recommendation?
Yes☒ No☐

All critical outcomes measured?
Yes☒ No☐

Is the intervention feasible for patients, their caregivers and healthcare providers?	☐ No ☐ Probably no ☐ Probably yes ☐ Yes ☒ Varies ☐ Don't know

Opioid deprescribing interventions: The guideline development group acknowledges that multidisciplinary and multimodal pain management services may be difficult to access or implement. This may particularly be the case in rural or remote areas, among socially-disadvantaged individuals, or in primary care settings where resources or access to multidisciplinary or specialist services are limited. In such cases the barriers to opioid deprescribing may make a recommendation difficult to implement without additional resources.

Are opioid deprescribing interventions generally available?
Yes☐ No☒

No, co-interventions to support opioid deprescribing may be difficult to access due to cost and accessibility barriers.

How large are the resource requirements (costs)?	☐ Large ☒ Moderate ☐ Neutral ☐ Moderate savings ☐ Large savings ☒ Varies ☐ Don't know

Opioid deprescribing may involve intensive co-interventions such as multidisciplinary and multimodal pain management services. Such interventions may be difficult to access or implement. This may particularly be the case in rural or remote areas, among socially-disadvantaged individuals, or in primary care settings where resources or access to multidisciplinary or specialist services are limited. In such cases the barriers to opioid deprescribing may make a recommendation difficult to implement without additional resources.

Opportunity cost: Is this intervention and its effects worth withdrawing or not allocating resources from other interventions?
Yes☒ No ☐

Economic and preventive benefits for harms at an individual and societal level.

Is there lots of variability in resource requirements across settings?

Medicare and the public hospital system provide free or low-cost access for all Australians to many healthcare services. Private health insurance provides choice outside the public system and requires individuals to contribute toward the cost of healthcare. Approximately 53% of the Australian population has some form of private health insurance. People living in major cities are the most likely to have private health insurance. Those with private health insurance may still incur out-of-pocket costs for 'medical gaps'.

Many allied health services are provided in the community, often by practitioners operating in private practices. Allied health services can usually be accessed directly by any patient paying privately without a referral. A range of national and state-based funding schemes and programs are available to help people access allied health services such as services provided by community or aboriginal health services, Medicare funded services, and allied health services provided by aged care or disability providers. In these cases, patients may need a referral, typically from a general practitioner. Access to these services can be limited by lengthy waiting times. Additional individual costs of accessing such treatment may include transport to and from appointments.

Opioid continuation: Opioids are a widely-available and feasible treatment option. Direct costs of prescription opioid analgesics to individuals are generally relatively low, although prescribing rules in Australia require frequent visits to healthcare providers for ongoing prescriptions which may result in higher out-of-pocket costs or may have an impact on work.

The societal costs of chronic non-cancer pain are significant. Potential costs to society of widespread use of opioids for chronic

Deprescribing in isolation is a low resource intervention, feasible for primary and long term care.

The addition of co-interventions to support deprescribing would increase the cost but may provide benefits in terms of efficacy, and clinical outcomes.

non-cancer pain include direct and indirect costs relating to overdose, misuse, dependence and altered productivity. The societal costs of opioid misuse and abuse and are also considerable. Indirect costs include the economic burden of untreated opioid dependence, drug-related crime, illicit opioid use and loss of productivity.

| What would be the impact on health equity? | ☐ Large
☒ Moderate
☐ Negligible
☐ Varies
☒ Don't know | Socioeconomic factors are important determinants of chronic pain, opioid use and opioid-related adverse outcomes. Variation in access to health professionals may delay surgical treatment or alternatives to opioid analgesics. | **Perspective taken**: Opioid deprescribing interventions may have moderate impacts on health equity. |

Populations which may require additional support or consideration when implementing opioid deprescribing co-interventions include: culturally and linguistically diverse populations, Aboriginal and Torres Strait Islander populations, Aged Care Facility residents, Individuals with co-morbidities such as dementia, those in the forensic system and those with a severe opioid use disorder.

Access to comprehensive and multidisciplinary chronic pain management services varies within Australia. Access may be limited for socially-disadvantaged people and those in regional and remote areas.

Source of equity: Equity implications discussed amongst guideline development group.

Source of variability, if any: We anticipate substantial variability in equity implications across population groups.

Method for determining equity satisfactory for this recommendation?
 Yes☒ No☐

All critical outcomes measured?
Yes☒ No☐

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