DEPRESCRIBING IN OLDER PEOPLE:

A clinical practice guideline

THE UNIVERSITY OF WESTERN AUSTRALIA

WESTERN AUSTRALIAN CENTRE FOR HEALTH AGEING

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Endorsements

Endorsement statements from organisations will be included upon finalisation of the guideline.

List of Abbreviations

Abbreviation	Definition
ACC	American College of Cardiology
ACG	American College of Gastroenterology
ACR	American College of Rheumatology
ACS	Acute Coronary Syndrome
ADE	Adverse Drug Event
ADL	Activities of Daily Living
ADWE	Adverse Drug Withdrawal Event
AF	Atrial Fibrillation
AFF	Atypical Femoral Fracture
AGREE II	Appraisal of Guidelines for Research and Evaluation II
AHA	American Heart Association
AIMS	Abnormal Involuntary Movement Scale
ASPREE	ASPirin in Reducing Events in the Elderly
ATC	Anatomical Therapeutic Chemical (Classification System)
AV	Atrioventricular
BMD	Bone Mineral Density
BP	Blood Pressure
BPH	Benign Prostatic Hyperplasia
BPRS	Brief Psychiatric Rating Scale
BPSD	Behavioural and Psychological Symptoms of Dementia
BWSQ	Benzodiazepine Withdrawal Symptom Questionnaire
CAC	Coronary Artery Calcium
CANMAT	Canadian Network for Mood and Anxiety Treatments
CBR	Consensus-Based Recommendation
CBT	Cognitive Behavioural Therapy
CGM	Continuous Glucose Monitoring
CI	Confidence Interval
CKD	Chronic Kidney Disease
COPD	Chronic Obstructive Pulmonary Disease
CRP	C-Reactive Protein
CT	Computed Tomography
CTX	C-Terminal Telopeptide
CV	Cardiovascular
CVD	Cardiovascular Disease
DANTON	Discontinuation of ANtihypertensive Treatment in Older people with dementia living in a Nursing home
DAPT	Dual Antiplatelet Therapy
DBI	Drug Burden Index
DBP	Diastolic Blood Pressure
DCM	Dementia Care Mapping
DISCUS	Dyskinesia Identification System Condensed User Scale
DLB	Dementia with Lewy Bodies
DXA	Dual-Energy X-ray Absorptiometry
EBR	Evidence-Based Recommendation

EF	Ejection Fraction
ESR	Erythrocyte Sedimentation Rate
FLEX	Fracture Intervention Trial Long-Term Extension
FLOW	Evaluate Renal Function with Semaglutide Once Weekly
FVC	Forced Vital Capacity
GDG	Guideline Development Group
GDMT	Guideline-Directed Medical Therapy
GI	Gastrointestinal
GINA	Global Initiative for Asthma
GORD	Gastro-Oesophageal Reflux Disease
GPS	Good Practice Statement
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GSM	Genitourinary Syndrome of Menopause
HFpEF	Heart Failure with preserved Ejection Fraction
HFmrEF	Heart Failure with mildly reduced Ejection Fraction
HFrEF	Heart Failure with reduced Ejection Fraction
HR	Hazard Ratio
ICS	Inhaled Corticosteroids
INR	International Normalised Ratio
IPSS	International Prostate Symptom Score
IV	Intravenous
LABA	Long-Acting Beta-Agonist
LAMA	Long-Acting Muscarinic Antagonist
LSC	Least Significant Change
LUTS	Lower Urinary Tract Symptoms
MACE	Major Adverse Cardiovascular Event
MADRS	Montgomery-Asberg Depression Rating Scale
mcg	microgram
mg	milligram
MD	Mean Difference
MHT	Menopausal Hormone Therapy
MI	Myocardial Infarction
MMSE	Mini-Mental State Examination
MRONJ	Medication-Related Osteonecrosis of the Jaw
NHMRC	National Health and Medical Research Council
NNT	Number Needed to Treat
NPI	Neuropsychiatric Inventory
NPI-NH	Neuropsychiatric Inventory Nursing Home Version
NRS	Numeric Rating Scale
NSAID	Non-steroidal Anti-Inflammatory Drug
OAC	Oral Anticoagulant
25[OH]D	25-hydroxyvitamin D
OR	Odds Ratio
P1NP	Procollagen Type 1 N Propeptide
PBS	Pharmaceutical Benefits Scheme
PCI	Percutaneous Coronary Intervention
PDD	Parkinson's Disease Dementia

PIM	Potentially Inappropriate Medicine
PPI	Proton Pump Inhibitor
PREVENTABLE	Pragmatic Evaluation of Events and Benefits of Lipid Lowering in Older Adults
PROMIS	Patient-Reported Outcomes Measurement Information System
PSQI	Pittsburgh Sleep Quality Index
QoL	Quality of Life
QOLAD	Quality of life in Alzheimer's Dementia
QUALID	Quality of Life in Late Stage of Dementia score
QUALIDEM	Quality of Life for People with Dementia
RA	Rheumatoid Arthritis
RCT	Randomised Controlled Trial
RLS	Restless Legs Syndrome
RR	Relative Risk
SAPT	Single Antiplatelet Therapy
SBP	Systolic Blood Pressure
SD	Standard Deviation
SELECT	Semaglutide Effects on Cardiovascular Outcomes in People with Overweight or Obesity
SIB	Severe Impairment Battery
SMB	Standardised Mean Difference
SNRI	Serotonin-Norepinephrine Reuptake Inhibitors
SoF	Summary of Findings
SSRI	Selective Serotonin Reuptake Inhibitors
STALD	Sheffield Test for Acquired Language Disorders
STAREE	STAtins in Reducing Events in the Elderly
START	Screening Tool to Alert to Right Treatment
SVT	Supraventricular Tachycardia
TCA	Tricyclic Antidepressants
TPV	Total Prostatic Volume
TURP	Transurethral Resection of the Prostate
UKPDS	United Kingdom Prospective Diabetes Study
ULT	Urate-Lowering Therapy
UPDRS	Unified Parkinson's Disease Rating Scale
VADT	Veterans Affairs Diabetes Trial

Consumer Preface

This section is written in collaboration with consumer representatives in the guideline development group.

Deprescribing is a systematic process of tapering, stopping, discontinuing, or withdrawing one or more medicines that are considered inappropriate or no longer beneficial to improve outcomes. This deprescribing guideline was developed in response to the growing need to provide guidance for optimising medication regimens in older people to reduce adverse outcomes and their treatment burden. It represents a collaborative partnership between consumers, carers, healthcare professionals, and researchers.

This guideline is not a strict mandate; rather, it serves as a resource to assist clinical decision-making in partnership with individuals, their families, and carers. We believe that open dialogue and transparent decision-making between healthcare professionals and individuals is essential. Healthcare professionals must place individuals at the centre of their care, adopting a holistic, whole-person perspective that honours each individual's unique journey.

The decision to deprescribe a medicine or a few medications is multifaceted, shaped by an interplay of clinical, psychological, sociodemographic, financial, and physiological factors – each of which may hold varying significance for different individuals. Emotional considerations, in particular, play a vital role for older people as they make treatment choices. Thoughtful attention to how culture, values, and preferences influence clinical contexts can ensure that older people feel valued, respected, and dignified, ultimately enhancing their healthcare experience.

At its core, deprescribing is a choice that must resonate with the values and preferences of the individual taking the medicine, alongside those of their caregivers and family members. The goals of care for the individual should be considered in the prescribing and deprescribing process. Every healthcare decision – whether it involves initiating, continuing, altering, or discontinuing treatment – necessitates informed consent from the individual or their substitute decision-maker. To facilitate a truly informed decision, adequate information must be consistently provided, especially regarding regular medicines, where the balance of risks, benefits, and alternative options may evolve over time.

As you engage with this guideline, remember the profound significance of centring individuals, their carers, and loved ones in decision-making. These are the people who best understand their personal circumstances, goals, and preferences, and whose lives will be directly impacted by any decisions.

We hope this guideline will serve as a valuable resource in your clinical practice, supporting informed, compassionate, and shared decision-making that truly prioritises the best interests of those you care for.

Plain Language Summary

Deprescribing is a process of reducing or stopping medicine(s) when they may no longer be necessary or when the potential risks of continuing the medicine outweigh the potential benefits.

The purpose of taking medicine is to treat or prevent illnesses or slow the progression of disease. However, a medicine that brings benefits also has the potential to cause unwanted or harmful effects. The decision to prescribe medicine involves weighing up the potential benefits for the person against the likelihood and potential severity of side effects. It requires a comprehensive understanding of the individual's life stage, medical history, current health (including other diagnoses), prognosis, the nature of the condition, and the characteristics of the available medicines. Prescribing should be a collaborative process that involves open communication between the healthcare professional and the expectations and preferences of the individual, their families, and/or carers. Similarly, deprescribing requires a thoughtful and structured approach, ensuring alignment with person-centred care principles.

Deprescribing is an important component of rational prescribing, aimed at optimising medication regimens to ensure quality use of medicines. Deprescribing involves ongoing monitoring for benefits, harmful effects, and adverse outcomes in collaboration with the individual and their support person(s). The essence of deprescribing is to acknowledge that a person's body (physiology), treatment preferences, and goals may change over time. To deprescribe is to simplify the medication regimen and to reduce potential risks associated with individual and combinations of medicines.

Deprescribing is a person-centred approach that includes identifying the priorities of both the individual and the healthcare provider in relation to the treatment plan, promoting shared decision-making, determining agreed actions, communicating actions, and regular monitoring. The decision to deprescribe should be a team effort between the healthcare provider and the individual, their families or carers, with the focus on finding the most suitable solution that reflects an individual's goals, values, and preferences, considering the available research evidence, cost-effectiveness, and value-based care.

Through a person-centred approach to deprescribing, previously unrecognised health priorities and concerns may emerge. In some cases, this process may lead to the initiation of new medicines that offer potential benefits while discontinuing others that are no longer necessary.

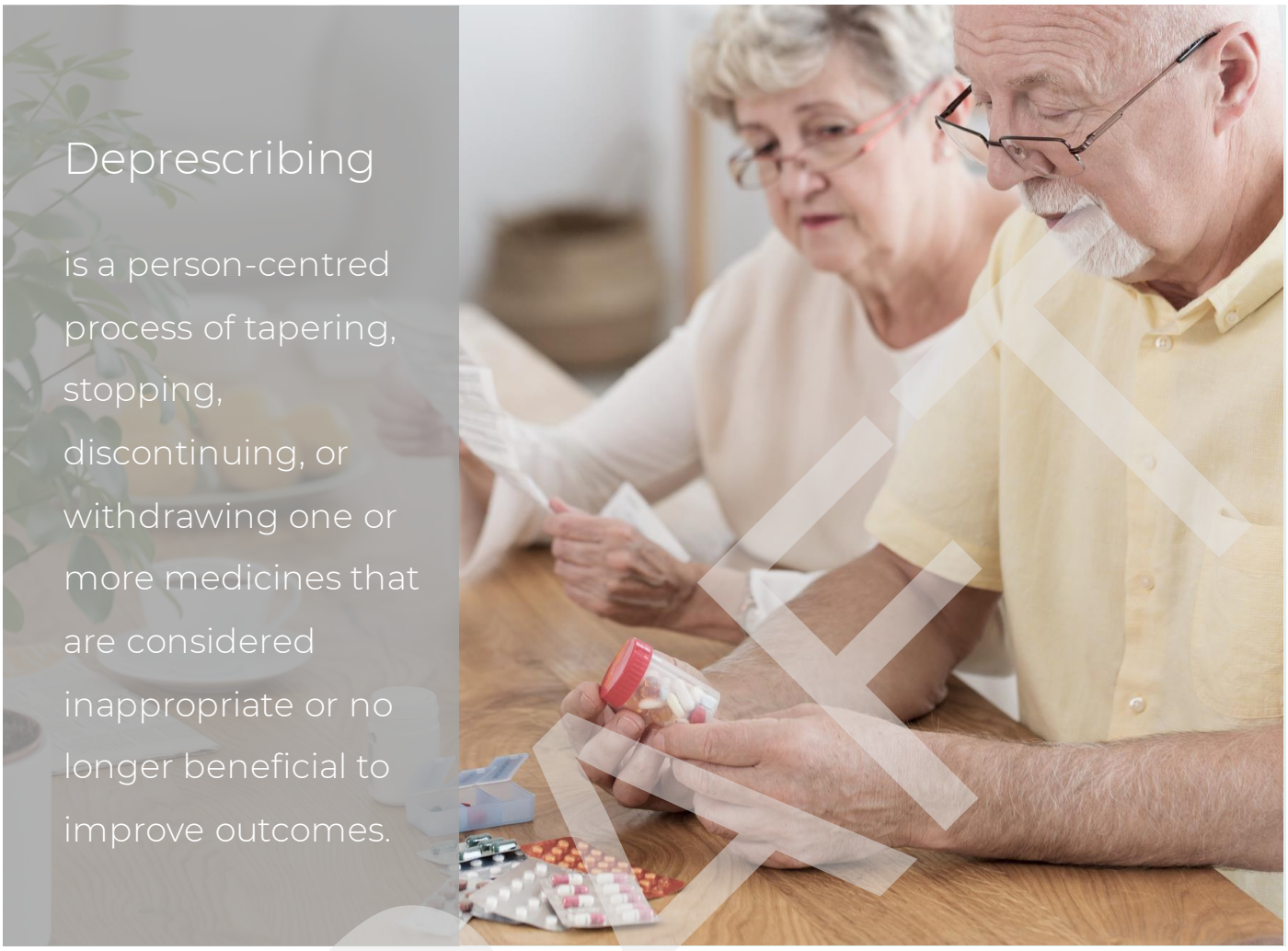
Older people are more likely than younger people to benefit from deprescribing as they may be more vulnerable to the risks associated with the use of multiple medicines due to age-related changes in organ function. These risks are further exacerbated by inadequate monitoring and a lack of ongoing, coordinated assessment of medicines, often prescribed by multiple healthcare practitioners.

However, deprescribing in practice is challenging. The purpose of this clinical practice guideline is to assist healthcare providers, especially medical practitioners, nurse practitioners, pharmacists, and other non-medical prescribers such as dental practitioners, podiatrists, and optometrists in the shared decision-making for deprescribing. Specifically, this guideline aims to provide a summary of recommendations for when, how and for whom deprescribing may be considered and offered with a shared decision-making process involving individuals, their family members, carers, or support persons to ensure decisions align with individual health goals, values, and preferences. Additionally, this guideline aims to identify monitoring requirements during the deprescribing process and address ongoing treatment needs as applicable. The recommendations and statements provided in this guideline are intended as guidance to be applied using a shared decision-making approach and are *not* prescriptive.

This guideline is applicable in the various settings where deprescribing decisions may be made, including primary care, hospital and residential care. It covers drug classes commonly dispensed to people aged 65 years and over, and less commonly used drug classes where there is evidence to inform deprescribing in people aged over 65 years (e.g. potassium, digoxin, nitrates, genito-urinary anticholinergics, teriparatide, bisphosphonates, levodopa, lithium, and cholinesterase inhibitors).

Healthcare professionals must actively involve individuals in shared decision-making that considers their values, preferences and treatment goals. This guideline is not a substitute for disease-specific therapeutic guidelines or non-pharmacological management resources.

Executive Summary



Introduction

Medicines play a critical role in preventing illness, managing chronic conditions, curing disease, and offering symptomatic relief that can significantly improve a person's functional capacity and quality of life. However, all medicines have the potential to cause harm. The use of a medicine is typically a trade-off between benefits and risks. Evidence suggests that an increasing number of medicines was associated with an increased risk of medicine-related harm [3].

Existing clinical practice guidelines are largely single-disease-focused and do not reflect the reality of multimorbidity (defined as the presence of two or more chronic health conditions) in practice [4]. The management of multimorbidity is often complex. Strictly following all the recommendations in current single-disease guidelines without incorporating individual preferences and circumstances can result in an overwhelming treatment burden for older people with multimorbidity [5].

For people with chronic diseases, the assessment of the benefits and risks of medicines is likely to evolve throughout their disease journey depending on their treatment experience, clinical situation, and changing needs [6]. As such, appropriate monitoring is essential as a medicine that was once beneficial may become less suitable over time. These medicines are referred to as potentially inappropriate medicines (PIMs) which are medicines where the risk of harm outweighs the benefits, that are used instead of a safer and more effective alternative or are used without an existing evidence-based indication [7, 8]. The use of PIMs is highly prevalent among older people worldwide [9, 10]. Multimorbidity and concurrent use of multiple medicines were associated with the high prevalence of PIM use [9, 11]. The use of PIMs in older people leads to negative health outcomes, including adverse drug events [12], hospitalisations [12, 13], and high healthcare expenses [14]. Among older people with dementia, the use of PIMs significantly

increased the risk of falls and fall-related injuries [15].

Deprescribing acknowledges that the need for medicines is dynamic as an individual's circumstances may evolve with time. It is a systematic process to optimise an individual's medication regimens with the ultimate goal of reducing harm as well as improving outcomes and quality of life [16]. Prescribing and deprescribing are two interconnected aspects of medicine management. While prescribing involves initiating medicines and deprescribing involves discontinuing or reducing the dose of a medicine, both are intended to improve health outcomes. Rational prescribing emphasises the continuous monitoring of treatment for efficacy and adverse outcomes.

Interprofessional collaboration

For optimal patient care and to ensure continuity of care, all healthcare providers involved in a patient's care must collaborate and align their treatment plans [17]. Any modifications to a person's medication regimen (whether prescribing or deprescribing) should be communicated to other healthcare providers involved in a patient's care with sufficient information to enable other healthcare providers to deliver the best possible care to their mutual patient.
Prescribers should also document any discussions held with other healthcare providers regarding the prescribing and deprescribing process. This includes recording the rationale for changes, the agreed-upon approach for medicine withdrawal (e.g. dose tapering, order of withdrawal), and the monitoring plan. Collaboration and communication with all prescribers help to maintain a unified, person-centred approach and avoid medication misadventures.

Person-centred care

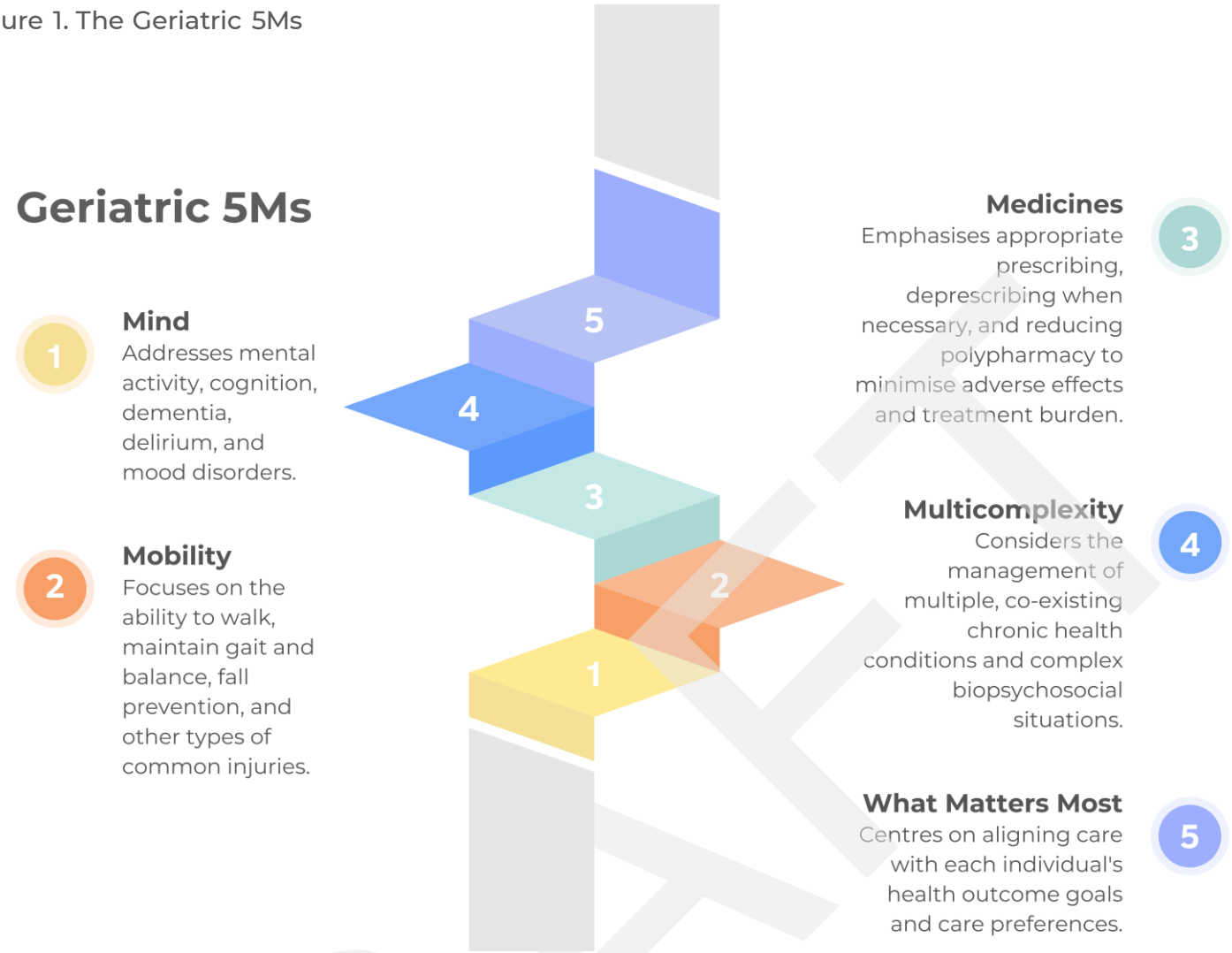
A critical attribute of deprescribing is person-centred care [18]. Person-centred care involves meeting the multidimensional needs and preferences of older people dependent on care, by considering the needs, goals, and abilities of the person, their carers as well as their families [19-21]. In the context of deprescribing, person-centred care must take into account an individual's goals, values, and preferences along with research evidence, cost-effectiveness, and value-based care in the decision-making process [22]. For older people who are receiving care from family members and/or formal or informal carers, the views and preferences of their families and/or carers are a part of the key aspects of person-centred care. The implementation of person-centred care can help to identify and contribute to meeting the needs of the family and/or carers of older people [23].

Values and preferences may differ substantially among people. Therefore, the decision to deprescribe should be personalised. Deprescribing should be a shared, collaborative decision-making process between individuals and healthcare providers involving the following steps [24]:

1. Creating awareness that options exist, and a decision can be made
2. Discussing the options and their potential benefits and harms
3. Exploring preferences for (attributes of) different options
4. Making the decision together with the person, their families, and/or carers

The decision to deprescribe appeared to be influenced by communication skills (e.g. risk, uncertainty, prognosis communication) [25, 26], the perceived experience of the healthcare provider [27], and a trusting relationship between the individual and the healthcare provider [26]. Treatment plans, including decisions to deprescribe, should be revisited periodically to adapt to the individual's changing needs and preferences [24]. The process should emphasise open communication, respect for the individual's autonomy, and shared responsibility in decision-making.

Figure 1. The Geriatric 5Ms



The Geriatric 5Ms is a framework to optimise the care for older people, focusing on five key domains. This framework [28] aligns well with deprescribing efforts, emphasising a holistic approach to managing medicines while considering broader aspects.

Through a person-centred approach to deprescribing, previously unrecognised health priorities and concerns may emerge. In some cases, this process may lead to the initiation of new medicines that offer potential benefits while discontinuing others that are no longer necessary.

Deprescribing competencies

The prescribing competencies framework currently exists, which describes the competencies required for healthcare professionals to prescribe medicines judiciously, appropriately, safely, and effectively [29]. Reviewing the outcomes of treatment is one of the key prescribing competency areas which includes stopping or modifying existing medicines and other treatments where appropriate. In addition to healthcare professionals often expressing low confidence and self-efficacy for deprescribing [30, 31], there is a lack of focus on teaching and assessing deprescribing skills within healthcare curricula in many countries [32]. To address these barriers, specific competencies required for deprescribing are now being proposed as part of the essential curriculum for pre-registration healthcare professionals in their entry-to-practice degree programs [1]. Deprescribing has been described as a key competency in medicine, dentistry, nursing, and pharmacy, that is viewed to be inextricably linked to prescribing to achieve high-quality healthcare. Farrell et al proposed the following seven deprescribing competencies to be applied by healthcare professionals in collaboration with individuals, their families, and/or carers within an interprofessional care team (see below).

Each of the seven competencies was expanded in detail in the paper, with descriptions of the knowledge and skills required to meet each competency [1]. Integrating this deprescribing competency framework into the education of other allied healthcare professionals (e.g. physiotherapists, occupational therapists, dietitians, speech-language pathologists, social workers) is also valuable as they play crucial roles in the holistic care of older people. Allied healthcare professionals can identify situations where deprescribing of a particular medicine may be considered [1].

Deprescribing competencies adapted from Farrell et al, 2023 [1]:

1. Conduct a comprehensive medicine history and health condition information (including prognosis and life stage) as well as understand the reason for medicine use and the expectations of the individual, their carers and/or families, their beliefs, values, goals of care and perspectives regarding medicine use and medical conditions

2. Interpret relevant information in the context of desired therapeutic outcomes and goals of care according to the individual, their families, and/or carers

3. Identify medicines without an indication (condition resolved or unconfirmed), with low or no efficacy, may have more harm than benefits, or are otherwise potentially inappropriate

4. Assess the deprescribing potential of each medicine by weighing the benefits and harms of continuation versus discontinuation of each medicine

5. Decide whether deprescribing a medicine is appropriate using shared decision-making with individuals, their families, and/or carers, and the healthcare team (e.g. explore their preferences, socio-demographic backgrounds, capacity in making informed medicine decisions such as health literacy, expectations for medicines, debunk misconceptions and/or explain why medicines may no longer be needed)

6. Design, document, and share a deprescribing and monitoring plan for deprescribing (including rationale and process) with an interprofessional care team, individuals, their families and/or carers (lay language) as appropriate

7. Monitor progress and provide support to individuals (including rounds of reviewing or making continuous adjustments to the treatment plan as needed)

In practice

Deprescribing in practice is challenging as it involves complex considerations in a fast-paced environment (some settings may be resource-poor), taking a person-centred approach that understands the individual's preferences in a particular situation, and coordinating care with multiple prescribers [33]. Drug class-specific deprescribing guidelines and algorithms are available to guide the process such as those developed by Primary Health Tasmania and New South Wales Therapeutic Advisory Group in Australia as well as the Bruyère Research Institute in Canada [34-36]. Evidence-based deprescribing clinical practice guidelines developed using a rigorous process exist for a number of drug classes, including cholinesterase inhibitors and memantine [37], opioid analgesics [38], benzodiazepine receptor agonists [39], proton-pump inhibitors [40], diabetes medicines [41], and antipsychotics [42]. Expert guidance on deprescribing antidepressants, benzodiazepines, gabapentinoids, and Z-drugs is also available [43].

Medicine management is often complex, with barriers existing for both prescribing and deprescribing. A key challenge in practice is the absence of robust evidence to guide decision-making, such as the lack of evidence in the management of gout and rheumatoid arthritis. Additionally, barriers specific to the application of deprescribing guidelines in clinical practice include time constraints and competing priorities during a consultation [44]. When a person is prescribed multiple medicines, it becomes increasingly challenging for healthcare providers to approach deprescribing, as existing drug-specific guidelines may lack guidance on how to manage the deprescribing of multiple medicines holistically. The complexity of discussing and implementing deprescribing for people with multiple morbidities and an increased risk of poor communication between parties involved in an individual's care have been cited in the literature [45]. When prescribing is directly influenced by individual requests for specific medicines, the resulting resistance or refusal to deprescribe medicines may also be a barrier to medicine cessation [46]. In addition, people may feel uneasy about deprescribing medicines prescribed by another healthcare professional, which may be a kind of loyalty to this person [47]. Similarly, physicians may be reluctant to deprescribe medicines prescribed by another healthcare professional or specialist due to concerns about undermining another practitioner's treatment plan [48]. For healthcare professionals, there are major concerns arising from deprescribing about undertreatment, underdosing, and not complying with the recommendations from existing treatment guidelines, particularly in the absence of clear and consistent high-quality evidence for deprescribing [49].

What does this guideline aim to achieve?

The overarching goal of this guideline is to bridge the gap from research to practice by translating research evidence into recommendations that are actionable, acceptable, feasible, and implementable in care practice for older people. Clinical practice guidelines for deprescribing exist for key drug classes. Our goal is to provide broad guidance for deprescribing medicines, that complements more detailed drug-specific deprescribing guidance, disease-specific therapeutic guidelines, and non-pharmacological management resources. The current guideline aims to provide a summary of recommendations for when, how, and for whom deprescribing may be considered and offered, with a shared decision-making process involving individuals, their family members, carers, or support persons to ensure decisions align with individual health goals, values, and preferences. Additionally, since deprescribing is not without risks, this guideline aims to identify monitoring requirements during the deprescribing process and address ongoing treatment needs as applicable. Although this guideline has been developed with a focus on medicines commonly used by people aged 65 and older in Australia, the guideline draws on evidence from studies conducted globally. We anticipate that this guideline will have international relevance. However, variations in medicine availability, regulatory frameworks and clinical practices may necessitate adaptations to align with country-specific treatment guidelines.

How to use this guideline?

Figure 2. How to use this guideline?

For section information, refer to "Guideline structure".

Summary of Recommendations

Summary of recommendations will be included upon finalisation of the guideline.

Introduction

Background

On 30 June 2020, one in six (approximately 4.2 million) Australians were aged 65 and over [50]. At least 250,000 hospital admissions in Australia annually are medicine-related, with the majority involving older people [51]. Two-thirds of these unplanned hospital admissions are potentially preventable [51]. The use of multiple concurrent medicines is especially prevalent among older people and is commonly referred to as polypharmacy [52]. Polypharmacy affects almost one million older Australians, and the number of people affected increased by 52% from 2006 to 2017 [53]. While some medicines are clinically indicated, polypharmacy in older people is associated with an increased risk of hospitalisations, functional impairment, geriatric syndromes (including confusion, falls, incontinence, frailty) and mortality [54]. Paradoxically, polypharmacy is also associated with under-prescribing, where people may not receive indicated medications for treating or preventing a condition due to concerns about further complicating their regimen [55].

Medicine safety is a health priority for Australia's ageing population. Medicine use in older people is a fine balance of managing the underlying symptoms or risks in accord with the older person's preferences, while at the same time, minimising drug-related problems through monitoring, reducing pill burden and avoiding unnecessary medicine use. Older people are at an increased risk of adverse drug events and harm arising from potentially inappropriate medicine use and adverse drug interactions [56-60]. Adverse drug events are defined as any injuries resulting from medical intervention related to a drug [61] which includes physical harm, mental harm, or loss of function. The incidence of adverse drug events increases with the number of medicines used [62]. Adverse drug events are frequently under-recognised and can be mistaken for symptoms requiring further treatment, which leads to inappropriate prescribing cascades or may be simply dismissed as an unavoidable consequence of ageing.

The reasons why older people are at an increased risk of medicine-related harm are multifactorial and include factors such as drug-drug interactions, prescribing cascades, frailty, physiological changes, and multimorbidity [63, 64]. The balance of benefits and risks associated with medicines shifts as people age, particularly in the management of chronic diseases. In these cases, deprescribing can play a crucial role in optimising care. Deprescribing is a person-centred process of withdrawing medicines that are either no longer required or where the risk of harm outweighs the risk of benefit, with the ultimate goal of improving quality of life [18]. It involves carefully evaluating whether the ongoing use of certain medicines continues to offer more benefits than risks, particularly as an individual's circumstances change. A medicine clinically indicated for an individual's condition at a specific point in time may not be appropriate or necessary in the future. As such, ongoing monitoring is important to adapt health management strategies based on their changing needs, goals, preferences, or priorities over time. Deprescribing provides an opportunity for medication reconciliation and optimising medication regimens to ensure the medicines are prescribed based on the best available evidence and aligned with the individual's goals, on the proposition that the person is likely to derive more benefit than harm.

Deprescribing is an intervention that is acceptable to older people, with over 90% of older people across a range of settings stating that they would like to stop one of their medicines if their doctor said it was possible [65]. However, deprescribing in clinical practice is a challenging process [63], and health professionals consistently cite the lack of synthesised evidence or guidance as a barrier to deprescribing [66]. Deprescribing is not a decision made in isolation but requires careful consideration of various individual factors, including overall health, quality of life, goals, preferences, affordability, pill burden, health literacy, and adherence to the current medication regimen [63]. Existing resources that support health professionals in identifying potential target medicines for deprescribing include lists of high-risk medicines and

decision aids [67]. Lists that identify high-risk medicines in older people can prompt prescribers to re-consider these potentially high-risk medicines. These lists do not require specialist in-depth knowledge; however, they are general in nature and do not provide specific advice or information on how to withdraw identified medicines in an individual and how to monitor the process of medicine withdrawal [67]. Most of these lists also do not suggest safer alternative treatments or therapies.

Purpose

The current clinical practice guideline ('guideline') aims to provide a resource for healthcare providers to guide the deprescribing of commonly encountered medicines in routine clinical care. It provides information to support healthcare providers in determining whether deprescribing is appropriate for specific drug classes as well as including overarching information for deprescribing in the context of polypharmacy or multiple drug classes. The target audience for the guideline is health practitioners involved in the care of older people (≥ 65 years), particularly medical practitioners, nurse practitioners, pharmacists, and other non-medical prescribers such as dental practitioners, podiatrists, and optometrists. All of whom may be involved in the shared decision-making for deprescribing. This guideline is applicable in the various settings where deprescribing decisions may be made including primary care, hospitals, and residential care. It is intended as a practical guidance to help prescribers decide with the individual which regular medicines can be considered for deprescribing. It provides a summary of recommendations for when, how and for whom deprescribing may be considered and offered, with a shared decision-making process involving individuals, their family members, carers, or support persons to ensure decisions align with individual health goals, values, and preferences. Additionally, this guideline aims to identify monitoring requirements during the deprescribing process and address ongoing treatment needs as applicable.

Scope

This guideline is for deprescribing in older people. While these recommendations are intended for this population, the guideline development team accepted that some guidance may also be applicable to people under 65 years of age. Furthermore, chronological age does not necessarily reflect an individual's health status. The evidence informing the review is for people over the age of 65, and cautious clinical judgement is required in applying the guidance to younger people.

This guideline does not address all medicines available in the market. It is intended to focus on the top 100 commonly dispensed medicines in the Australian Pharmaceutical Benefits Scheme (PBS) for people over 65 years. The guideline development group reviewed and considered the inclusion of less commonly used medicines (not part of the top 100) where evidence for deprescribing is identified in the literature search. Additionally, depending on the available evidence, this guideline may not address all medicines in the same drug class as the common PBS medicines. A limitation of using the PBS data to estimate common medicines is the data does not include medicines available without a prescription, such as over-the-counter and complementary medicines, or medicines dispensed on private prescriptions.

The guideline includes medicines prescribed for regular use and excludes medicines prescribed for short-term, intermittent, as-required, or acute use only (e.g. systemic or topical antibiotics). Where recommendations involve tapering a dose, healthcare professionals are advised to consult relevant resources and available medicine information to determine the most appropriate method for dose adjustment based on the medicine, its formulation, and person-specific factors. This guideline is not intended to be used as a substitute for disease-specific therapeutic guidelines and evidence-based resources related to non-pharmacological strategies for the management of a medical condition.

Under-prescribing is another important aspect of medicine management which occurs when a clinically indicated medicine is not being prescribed for a person. This guideline does not consider appropriate medicines that are not present, or omissions as this is beyond the scope of this guideline. It is likely that, in some cases, clinically indicated medicines may be identified during the deprescribing process. The information provided in this guideline should be considered in the context of an individual's circumstances (including health and financial status), life experience, goals and expectations as well as cultural and personal values and beliefs.

Guideline structure

There are two main parts to this guideline. The first section "Polypharmacy/Multiple Drug Classes" can be viewed as the general principles for deprescribing. This section includes evidence on deprescribing without specifically targeting specific drug classes which includes studies targeting polypharmacy, three or more drug classes, or medicines with a certain pharmacological action covering multiple drug classes. Subsequent sections are organised by specific drug classes. Within each section, individual medicines or drug classes are discussed.

Deprescribing is inherently intertwined with and an essential part of good prescribing practice. In each specific drug class section of this guideline, a brief review of relevant guidance for the appropriate use and continuation of medicines is provided. This review is **not** based on a systematic literature review but incorporates evidence from a non-systematic review of sources including clinical practice guidelines, position statements, and expert consensus documents.

Further details on the recommendation types can be found in the Methodology section. The Summary of Recommendations provides a brief overview, serving as a quick reference to support clinical decision-making. For more information on the evidence review process, refer to the individual drug class sections in the appendices of the Technical Report. The Technical Report documents the methodology, evidence synthesis, and decision-making framework behind the recommendations, including considerations of benefit-risk balance, values and preferences, resource implications, acceptability, and feasibility.

Methodology

This clinical practice guideline follows the National Health and Medical Research Council (NHMRC) Guideline Development Methodology and the Appraisal of Guidelines for Research & Evaluation (AGREE) II Instrument and User's Manual [68, 69]. The process for the development of this clinical practice guideline can be found in the Technical Report. Briefly, a systematic literature review was conducted for existing evidence on the benefits and harms of deprescribing as part of the guideline search strategy and the evidence identified was graded according to an NHMRC-approved method (i.e. GRADE framework).

This guideline targeted the top 100 dispensed medicines on the Australian PBS for people aged over 65 years, both by prescription dispensing volume and by the number of unique persons dispensed in 2023 (Table 1). The volume-based refers to the total number of dispensing in a calendar year, while the person-based metric refers to the number of people who received the medicine in a calendar year. The latter approach accounts for medicines that may be prescribed to a large number of individuals despite having lower dispensing frequencies due to less frequent dosing (e.g. denosumab typically administered once every six months). Additionally, we also included less commonly used drug classes where there is evidence to inform deprescribing in people aged over 65 years (e.g. potassium, digoxin, nitrates, genito-urinary anticholinergics, teriparatide, bisphosphonates, levodopa, lithium, and cholinesterase inhibitors).

Depending on the available evidence, this guideline may not address all medicines in the same drug class as the common PBS medicines. A limitation of using the PBS data to estimate common medicines is the data does not include medicines available without a prescription, such as over-the-counter and complementary medicines, or medicines dispensed on private prescriptions.

For further information, refer to the Scope section in this guideline.

Table 1. Top 100 medicines dispensed under the Australian Pharmaceutical Benefits Scheme for people aged over 65 years (based on dispensing volume and the number of unique recipients in 2023), categorised according to the World Health Organisation Anatomical Therapeutic Chemical (ATC) Classification System [70]

ATC therapeutic class first level	ATC therapeutic class 2nd/3rd/4th level	**Top 100 dispensed** PBS medicines/ combination products*
ALIMENTARY TRACT AND METABOLISM (A)	Proton-pump inhibitors (A02BC)	Esomeprazole Omeprazole Pantoprazole Rabeprazole
	Other antiemetics (A04AD)	Prochlorperazine# (PBS classification)
	Osmotically acting laxatives (A06AD)	Macrogol laxatives
	Drugs used in diabetes (A10)	Dapagliflozin Empagliflozin Empagliflozin + metformin Gliclazide Insulin glargine# Linagliptin Metformin Semaglutide Sitagliptin Sitagliptin + metformin
BLOOD AND BLOOD FORMING ORGANS (B)	Antithrombotic agents (B01A)	Apixaban Clopidogrel Rivaroxaban Warfarin
	Anti-anaemic preparations (B03)	Ferric carboxymaltose# Hydroxocobalamin#
CARDIOVASCULAR SYSTEM (C)	Digitalis glycosides (C01AA)	Digoxin#
	Organic nitrates (C01D)	Glyceryl trinitrate# Isosorbide mononitrate
	Antiadrenergic agents, centrally acting (C02A)	Moxonidine
	Antiadrenergic agents, peripherally acting (C02C)	Prazosin
	Diuretics (C03)	Furosemide Spironolactone
	Beta-blocking agents (C07)	Atenolol Bisoprolol Metoprolol tartrate Nebivolol Sotalol
	Calcium channel blockers (C08)	Amlodipine Diltiazem Felodipine Lercanidipine Verapamil

ATC therapeutic class first level	ATC therapeutic class 2nd/3rd/4th level	**Top 100 dispensed** PBS medicines/ combination products*
CARDIOVASCULAR SYSTEM (C)	Agents acting on the renin-angiotensin system (C09)	Amlodipine + valsartan + hydrochlorothiazide Amlodipine + valsartan Amlodipine + atorvastatin Candesartan Candesartan + hydrochlorothiazide Irbesartan Irbesartan + hydrochlorothiazide Olmesartan Perindopril Perindopril + indapamide Perindopril + amlodipine Ramipril Sacubitril + valsartan Telmisartan Telmisartan + hydrochlorothiazide Telmisartan + amlodipine
	Lipid-modifying agents (C10)	Atorvastatin Atorvastatin + amlodipine Ezetimibe Ezetimibe + atorvastatin Ezetimibe + rosuvastatin Ezetimibe + simvastatin Fenofibrate Pravastatin Rosuvastatin Simvastatin
DERMATOLOGICALS (D)	Corticosteroids, plain (D07A)	Betamethasone dipropionate Methylprednisolone# Mometasone# Triamcinolone#
GENITO URINARY SYSTEM AND SEX HORMONES (G)	Estrogens (G03C)	Estradiol Estriol#
	Drugs used in benign prostatic hypertrophy (G04C)	Dutasteride + tamsulosin
SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS (H)	Glucocorticoids (H02AB)	Prednisolone Prednisone#
	Thyroid hormones (H03AA)	Levothyroxine
MUSCULOSKELETAL SYSTEM (M)	Anti-inflammatory and antirheumatic products, non-steroids (M01A)	Celecoxib Meloxicam
	Antigout preparations (M04A)	Allopurinol Colchicine#
	Drugs affecting bone structure and mineralisation (M05B)	Denosumab Risedronate

ATC therapeutic class first level	ATC therapeutic class 2nd/3rd/4th level	**Top 100 dispensed** PBS medicines/ combination products*
NERVOUS SYSTEM (N)	Analgesics (N02)	Buprenorphine Oxycodone Oxycodone + naloxone Paracetamol + codeine Tapentadol Tramadol Paracetamol Pregabalin
	Dopaminergic agents (N04B)	Levodopa + carbidopa
	Anxiolytics (N05B)	Diazepam
	Hypnotics and sedatives (N05C)	Temazepam
	Antidepressants (N06A)	Amitriptyline Citalopram Desvenlafaxine Duloxetine Escitalopram Mirtazapine Sertraline Venlafaxine
	Anti-dementia drugs (N06D)	Donepezil
RESPIRATORY SYSTEM (R)	Drugs for chronic obstructive airway diseases (R03)	Budesonide + formoterol Fluticasone furoate + umeclidinium + vilanterol Fluticasone propionate + salmeterol Tiotropium
SENSORY ORGANS (S)	Corticosteroids, plain (S01BA)	Dexamethasone# Fluorometholone#
	Antiglaucoma preparations and miotics (S01E)	Latanoprost Bimatoprost + timolol
	Other ophthalmologicals (S01X)	Liquid paraffin + glycerol + tyloxapol + poloxamer-188 + trometamol hydrochloride + trometamol + cetalkonium chloride

Medicines intended for short-term, intermittent, as required, or acute use only (e.g. systemic or topical antibacterial, salbutamol) are not within the scope of this guideline. Common medicines are defined based on the Pharmaceutical Benefits Scheme (PBS) prescription dispensing volume unless otherwise stated. Plain products refer to products containing only one active ingredient.
 # Common PBS medicines are defined by the number of unique persons dispensed in a calendar year.

Presenting evidence and certainty of evidence

A Summary of Findings (SoF) table was prepared for each drug class and included in the main guideline to provide key information underlying a recommendation [71]. The SoF tables serve as a concise and accessible summary for each of the included outcomes along with the final rating for certainty of evidence.

Effect measures were reported as odds ratios (OR) for dichotomous data and mean differences (MD) for continuous data, each accompanied by 95% confidence intervals (CI). An OR of less than 1 favoured the deprescribing group, while an OR greater than 1 favoured the control group. For continuous data, when reverse scales were used (where higher values represented better outcomes), the outcome values were multiplied by -1 to ensure consistent directional reporting across all measures in the meta-analysis. An MD of less than zero favoured the deprescribing group, whereas an MD greater than 0 favoured the control group.

For single-arm studies, unless otherwise stated, effect measures were reported as the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values (if stated in the study).

For each outcome, there are four possible ratings which were high, moderate, low, or very low shown in Table 2.

Table 2. GRADE certainty of evidence ratings

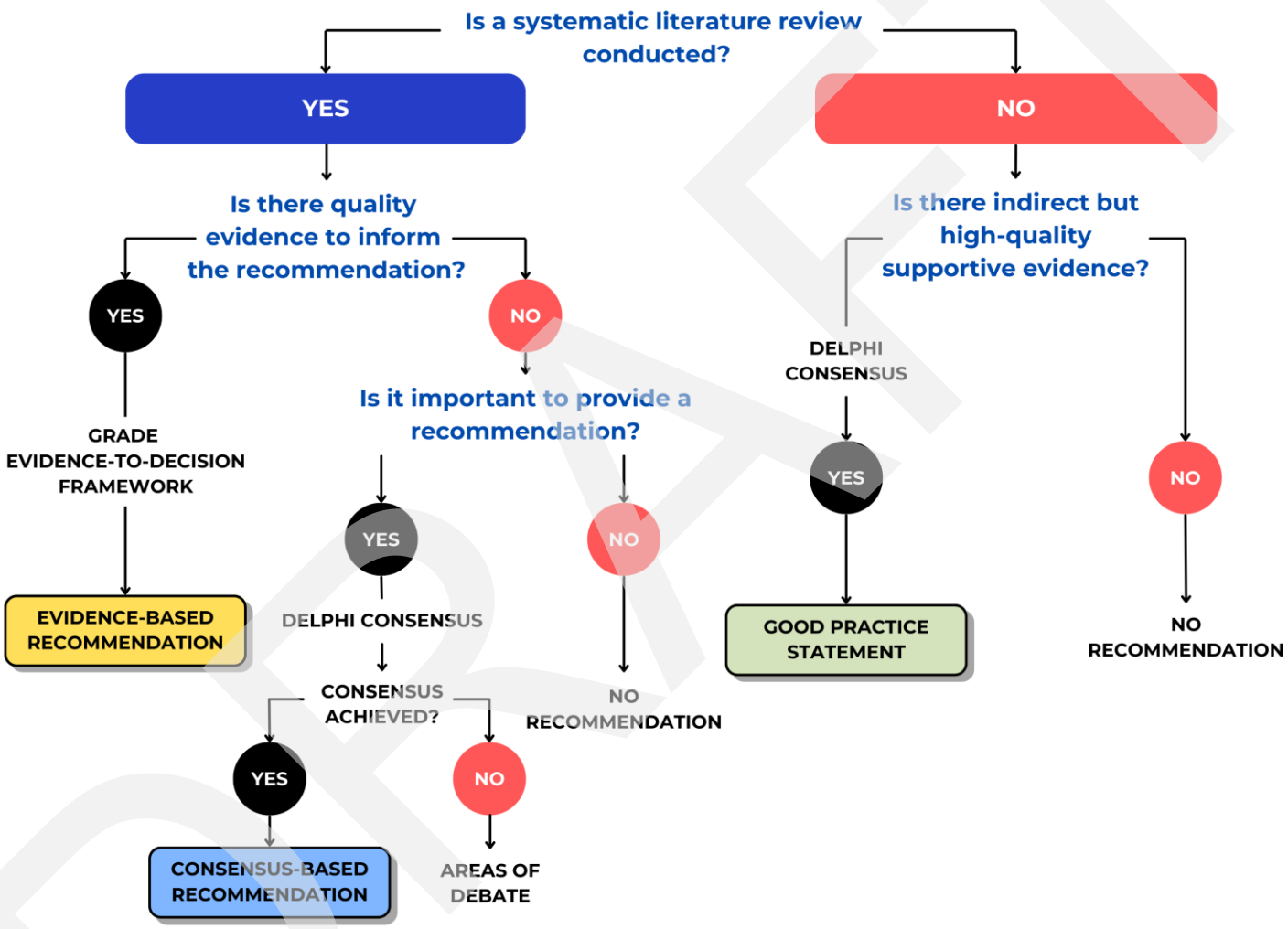
GRADE ratings		Definitions
High		We are very confident that the true effect is close to the estimated effect.
Moderate		We are moderately confident in the estimated effect. The true effect is probably close to the estimated effect, but there is a possibility that it is substantially different.
Low		We have limited confidence in the estimated effect. The true effect may be substantially different from the estimated effect.
Very low		We have very little confidence in the estimated effect. The true effect is likely to be substantially different from the estimated effect.

Types of recommendations

Each recommendation was classified as one of three possible types: evidence-based recommendation (EBR), consensus-based recommendation (CBR), or good practice statements (GPS). The section below and Figure 3 provide further details to differentiate the three types of recommendations.

In this guideline, no recommendations are classified as EBRs due to the lack of high or moderate quality evidence on which to base a recommendation. The consensus process for CBRs and GPS followed a Delphi method and was single-blinded, with only the guideline steering committee having knowledge of the vote for each GDG member (see Technical Report).

Figure 3. Types of guideline recommendations



Evidence-based recommendation (EBR)

If sufficient quality evidence is available to support the recommendations, they are classified as EBRs. These EBRs are assigned a rating and strength based on the GRADE framework (see Table 2 & Table 3) and worded to indicate the direction of the recommendation – either for or against deprescribing [72]. Strong EBRs are based on high or moderate quality evidence generally, implying that the implementation of deprescribing is strongly recommended by most if not all people. However, it is important to note that the strength of a recommendation is not based solely on the certainty of the evidence, but also dependent on other important GRADE elements listed above (balance and trade-off, values and preferences, resources, acceptability, and feasibility). Recommendations are more likely to be conditional rather than strong when:

1. the certainty of the evidence is low;
2. there is a close balance between desirable and undesirable effects; or
3. there is substantial variability in individual circumstances, values and preferences [73].

The wording "we recommend…" was used to represent a strong evidence-based recommendation. For conditional evidence-based recommendations, "we suggest…" was used. This was decided in accordance with the GRADE framework for clarity. This difference in wording characterises the two categories of strength for the recommendations in this guideline.

Table 3. GRADE strength of evidence-based recommendations

GRADE strength	Definitions
Strong	The guideline development group is confident that most or all people will be best served by the recommended course of action.
Conditional	The guideline development group is confident that not all people will be best served by the recommended course of action. There is a need to consider more carefully than usual the individual's circumstances, values, and preferences.

The wording "**we recommend…**" was used to represent a strong evidence-based recommendation. For conditional evidence-based recommendations, "**we suggest…**" was used. This was decided in accordance with the GRADE framework for clarity. This difference in wording characterises the two categories of strength for the recommendations in this guideline.

Consensus-based recommendation (CBR)

CBRs are developed when there is either a lack of evidence or insufficient quality of evidence for deprescribing (i.e. low or very low certainty of outcomes) on which to base a recommendation following a systematic search, but the GDG still considers it important to provide a recommendation. When drafting the CBRs, relevant evidence identified from the systematic literature review related to the benefits and harms of deprescribing was considered, along with other existing resources (e.g. Therapeutic Guidelines, Australian Medicines Handbook, clinical practice guidelines, position statements, and expert consensus documents) for deprescribing or prescribing where appropriate. The resulting recommendations using this process were ungraded and labelled as CBRs. CBRs can be given for or against deprescribing. Although the recommendations are labelled as 'consensus-based', these recommendations are developed rigorously with consideration of any available evidence following a systematic review of the literature for deprescribing. For the purpose of this guideline, the term 'consensus' was chosen for clarity of language, to distinguish these recommendations from EBRs which are guided by quality evidence. CBRs are developed following a structured Delphi consensus process.

All consensus-based recommendations were phrased as "we suggest...".

All consensus-based recommendations were phrased as "**we suggest...**".

Good practice statement (GPS)

GPS are also not graded and developed following a structured Delphi consensus process. GPS are an actionable statement developed by the GDG to support recommendations, or to guide deprescribing processes when there is indirect but high-quality supportive evidence and other criteria for GPS development are met (see Table 4). GPS are developed when the GDG deems implementing a course of action clearly doing more good than harm; while conducting a formal evidence review would not be a good use of resources.

The wording "we recommend" for strong EBRs and "we suggest" for conditional EBRs or CBRs are not used for GPS. Instead, the statement **"ungraded good practice statement"** is used in parenthesis after each GPS. This was decided to clarify that GPS are not graded and a formal evidence review was not conducted [2].

Table 4. Five criteria for developing good practice statements

Criteria	Descriptions
1	The statement is clear and actionable
2	The message is necessary regarding healthcare practice
3	The implementation of the statement is likely to result in large net positive consequences
4	The summarisation of evidence would be a poor use of the guideline panel's time
5	The rationale connecting the indirect evidence used to support the statement is clear and explicit

The statement **"ungraded good practice statement"** is used in parenthesis after each GPS. This was decided to clarify that GPS are not graded and a formal evidence review was not conducted [2].

POLYPHARMACY/ MULTIPLE DRUG CLASSES

This section includes evidence from studies that targeted:

- General polypharmacy (commonly defined as the concurrent use of five or more medicines)
- Medicines with a certain pharmacological action spanning multiple drug classes (e.g. medicines with anticholinergic and sedative properties)
- Three or more drug classes

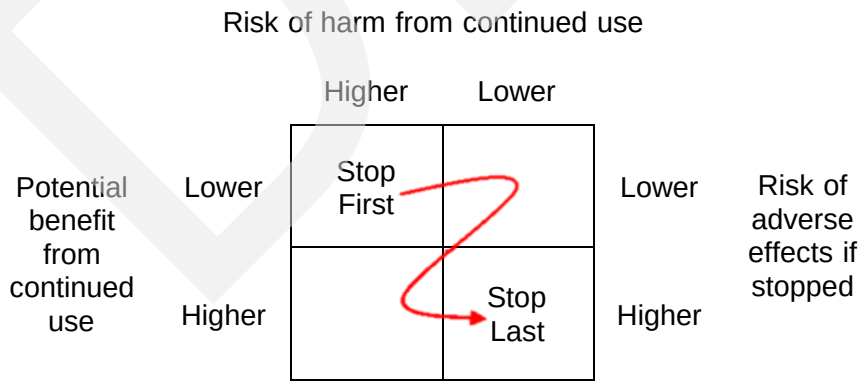
POLYPHARMACY/ MULTIPLE DRUG CLASSES

Type	Recommendation
When to deprescribe	
CBR	Given the potential clinical and economic benefits in reducing inappropriate polypharmacy, we suggest that in addition to applying a targeted approach to deprescribe specific drug classes, regular medication review is offered to older people taking multiple long-term medicines. We suggest deprescribing medicines in the following order: 1. With no clear indication, an obvious contraindication, or if there is an inappropriate prescribing cascade 2. With adverse effects or interactions that outweigh the potential benefits 3. Used for symptomatic relief, where the symptoms are resolved and unlikely to recur 4. Used for prevention, when the potential benefits are uncertain or unlikely to be realised
GPS	In the context of multimorbidity and polypharmacy, healthcare providers should refer to existing high-quality disease-specific guidelines relevant to the condition to identify medicines that may be suitable for deprescribing (ungraded good practice statement).
GPS	Deprescribing should be a preference-sensitive decision, requiring a shared decision-making approach (ungraded good practice statement).
Ongoing treatment	
CBR	We suggest continuing medicines after confirming that the pharmacotherapy is clearly indicated, the benefits of the medicine are expected to outweigh the potential harms and that this aligns with the individual's goals and preferences. In the context of multimorbidity and polypharmacy, deprescribing one medicine may necessitate a change in other pharmacotherapies due to a potential increase or reduction in risks (e.g. drug-drug or drug-disease interactions). There may be a need for a "deprescribing cascade" or prescribing of another more suitable medicine to optimise therapy.
How to deprescribe	
CBR	**Methods** When a medicine is identified as being suitable for deprescribing, we suggest developing an individualised deprescribing plan in collaboration with the person and/or their carers/family members, by referring to the specific guidance in individual drug sections in this guideline. **Broadly,** for medicines where adverse drug withdrawal events (ADWEs) or disease recurrence are likely, we suggest tapering the dose rather than abrupt cessation. For tapering,* we suggest halving the dose at two to four weeks intervals, until half of the lowest standard dose formulation is reached, then ceasing the medicine completely. However, smaller dose reductions may be appropriate (e.g. high baseline dose or high risk of symptom recurrence). We suggest switching from regular doses to *pro re nata* doses be considered if appropriate (e.g. antipsychotics). For medicines with longer half-lives, we suggest tapering may not be required. We suggest deprescribing one medicine at a time. However, up to three medicines may be deprescribed simultaneously if unlikely to cause ADWEs and practical, or if withdrawal effects can be clearly attributed to an individual medicine. If deprescribing cannot be fully implemented and/or maintained, we suggest the following options be considered and offered to the individual as appropriate: • Continue with a tapered dose and delay further dose reductions by an agreed interval for stabilisation; or • Continue with the tapered dose but forego further dose reductions; or • Restart the target medicine(s) at approximately 75% of the previously tolerated dose; or • Restart the target medicine(s) at the original dose. **When deprescribing fixed-dose combinations, if tapering of one active component is required, consider prescribing separate (i.e. free-dose) combination products.*
CBR	**Sequence of deprescribing target medicines** Once the medicines for deprescribing are agreed upon, we suggest the order of deprescribing be decided collaboratively between the individual and their prescriber.

	We suggest considering the priorities of the person, including their preference and impact on well-being, alongside the characteristics of the medicines, taking into account the balance of potential risks and benefits:* 1. Prioritising deprescribing of medicines with a high risk of harm and a low potential benefit from continued use 2. Next, deprescribing medicines with a low risk of harm from continued use and a low risk of adverse effects if ceased 3. Next, deprescribing medicines with both a high risk of harm and a high potential benefit from continued use; and 4. Finally, deprescribing medicines with a low risk of harm from continued use and a high risk of adverse effects if ceased **See Figure 4. Prioritisation matrix for deprescribing*
GPS	With informed consent from the individual or their substitute decision-maker, prescribers should provide written prescribing and deprescribing plans to relevant healthcare providers involved in the person's care (ungraded good practice statement).
GPS	Prescribers should document informed consent, the rationale for prescribing or deprescribing, and, if applicable, the dose tapering schedule, order of withdrawal, and monitoring plan (ungraded good practice statement).
Monitoring	
CBR	In general, we suggest closely monitoring for ADWEs and any health-related outcomes (e.g. physical/ psychological changes) every two weeks following each dose adjustment until at least four weeks after the medicine is fully discontinued. After this initial period, we suggest monthly monitoring for at least three months, followed by monitoring every six months thereafter. If in-person visits are not practical, we suggest informing people to report symptom recurrence and/or any appearance of new symptoms during monitoring and setting parameters for people for which point to initiate contact. We suggest individualising monitoring intervals (more or less frequent) in partnership with the person and their carers based on practicality, individual preferences, responses and tolerance. For instance, deprescribing multivitamins taken without a current indication in a robust person may require less frequent monitoring than other drug classes such as an antihypertensive or an antipsychotic. For specific guidance, we suggest referring to the individual drug sections in the guideline. Additionally, we suggest monitoring should occur at any time there is a change in the individual's risk-benefit profile (e.g. if the person becomes unwell or there is a change in their clinical status or preferences).

CBR, consensus-based recommendation; GPS, good practice statement

Figure 4. Prioritisation matrix for deprescribing



Introduction

As discussed earlier in the introduction and summaries, medicine optimisation is one of the integral parts of the healthcare of older people. Medicines are prescribed to manage symptoms or prevent disease-related outcomes. As people age, they are more likely to develop diseases resulting in the use of more medicines. The concurrent use of multiple medicines is commonly referred to as polypharmacy [52].

Narrative summary of evidence on deprescribing

As shown in Table 5, deprescribing to reduce polypharmacy or multiple drug classes was not found to have a significant impact on mortality in randomised controlled trials (odds ratio, OR 0.97, 95% CI 0.87, 1.08; studies = 25; participants = 15,374; low certainty) and non-randomised studies (OR 0.70, 95% CI 0.36, 1.38; studies = 6; participants = 853; very low certainty). The deprescribing group had significantly increased adverse drug withdrawal effects (ADWEs) (OR 2.29, 95% CI 0.60, 8.77; studies = 4; participants =3096; low certainty) compared to the continuation group. ADWE is referred to as a clinically significant set of signs or symptoms caused by the discontinuation of a drug [74].

There was no statistically significant difference between deprescribing and continuation groups in the following outcomes:

- Exacerbation of underlying conditions (OR 6.75, 95% CI 0.33, 136.91; study = 1; participants = 58; very low certainty)
- Falls (OR 0.88, 95% CI 0.66, 1.17; studies = 11; participants = 8416; very low certainty)
- Fractures (OR 0.97, 95% CI 0.60, 1.57; studies = 5; participants = 4867; low certainty)
- Adverse drug events (OR 1.11, 95% CI 0.64, 1.91; studies = 3; participants = 5492; very low certainty)
- Emergency department presentations (OR 0.85, 95% CI 0.72, 1.01; studies = 6; participants = 4287; low certainty)
- Unplanned hospital admissions (OR 0.99, 95% CI 0.82, 1.21; studies = 13; participants = 11,157; low certainty).

In one study involving deprescribing potentially inappropriate polypharmacy, a significantly smaller proportion of participants in the intervention group reported worsening anxiety or depression at follow-up (OR 0.37, 95% CI 0.15, 0.93, n = 137). Deprescribing did not lead to a significant difference in cognition and quality of life in most studies measured using standardised measures.

Overall, there is a paucity of direct evidence indicating significant harms or benefits associated with the general deprescribing targeting multiple medicines. The certainty of evidence is low and very low. There is also a wide variation in the reported person-oriented outcomes such as morbidity, physical function, cognitive function, and quality of life. The substantial healthcare expenditure associated with inappropriate medicine use and the broad applicability of deprescribing intervention in different healthcare settings provided the basis for formulating consensus-based recommendations in the absence of quality evidence.

For more information relating to the certainty of evidence for each outcome, please refer to the Technical Report.

Narrative evidence summary: withdrawal schedules

Various methods were used for deprescribing in the included studies due to different targeted medicines and there was no direct evidence that any particular method was associated with the greatest benefits and harms. However, compared to abrupt cessation, dose tapering is likely more acceptable for most people and practical to determine the lowest effective dose for some people requiring dose reduction rather than complete cessation.

GRADE Summary of Findings (SoF) Table

Table 5. Summary of findings for deprescribing multiple drug classes

Number of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
25 [75-99]	Randomised controlled trials (RCTs)	7618	7756	OR 0.97 (0.87, 1.08)	
6 [100-105]	Non-randomised studies	440	413	OR 0.70 (0.36, 1.38)	
6 [106-111]	Non-controlled studies	1139	N/A	19% [109] 14% [108] 38% [106] 1% [111] 27% [107] 0% [110]	
2. Adverse drug withdrawal events (ADWEs)					
ADWEs					
4 [85, 90, 96, 98]	RCTs	1535	1561	OR 1.98 (1.48, 2.66)	
1 [109]	Non-controlled study	132	N/A	47%	
Exacerbation or return of underlying condition					
1 [79]	RCT	31	27	OR 6.75 (0.33, 136.91)	
1 [108]	Non-controlled study	70	N/A	2%	
3. Health outcomes					
Adverse drug events					
6 [83, 85, 93, 99, 112, 113]	RCTs	4153	4798	The number of participants who experienced at least one adverse drug event did not differ significantly between the deprescribing and continuation groups (OR 1.11, 95% CI 0.64, 1.91, studies = 3, n = 5492) [85, 99, 113]. In one cluster RCT, deprescribing was associated with a significantly fewer number of adverse drug events (MD -0.30, 95% CI -0.48, -0.12, study = 1, n = 3185) [93].	

				Deprescribing was not associated with a significant difference in the frequency of medication side effects (MD -0.40, 95% CI -1.23, 0.43, study = 1, n = 202) [83], the number of participants with adverse events within 30 days of discharge (OR 0.92, 95% CI 0.82, 1.04, study = 1, n = 4988) [113], or the change in the number of adverse drug events (MD 0.11, 95% CI -0.23, 0.45, study = 1, n = 72) [112].	
1 [102]	Non-randomised study	32	132	OR 0.20 (0.03, 1.59)	
1 [114]	Non-controlled study	873	N/A	5%	
Falls					
14 [79, 81, 83, 87-89, 92, 93, 95, 97, 113, 115-117]	RCTs	5972	6538	Deprescribing was not associated with a significant difference in the number of participants who had at least one fall (OR 0.88, 95% CI 0.66, 1.17, studies = 11, n = 8416) [79, 81, 87-89, 92, 95, 97, 113, 115, 116]. The mean number of falls did not differ significantly between the deprescribing and continuation groups (MD -0.01, 95% CI -0.09, 0.07, studies = 3, n = 3843) [79, 83, 93]. In one study, the risk of experiencing at least one fall did not differ significantly between the deprescribing and continuation groups (OR -0.22, 95% CI -0.53, 0.09, study = 1, n = 885) [88]. In one study, there was no statistically significant difference in fall-related emergency department visits between patients who had modifications to medications following pharmacist reviews and those who had not implemented changes (OR 0.87, 95% CI 0.52, 1.46, n = 309) [117].	
5 [104, 118-121]	Non-randomised studies	580	741	Deprescribing was not associated with a significant difference in the number of participants who had at least one fall (OR 0.75, 95% CI 0.55, 1.03, studies = 5, n = 1321) [104, 118-121]. In one study, the mean number of falls did not differ significantly between the deprescribing and continuation groups (MD -2.30, 95% CI -4.94, 0.34, study = 1, n = 141) nor the risk of experiencing at least one fall (OR 0.48, 95% CI 0.23, 1.00, study = 1, n = 141) [121].	
2 [122, 123]	Non-controlled studies	1062	N/A	Non-controlled studies reported that deprescribing was associated with a 7% reduction in the proportion of patients who had at least one fall (study = 1, n = 49) [123] and a 1.09% increase in the rate of falls (p=0.77, study = 1, n = 1013) [122].	
Health service use					
20 [77, 79-81, 86-89, 92-96, 98, 99, 124-128]	RCTs	7628	7802	Deprescribing was not associated with a significant difference in the number of participants with unplanned hospital admissions (OR 0.99, 95% CI 0.82, 1.21, studies = 13, n = 11157) [77, 79, 81, 86, 88, 89, 92-96, 98, 99], number of hospital outpatient visit (MD 0.40, 95% -0.31, 1.11, study = 1, n = 2470) [125], the number of hospitalisations (MD -0.01, 95% -0.29, 0.27, study = 1, n = 521) [128], or percentage of difference in the time to first 90-day unplanned emergency department visit/hospital readmission/death (MD -0.15, 95% CI -0.40, 0.10, n = 283) [126]. Deprescribing was not associated with a significant difference in the length of hospital stay (MD -0.37, 95% CI -1.92, 1.18, studies = 2, n = 462) [79, 129], institutionalisation (OR 1.01, 95% CI 0.56, 1.82, studies = 2, n = 496) [86, 87], intensive care unit transfer (OR 0.75, 95% CI 0.16, 3.38, study =	

				1, n = 372) [96], number of emergency room presentation (MD 0.13, 95% CI -0.11, 0.37, study = 1, n = 229) [129], and the number of participants with emergency room presentation or readmission (OR 0.85, 95% CI 0.72, 1.01, studies = 6, n = 4287) [77, 80, 81, 86, 96, 124].	
8 [100, 102-104, 120, 130-132]	Non-randomised studies	547	656	Deprescribing was not associated with a significant difference in the number of participants with unplanned hospital admissions (OR 0.81, 95% CI 0.55, 1.18, studies = 6, n = 870) [100, 102, 104, 120, 130, 132]. Deprescribing was not associated with a significant difference in the number of participants with emergency room presentation or readmission (OR 0.81, 95% CI 0.47, 1.38, studies = 2, n = 350) [104, 120], or readmission risk (OR 0.74, 95% CI 0.48, 1.15, studies = 2, n = 346) [103, 104]. Deprescribing was not associated with a significant change in the rate of hospital discharge to home (OR 0.82, 95% CI 0.42, 1.59, study = 1, n = 153) [131].	
5 [107, 111, 123, 133, 134]	Non-controlled studies	382 (one study not stated)	N/A	Deprescribing was associated with a 14% reduction in hospital admissions (n = not stated) [133], 10% of the participants had at least one hospital admission (n = 49) [123], 9-49% were hospitalised following deprescribing (studies = 3, n = 574) [107, 111, 134], 2.5-18% had emergency department visit following deprescribing (studies = 2, n = 333) [111, 134], and 32.5% had an outpatient hospital visit following deprescribing (n = 35) [134]. There was no significant change in the number of emergency department visits (+0.03, p=0.26, n= 99), and non-elective hospitalisations (-0.01, p = 0.78, n = 99) six months after deprescribing [110].	
Sleep					
2 [78, 92]	RCTs	24	23	Deprescribing was not associated with a significant difference in sleep quality (MD 1.00, 95% CI -0.68, 2.68, studies = 2, n = 47) [78, 92].	
2 [106, 107]	Non-controlled studies	475	N/A	A non-controlled study reported that 13% of participants had worsened night-time sleep quality and 10% had worsened daytime wakefulness (n = 193) following deprescribing. Another study by the same author reported that 31% of participants had improved night-time sleep quality and 18% had improved daytime wakefulness following deprescribing (n=282) [107].	
Fractures					
5 [81, 83, 89, 92, 93]	RCTs	2446	2421	Deprescribing was not associated with a significant difference in any fractures (OR 0.97, 95% CI 0.60, 1.57, studies = 5, n = 4867) [81, 83, 89, 92, 93] or non-vertebral fractures (OR 0.66, 95% CI 0.37, 1.18, studies = 2, n = 223) [81, 92, 93].	
1 [102]	Non-randomised study	32	132	Deprescribing was not associated with a significant difference in any fractures (OR 0.81, 95% CI 0.22, 2.97, study = 1, n = 164).	
Mental status					
1 [130]	Non-randomised study	73	64	Deprescribing was associated with a significantly smaller proportion of participants who reported worsened anxiety or depression scores at follow-up (OR 0.37, 95% CI 0.15, 0.93, study = 1, n = 137).	
3 [106, 107, 122]	Non-controlled studies	1488	N/A	A non-controlled study [106] reported that 14% had worsened mental status (mood, depression) following deprescribing (n=193) and another study by the same author reported that 41% of participants had improved mental status following deprescribing (n=282) [107]. Another study [122] reported a lower rate of depression (-0.78%, p=0.65, n = 1013).	

Adverse events/ serious adverse events/ cardiovascular events					
1 [102]	Non-randomised study	32	132	Cardiovascular events OR 0.15 (0.01, 2.57)	
1 [106]	Non-controlled study	193	N/A	Vascular complications 17%	
Delirium					
3 [102, 104, 120]	Non-randomised studies	215	305	OR 0.87 (0.56, 1.35)	
Morbidity					
2 [87, 129]	RCTs	271	292	Different measures were used for reporting morbidity in two studies. Morbidity, measured using the Functional Comorbidity Index, showed significant deterioration with deprescribing (MD 1.20, 95% CI 0.50, 1.90, p = 0.0008, study = 1, n = 159) [87] whereas morbidity significantly improved with deprescribing in one study that used the Global Multimorbidity Treatment Burden questionnaire (MD -4.72, 95% CI -8.63, -0.81, p = 0.02, study = 1, n = 404) [129]. Higher scores represent greater comorbidity in both measures.	
Behavioural and psychological symptoms					
3 [83, 92, 135]	RCTs	427	378	Neuropsychiatric symptoms measured using the Neuropsychiatric Inventory-Nursing Home (NPI-NH) with high scores indicate worse neuropsychiatric symptoms. MD -0.56 (-1.81, 0.69)	
1 [122]	Non-controlled study	1013	N/A	A non-controlled study reported that deprescribing was associated with a significant change in the rate of disruptive behaviours (-6.85%, p = 0.02).	
Physical function					
5 [87, 92, 112, 135, 136]	RCTs	445	440	Two RCTs measured the dependency in activities of daily living using the modified Barthel Index [83, 92] where a lower score indicates higher dependency and reported no significant difference between the deprescribing and continuation groups (SMD 0.22, 95% CI -0.02, 0.46, studies = 2, n = 266). One study measured the dependency in activities of daily living using the Physical Self-Maintenance Scale where higher scores indicate higher dependency and reported an improvement in dependency following deprescribing (MD -1.50, 95% CI -2.81, -0.19, study = 1, n = 397 [135]. Physical function, measured using the short physical performance battery MD 0.50 (-0.60, 1.60) [87]. Change in frailty measured using Frailty Scale (MD 0.60, 95% CI -0.07, 1.27, n = 63) [112] Change in activities of daily living measured using modified Barthel Index (MD 2.20, 95% CI -8.13, 12.53, n = 63) [112]	

1 [105]	Non-randomised study	32	21	One study measured the dependency in activities of daily living using the modified Barthel Index where a lower score indicates higher dependency and reported no significant difference between the deprescribing and continuation groups (MD 3.80, 95% CI -2.59, 10.19).	
5 [106, 107, 122, 133, 137]	Non-controlled studies	1539	N/A	A non-controlled study [106] reported that 45% of participants had worsened functional status following deprescribing (n=193) and another study by the same author reported that 18% of participants had improved functional status following deprescribing (n=282) [107]. A study reported a significant reduction in frailty, assessed using the Edmonton Frailty Scale (MD 1.35, 95%, CI − 2.22, − 0.48, n = 46) [138]. A study reported that deprescribing was associated with a significant change in the rate of increased need for activities of daily living (-4.6%, p = 0.09) [122]. A small pilot study (n=5) reported improvements in [137]: • gait speed measuring using the 10-meter walk test normal pace from 0.95 ± 0.20 to 1.13 ± 0.26 meter/second, p-value unstated • Short Physical Performance Battery (balance, gait speed, and chair stand, each scoring up to four points for a total score of 12; where a higher score indicates a better lower extremity function) from 8.8 ± 2.4 to 11.0 ± 1.0, p-value unstated mini-BESTest (anticipatory postural adjustments, reactive postural control, sensory orientation, and dynamic gait with a maximum score of 28 and a higher score indicating better balance) from 18.2 ± 7.0 to 20.6 ± 1.9, p-value unstated	
Clinical Global Impressions of Change					
1 [135]	RCT	214	183	MD -0.20 (-0.41, 0.01)	
Pain					
2 [107, 122]	Non-controlled study	498	503	The measures used for reporting cognitive functions were heterogeneous across the studies. Deprescribing was not associated with a significant difference in cognitive functions measured using Mini-Mental State Examination (MD 0.62, 95% CI -0.24, 1.48, studies = 4, n = 353) [78, 83, 92, 112]. In one study, there was a modest but significant decrease in cognitive function measured using Mini-Cog (MD -0.50, 95% CI -0.88, -0.12, study = 1, n = 159) [87]. In two other studies, deprescribing was not associated with a significant difference between the two groups in the number of participants with cognitive impairment (score ≥ 8 points on 6-Item Cognitive Impairment Test) (OR 0.98, 95% CI 0.65, 1.47, study = 1, n = 485) [89], memory (MD 7.00, 95% CI -0.20, 14.20) or cognition (MD 2.00, 95% CI -1.92, 5.92) measured using the Neuropsychological Assessment Battery (study = 1, n = 9) [139].	
4. Cognitive function					
7 [78, 83, 87, 89, 92, 112, 139]	RCTs	464	481	The measures used for reporting cognitive functions were heterogeneous across the studies. Deprescribing was not associated with a significant difference in cognitive functions measured using Mini-Mental State Examination (MD 0.62, 95% CI -0.24, 1.48, studies = 4, n = 353) [78, 92, 112, 136]. In one study, there was a modest but significant decrease in cognitive function measured using Mini-Cog (MD -0.50, 95% CI -0.88, -0.12, study = 1, n = 159) [87]. In two other studies, deprescribing was not associated with a significant difference between the two groups in the	

				number of participants with cognitive impairment (score ≥ 8 points on 6-Item Cognitive Impairment Test) (OR 0.98, 95% CI 0.65, 1.47, study = 1, n = 485) [89], memory (MD 7.00, 95% CI -0.20, 14.20) or cognition (MD 2.00, 95% CI -1.92, 5.92) measured using the Neuropsychological Assessment Battery (study = 1, n = 9) [139].	
1 [105]	Non-randomised study	32	21	Deprescribing was not associated with a significant change in cognitive function measured using the Mini-Mental State Examination (MD -0.40, 95% CI -1.39, 0.59, study = 1, n = 53).	
2 [106, 108]	Non-controlled studies	352	N/A	Two non-controlled studies reported that 4-8% of participants had improved cognition (n = 352) [106, 107]. One of these studies [106] reported that 32% of participants had worsened cognitive status (n = 193) following deprescribing.	
5. Quality of life (QoL)					
11 [78, 81, 83, 85, 91, 92, 112, 135, 140-142]	RCTs	992	919	The measures used for reporting quality of life were heterogeneous across the studies, and some studies adopted multiple measures in one study. Deprescribing was not associated with a significant difference in the quality of life reported using EQ-5D utility score (MD 0.04, 95% CI -0.06, 0.15, studies = 7, n = 1654) [78, 83, 92, 112, 135, 140, 141], Quality of Life for People with Dementia (QUALIDEM) (MD -0.03, 95% CI -1.46, 1.40, studies = 2, n = 620) [81, 135], ICEpop CAPability measure for Older people (ICECAP-O) (MD 0.09, 95% CI -0.11, 0.29, study = 1, n = 50) [81], Quality of life in Alzheimer's Dementia (QOLAD) (MD 0.00, 95% CI -2.98, 2.98, study = 1, n = 37) [92], Quality of Life in Late Stage of Dementia score (QUALID) (MD -0.60, 95% CI -2.37, 1.17, study = 1, n = 545) [135], Short Form-12 mental component (MD 0.10, 95% CI -1.54, 1.74, study = 1, n = 541) [140], and Short Form-12 physical component (MD -1.30, 95% CI -2.73, 0.13, study = 1, n = 541) [140]. Deprescribing was associated with a significant deterioration in the quality of life reported using the 15-dimension instrument of health-related quality of life (MD -0.03, 95% CI -0.06, -0.01, study = 1, n = 189) [91] and Short Form-36 (MD -2.18, 95% CI -2.67, -1.68, studies = 3, n = 257) [78, 85, 142].	
1 [103]	Non-randomised study	118	62	EQ-5D index, MD -0.07 (-0.17, 0.03) VAS score, MD -2.90 (-9.58, 3.78)	
2 [108, 110]	Non-controlled study	169	N/A	88% of the participants reported improvement in perceived general health pertaining to mood and functional and cognitive capacity following deprescribing (n=70) [108]. However, in another study, there was no significant change in the mean EQ-5D-5L summary score (-0.024, p=0.18) or EQ-5D-5L VAS score (1.53, p=0.45) six months after deprescribing (n=99) [110].	

*For randomised or non-randomised controlled studies, effect measures are either reported as odds ratio (OR) for dichotomous data or mean difference (MD) for continuous data, with their 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation or the mean differences with corresponding p-values.

ALIMENTARY TRACT AND METABOLISM

This section includes:

- Proton-pump inhibitors
- Prochlorperazine
- Macrogol laxatives
- Drugs used in diabetes
- Potassium

Proton-pump inhibitors (PPIs)

PPIs include esomeprazole*, lansoprazole, omeprazole*, pantoprazole* and rabeprazole*.

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	Given the potential adverse effects associated with prolonged use, we suggest deprescribing be offered to older people taking PPIs: 1. Originally for a short-term indication i.e. • Up to 8 weeks for gastroesophageal reflux disease (GORD) • Up to 12 weeks for peptic ulcer disease • Up to 2 weeks for uncomplicated *H. pylori* eradication (as part of the eradication regimen) • During an intensive care unit admission for stress ulcer prophylaxis 2. Without a clear or known indication
Ongoing treatment	
CBR	In people with complicated gastrointestinal pathologies (e.g. Barrett's oesophagus, severe erosive disease) or those with a high risk of gastrointestinal complications using PPI for gastroprotection, we suggest continuing PPI therapy on the lowest effective dose according to the clinical indication, individual tolerance, and responses, provided this aligns with the individual's goals and preferences, following informed consent.
CBR	If deprescribing is unsuccessful despite multiple attempts, taking into account the possibility of rebound acid hypersecretion (occurred typically within four to eight weeks after PPI discontinuation), we suggest maintaining the person on the lowest effective dose; however, reassessing the need for long-term therapy periodically.
How to deprescribe	
CBR	We suggest individualising the tapering schedule and adjusting it according to the individual's response. In general, we suggest reducing the dose by 50% every two weeks (noting that enteric-coated formulations should not be broken*), ensuring individuals remain symptom-free before initiating each tapering. Once half the lowest standard dose formulation is reached, we suggest switching to alternate-day dosing or discontinuing PPI therapy completely and switching to on-demand or intermittent use of PPIs, antacids, alginates, or H2 receptor antagonists (H2RAs) at the lowest effective dose. We suggest a slower tapering for people taking a high dose (e.g. 20 mg omeprazole twice daily) prior to deprescribing to minimise rebound acid hypersecretion. If symptoms recur during tapering, we suggest restarting PPIs at the previously tolerated dose until symptoms resolve or using an antacid, alginate, or H2RAs as a "rescue therapy" for occasional symptoms, delaying further dose reductions by an agreed interval for stabilisation, and planning for a more gradual taper.

	** Marketed PPI dose forms that may be simpler to titrate include dispersible enteric tablets (omeprazole and esomeprazole), orally disintegrating tablets (lansoprazole), oral liquids (omeprazole) and granules (pantoprazole).*
CBR	For people on combination therapy of PPI and either an antacid or H2RA, we suggest deprescribing one at a time, prioritising antacids and then H2RAs as these are typically associated with a lower risk of harm when discontinued compared to PPIs and can be used as "rescue therapy" for occasional symptoms while tapering PPIs. Tapering of H2RAs can generally follow the same approach as PPI tapering (i.e. halving the dose every two weeks); however, we suggest individualising the tapering schedule and adjusting it according to the individual's response. Antacids and alginates typically do not require tapering unless used regularly and following patient preference. The dose for concomitant acid suppressants may also need to be adjusted temporarily to compensate for the lower dose of the other agent.
GPS	Healthcare providers should offer education on diet and lifestyle modifications (or referral to other relevant healthcare providers) and clearly differentiate between symptom recurrence or exacerbation due to lifestyle factors and adverse drug withdrawal events (ungraded good practice statement).
Monitoring	
CBR	We suggest closely monitoring for disease exacerbations (e.g. symptom recurrence) or adverse drug withdrawal events (e.g. rebound acid hypersecretion), every two weeks following each dose adjustment until at least eight weeks after the medicine has fully ceased, if practical. After this initial period, we suggest monthly monitoring for at least three months, followed by monitoring every six months thereafter. However, this should be tailored based on individual factors such as their preferences, responses and tolerance to deprescribing. If monitoring visits are impractical, we suggest advising people to report symptom recurrence (e.g. acid-related gastrointestinal symptoms) and/or any appearance of new symptoms as needed.
GPS	In individuals with recurrent symptoms after deprescribing, healthcare providers should test for *H. pylori* infection and proceed with eradication if the infection is present (ungraded good practice statement).

CBR, consensus-based recommendation; GPS, good practice statement

Introduction

PPIs relieve symptoms in many conditions such as gastroesophageal reflux disease (GORD), dyspepsia, peptic ulcer disease, and hypersecretory conditions (e.g. Zollinger-Ellison syndrome), and as part of the eradication therapy for *Helicobacter pylori (H. pylori)* [143].

Existing studies suggest that older people are commonly prescribed PPI therapy for prolonged periods without an appropriate clinical indication [144-146]. According to a 2017 Cochrane review, approximately 25% to 70% of people are prescribed a PPI inappropriately [147]. Both overprescribing and underprescribing of PPIs were reported in older people at hospital discharge [148]. Overprescribing was found to be associated with younger age and a lower burden of depression whereas underprescribing in people requiring gastroprotection due to increased risk of bleeding is more frequent in older age and those with greater comorbidities and polypharmacy [148]. Another study using administrative health claims data from the Australian Government Department of Veterans' Affairs revealed that 31% of veterans included in the study received a PPI, suggesting there is a scope to further improve the use of PPIs among older Australians [149]. A clear plan for periodic evaluation of the possibility of reducing the dose of PPI to the lowest effective dose is required. Chronic PPI use without ongoing reassessment contributes to polypharmacy and increases the risk of drug-drug interactions and adverse events.

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

Although PPIs are relatively safe when used in accordance with guideline duration, long-term use of PPIs has been associated with adverse events in several observational studies, including infections (pneumonia, enteric infection), nutritional deficiencies (hypomagnesaemia, vitamin B12 deficiency, iron deficiency, hypocalcaemia), fractures, dementia, gastric cancer, cardiovascular disease (ischemic heart disease, stroke), hepatic diseases (hepatic encephalopathy) and renal diseases (acute kidney injury, chronic kidney disease) [150-155]. While more high-quality studies are required to establish causation between the adverse effects and long-term PPI use, potential safety concerns warrant careful consideration and individualised risk-benefit assessment before continuing prolonged therapy [156]. However, the decision to discontinue PPI should not be based solely on PPI-associated adverse effects as a direct causation cannot be confirmed from existing observational studies [143]. Some individuals may prefer to continue taking PPIs due to a variety of reasons stemming from personal beliefs about the necessity of treatment [157]. In this instance, healthcare providers play a critical role in assessing and understanding their beliefs through person-centred discussions to manage any potential issues with suboptimal medicine use [158].

PPIs are typically indicated for short-term use of up to eight to 12 weeks except when a complicated gastrointestinal pathology is present, or gastroprotection is required in the presence of significant risk factors for gastrointestinal bleeding [144, 145, 159].

1. Complicated gastrointestinal pathologies

People with complicated gastrointestinal pathologies were typically excluded from deprescribing trials as long-term PPI therapy is indicated. These conditions include:

i. Barrett's oesophagus
ii. Endoscopically confirmed severe erosive disease (e.g. severe erosive oesophagitis)
iii. Gastroprotection in the following situations
    - Secondary prevention of complicated peptic ulcer or uncomplicated peptic ulcer with concurrent treatment with NSAIDs, antiplatelets, oral anticoagulants or corticosteroids
    - People receiving dual antiplatelet therapy (DAPT) or dual/triple antithrombotic therapy

- People receiving single antiplatelet therapy, either with a history of peptic ulcer disease, concomitant treatment with NSAIDs or steroids, or two of the following: 65 years or older, gastrointestinal reflux symptoms, or dyspepsia symptoms
- People receiving single anticoagulant therapy with at least one of the following risk factors: 75 years or older, history of peptic ulcer disease, or concomitant use of NSAIDs
- People with an increased risk of gastrointestinal bleeding who are receiving concomitant treatment with NSAIDs, corticosteroids or an SSRI in combination with an NSAID or anticoagulant

iv. Recurring, uncontrolled, or persistent symptoms in the following situations:

- Endoscopy-negative GORD
- Functional dyspepsia
- Upper airway symptoms associated with laryngopharyngeal reflux (e.g. cough, dysphonia)

2. Gastroprotection

2a) Non-steroidal anti-inflammatory drugs (NSAIDs)

The American College of Gastroenterology (ACG) provides guidance on risk stratification for NSAID gastrointestinal toxicity and recommendations for prevention of NSAID-related ulcer complications (see Table 6) [160]. In addition to the risk factors for NSAID-related gastrointestinal complications outlined in Table 6 below, *H. pylori* infection is an independent and additive risk factor that further increases the likelihood of these complications. The ACG recommends testing for *H. pylori* infection before initiating long-term NSAID therapy and, if the infection is present, proceeding with eradication. The need for co-therapy with a gastroprotective agent (e.g. PPI) after eradication depends on the individual's underlying gastrointestinal risk.

Table 6. Recommendations for preventing NSAID-related ulcer complications based on risk stratification for NSAID gastrointestinal toxicity and cardiovascular risk (adapted from Lanza et al., 2009 [160])

Cardiovascular (CV) risk	**Risk factors for NSAID gastrointestinal (GI) toxicity** • Age > 65 years • High-dose NSAID therapy • Previous history of peptic ulcer disease (with or without complication) • Concomitant use of NSAID and other NSAIDs (including low-dose aspirin), corticosteroids, anticoagulants, or other antiplatelet agents (e.g. clopidogrel)		
	High GI risk History of ulcer complications or more than two of the above risk factors	**Moderate GI risk** One or two of the above risk factors	**Low GI risk** No risk factors
High CV risk*	Avoid NSAIDs or COX-2 inhibitors and use alternative therapy	Naproxen + PPI/misoprostol	Naproxen + PPI/misoprostol
Low CV risk	Alternative therapy if possible, or COX-2-specific NSAID + PPI/misoprostol	NSAID+ PPI/misoprostol	NSAID alone (the least ulcerogenic NSAID at the lowest effective dose)

** arbitrarily defined as low-dose aspirin required*

2b) Antithrombotic agents

Current guidelines provide clear recommendations for co-therapy with a PPI for gastroprotection in the following situations [161]

i. Dual antiplatelet therapy (DAPT)
ii. Dual and triple antithrombotic therapy (i.e. combination antiplatelet and anticoagulant therapy)
iii. Single antiplatelet therapy in the presence of at least one risk factor:
    - History of peptic disease;
    - Concomitant treatment with NSAIDs or steroids; or
    - Two of the following: 65 years or older, gastrointestinal reflux symptoms, or dyspepsia symptoms.
iv. Single anticoagulant therapy in the presence of at least one risk factor:
    - 75 years or older;
    - History of peptic ulcer disease;
    - Concomitant use of NSAIDs.

2c) Corticosteroids

In people taking corticosteroids, routine use of PPI for gastroprotection is generally not required, unless in the presence of other risk factors for gastrointestinal complications such as active peptic ulcer disease or when the steroid therapy is combined with NSAIDs or anticoagulants [162].

2d) Selective serotonin reuptake inhibitors (SSRIs)

SSRIs have been associated with an increased risk of gastrointestinal bleeding, especially when combined with NSAID therapy [163]. The risks and benefits of concomitant therapy with SSRIs and NSAIDs should be reviewed periodically and communicated to people as appropriate. Gastroprotection can be considered if there is a clear indication to continue NSAIDs or SSRIs in people with a higher risk of gastrointestinal bleeding.

Narrative summary of evidence on deprescribing

We identified 12 before-and-after studies related to PPI deprescribing from the systematic review and meta-analysis [164-175].

Overall, these studies suggest that deprescribing PPIs can be achieved but most studies did not report clinically meaningful outcomes (see Table 7). The current evidence on health-related outcomes is derived from only two single-arm studies of small sample sizes and evidence is very low in certainty. The evidence at this stage is insufficient to inform evidence-based recommendations.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Lee 2017 recruited nursing home participants taking either pantoprazole or esomeprazole (for longer than six months) without an ongoing indication for long-term use and successfully discontinued PPIs in 19/27 (70%) of participants eight weeks after the intervention [167].

McDonald 2015 implemented an educational initiative paired with a web-based quality improvement tool to reduce inappropriate PPI discharge prescriptions in a hospital. The appropriateness of PPIs and suitability for trial withdrawal was determined based on a list of consensus indications. These indications were:

- Gastric or duodenal ulcer within the past three months;
- Pathological hypersecretory conditions;

- GORD within the last three months not responsive to H2 receptor antagonists (H2RAs) and non-pharmacological strategies;
- Erosive esophagitis;
- Recurring symptoms recently associated with severe indigestion within the last three months not responsive to H2RAs or non-pharmacological strategies;
- *H. pylori* eradication;
- Dual antiplatelet therapy;
- Antiplatelet therapy with anticoagulants;
- Antiplatelet or anticoagulant therapy with a history of previously complicated ulcer; and
- Antiplatelet or NSAID with two of the following: concomitant systematic corticosteroids, age > 60, previously complicated ulcer, concomitant NSAID, or antiplatelet/anticoagulant.

The study reported that 17/18 (94%) patients who had their inappropriate PPI therapy deprescribed during a hospital admission remained off treatment at three months follow-up, with one patient restarting the PPI due to reflux symptoms [170].

Reeve 2015 recruited six people from a hospital outpatient clinic who were taking PPIs with complex polypharmacy and consented to participate in a PPI deprescribing trial. PPI appropriateness was determined using study-specific PPI assessment guidelines developed via a literature review and independent assessment by a gastroenterologist. Appropriate indications included Barrett's oesophagus, secondary prevention of peptic ulcer disease in high-risk patients, primary prevention of peptic ulcer disease in NSAID users, and GORD with currently uncontrolled symptoms. Likely appropriate indications included PPI initiated by a gastroenterologist and primary prevention of peptic ulcer disease in high aspirin or corticosteroid users. All six participants either ceased (n=3) or reduced (n=3) their PPIs during the trial, although at six months, only four patients remained without their PPIs [171].

Wahking 2018 reported a pharmacist-led inpatient PPI stewardship program to reduce PPI use, both during hospitalisation and upon discharge. PPI appropriateness was determined using study-specific criteria for continuation developed by the hospital PPI stewardship team. Criteria for inpatient continuation of PPI include Barrett's oesophagus, upper gastrointestinal bleeding, erosive esophagitis, ulcer diagnosed in the past eight weeks, or longer but with documented persistent GORD symptoms, *H pylori* eradication, oesophageal strictures secondary to acid reflux, hypersecretory disorder, gastric malignancy or previous oesophageal or gastric surgery (excluding total gastrectomy), chronic kidney disease IV or Va, current diagnosis of acid-related disorder, active cancer, PPI initiated by a gastroenterologist, and previously failed attempts at deprescribing. In the study, inpatient PPI therapy was successfully discontinued in 211/220 (96%) patients. Upon discharge, among the patients who had their inpatient PPI discontinued, 24/42 (57%) maintained PPI discontinuation at three months, while 18/22 (82%) patients maintained dose reduction at three months [174].

Bhardwaj 2022 conducted a PPI deprescribing telehealth program led by student pharmacists to evaluate PPI appropriateness in veterans via remote chart reviews based on the study-specific PPI deprescribing protocol listing appropriate long-term indications. Out of the 24 veterans who consented to attempt deprescribing and lacked an appropriate indication for their long-term PPI therapy, 13/24 (54%) had their PPI discontinued and 4/24 (17%) had their dose reduced at study completion (duration was not stated) [164].

Calvo 2021 applied a deprescribing algorithm in hospitalised patients with inappropriate long-term PPI use (daily PPI use of 8 weeks or more) before admission, did not meet the criteria of the current clinical practice guidelines, and asymptomatic and reported 61/75 (81%) remaining off their PPIs at week four with 54/75 (72%) remaining off at week 24 [165].

Leszcynski 2023 reported that inappropriate PPI use significantly reduced from 84% to 44% at 12 months ($p < 0.0001$) after the implementation of a pharmacist-led deprescribing algorithm in a primary care geriatric ambulatory office [168]. The study determined PPI appropriateness based on a study-specific algorithm developed using components of the PPI deprescribing clinical practice guideline and information from previously published PPI deprescribing trials.

Czikk 2022 conducted a deprescribing trial informed by absolute indications from a PPI deprescribing clinical practice guideline and the Choosing Wisely guideline. Absolute indications for PPIs include:

- Erosive esophagitis
- Barrett's oesophagus
- Gastrointestinal bleeding secondary to an ulcer
- NSAID user plus one other risk factor (age > 65 years, prior ulcer, concomitant anticoagulant, antiplatelet, or prednisone)
- Antiplatelet user plus one other risk factor (history of ulcer, concomitant anticoagulant or NSAID) or two other risk factors (age > 65 years, concurrent use of prednisone, GORD)
- Dual antiplatelet therapy plus one other risk factor (age > 65, concomitant anticoagulants, prednisone or NSAIDs).

There were 29 patients with end-stage kidney disease in a haemodialysis unit of a hospital who did not have an absolute indication for a PPI. At eight weeks, 14 restarted their PPI due to reoccurrence of GORD (n = 10), gastrointestinal bleeding (n = 2, of which one case was fatal), gastrointestinal complaints (n = 1), and initiation of dual antiplatelet therapy (n = 1) [166].

Tandun 2019 conducted a pharmacist-led PPI deprescribing intervention in a long-term care facility and reported that 24/30 (80%) residents who received an active order of either pantoprazole or esomeprazole at any dose had their PPI successfully deprescribed (complete discontinuation or maintained on reduced dose) by the end of the four months study period [172]. The method of determining the appropriateness of PPI and suitability for trial withdrawal was not mentioned.

Visser 2021 targeted both statins and PPIs by applying study-specific evidence-based implicit deprescribing algorithms in nursing home residents [173]. In this study, 34/66 (52%) of the residents had their PPI and/or statin dosage either successfully reduced or discontinued after three months which were maintained at six months. Of the 31 residents who were using a PPI, 22 (71%) had their PPIs discontinued, five (16%) had their dose reduced by 50%, two (6%) continued their PPIs, two (6%) had their PPIs initially discontinued but restarted due to withdrawal effects which resolved after restarting PPI at a lower dose than they initially had.

Mati 2024 reassessed PPI use in 97 patients within the long-term care department of a geriatric hospital. All patients had been on PPIs for over eight weeks, with the mean treatment duration being four years. During the reassessment, the initial indication for PPI, use of antithrombotic agents or NSAIDs, risk of gastrointestinal bleeding, risk of infection, risk of bone fractures, history of hyponatremia and hepatic risk were recorded. The reassessment resulted in one of three outcomes: PPI continuation, dose adjustment, or gradual discontinuation. Among the 97 patients, 53 (55%) underwent gradual PPI discontinuation, three (3%) had their dose adjusted, and 41 (42%) continued PPI therapy. At the three-month follow-up, 38 of the 53 patients (72%) who discontinued PPIs remained off treatment, nine (17%) resumed PPI therapy, and six (11%) had died with causes of death not stated. Of those who restarted PPIs, six (67%) did so within the first month of discontinuation, while the remaining three (33%) resumed within three months. The primary reasons for PPI resumption were recurrent gastro-oesophageal reflux disease (GORD) with epigastric pain (n=5, 56%) and suspected peptic ulcer with acute anaemia (n=4, 44%) [175].

Linsky 2022 targeted diabetes medicines and PPIs by mailing patient-centred educational brochures to veterans two weeks prior to their scheduled primary care appointments. Targeted veterans were either taking a PPI for at least 90 consecutive days or were at an increased hypoglycaemia risk (diabetes diagnosis with a prescription for insulin or sulfonylurea, most recent HbA_{1c} < 7%, and either aged 65 or over, had renal insufficiency, or cognitive impairment). PPI appropriateness was not determined from administrative data as the goal of the study was to promote discussion of deprescribing. Compared to a historical control group, targeted veterans (i.e. intervention group participants) were more likely to have their medicines discontinued or reduced (14% versus 4%, p = 0.009) and more likely to discuss with their healthcare providers about the target medicine (12% versus 1%, p = 0.001) [169].

Narrative evidence summary: withdrawal schedules

Various methods were used for deprescribing in the included studies and there was no direct evidence that any particular method was associated with the greatest benefits and harms. However, compared to abrupt cessation, dose tapering is likely more acceptable and helpful in determining the lowest effective dose for some patients requiring dose reduction rather than complete cessation. There was also a lack of clear differentiation between rebound acid hypersecretion and relapse of the initial condition. Rebound acid hypersecretion may occur with abrupt discontinuation of prolonged PPI therapy due to reversal of long-term inhibition of gastric acid secretion, which can be mistaken as a need to restart PPI therapy even when it is not indicated. Rebound acid hypersecretion, if it occurs, is typically within four to eight weeks after PPI discontinuation, although in some cases it may last up to 26 weeks [176]. There are several strategies to manage rebound acid hypersecretion, such as using histamine type 2 receptor antagonists/blockers (H2 blockers) or over-the-counter antacids on demand. Another reasonable strategy is the use of PPI on-demand until symptoms are controlled. If symptoms are not controlled two months after deprescribing PPI, continuation of PPI therapy may be indicated.

Three non-controlled trials reported important or critical outcomes of very low certainty. In the study by Reeve 2015 (n=6) [171], the PPI dose was halved every two weeks, and if participants remained asymptomatic on the reduced dose, the daily dose was changed to as-required administration. In the study by Czikk 2022 (n=29) [166], PPI was withdrawn over two weeks. Finally, in the study by Mati 2024, PPI was gradually discontinued every two days for 3 weeks until the lowest possible marketed dose was reached [175].

Other studies did not report important or critical outcomes associated with deprescribing; however, the withdrawal schedules are summarised below:

- Slowly tapered according to a study-specific protocol (study=1, n=170) [164]
- Dose halved every two to four weeks until the lowest dose (study=1, n=228) [168]
- Abrupt discontinuation or dose reduction (study=1, n=220) [174]
- Abrupt cessation, gradual taper, or switching to “on-demand” dosing (study=1, n=75) [165]
- Abrupt cessation (study=1, n=28) [167]
- Individualised (studies=2, n=124) [172, 173]
- Not described (studies=2, n=500) [169, 170]

GRADE Summary of Findings (SoF) Table

Table 7. Summary of findings for deprescribing PPIs

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
3 [166, 171, 175]	Non-controlled studies	88	N/A	0/6 (0%) [171] 1/29 (3%) [166] 6/53 (11%) [175]	
2. Adverse drug withdrawal events (ADWEs)					
Exacerbation/return of underlying condition					
1 [166]	Non-controlled study	29	N/A	10/29 (34%) (10 had a reoccurrence of gastroesophageal reflux disease).	
ADWEs					
3 [166, 171, 175]	Non-controlled studies	88	N/A	3/29 (10%) had gastrointestinal bleeding (of which one was fatal). 2/3 (67%) of those with a dose reduction did not remain symptom-free at six months. 9/53 (17%) restarted PPI of whom 5/53 (9%) had recurrent gastro-oesophageal reflux disease (GORD) with epigastric pain and 4/53 (8%) had suspected peptic ulcer with acute anaemia.	
3. Health outcomes					
No available evidence					
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*Effect measures are reported as the proportion of individuals with the outcome of interest.

Prochlorperazine

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing be offered to older people taking long-term prochlorperazine: 1. Originally for a short-term indication (e.g. symptoms of acute vertigo typically resolve within hours to days); or 2. With no clear or known indication; or 3. For the indication of drug-induced nausea and vomiting/dizziness, where the original drug can be suitably reduced, discontinued, or replaced by another drug (e.g. inappropriate prescribing cascade)
Ongoing treatment	
CBR	Given the harms of long-term prochlorperazine use are likely to outweigh the benefits in most cases, we generally suggest against the use of long-term prochlorperazine in older people and trial on-demand or intermittent use at the lowest effective dose in addition to appropriate investigation to identify and subsequently treat a cause. If symptoms are chronic and persistent, we suggest considering appropriate non-pharmacological therapies and/or safer alternatives for symptoms, provided this aligns with the individual's goals and preferences, following informed consent.
How to deprescribe	
CBR	We suggest individualising the tapering schedule and adjusting it according to the individual's response. In general, given the likelihood of symptom recurrence in long-term users, we suggest reducing the dosing frequency every one to two weeks: • For those on three times daily, reduce to twice daily, then once daily, then cease completely; or • For those on twice daily, reduce to once daily, then cease completely and switch to on-demand or intermittent use at the lowest effective dose. If symptoms recur during tapering, we suggest restarting at the previously tolerated tapered dose until symptoms resolve, delaying further dose reductions by an agreed interval for stabilisation, and planning for a more gradual taper.
Monitoring	
CBR	We suggest closely monitoring for disease exacerbations (e.g. symptoms recurrence) or adverse drug withdrawal events (ADWEs, e.g. withdrawal-emergent abnormal movements), every two weeks following each dose adjustment until at least four weeks after the medicine is fully ceased if practical. After this initial period, we suggest monthly monitoring for at least three months, followed by monitoring every six months thereafter. However, this should be tailored based on individual factors such as their preferences, responses and tolerance to deprescribing. For persistent ADWEs, we suggest collaborating with other relevant healthcare providers (e.g. physiotherapist and speech pathologist) to evaluate their impact and seriousness and develop strategies to resolve them. If in-person visits are impractical, we suggest informing people to report symptom recurrence (e.g. dizziness) and/or any appearance of new symptoms as needed.

CBR, consensus-based recommendation

Introduction

Prochlorperazine is a dopamine antagonist indicated for symptomatic relief of acute vertigo and to prevent or treat both nausea and vomiting [177]. Prochlorperazine and other anti-vertigo medications should be limited to acute use and administered for the shortest duration possible. Vestibular rehabilitation should be considered as part of the management plan where appropriate. Furthermore, people with benign paroxysmal positional vertigo would benefit from Epley manoeuvres as the first-line treatment. When performed by a trained healthcare provider, Epley manoeuvres can usually resolve symptoms [178].

Narrative summary of evidence on deprescribing

We were unable to identify any direct evidence related to the deprescribing of prochlorperazine in older people from the systematic review and meta-analysis. Recommendations are provided in this section following a Delphi consensus process.

Justification of recommendations

Long-term use of prochlorperazine to treat dizziness and vertigo is not recommended due to the potential sedative and hypotensive effects that may increase the risk of falls, especially in older people [177]. The risk of more serious side effects including extrapyramidal symptoms (usually acute dystonic reactions) increases with cumulative dose and length of treatment [177]. Extra caution is required for older people, particularly those with Parkinson's disease where it is recommended to best avoid (Beers Criteria) [177, 179]. Prochlorperazine also causes many anticholinergic side effects including confusion, delirium, hallucinations, visual disturbance, urinary retention, constipation and tachycardia [180]. In older people, these may be severe and lead to cognitive impairment, falls and increased all-cause mortality [180]. Prochlorperazine is commonly initiated due to dizziness as a side effect of other medicines such as diuretics (i.e. a prescribing cascade) [181]. A significant association between cardiovascular medicines, NSAIDs, opioids and sedatives and the subsequent initiation of prochlorperazine has previously been reported [181]. It is crucial to identify dizziness as a potential side effect of other medicines before initiating treatment to avoid inappropriate prescribing cascades.

The tapering approach is based on pharmacological rationale and clinical experience, considering the possible recurrence of symptoms and the risk of withdrawal-emergent abnormal movements in long-term users.

Given the lack of deprescribing-specific evidence, the monitoring plan should be informed by known adverse effects associated with dopamine antagonists and the clinical consensus on safe withdrawal practices in older populations. ADWEs such as extrapyramidal symptoms may emerge during or after dose reduction and should be closely observed.

Note: While metoclopramide is part of the top 100 PBS medicines, it is not covered in this guideline as it is typically used short term (up to five days).

Macrogol laxatives

Type	Recommendation
When to deprescribe	
CBR	To minimise the risk of electrolyte imbalance (particularly for the use of macrogol with electrolytes in people with congestive heart failure, renal disease, or severe dehydration), we suggest deprescribing be offered to older people taking long-term macrogol laxatives: 1. Without an ongoing indication in people who are/have been asymptomatic 2. For drug-induced constipation where the original drug can be suitably reduced, discontinued, or replaced by another drug (e.g. inappropriate prescribing cascade)
Ongoing treatment	
CBR	We suggest continuing macrogol laxatives when there is a clear indication (e.g. opioid-induced constipation for the duration of opioid treatment, chronic slow-transit constipation), provided this aligns with the individual's goals and preferences, following informed consent.
CBR	If deprescribing is unsuccessful despite multiple attempts, we suggest maintaining the lowest effective dose; however, reassessing the need for long-term therapy periodically.
How to deprescribe	
CBR	We suggest individualising the tapering schedule and adjusting it according to the individual's current bowel function, risk of recurrence, frequency and consistency of the stools. In general, given the likelihood of recurrence of constipation, we suggest reducing by one sachet and then alternate day dosing every one to two weeks and switching to on-demand or intermittent use at the lowest effective dose. Once dosing every other day and regular bowel movements occur without difficulty, discontinue the medicine. If constipation recurs during tapering, we suggest restarting at the previously tolerated tapered dose or original dose until constipation is resolved, delaying further dose reductions by an agreed interval for stabilisation, and planning for a more gradual taper. For people on combination therapy of laxatives, we suggest deprescribing one at a time, prioritising medicines with a higher risk of harm and a lower potential benefit from continued use. However, the dose for concomitant laxatives may also need to be adjusted temporarily to compensate for the lower dose of the other agent. We suggest individualising the tapering schedule and adjusting it according to the individual factors above.
GPS	Healthcare providers should offer appropriate education on fluid intake, fibre intake, mobility and referral to other relevant healthcare providers whenever applicable (ungraded good practice statement).
Monitoring	
CBR	We suggest closely monitoring for recurrence of constipation following each dose adjustment and advising people that they may revert to the previously tolerated tapered dose or original dose if constipation recurs. For people who have concomitant diagnoses of heart failure, or renal failure or who are using lithium, potassium, magnesium or salt (sodium) supplements, we suggest monitoring for electrolytes as dosing may need to be adjusted.

	We suggest monitoring for changes in mobility, fluid and fibre intake and adapting strategies to deprescribing as appropriate.

CBR, consensus-based recommendation; GPS, good practice statement

Introduction

Constipation is a common issue in older people [182] with various causes ranging from dietary, lifestyle, and pelvic floor dysfunction [183]. Many medicines commonly used by older people can also inhibit gastric emptying and peristalsis in the gastrointestinal tract, thereby causing constipation [182]. For instance, opioids, calcium supplements, calcium channel antagonists (e.g. verapamil) and oral iron supplements may contribute to or aggravate constipation [182]. It is important to note that there are medicines that may cause dehydration through mechanisms such as 1) the increase of water elimination through either diarrhoea, urine or sweat (e.g. diuretics), 2) a decrease in thirst sensation or appetite (e.g. selective serotonin reuptake inhibitors), or 3) the alteration of central thermoregulation (e.g. angiotensin-converting enzyme inhibitors) [184]. Dehydration may consequently lead to constipation [182].

Narrative summary of evidence on deprescribing

We were unable to identify any direct evidence related to the deprescribing of macrogol in older people from the systematic review and meta-analysis. Recommendations are provided in this section following a Delphi consensus process.

Justification of recommendations

In many cases, constipation is induced by medicines and changing the causative agent alone can restore bowel function [183]. An inappropriate prescribing cascade can be seen when a laxative is initiated when the constipation is induced by a medicine where the original medicine can be suitably reduced, discontinued, or replaced by another medicine. The use of laxatives should follow a stepwise approach with the possibility of stepping down being considered periodically [183]. Macrogol is an osmotic laxative commonly used in older people when first-line interventions such as lifestyle modifications or bulk-forming agents are inadequate [182]. However, inappropriate long-term use of osmotic laxatives, especially macrogol with electrolyte formulations, may increase the risk of fluid and electrolyte disturbances that can potentially lead to serious complications [183]. The continuation or discontinuation of macrogol laxatives requires careful consideration of potential benefits and risks, ensuring that the approach aligns with the person's overall health goals.

Individuals with congestive heart failure, renal disease, or severe dehydration may have a higher baseline risk of fluid electrolyte disturbances [185]. In contrast, other people may be more likely to derive substantial benefits from continuing treatment and may be willing to accept a tolerated level of risk. For example, the benefits of continuing macrogol laxatives for conditions such as chronic constipation to maintain bowel regularity and provide symptomatic relief may outweigh the associated risks [186, 187]. In people with opioid-induced constipation where opioid use is considered appropriate and other measures to reduce the risk of opioid-induced constipation are not effective (e.g. lifestyle interventions, considerations of alternative formulation or concurrent medicines, considerations of changing therapy or reducing the dose), ongoing macrogol therapy for the duration of opioid therapy may be considered suitable [188].

The tapering and monitoring approach is based on pharmacological rationale and clinical experience, considering the likelihood of recurrence of constipation.

Note: Other laxatives (bulk-forming, stimulant, and stool softener) are not covered in this guideline as these medicines are widely available over the counter. Although beyond the scope of this guideline, it is important to point out that excessive use of other laxatives is also associated with harm, particularly stimulant laxatives [183]. Therefore, periodic reviews of the possibility of deprescribing these agents and reiterating dietary/lifestyle advice are equally important.

Medicines for diabetes include:

- Alpha-glucosidase inhibitors: Acarbose
- Biguanide: Metformin*
- Dipeptidyl peptidase 4 (DPP-4) inhibitors: Alogliptin, linagliptin*, saxagliptin, sitagliptin*, vildagliptin
- Glucagon-like peptide-1 (GLP-1) analogues: Dulaglutide, liraglutide, semaglutide*
- Sodium-glucose co-transporter 2 (SGLT2) inhibitors: Dapagliflozin*, empagliflozin*
- Sulfonylureas: Glibenclamide, gliclazide*, glimepiride, glipizide
- Thiazolidinediones: Pioglitazone
- Insulins*
- Combinations of oral blood glucose-lowering drugs:
  - Saxagliptin with dapagliflozin
  - Empagliflozin with linagliptin
  - Metformin with sitagliptin*/ empagliflozin*/ alogliptin/ dapagliflozin/ linagliptin/ glibenclamide/ saxagliptin/ vildagliptin

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	We suggest individualising HbA_{1c} targets based on individual factors and preferences, aiming to avoid hypoglycaemia. In general, we support the suggested HbA_{1c} targets: • < 7.0 - 7.5% (53-58 mmol/mol) for robust older people (two or fewer coexisting chronic conditions and intact cognitive and functional status) • < 8.0% (64 mmol/mol) for older people with complex/intermediate health status (three or more coexisting chronic conditions requiring medicines/lifestyle interventions, two or more instrumental activities of daily living impairments, or mild-to-moderate cognitive impairment) • Avoid specifying strict HbA_{1c} targets in older people with moderate-to-severe cognitive impairment, two or more impairments in activities of daily living, chronic illnesses with significant symptoms/impairment of functional status, or limited life expectancy.
CBR	We suggest that deprescribing decisions be made in collaboration with the individual and their diabetes care team, including specialist providers. For older people using diabetes medicines to manage glycaemic control in **type 2 diabetes mellitus** (T2DM), we suggest offering deprescribing: 1. If the two most recent consecutive HbA_{1c} levels are below the individualised target, prioritising deprescribing insulin therapy, then sulphonylureas next (given the higher risk of hypoglycaemia); or 2. In the presence of side effects impacting quality of life (e.g. infections attributed to SGLT2 inhibitors or other agents, gastrointestinal adverse effects, and weight loss attributed to metformin) where the benefit of discontinuation outweighs the risk.
CBR	In older people taking SGLT2 inhibitors or GLP-1 analogues for indications other than their glycaemic control benefits (e.g. **cardiovascular and/or renal risk reduction**), we suggest deprescribing be offered if these medicines are associated with adverse effects (e.g. potential muscle wasting which can exacerbate frailty), ensuring the benefit of discontinuation outweighs the risk and other management strategies are in place. We

	suggest that deprescribing decisions be made in collaboration with the individual and their diabetes care team, including specialist providers.
Ongoing treatment	
CBR	We suggest continuing diabetes medicines used for **glycaemic control** in older people where the benefits generally outweigh the risks, including those who: • Have type 1 diabetes, hybrid forms of diabetes, or diseases of the exocrine pancreas; or • Experience hyperglycaemic symptoms and are not at an increased risk of hypoglycaemia; or • Are robust without reduced life expectancy and are not at an increased risk of hypoglycaemia.
How to deprescribe	
CBR	We suggest discontinuing oral diabetes medicines without the need for tapering with the possibility of restarting the medicine if needed, provided this approach aligns with the individual's goals and preferences, following informed consent. Seek expert advice for the tapering of injectable diabetes medicines
CBR	For people on combination therapy of diabetes medicines, we suggest: • Deprescribing one at a time; and • Prioritising medicines most likely to cause hypoglycaemia; and • Considerations be given to the impact of diabetes medicines on weight. For instance, prioritising short-acting insulins and sulfonylureas and last for other agents with additional cardiovascular risk reduction if considered appropriate to deprescribe. In people taking other medicines that impact blood glucose levels (e.g. centrally acting medicines, beta-blockers, thiazide diuretics, antipsychotics, corticosteroids, quinolones, ACE inhibitors), we suggest close monitoring of blood glucose levels for the first two weeks when deprescribing diabetes medicines.
Monitoring	
CBR	We suggest monthly monitoring of the overall risk-benefit profile and lifestyle changes for at least three months, then every six months thereafter. However, this should be tailored based on individual factors such as their preferences, responses and tolerance to deprescribing. We suggest careful monitoring for signs and symptoms of hypoglycaemia and hyperglycaemia, as the presentation can often be different in older people and easily missed in older people.
CBR	**Self-monitoring of blood glucose** For people who are already self-monitoring blood glucose, we suggest advising people to self-monitor random and fasting blood glucose concentrations at least once daily during tapering, and self-monitor for symptoms of hyperglycaemia (e.g. increased nocturia or thirst), as well as reporting to their healthcare provider if symptomatic or if their blood glucose concentration becomes elevated. **HbA_{1c} monitoring** We suggest reviewing HbA_{1c} levels once after approximately three months, and then twice a year for people who are stable and well-controlled.
GPS	**Continuous glucose monitoring (CGM)** CGM should be considered and offered to people with diabetes to detect glucose fluctuations throughout the day, noting that CGM is not subsidised by the National Diabetes Services Scheme for individuals who do not have Type 1 diabetes at the time

	of writing. Where it is safe to do so, de-escalate blood glucose monitoring in line with patient preferences and goals of treatment to reduce the daily burden of disease monitoring (ungraded good practice statement).
GPS	Healthcare providers should reinforce the benefits of optimal dietary intake and physical activity (ungraded good practice statement).

CBR, consensus-based recommendation; GPS, good practice statement

Introduction

The optimal intensity of glycaemic control for older people with type 2 diabetes is highly debated. Type 2 diabetes remission is possible and occurs more frequently in people over 75 years of age and people who had a substantial weight loss (over 15 kg) [189]. This could be due to reduced nutritional intake in older people coupled with age-related metabolic changes. As a result, adjustments in diabetes treatment are often necessary in this population to avoid overtreatment. Overly intensive glycaemic control (HbA_{1c} <7%) in older people has been associated with recurrent episodes of hypoglycaemia, which can have serious consequences, including an increased risk of cardiovascular and cerebrovascular events, cognitive decline, falls, and mortality [190-193]. Among diabetes medicines, insulin and sulfonylureas carry the highest risk of hypoglycaemia, with the risk heightened in older people due to the higher rate of renal or hepatic impairment, malnutrition, and low body weight which were found to be risk factors for hypoglycaemia [177, 194]. Hypoglycaemia in older people may have different presentation, with neurological symptoms such as dizziness, visual disturbances, agitation, confusion, or behavioural changes being more prominent than autonomic symptoms. In people with dementia, these neurological symptoms can be misinterpreted as dementia-related symptoms [195]. Furthermore, symptoms of hypoglycaemia are less specific with increasing age and asymptomatic hypoglycaemia is also common in older people, further complicating its management. While hypoglycaemia poses significant risks, undertreatment of diabetes can increase the likelihood of both microvascular and macrovascular complications.

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

Glycaemic control

Below we summarised the findings from key trials that contributed to the guidelines for glycaemic control in older people. Findings from the studies suggest that deintensifying glycaemic control in older people or those with longstanding diabetes may be unlikely to worsen microvascular outcomes in the short term. However, before de-intensifying treatment, it is essential to review medicines that can affect glycaemic control in people with diabetes. Some medicines are known to cause hyperglycaemia, including thiazide diuretics, atypical antipsychotics (particularly olanzapine), and corticosteroids. Conversely, alcohol is associated with hypoglycaemia in addition to other medicines such as salicylates, quinolones, beta-blockers, and ACE inhibitors.

For individuals who are already self-monitoring their blood glucose, checking random or fasting blood glucose levels after deprescribing, such as at least once daily, can help track glycaemic control [196]. However, the frequency of monitoring should be individualised based on the person's medication regimen, clinical stability, and preferences. Where safe and appropriate, blood glucose monitoring can be de-escalated in line with the individual's goals and preferences to reduce the daily burden of disease management [197]. When encouraging self-monitoring, it may be helpful to provide examples of common symptoms of hyperglycaemia (e.g. increased thirst or nocturia), as many people may not recognise that these non-specific symptoms could indicate elevated blood glucose. Continuous glucose monitoring (CGM) should be considered and offered as an alternative to identify trends in blood glucose levels and reduce the need for frequent fingerstick testing. Additionally, HbA_{1c} levels reflect glycaemic control over the preceding six to eight weeks [198]. It

may be appropriate to test HbA_{1c} once around three months after deprescribing, and then every six months for individuals who are stable and well-controlled.

The United Kingdom Prospective Diabetes Study (UKPDS) was a pivotal RCT that compared intensive glycaemic control (fasting plasma glucose, FPG <6 mmol/L) with conventional control (FPG <15 mmol/L) in 5,102 patients with newly diagnosed type 2 diabetes. Participants had a median age of 54 years (IQR 48–60) and were followed for over 10 years while receiving intervention with diet alone (conventional), metformin, sulfonylureas, or insulin (intensive) [199]. The study found that intensive glycaemic control with metformin, sulfonylureas, or insulin reduced the risk of microvascular complications but had no significant effect on macrovascular disease (approaching statistical significance, p = 0.052) during the trial period.

A follow-up conducted 10 years after the UKPDS RCT concluded demonstrated long-term benefits, with a reduced rate of microvascular disease, myocardial infarction, and mortality in those who had received intensive treatment [200]. This glycaemic "legacy effect" suggests the potential long-term benefits of early intensive glycaemic control.

Participants in the UKPDS were approximately 10 years younger at baseline compared to those in the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation) and the ACCORD (Action to Control Cardiovascular Risk in Diabetes trials) (mean age = 66 and 62 years respectively) [201, 202]. The mean diabetes duration was 8 years in ADVANCE and 10 years (median) in ACCORD. In contrast to UKPDS, these two studies found that intensive glycaemic control was associated with an increased risk of mortality. These differences in age and diabetes duration have important implications when adjusting treatment intensity, particularly in the context of deprescribing.

Similarly, the 2009 Veterans Affairs Diabetes Trial (VADT) included 1,791 military veterans (mean age = 60 years) with type 2 diabetes who were nonresponsive to at least one oral diabetes medicine at the maximum dose and/or daily insulin injections, with nonresponse defined as a central HbA_{1c} ≥ 7.5% or local HbA_{1c} ≥ 8.3% [203]. The mean diabetes duration was 11.5 years. This study found no significant differences between the intensive and standard glycaemic control groups in major cardiovascular events, cardiovascular mortality, all-cause mortality, or microvascular complications, except for a reduced progression of albuminuria in the intensive group.

Table 8. Possible HbA_{1c} target (adapted from ElSayed et al., 2023 [204])

Possible HbA_{1c} target	Populations
< 7.0 - 7.5% (53-58 mmol/mol)	Robust older people (two or fewer co-existing chronic conditions, intact cognitive and functional status)
< 8.0 % (64 mmol/mol)	Older people with complex/intermediate health status (three or more co-existing chronic conditions requiring medicines/lifestyle interventions, two or more instrumental ADL impairments, or mild-to-moderate cognitive impairment)
Avoid specifying strict HbA_{1c} targets	Older people with complex or poor health (moderate-to-severe cognitive impairment, two or more impairments in activities of daily living, chronic illnesses with significant symptoms/impairment of functional status, limited life expectancy) as symptom management and quality of life may be more relevant than HbA_{1c} targets.

International guidelines provide general glycaemic goals for older people (see Table 8) but emphasise the importance of individualising these goals based on unique characteristics through shared decision-making to address individual needs and preferences [205]. Other important factors

that should be considered include frailty, diabetes duration and presence of cardiovascular diseases as discussed above, in addition to hypoglycaemia awareness, history of severe hypoglycaemia, diabetes-related distress, and concerns such as fear of hypoglycaemia [206]. For example, a robust person aged 70 years with no established cardiovascular diseases may aim for an HbA_{1c} target of less than 7%. If a person had a 15-year history of diabetes or an established cardiovascular disease, a less intensive target of less than 7.5%, or even below 8% in the presence of additional comorbidities or hypoglycaemia risk, may be considered.

Cardiovascular and/or renal benefits

As discussed, many RCTs of diabetes medicines were conducted prior to the introduction of newer agents (SGLT2 inhibitors and GLP-1 receptor agonists). These newer agents have demonstrated cardiovascular or renal benefits independent of their benefits in glycaemic control. As such, less intensive glycaemic targets, combined with the careful selection of these medicines, may offer a safer and more favourable benefit-risk profile for certain people.

Below we summarised the findings from key trials for SGLT2 inhibitors and GLP-1 receptor agonists in the context of cardiovascular and/or renal benefits.

SGLT2 inhibitors

A systematic review and meta-analysis that included 35 RCTs that assessed the cardiovascular effects of SGLT2 reported that SGLT2 inhibitors significantly reduce the incidence of mortality, major adverse cardiac events, non-fatal myocardial infarction and heart failure in patients with Type 2 diabetes [207]. Among the studies included in the review, the 2015 EMPA-REG OUTCOME trial (Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes) was a prominent study [208]. This randomised, double-blind, placebo-controlled trial included 7,020 patients (mean age = 63 years) with Type 2 diabetes and at high risk for cardiovascular events. Patients were included if they had an HbA_{1c} of between 7% - 9% (for those who had not received glucose-lowering agents for at least 12 weeks before randomisation) or 7% - 10% (for those who had received stable glucose-lowering therapy for at least 12 weeks before randomisation). Participants who were randomised to 10 mg or 25 mg of empagliflozin (an SGLT2 inhibitor), in addition to standard care, had significantly lower cardiovascular mortality, all-cause mortality, and hospitalisation for heart failure compared to placebo. However, there were no significant between-group differences in the risk of nonfatal myocardial infarction or nonfatal stroke and hospitalisation for unstable angina. In terms of adverse events, there was a significant increase in genital infection among patients who received 10 mg or 25 mg empagliflozin compared to placebo but no significant difference between the two groups in other adverse events including hypoglycaemia, acute renal failure, diabetic ketoacidosis, thromboembolic events, bone fracture, and events consistent with volume depletion.

The 2022 EMPA-KIDNEY trial (Study of Heart and Kidney Protection with Empagliflozin) randomised 6,609 patients (mean age = 64 years) with chronic kidney disease (CKD), a wide range of GFRs, levels of albuminuria, and causes of CKD to receive empagliflozin (10 mg once daily) or placebo [209]. The study included patients with or without diabetes. There was a significantly lower risk of progression of kidney disease or death from cardiovascular causes in the group who received empagliflozin. Results were consistent among patients with or without diabetes. The group who received empagliflozin also had a significantly lower risk of all-cause hospitalisation. In the subsequent 2024 follow-up study involving 4,891 (74%) surviving patients who consented, findings suggest that empagliflozin may have residual cardiorenal benefits for up to 12 months after it was discontinued [210].

The 2017 CANVAS (Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes) trial assessed the effects of the SGLT2 inhibitor canagliflozin on cardiovascular, renal, and safety outcomes in 10,142 participants with Type 2 diabetes and high cardiovascular risk [211]. The 2019

CREDENCE (Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation) trial assessed the effects of the SGLT2 inhibitor canagliflozin on renal outcomes in 4,401 participants with type 2 diabetes and albuminuric chronic kidney disease [212]. Both trials (both mean age = 63 years) reported that canagliflozin significantly reduced the risk of cardiovascular death, myocardial infarction, stroke, and heart failure hospitalisation. These studies consolidated previous findings of the renal and cardiovascular protection of SGLT2 inhibitors.

More recently, a 2025 post hoc analysis utilised the data from the CANVAS and CREDENCE trials to assess the efficacy and safety of SGLT2 inhibitors in people with frailty [213]. From the pooled, individual participant-level data analysis, frailty (defined as Frailty Index > 0.25) was present in 56% of all participants in the two trials (n = 10,142). This post hoc analysis reported that the benefits of canagliflozin in improving cardiovascular and mortality outcomes were observed in people with type 2 diabetes irrespective of their frailty status, and canagliflozin did not further increase the risk of adverse events except for osmotic diuresis (where the opposite was reported, i.e. osmotic diuresis was less common in frail participants compared with non-frail). However, it is important to note that all participants had a significantly higher risk of adverse events (including fracture, volume depletion, osmotic diuretic, amputation, diabetic ketoacidosis, and genital infection) with canagliflozin use. In these trials, only 0.2% (25/14,543) of all participants were underweight with a BMI < 18.5 whereas the majority of the participants were overweight (4608/14,543; 32%) or obese (8375/14,543; 58%).

An individualised approach is needed to optimise therapy for people with frailty. Evidence suggests the benefits of the SGLT2 and GLP-1 agonists in people who are underweight, anorexic, and malnourished are lacking as they are often underrepresented or excluded in clinical trials [214]. It is possible that some individuals may not be able to tolerate these newer therapies due to the associated risk of causing further weight loss, dehydration, and hypotension that may further exacerbate frailty.

GLP-1 receptor agonists

A 2025 meta-analysis that included 11 RCTs that assessed the cardiovascular and renal effects of GLP-1 receptor agonists reported that GLP-1 receptor agonists led to a significant reduction in clinically important kidney events, kidney failure, and cardiovascular events [215]. Among the studies included in the meta-analysis, the Semaglutide Effects on Cardiovascular Outcomes in People with Overweight or Obesity (SELECT) and the Evaluate Renal Function with Semaglutide Once Weekly (FLOW) trials were two recent trials conducted in 2023 and 2024 respectively.

In the 2023 SELECT trial, 17,604 patients (mean age = 62 years) with no diabetes who had pre-existing cardiovascular disease, overweight or obese (body-mass index of ≥ 27) were randomised to receive once-weekly semaglutide (a GLP-1 receptor agonist) or placebo and followed up for a mean of 40 months [216]. Participants who had received semaglutide had a significantly lower risk of primary composite outcome (cardiovascular mortality, nonfatal myocardial infarction, or nonfatal stroke). However, the semaglutide group had experienced a significantly higher rate of adverse events leading to permanent discontinuation.

In the FLOW trial, 3,533 patients (mean age = 67 years) with type 2 diabetes and CKD who were at very high risk for kidney disease progression, kidney failure, cardiovascular events, or death (according to the Kidney Disease: Improving Global Outcomes risk calculators) were included [217]. Compared to placebo, The group who had received semaglutide had a significantly lower risk of clinically important kidney outcomes and death from cardiovascular causes in patients with type 2 diabetes and chronic kidney disease.

Narrative summary of evidence on deprescribing

We identified five studies (four cohort studies and one before-and-after study) related to deprescribing diabetes medicines from the systematic review and meta-analysis [169, 218-221].

Overall, there is limited evidence suggesting significant benefit or harm associated with the discontinuation of diabetes medicines. Most studies were cohort studies, and although one of these studies showed that deprescribing was associated with a reduction in hypoglycaemic episodes, the certainty of this evidence is very low and insufficient to support evidence-based recommendations.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Sjöblom 2008 included 32 older Swedish nursing home residents with type 2 diabetes and intensive (HbA_{1c} ≤ 6%) glycaemic control in a prospective cohort study [221]. Diabetes medicines remained deprescribed in 24 (75%) participants three months after the initial dose reduction or withdrawal. At six months, the mean HbA_{1c} in the deprescribing group was lower, 5.8 ± 1.1% compared to 6.6 ± 1.4% in the continuation group. However, continuation group participants had a higher baseline HbA_{1c} compared to the intervention group (7.1 ± 1.6% vs 5.2 ± 0.4%). Four participants in the deprescribing group reported hyperglycaemia (OR 21.0, 95% CI 1.09, 403.01) and subsequently dropped out of the study. Their plasma glucose levels were 14.6, 16.6, 17.4, and 18.3 mmol/L respectively.

Hui 2019 conducted a retrospective study that included older people with type 2 diabetes who have a prescription for diabetes medicines other than metformin and either two most recent consecutive HbA_{1c} ≤ 6.5% or ≤ 7.0% but had either visited the emergency department or were hospitalised for hypoglycaemia in two years prior. The study reported that the discontinuation of diabetes medicines significantly reduced the risk of hypoglycaemia (OR 0.46, 95% CI 0.24, 0.90) and all-cause mortality (OR 0.40, 95% CI 0.24, 0.69) [218]. Additionally, there was no significant difference in the proportion of patients who experienced hyperglycaemia between the deprescribing group and the continuation group (OR 0.43, 95% CI 0.13, 1.43).

Niznik 2022 conducted a retrospective cohort study that included veteran nursing home residents with advanced dementia or limited life expectancy with HbA_{1c} ≤ 7.5%. Type 1 and type 2 diabetes could not be distinguished using administrative data. The study reported that deintensifying diabetes medicines (dose reduction or discontinuation) was not associated with all-cause emergency department visits, hospitalisation, or death in weighted analyses for 60 days after deintensification [219].

Silverii 2020 conducted a retrospective cohort study that included outpatients with type 2 diabetes aged over 75 years. Within the cohort in which deprescribing of diabetes medicines was performed (n=46), there was a reduction in the rate of severe hypoglycaemia six months following deprescribing (none versus five cases in the prior six months) while mean HbA_{1c} increased significantly from 6.4 ± 2.6% to 7.0 ± 3.3% ($p < 0.05$) [220].

Linsky 2022 targeted diabetes medicines and PPIs by mailing patient-centred educational brochures to veterans two weeks prior to their scheduled primary care appointments. Targeted veterans were either taking a PPI for at least 90 consecutive days or were at an increased hypoglycaemia risk (diabetes diagnosis with a prescription for insulin or sulfonylurea, most recent HbA_{1c} < 7%, and either aged 65 or over, had renal insufficiency, or cognitive impairment). Medicine appropriateness was not determined from administrative data as the goal of the study was to promote discussion of deprescribing. The study reported that the intervention group was more

likely to have the target medicine discontinued or reduced (14% versus 4%, p = 0.009) and have discussions with their healthcare providers about the target medicine (12% versus 1%, p = 0.001) [169].

Narrative evidence summary: withdrawal schedules

There was a lack of description on the method of deprescribing in most studies and no direct evidence indicates tapering or abrupt discontinuation was associated with the greatest benefits and harms.

Four studies reported important/critical outcomes of very low certainty. In the study by Hui 2019, withdrawal schedules were likely individualised following a pharmacist-led assessment (n=2740) [218]. In the study by Sjöblom 2008, diabetes medicines were discontinued abruptly except for insulin over 20 units/day for which the dose was reduced by half (n=32) [221]. Methods were not described in the other two studies (n=2128) [219, 220].

The other study by Linsky 2022 did not report important or critical outcomes associated with deprescribing and the method of deprescribing was not described (n=348) [169].

GRADE Summary of Findings (SoF) Table

Table 9. Summary of findings for deprescribing drugs used in diabetes

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
2 [218, 219]	Non-randomised studies	1239	3583	OR 0.85 (0.20, 3.60)	
2. Adverse drug withdrawal events (ADWEs)					
Exacerbation/return of underlying condition					
2 [218, 221]	Non-randomised studies	717	2121	OR 2.35 (0.05, 103.89)	
3. Health outcomes					
Health service use					
1 [219]	Non-randomised study	554	1528	OR 1.10 (0.89, 1.36)	
Adverse drug events					
1 [218]	Non-randomised study	685	2055	Incidence of hypoglycaemic episodes OR 0.46 (0.24, 0.90)	
Glycated haemoglobin, HbA_{1c} levels					
1 [220]	Non-controlled study	46	N/A	Baseline to endpoint 6.4 ± 2.6% (46.0 ± 5.3 mmol/mol) to 7 ± 3.3% (53.0 ± 12.5 mmol/mol)	
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

Potassium

Type	Recommendation
When to deprescribe	
CBR	To minimise potential prescribing cascades and risk of adverse outcomes associated with electrolyte imbalance, especially in people with an increased risk of hyperkalaemia (e.g. renal impairment, concurrent use of medicines affecting serum potassium levels), we suggest deprescribing be offered to older people taking long-term potassium: 1. Without an ongoing indication (e.g. past use for diuretic-induced hypokalaemia and current normal serum potassium) 2. For drug-induced hypokalaemia where the original drug can be suitably reduced, discontinued, or replaced by another drug (e.g. inappropriate prescribing cascade) 3. With no clear or known indication (e.g. prophylaxis in people with a low risk of hypokalaemia)
Ongoing treatment	
CBR	We suggest continuing potassium in older people with persistent potassium depletion due to causes that cannot be resolved: • Advanced liver disease; or • Secondary hyperaldosteronism with renovascular hypertension; or • Gastrointestinal losses; or • Concomitant medicines known to affect potassium status adversely that cannot be deprescribed provided treatment aligns with the individual's goals and preferences, following informed consent.
How to deprescribe	
CBR	We suggest discontinuing potassium without the need for tapering with the possibility of restarting if needed. If tapering is preferred [e.g. for people taking a high dose (i.e. > 1200 mg three times daily) prior to deprescribing], we suggest reducing the dose by 50%* every two weeks to minimise the risk of hypokalaemia. Once the lowest dose is reached, we suggest discontinuing potassium completely. **Tapering can be performed by reducing the dosing frequency. Effervescent tablet formulation is available, presenting additional options for tapering doses.*
Monitoring	
CBR	We suggest closely monitoring serum potassium concentration with the time frame to be determined by the baseline dose. In general, we suggest reassessing serum potassium concentration once, one week after deprescribing. We suggest periodic monitoring for dietary changes (i.e. intake of potassium-containing foods), and symptoms or signs attributable to hypokalaemia (e.g. muscle weakness, cramps, spasms, fatigue, and palpitations).

CBR, consensus-based recommendation

Introduction

Hypokalaemia is widely defined as a serum potassium concentration of <3.5 mmol/L [222]. A cross-sectional study reported that hypokalaemia is significantly more prevalent in older people with a diagnosis of hypertension, especially those taking potassium-losing diuretics [222]. In contrast, the incidence of hypokalaemia did not significantly differ between older people with heart failure and those without [222]. Mild-to-moderate hypokalaemia is typically treated with an oral potassium

supplement. Enteral preparations are often poorly tolerated due to common gastrointestinal side effects including nausea, vomiting, diarrhoea, and abdominal pain [223].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

The benefits of potassium supplements and medicines that increase serum potassium levels must be carefully balanced against the risk of hyperkalaemia, as the risk of hyperkalaemia becomes more pronounced with advancing age and the presence of comorbidities such as chronic kidney disease and diabetes [224].

Maintaining serum potassium within the optimal range is essential as dyskalaemia (encompassing both hypokalaemia and hyperkalaemia) can cause neuromuscular, gastrointestinal, and cardiac abnormalities [225]. In people with heart failure, hypokalaemia is associated with a higher risk of morbidity and mortality [225]. Similarly, both hypokalaemia and hyperkalaemia are linked to increased mortality risks in people with arrhythmias or acute myocardial infarction [226, 227].

People with persistent potassium depletion due to irreversible causes (e.g. advanced liver disease, secondary hyperaldosteronism with renovascular hypertension, gastrointestinal losses) may require ongoing potassium supplementation to maintain adequate levels [228].

The major risk factors for hyperkalaemia are renal impairment, history of diabetes mellitus, adrenal disease and concurrent use of medicines affecting serum potassium levels such as angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and potassium-sparing diuretics [229]. A common example of a prescribing cascade involves lower extremity oedema, which may occur as a side effect of a calcium channel blocker. Rather than discontinuing the causative medicine, a diuretic is often added, followed by potassium supplementation to counteract diuretic-induced potassium loss [230]. In some cases, the original medication affecting serum potassium levels may be discontinued, yet potassium supplementation is unnecessarily continued as a 'relic' of prior prescribing [231]. In individuals with normal serum potassium levels and no clear ongoing indication, deprescribing may be appropriate to reduce the risk of dyskalaemia.

If potassium is considered suitable to deprescribe, monitoring serum potassium concentration is necessary along with dietary changes (i.e. intake of potassium-containing foods), and symptoms or signs attributable to hypokalaemia [228]. It may be helpful to provide examples of common symptoms of hypokalaemia (e.g. muscle weakness, cramps, spasms, fatigue, and palpitations) when encouraging individuals to self-monitor and report symptoms to their healthcare professionals. As some symptoms are non-specific, many individuals may not recognise that they could be indicative of hypokalaemia.

Narrative summary of evidence on deprescribing

We identified one before-and-after study related to deprescribing potassium from the systematic review and meta-analysis. The current evidence for deprescribing potassium is based on a single-arm study. Although approximately half of the participants on diuretics for heart failure were able to discontinue potassium without a significant change in their mean erythrocyte potassium level, the certainty of the evidence is of very low certainty due to a surrogate outcome, very small sample size, lack of a comparison group, and other methodological limitations. The evidence at this stage is insufficient to inform evidence-based recommendations.

Key study characteristics and results

Henschke 1981 conducted a before-and-after study that involved 14 male veterans living in a veterans' care complex who were taking diuretics for heart failure as well as potassium supplements as routine prophylaxis against potassium depletion. All 14 veterans received an average daily potassium content of 100 mEq and had their oral potassium supplements withdrawn [232]. Six weeks after withdrawal of potassium supplements, plasma potassium levels significantly fell by a mean of 0.37 mmol/L ($p < 0.001$) but there was no significant change in mean erythrocyte potassium level (from 107.3 ± 6.3 mmol/L and 105.7 ± 7.4 mmol/L). No deaths were reported. For a further six weeks after the withdrawal period, seven participants (50%) were given a combination of 25 mg spironolactone (potassium-sparing diuretic) and 25 mg hydrochlorothiazide. Plasma potassium level increased significantly but the erythrocyte potassium level remained unchanged. None of the participants reported adverse effects or symptoms attributable to hypokalaemia during the period of study.

Narrative evidence summary: withdrawal schedules

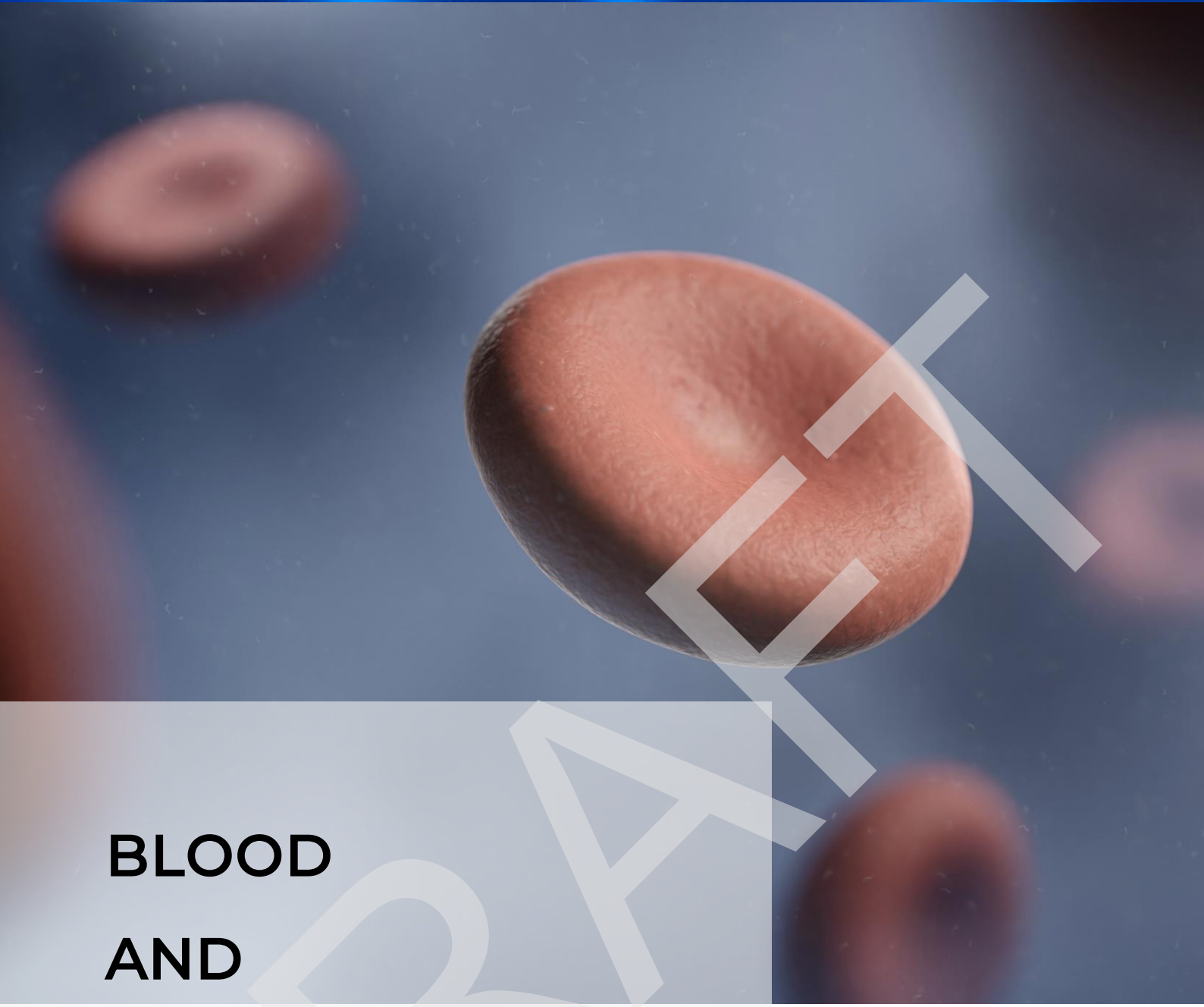
The method of deprescribing was not specified in the study, but it appears to have involved abrupt discontinuation .

GRADE Summary of Findings (SoF) Table

Table 10. Summary of findings for deprescribing potassium

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
1 [232]	Non-controlled study	14	N/A	0%	
2. Adverse drug withdrawal events (ADWEs)					
1 [232]	Non-controlled study	14	N/A	Adverse effects or symptoms attributable to hypokalaemia during withdrawal, 0% Change in serum potassium levels over three months, - 0.37 mmol/L	
3. Health outcomes					
No available evidence					
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*Effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.



BLOOD AND BLOOD-FORMING ORGANS

This section includes:

- Iron/ Vitamin B12 (Anti-anaemic preparations)
- Antithrombotic agents (anticoagulants and antiplatelets)

BLOOD AND BLOOD FORMING ORGANS

Antithrombotic agents (anticoagulants and antiplatelets)

Antithrombotic agents include:

Anticoagulants

- Vitamin K antagonists: Warfarin*
- Heparins: Dalteparin, danaparoid, enoxaparin, heparin, nadroparin
- Direct thrombin inhibitors: Bivalirudin, dabigatran
- Direct factor Xa inhibitors: Apixaban*, rivaroxaban*
- Other antithrombotic agents: Fondaparinux

Antiplatelets

- Platelet aggregation inhibitors excluding heparin: Aspirin, clopidogrel*, ticagrelor, prasugrel, tirofiban, eptifibatide, dipyridamole

Combination antiplatelets: Aspirin with clopidogrel or dipyridamole

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing decisions be made in consultation with the person and their GP and/or specialist providers to ensure it aligns with their preferences, goals and overall treatment plans. We suggest deprescribing be offered to older people taking **oral anticoagulants**: • For short-term indications (e.g. acute venous thromboembolism for over 6-12 months in people without recurrent unprovoked venous thromboembolism or not at an increased risk of recurrence); or • When the risk of major/recurrent bleeding outweighs the benefit of prevention of ischaemic stroke or thromboembolism, following a shared informed decision-making process with the person and/or family/carers. We suggest deprescribing of **warfarin** be offered to older people with advanced chronic kidney disease (CKD IV-V/ESKD) as the risk of complications may outweigh the potential benefits of anticoagulation.
CBR	We suggest deprescribing decisions be made in consultation with the person and their GP and/or specialist providers to ensure it aligns with their preferences, goals and overall treatment plans. We suggest deprescribing of **antiplatelets** be offered to older people: • Taking aspirin for the **primary prevention** of cardiovascular events due to the progressive reduction in net benefit relative to increased risk of major bleeding in older people • Taking **dual antiplatelet therapy** for short-term indications (e.g. beyond 6-12 months post-acute coronary syndrome [or shorter duration in selected high bleeding risk populations); and continue with antiplatelet monotherapy) • Taking triple antithrombotic therapy [i.e. dual antiplatelet therapy plus an anticoagulant (for an oral anticoagulation indication such as atrial fibrillation)] beyond 1 to 4 weeks post-percutaneous coronary intervention; continue single antiplatelet therapy plus an anticoagulant for 6 to 12 months; then anticoagulant monotherapy for the long-term oral anticoagulation indication

	provided the person is stable and the risks of bleeding outweigh the benefits of continued dual therapy.
Ongoing treatment	
CBR	We suggest continuing antithrombotics in robust older people with cardiovascular risk factors taking: • **Anticoagulants** for the primary prevention of thromboembolic events due to atrial fibrillation or secondary prevention of cardiovascular events • **Antiplatelets** for the secondary prevention of cardiovascular events (e.g. in people with stable coronary artery disease, peripheral artery disease or cerebrovascular disease) provided there are no life-limiting diseases (where potential risks often outweigh potential benefits) or significant bleeding risk, and this aligns with the individual's goals and preferences, following informed consent.
GPS	Healthcare providers should reassess an individual's cardiovascular and bleeding risk at least annually or more frequently, based on clinical indications or changes in health status, using a validated tool appropriate for the patient population (e.g. HAS-BLED for estimating major bleeding risk in people receiving anticoagulation for atrial fibrillation, and CHA_2DS_2-VASc for calculating stroke risk) (ungraded good practice statement).
How to deprescribe	
CBR	We suggest ceasing anticoagulants and/or antiplatelets, without the need for tapering.
Monitoring	
CBR	**Routine monitoring** We suggest close monitoring of ongoing risk factors (e.g. risk of bleeding and cardiovascular events), at least monthly for the first six months after deprescribing, followed by monitoring every six months thereafter to maintain the therapeutic relationship while working on potentially modifiable cardiovascular risk factors through lifestyle optimisation. However, this should be tailored based on individual factors such as their preferences, responses and tolerance to deprescribing. For **warfarin**, routine monitoring of the international normalised ratio (INR) when stopping is generally not required, especially if the INR is within the therapeutic range. However, closer monitoring (a few days after cessation) may be preferred if there are concurrent illnesses or medicine changes (including prescribed, over-the-counter medicines, complementary and alternative medicines). For people who need to restart warfarin therapy, closely monitoring the INR is essential to achieve the therapeutic range.
CBR	We suggest advising people to present for medical attention in case of concerning symptoms (e.g. dyspnoea, chest pain, or painful and/or swollen calf suggestive of venous thromboembolism).

CBR, consensus-based recommendation; GPS, good practice statement

Introduction

Anticoagulants

Anticoagulants are indicated for deep vein thrombosis, pulmonary embolism, ischaemic stroke, transient ischaemic attack, and during the acute hospitalisation phase of acute coronary syndromes (ACS) [177]. Independent risk factors for the long-term risk of major bleeding include age > 65 years, concomitant antiplatelet therapy, renal impairment (creatinine clearance <50 mL/min), anaemia, and history of major bleeding [233, 234]. In clinical practice, anticoagulants for stroke prevention are often under-prescribed in older people with newly diagnosed atrial fibrillation (AF), likely due to the perceived risk of severe haemorrhage outweighing anticoagulation benefits [235, 236].

The factors influencing the prescribing of direct oral anticoagulants and warfarin in older people with AF include a history of dementia, falls, major bleeds, and fractures [237]. Optimal prescribing of anticoagulants requires the healthcare provider to assess the benefits of reduced thromboembolic events against the risk of major bleeding. In people who require long-term anticoagulation, at least an annual reassessment of risks and benefits is essential [233]. Excessive anticoagulation may lead to serious harm including anticoagulant-related nephropathy and bleeding [177]. Anticoagulant-related nephropathy is a type of acute kidney injury, but it may also result in permanent kidney damage and increased mortality [177].

Antiplatelets

Antiplatelets are indicated for the prevention of ACS or cerebral vascular disease [177]. Its use can be separated into primary (without established cardiovascular disease) or secondary prevention (with a prior cardiovascular event).

Dual antiplatelet therapy (DAPT)

Other antiplatelet agents (P2Y12 antagonists e.g. clopidogrel, ticagrelor, prasugrel) are often used as secondary prevention agents to prevent the recurrence of cardiovascular events. DAPT, consisting of aspirin and P2Y12 receptor antagonists, is often initiated post-hospitalisation for ACS or stroke. Recommended duration varies depending on the initial indication, and individual bleeding and ischaemic risks.

The 2025 Australian clinical guideline for the diagnosis and management of ACS provided a strong recommendation that DAPT (with aspirin and a P2Y12 inhibitor) should be prescribed for [238]:

- Six to 12 months in people discharged post-ACS who are at high ischaemic and/or low bleeding risk
- One to three months post-ACS in low ischaemic and/or high bleeding risk, followed by single antiplatelet therapy (SAPT)

In addition, the 2025 American College of Cardiology (ACC) and American Heart Association (AHA) joint guideline for the management of ACS provides updated recommendations on dual antiplatelet therapy (DAPT) duration and strategies to reduce the risk of bleeding [239]:

- For people not at high bleeding risk, a standard 12-month DAPT regimen consisting of aspirin and an oral P2Y12 inhibitor is recommended to reduce the risk of major adverse cardiovascular events (MACE)
- In patients with ACS who have tolerated DAPT (aspirin and ticagrelor), discontinuation of aspirin and continuation with ticagrelor monotherapy after one to three months post-PCI may be considered to lower bleeding risk. Alternatively, de-escalation of P2Y12 inhibitor potency (from aspirin + ticagrelor/prasugrel to aspirin + clopidogrel) can be considered to reduce bleeding risk
- In patients with ACS at high bleeding risk, early transition to single antiplatelet therapy (either aspirin or a P2Y12 inhibitor) after one month post-PCI may be reasonable

Evidence supports shortened DAPT durations in selected post-PCI populations to balance the risks of bleeding and MACE. A 2024 systematic review and meta-analysis of 14 RCTs found that abbreviated DAPT regimens of one or three months were associated with significantly lower bleeding risk compared to six months of DAPT, without an increase in net adverse clinical events or MACE [240]. Additionally, three months of DAPT was associated with a lower risk of bleeding compared to 12 months [240]. Additionally, when comparing aspirin monotherapy with clopidogrel monotherapy, a secondary analysis of the STOPDAPT-3 trial found no significant difference in cardiovascular or bleeding outcomes beyond 1 month and up to 12 months after PCI with drug-eluting stents [241].

Concurrent antiplatelet and anticoagulant therapy
Certain clinical situations necessitate the temporary use of combined antiplatelet therapy and oral anticoagulants (OAC), after which a clinical decision should be made to discontinue either therapy. Combining antiplatelet with OAC should only occur in people who require anticoagulation for thromboembolic prevention (e.g. AF, venous thromboembolism) but also have an indication for antiplatelet therapy (e.g. recent ACS or percutaneous coronary intervention) [242].

Triple antithrombotic therapy (an oral anticoagulant, aspirin and a P2Y12 inhibitor) is commonly indicated for people requiring long-term anticoagulation therapy (e.g. for AF, venous thromboembolism, and prosthetic heart valves) plus an indication for dual antiplatelet therapy following coronary stent insertion for ACS. The balance between ischaemic and bleeding risks must be carefully considered.

Justification of recommendations
Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

1. Anticoagulants
Although AF primarily affects older people, they are often under-represented in RCTs, particularly those who are frail. Australian clinical guidelines recommend anticoagulation for all people aged 75 years and older with non-valvular AF [243]. In people with acute ischemic stroke and AF, OAC is often switched to antiplatelet therapy until the risk of haemorrhagic transformation is low, normally up to two weeks, depending on the size of the infarcted area, after which the OAC is re-started [244]. The risk of major bleeding in people taking OAC for stroke prophylaxis is 2-3% per year, with approximately half of these events being gastrointestinal bleeding [245]. Similar rates were observed when OAC was used for venous thromboembolism prophylaxis [246]. However, anticoagulant-related major bleeding is more likely to be fatal than recurrent venous thromboembolism [234]. In people with AF, anticoagulation is only recommended when the net clinical benefit of reducing ischaemic stroke risk outweighs the potential harm from major bleeding. The bleeding risk in people prescribed long-term anticoagulation for atrial fibrillation can be estimated using the HAS-BLED score. In older people with advanced chronic kidney disease (CKD IV-V/ESKD), the risk of bleeding complications with warfarin use often outweighs the potential benefits of anticoagulation [247].

CHA_2DS_2–VASc is a point-based tool that can be used to calculate stroke risk in people with atrial fibrillation [248]. The tool was validated to predict the patients at high risk for mortality within three to five years in people with atrial fibrillation [248]. The scores for stratifying risk levels were score 0 (low risk), score 1 (medium risk), and score ≥ 2 (high risk) [248]. For people with a CHA_2DS_2–VASc score of ≥ 2 (high risk), anticoagulant therapy is recommended, whereas in those with a CHA2DS2-VA score of 1 (medium risk), anticoagulant therapy should be considered following a person-centred approach and careful assessment of other thromboembolic risk factors if present [242].

However, the tools are not sufficient on their own to justify withholding anticoagulants in AF [243]. A study involving approximately 25,000 people with AF found that for those with a HAS-BLED score of 3 or more, continuing OAC was associated with better clinical outcomes, including stroke prevention, reduced major bleeding, and lower all-cause mortality [249]. Higher HAS-BLED scores may be used as a prompt to identify and address modifiable bleeding risk factors, such as uncontrolled hypertension, excessive alcohol intake, concomitant antiplatelet use, and the need for fall prevention. Restarting anticoagulation after a bleeding episode must balance stroke prevention with the risk of recurrent bleeding. A systematic review reported that many people with AF were willing to accept a moderate increase in the risk of bleeding to reduce stroke risk [250]. However, recommendations for clinical practice are rarely straightforward, especially in the care of people who

are frail. An individualised approach should be implemented, involving informed decision-making with the person, their carer and/or family.

The anticoagulant effect of warfarin diminishes upon cessation, with normal coagulation typically restored in a few days. Warfarin has a mean half-life of 40 hours and the duration of effect is typically two to five days [251]. When stopping warfarin, routine monitoring of the international normalised ratio (INR) is generally not required, particularly if the INR is within the therapeutic range at the time of discontinuation. However, closer monitoring a few days after cessation may be appropriate in the presence of concurrent illness or changes in medications, including prescribed, over-the-counter, complementary, or alternative therapies. For individuals who require reinitiation of warfarin, close INR monitoring is essential to ensure a return to and maintenance of the therapeutic range.

2. Antiplatelets

Older people who are otherwise well, functionally independent, and have a life expectancy of five years or more are likely to derive the most benefits from antiplatelet therapy as secondary prevention [252]. However, the net benefit in primary prevention declines with advanced age due to underlying comorbidities. In older people without a history of cardiovascular, cerebrovascular, or peripheral arterial disease, the risk of major gastrointestinal or intracranial bleeding from aspirin often offsets the risk reduction in preventing cardiovascular events [177].

The ASPirin in Reducing Events in the Elderly (ASPREE) trial included 19,114 community-dwelling older people aged 70 years or above in Australia and the United States without a history of dementia or cardiovascular disease [253]. The study reported no benefit of prophylactic aspirin in lowering cardiovascular risk but resulted in a significantly higher risk of major bleeding events [254].

Furthermore, post-hoc subgroup analysis of the ASPREE trial demonstrated aspirin did not improve outcomes in older people with CKD while increasing bleeding risks [255]. CKD was defined as either baseline eGFR <60mL/min/1.73m^2 or urine albumin to creatinine ratio $\geq$ 3 mg/mmol.

The routine use of aspirin for primary prevention of cardiovascular disease in patients with chronic kidney disease is generally not recommended [256]. This is due to an increased bleeding risk in people with chronic kidney disease and clear benefit in the reduction of cardiovascular events lacking for primary prevention.

Coronary artery calcium (CAC) scoring, used for predicting future cardiovascular risk, may be useful in identifying a subgroup of people who are more likely to benefit from antiplatelet therapy for primary prevention. People with a CAC score of more than 100 were estimated to have a favourable risk/benefit profile for aspirin use in the primary prevention of coronary heart disease, with the greatest benefit observed in those with a score exceeding 400. However, these effects have not been well studied in people over the age of 70 [257, 258].

The use of DAPT beyond six to 12 months (or beyond one to three months in certain people post-PCI) is rarely indicated [238, 239], as it increases bleeding risk without additional benefit in reducing cardiovascular or all-cause mortality for most people [259]. However, individual assessment of bleeding and ischemic risk is essential to guide DAPT duration. For stroke, DAPT is recommended to be used for only 21 days following an acute ischaemic stroke or transient ischaemic attack. A meta-analysis of four trials has found the net benefit of DAPT occurred within the first 21 days and DAPT beyond three months significantly increased bleeding and mortality risk with no reduction in major vascular events [260]. DAPT therapy to reduce ischaemic risks needs to be weighed against the higher bleeding risk and all-cause mortality [259]. The PRECISE-DAPT score, validated in 21 studies, was developed to assess bleeding risk in people treated with DAPT following coronary stent

insertion for coronary artery disease. Older people with either prior bleeding, anaemia Hb <100g/L or CKD stage IV or V are recommended to have a shortened DAPT duration [261].

3. Concurrent antiplatelet and anticoagulant therapy

In people with an indication for oral anticoagulation (e.g. AF) undergoing percutaneous coronary intervention, triple therapy should be continued for up to seven days or extended up to one month in people at high ischaemic risk [239]. After this, the person should transition (i.e. step down) to OAC plus SAPT, preferably with a P2Y12 inhibitor (clopidogrel) due to its lower bleeding risk, for up to six months (in people not at high ischaemic risl) or 12 months (in people at high ischaemic risk) post-event (including duration of triple therapy), then stepping down to OAC alone ongoing for the oral anticoagulation indication [238, 239, 262]. During the first 12 months of therapy, any new ischemic or bleeding event should prompt a re-evaluation of antithrombotic therapy [243].

To date, only two RCTs have evaluated the efficacy of OAC monotherapy versus OAC plus SAPT for maintenance thrombotic prevention in people with AF, both conducted in Asian populations. The OAC-ALONE trial was terminated prematurely due to slow enrolment [263]. The AFIRE trial which followed 2,236 people over 23 months, compared rivaroxaban monotherapy with rivaroxaban plus SAPT (either aspirin or a P2Y12 inhibitor) was also stopped early due to increased mortality in the combination therapy group [264].

Several ongoing RCTs are expected to provide further insights into this area, including SoSTART, APACHE-AF, and ASPIRE trials. Although the evidence remains inconclusive, some guidelines, such as those from the European Society of Cardiology [265] and the National Heart Foundation of Australia [243], recommend OAC monotherapy for stroke prevention after six to 12 months of stenting in people with AF.

Narrative summary of evidence on deprescribing

We identified one study related to anticoagulant deprescribing from the systematic review and meta-analysis [266]. Additionally, we identified five studies (two cohort studies and three before-and-after studies) related to antiplatelet deprescribing [254, 267-270].

Overall, the current evidence supporting the deprescribing of antithrombotic agents is of very low certainty. Available studies suggest that discontinuing low-dose aspirin used for primary prevention in patients without cardiovascular comorbidities may reduce the risk of mortality and bleeding. In contrast, for individuals with cardiovascular comorbidities, stopping low-dose aspirin prescribed for secondary prevention may increase the risk of mortality or acute cardiovascular events, particularly within the first six months of discontinuation. However, there is a lack of quality evidence to inform evidence-based recommendations. If deprescribing is considered appropriate, close monitoring of ongoing risk factors, such as bleeding risk and cardiovascular risk, is essential. Regular follow-up, ideally at least monthly during the first six months may be necessary while concurrently addressing modifiable cardiovascular risk factors through lifestyle optimisation.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Anticoagulants

Patel 2013 reported a post-hoc analysis of a double-blind RCT comparing rivaroxaban and warfarin in people with nonvalvular AF who subsequently transitioned to open-label therapy (most commonly warfarin) at the conclusion of the study. This study compared the incidence of stroke or non-central nervous system embolism during the transition in participants previously treated with rivaroxaban versus warfarin of which both groups had a temporary interruption of therapy.

The rivaroxaban group had poor anticoagulant coverage through the transition, whereas the warfarin group had no uncovered period, as evidenced by the time to a therapeutic INR. There were significantly more acute cardiovascular events (defined as ischemic stroke, non-central nervous system embolism, myocardial infarction, or vascular death) in the group that transitioned from rivaroxaban to open-label therapy at the end of the blinded RCT (compared to the warfarin group that continued open-label therapy; OR 3.73, 95% CI 1.51 to 9.21). There were also significantly more major bleeding events in the group that discontinued rivaroxaban and transitioned to open-label therapy, compared to the warfarin group that continued open-label therapy (OR 3.64, 95% CI 1.57 to 8.42).

Antiplatelets

Derogar 2013 [267] reported the discontinuation of low-dose aspirin therapy in 118 patients who were hospitalised for bleeding peptic ulcers. Among older patients with cardiovascular comorbidities (n = 76), discontinuation of low-dose aspirin therapy was associated with a substantial increase in the risk of death *or* acute cardiovascular events within the first six months of follow-up (OR 10.67, 95% CI 2.07, 55.07). Cardiovascular comorbidities included chronic ischemic heart disease or angina, chronic heart failure, previous myocardial infarction, AF, previous stroke or transient cerebral ischemia. However, there was no significant difference in mortality after the initial six-month follow-up (median follow-up duration of 24 months) (OR 0.97, 95% CI 0.32, 2.95). This retrospective cohort study did not report such an association in death or acute cardiovascular events in patients without any cardiovascular comorbidities. Among patients without cardiovascular comorbidities (n = 42), there was no death or acute cardiovascular events within the first six months of follow-up. Again, after the initial six-month follow-up, there was no significant difference in mortality between the two groups (OR 1.87, 95% CI 0.39, 9.12).

Sambu 2011 [268] included 33 patients who were taking low-dose aspirin clopidogrel 75 mg and statin treatment who had undergone PCI with a drug-eluting stent and were due to discontinue clopidogrel at one year. Following clopidogrel discontinuation, an increase in markers of platelet reactivity was observed. Although more evidence is required, discontinuation of clopidogrel may lead to a clustering of adverse events attributed to the increasing platelet activity after discontinuation.

Ramos 2024 [269] reported a pharmacist-led deprescribing before-and-after study conducted in a hospital outpatient setting. Patients aged 70 years or older who were taking aspirin for primary prevention without a documented history of atherosclerotic cardiovascular disease were contacted by pharmacists. These patients engaged in discussions with pharmacists regarding the risks and benefits of aspirin for primary prevention and were offered the option to discontinue its use. Of the 131 participants who met the eligibility criteria and were contacted, 78 (60%) discontinued aspirin following their consultation with a pharmacist.

Varghese 2024 [270] described a study involving veterans in a primary care setting who were aged 70 years or older and were taking aspirin for primary prevention of atherosclerotic cardiovascular disease. Participants were excluded if they were prescribed clopidogrel or had other indications for aspirin use. The control group received education from primary care providers on the risks and benefits of aspirin for primary prevention in older veterans. In the intervention group, in addition to provider education, a pharmacist discussed the risks and benefits of aspirin use with each eligible patient. Among the 57 patients who received care from the control group's primary care providers, 10 (18%) discontinued aspirin by the end of the four-month study. Compared with the control group, a significantly greater proportion of patients in the intervention group who were contacted by a pharmacist discontinued aspirin (35/65, 54%, p = 0.0001).

Zhou 2024 [254] conducted a post-hoc analysis of the ASPREE trial using a target trial emulation framework. As previously noted, the ASPREE trial included community-dwelling older people aged

70 years or above in Australia and the United States who had no history of dementia or cardiovascular disease. The current study analysed data from 6,103 participants during the immediate post-trial period (2017–2021), identifying 5,427 participants who had discontinued aspirin and 676 who had continued its use. At 48 months, no significant difference was observed between the discontinuation and continuation groups for cardiovascular disease (OR 0.75, 95% CI 0.54, 1.03) or major adverse cardiovascular events (OR 0.88, 95% CI 0.60, 1.30). Participants in the discontinuation group had a significantly lower risk of major bleeding events (OR 0.64, 95% CI 0.42, 0.99) and all-cause mortality (OR 0.69, 95% CI 0.53, 0.90). However, after propensity score adjustment, there was no significant difference in all-cause mortality between the two groups at 48 months (HR 0.79, 95% CI 0.61, 1.03).

Narrative evidence summary: withdrawal schedules

The method of deprescribing was not described in all studies, but it appears to have involved abrupt discontinuation.

GRADE Summary of Findings (SoF) Table

Table 11. Summary of findings for deprescribing antithrombotic agents

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
1 [254]	Non-randomised study	5427	676	**In patients without cardiovascular comorbidities:** Mortality at 48-month OR 0.69 (95% CI 0.53, 0.90)	
1 [268]	Non-controlled study	33	N/A	0%	
2. Adverse drug withdrawal events (ADWEs)					
Adverse events/ serious adverse events/ cardiovascular events					
1 [266]	RCT	4587	4652	The study reported an increased risk of stroke and systemic embolism for patients who transitioned from rivaroxaban compared with those who transitioned from warfarin (OR 3.73, 95% CI 1.51, 9.21).	
1 [267]	Non-randomised study	26	50	**In patients with cardiovascular comorbidities** Death or cardiovascular events in patients with cardiovascular comorbidities at 6 months 10.67 (2.07, 55.07) Death or cardiovascular events in patients with cardiovascular comorbidities after the initial follow-up (median 24 months) 0.97 (0.32, 2.95) **In patients without cardiovascular comorbidities** Death or cardiovascular events after the initial follow-up (median 24 months) 1.87 (0.39, 9.12)	
1 [254]	Non-randomised study	5427	676	Cardiovascular disease OR 0.75 (0.54, 1.03) Major adverse cardiovascular events OR 0.88 (0.60, 1.30)	
1 [268]	Non-controlled study	33	N/A	Stent thrombosis 3%	
3. Health outcomes					
Health service use					
1 [267]	Non-randomised study	47	71	Re-hospitalised due to peptic ulcer bleeding OR 2.11 (0.45, 9.88)	
Adverse drug events					
1 [266]	RCT	4587	4652	The study reported an increased risk of major bleeding for patients who transitioned from rivaroxaban compared with those who transitioned from warfarin (OR 3.64, 95% CI 1.57, 8.42).	
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

Iron/ Vitamin B12 (Anti-anaemic preparations)

Type	Recommendation
When to deprescribe	
CBR	If haemoglobin and ferritin/B12 levels are within an acceptable range, we suggest deprescribing be offered to older people taking iron and/or vitamin B12: 1. Without an ongoing indication (e.g. underlying cause of iron deficiency has been addressed) 2. For drug-induced indication where the original drug can be suitably reduced, discontinued, or replaced by another drug (e.g. inappropriate prescribing cascade related to metformin or proton pump inhibitors and B12) 3. With no clear or known indication (e.g. no documented history of iron/B12 deficiency or pernicious anaemia)
Ongoing treatment	
CBR	We suggest continuing iron or vitamin B12 therapy in older people whose deficiency is due to permanent underlying conditions, such as a history of gastric surgery, pernicious anaemia, or unmodifiable dietary limitations (e.g. vegetarian or vegan diet).
How to deprescribe	
CBR	We suggest ceasing iron and/or vitamin B12 therapy without the need for tapering. We suggest before deprescribing, assessing nutritional status and other relevant health factors, as part of a comprehensive care plan to ensure ongoing patient well-being.
Monitoring	
CBR	We suggest offering laboratory monitoring of complete blood count, iron studies/B12 periodically to promptly identify any recurrence of iron/B12 deficiency.
CBR	We suggest advising patients to report to their healthcare providers symptoms of iron/B12 deficiency such as unexplained lack of energy, shortness of breath, headache, and heart palpitations, or B12 deficiency symptoms of glossitis (tongue soreness), and neuropathy (numbness involving fingers/toes).

CBR, consensus-based recommendation

Introduction

Anaemia is highly prevalent in older people and is particularly common among the oldest and most frail [271]. The most common causes of anaemia in older people are chronic diseases and nutritional deficiencies (e.g. iron deficiency anaemia, vitamin B12 deficiency) [272]. Anaemia in older people is associated with an increased risk of mortality, morbidity, and all-cause hospitalisation [271].

Narrative summary of evidence on deprescribing

We were unable to identify any direct evidence related to the deprescribing of iron and vitamin B12 in older people from the systematic review and meta-analysis. Recommendations are provided in this section following a Delphi consensus process.

Justification of recommendations

Iron and vitamin B12

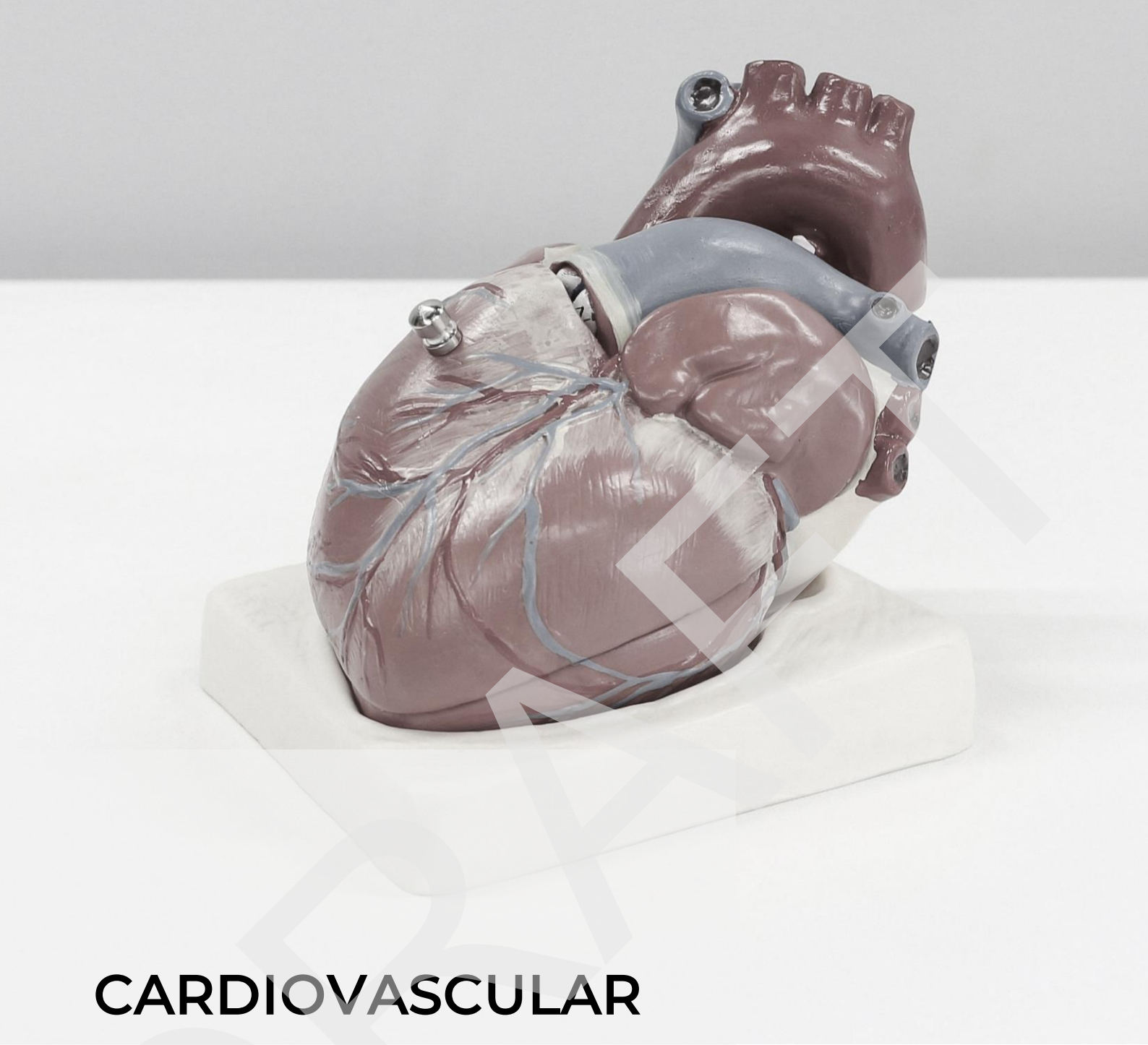
Iron supplementation is usually required until iron stores are replenished, and the serum ferritin concentration is within an acceptable range which could take three to six months [273]. Long-term use of iron supplementation may only be required after appropriate investigations have been carried out to determine the underlying cause of iron deficiency and that the cause cannot be corrected [273]. If haemoglobin levels are within an acceptable range, and there is no clear ongoing indication for continued use (i.e. irreversible cause), deprescribing may be appropriate.

Vitamin B12 is indicated for neurological symptoms in addition to anaemia caused by vitamin B12 deficiency [274]. Deficiency can lead to neurological symptoms including peripheral neuropathy, gait abnormalities, and cognitive impairment [275]. Therefore, assessing B12 levels in older people with neurological symptoms may help prevent potentially irreversible neurological complications. Most people with vitamin B12 deficiency caused by permanent underlying conditions (e.g. gastric surgery, pernicious anaemia) often require lifelong maintenance therapy after the initial treatment [274, 275]. Early detection and treatment for the underlying cause is crucial. Those with deficiency caused by the long-term use of other drugs (e.g. metformin, PPIs) that affect B12 absorption may benefit from deprescribing the causative agent where possible. Additionally, in the absence of anaemia or neurological and cognitive signs or symptoms, an RCT found that correcting moderate vitamin B12 deficiency did not provide any neurological or cognitive benefits in later life [276]. In this population, deprescribing may be appropriate.

If considered suitable to deprescribe, iron and/or vitamin B12 therapy generally do not require tapering as they do not cause physiological dependence or withdrawal/rebound syndromes.

Laboratory monitoring, if indicated, may be undertaken periodically to promptly identify any recurrence of iron/B12 deficiency [275]. General symptoms of B12 deficiency include glossitis (tongue soreness), and neuropathy (numbness involving fingers/toes) [277]. In addition, common iron deficiency includes an unexplained lack of energy, shortness of breath, headache, and heart palpitations [278].

It may be helpful to provide examples of common symptoms when encouraging individuals to self-monitor and report symptoms to their healthcare professionals. As some symptoms are non-specific, many individuals may not recognise that they could be indicative of iron and/or vitamin B12 deficiency.



CARDIOVASCULAR SYSTEM

This section includes:

- Digoxin/ Sotalol
- Organic nitrates
- Antihypertensives
- Diuretics
- Lipid-modifying agents

CARDIOVASCULAR SYSTEM

Digoxin/ Sotalol

Type	Recommendation
When to deprescribe	
CBR	**Digoxin** We suggest deprescribing decisions be made in consultation with the individual and their GP and/or specialist providers to ensure it aligns with their preferences, goals and overall treatment plans. Given the risks of digitalis toxicity and drug-drug interactions potentially outweigh the benefits in older people, especially in those with declining renal function or polypharmacy, we suggest offering deprescribing digoxin: • For individuals with heart failure with reduced ejection fraction (HFrEF) who are in sinus rhythm and have been stabilised on one or more of the "four pillars" of the guideline-directed medical therapy (GDMT) • For individuals with atrial fibrillation treated with digoxin in combination with other agents (such as beta-blockers, diltiazem or verapamil) and have achieved the target heart rate [i.e. resting heart rate of < 110 beats per minute (bpm), or stricter control of < 80 bpm for those with persistent symptoms of atrial fibrillation especially breathlessness] • For individuals experiencing potential adverse effects (e.g. cardiac disturbances, gastrointestinal symptoms)
CBR	**Sotalol** Given the risk of adverse effects (e.g. arrhythmia) potentially outweighing the benefits, we suggest deprescribing be offered to older people taking sotalol who: • Have permanent atrial fibrillation without an intention to restore or maintain sinus rhythm; or • Have been stabilised and in normal sinus rhythm for at least two to three months
Ongoing treatment	
CBR	We suggest continuing GDMT for heart failure or beta-blockers for atrial fibrillation.
How to deprescribe	
CBR	**Digoxin** We suggest individualising the tapering schedule based on the individual's clinical context. When digoxin is identified as being suitable for deprescribing, we suggest abrupt cessation if the serum level is subtherapeutic. We suggest abrupt cessation when clinically indicated, such as in cases of digitalis toxicity (e.g. bradycardia), and introducing an alternative agent for rate control if indicated. If tapering is preferred and the individual is experiencing symptoms of tachycardia, we suggest reducing the dose by 50% every two weeks until the dose reaches ≤ 62.5 microgram, then cease completely.
CBR	**Sotalol** We suggest gradual tapering of the dose by 25% every one to two weeks, ensuring individuals remain symptom-free before initiating each tapering. Once half the lowest standard dose formulation is reached, we suggest ceasing completely. If clinically indicated, consider an alternative for rate control, preferably a beta-blocker. *Note: This suggestion does not apply to cases of sotalol poisoning, where urgent procedures are required to monitor and treat QT-interval prolongation and torsades de pointes. Refer to relevant clinician resources, such as the Therapeutic Guidelines toxicology section (https://www.tg.org.au/content-updates/toxicologyandtoxinology/).*

Monitoring	
CBR	**Digoxin and sotalol** We suggest closely monitoring for changes in heart rate and/or signs of cardiac decompensation (e.g. shortness of breath) including addressing electrolyte disturbances, every one to two weeks until at least four weeks after the medicine is fully ceased if practical. After this initial period, we suggest monitoring at three and six months, followed by monitoring every six months thereafter. However, this should be tailored based on individual factors such as their other medications, preferences, responses, and tolerance to deprescribing. If in-person visits are impractical, we suggest advising people to self-monitor symptoms using pulse monitors and report to their healthcare providers as needed.

CBR, consensus-based recommendation

Introduction

Atrial fibrillation (AF)

AF is the most common arrhythmia affecting older people [279]. Beta-blockers are the preferred rate control agents in this population due to their favourable safety profile compared to digoxin, which has a narrow therapeutic index.

Digoxin, a cardiac glycoside, is used as a rate control agent for atrial fibrillation with rapid ventricular response and heart failure. However, its clinical role has declined over time due to safety concerns. If prescribed, serum digoxin concentration should be monitored to maintain a concentration below 1.2 ng/mL, particularly in older people with renal impairment [280]. However, in practice, routine monitoring of serum digoxin concentration in the community is rarely undertaken.

Sotalol, a class III anti-arrhythmic with beta-blocking properties, is predominantly used for rhythm control in AF [280]. Its use in older people requires caution due to its significant risk of QTc prolongation, which can lead to polymorphic ventricular tachycardia, including Torsades de Pointes. The incidence of Torsades de Pointes, a potentially life-threatening arrhythmia, ranges from 0.4% to 2.3% globally, with a higher risk during therapy initiation [280]. A study of people aged over 80 years who were newly prescribed sotalol found that 40% required dose reduction or discontinuation due to safety concerns [281].

Heart failure

A 2015 study highlighted that inappropriate prescribing of digoxin (defined as prescribing digoxin for HFrEF patients who are not receiving an ACE inhibitor or beta-blocker) remains prevalent [282]. In this study, 99 consecutive patients hospitalised for digoxin toxicity were assessed, and 67% of them were prescribed digoxin without appropriate indications.

The management of heart failure has advanced over the past decade. The 2022 American College of Cardiology/American Heart Association/Heart Failure Society of America guideline for the management of heart failure recommends guideline-directed medical therapy (GDMT) for people with heart failure and reduced ejection fraction (HFrEF) [283]. The GDMT, also known as the “four pillars”, includes a renin-angiotensin system inhibitor, a heart-failure specific beta-blocker, a mineralocorticoid receptor antagonist and a sodium-glucose cotransporter 2 inhibitor, as the four main recommended drug treatment regimens for HFrEF. This quadruple therapy is recommended as the regimen for HFrEF due to its demonstrated benefits in reducing morbidity and mortality [284].

Comorbid atrial fibrillation and heart failure

AF and heart failure often coexist, with a complex interplay between the two conditions that complicate management [285]. AF can worsen heart failure by reducing cardiac output due to the loss of atrial contraction, promoting tachycardia, neurohormonal activation, and irregular ventricular contractions. Conversely, heart failure increases the risk of AF through structural atrial remodelling, mitral regurgitation, and neurohormonal changes [286].

Pharmacological treatment for comorbid AF and heart failure, whether for rhythm or rate control, requires an individualised approach, especially in older people. Treatment decisions should be based on symptom burden, the success of reversion strategies, ejection fraction, and comorbidities [287]. Rhythm control strategies, such as cardioversion or catheter ablation, may benefit certain people with HFrEF and have shown superiority over pharmacological therapy in reducing mortality and hospitalisations related to worsening heart failure [288]. This further diminishes the role of digoxin in the management of coexisting AF and heart failure. From a deprescribing perspective, managing these conditions requires careful evaluation and regular review of treatment regimens to ensure therapies align with evolving clinical goals and priorities.

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

In the era of GDMT, the role of digoxin in heart failure management is very limited as it has not been shown to improve mortality in this context [289]. Current guidelines offer a class IIb recommendation (weak recommendation) for the use of digoxin in patients with symptomatic HFrEF despite GDMT or in those who cannot tolerate GDMT, to reduce hospitalisations related to heart failure [290]. The risk of digoxin toxicity increases significantly with age, particularly in the presence of renal impairment, hypokalaemia, or acute illness, and can lead to severe arrhythmias or death. Notably, digoxin toxicity accounts for 3% of all emergency department visits for adverse drug effects in older people [291]. For acute rate control during critical illness in hospitalised patients, digoxin or amiodarone may be added if beta-blockers alone are insufficient. However, for long-term rate control in older people in the community, digoxin should be limited to specific situations, such as in cases of poor tolerance to beta-blockers or non-dihydropyridine calcium channel blockers, or for persistent tachycardia (>110 bpm). Given the significant risk of toxicity, digoxin should be used with extreme caution when combined with amiodarone, as drug-drug interactions can markedly increase digoxin levels. For people without heart failure, digoxin is an independent predictor of mortality [292].

Sotalol should not be used in permanent AF where rhythm control is deemed futile. For long-term rate control in people with AF, an alternative beta-blocker is recommended as the choice of agent [280]. As with all treatment choices, long-term use of pharmacological rhythm control should balance the possible adverse effects, along with the individual comorbid conditions, symptoms, as well as values and preferences. Considerations to deprescribe sotalol may be reasonable in people who have been stabilised and in normal sinus rhythm for at least two to three months if the risk of adverse effects (e.g. QT prolongation, arrhythmia, hypokalaemia, hypomagnesemia) outweighs the potential benefits. In older people, impaired kidney function can further prolong the half-life of sotalol, increasing the risk of adverse effects. If sotalol is considered suitable to deprescribe, gradual tapering is necessary, such as reducing the dose by 25% every one to two weeks to avoid beta-blocker withdrawal syndrome [293]. If sotalol is considered suitable to deprescribe, gradual tapering may be appropriate to avoid beta-blocker withdrawal syndrome, such as reducing the dose by 25% every one to two weeks [293].

Narrative summary of evidence on deprescribing

We identified six non-controlled studies related to digoxin deprescribing from the systematic review and meta-analysis; however, no studies related to sotalol deprescribing [294-299].

Overall, the current evidence for deprescribing digoxin is derived from studies conducted in the 90s. These are single-arm studies with very small sample sizes and are of very low certainty due to significant methodological limitations. Most participants without evidence of heart failure or AF in these studies were able to safely discontinue digoxin, particularly in people who had been in sinus rhythm before withdrawal. However, the evidence is insufficient to support the development of evidence-based recommendations. Close monitoring of pulse rate and/or signs of cardiac decompensation (e.g. shortness of breath) including addressing electrolyte disturbances may be appropriate.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Daly and Edwards 1983 [294] recruited people on maintenance digoxin with a mean daily dosage between 62.5mcg to 375mcg. Deprescribing was attempted in 15 participants with subtherapeutic digoxin concentrations without heart failure. Among the 15 participants, 11 (73%) remained asymptomatic while three participants developed tachycardia during the one-month follow-up and one participant withdrew from the study.

Fair 1990 [295] reported deprescribing digoxin in 32 participants receiving long-term digoxin while only two participants received beta-blockers. 18 (56%) participants restarted their digoxin due to tachycardia, but digoxin was successfully discontinued in the remaining 14 participants (44%). Successful withdrawal was more likely in participants who had been in sinus rhythm before withdrawal.

Fonrose 1974 [296] reported deprescribing digoxin in 31 participants of whom 15 had an original indication for congestive heart failure, two for AF, and the reason was not known in 14 participants. Of the 31 participants, 15 (48%) successfully discontinued digoxin at the end of four months. Digoxin was restarted in the remaining 16 participants due to signs and symptoms indicative of cardiac decompensation. These signs and symptoms were chest pain, gallop rhythm, dyspnoea, pulmonary congestion, venous dilatation, and recurrence of oedema.

Macarthur 1990 [297] reported deprescribing maintenance digoxin in 14 nursing home residents in sinus rhythm without evidence of atrial dysrhythmia or AF during examinations before trial inclusion. Of the 14 residents, 12 (86%) successfully discontinued digoxin without deleterious effects or a change in exercise tolerance over the 18-month follow-up. Digoxin was restarted in one resident who had a history of supraventricular tachycardia (SVT) following an episode of SVT, whereas one other resident developed heart failure requiring a diuretic.

Sommers 1981 [298] reported deprescribing digoxin in 20 participants with a history of left ventricular failure but had been in sinus rhythm for at least four months without a record of previous AF. Of the 20 participants, 18 (90%) successfully discontinued digoxin without detrimental effects, one developed tachyarrhythmia and signs indicative of heart failure due to hyperthyroidism whereas one other participant also showed signs indicative of heart failure.

Wilkins and Khurana 1985 [299] reported deprescribing digoxin in 19 nursing home residents with sinus rhythm, and no evidence of congestive heart failure or AF during examinations before trial inclusion. Of the 19 residents, 16 (84%) discontinued digoxin without a change in clinical status,

one resident with a history of fibrillation restarted digoxin due to AF, one resident developed shortness of breath and was subsequently started on diuretic, and another resident with pancreatic carcinoma restarted digoxin due to tachycardia and poor general condition. During the first week of withdrawal, nine residents (47%) had an increase in pulse rate, nine (47%) had no change, and one (5%) had a decrease in pulse rate. Ten (52%) residents showed weight gain and five (26%) showed weight loss.

Narrative evidence summary: withdrawal schedules

The method of deprescribing was not described in all identified studies, except one where digoxin was ceased abruptly on the first day of the trial and participants were seen weekly for five consecutive weeks [298].

The half-life of digoxin is between 36 to 48 hours but may be prolonged in certain individuals such as those with renal impairment [300]. If digoxin is identified as being suitable for deprescribing, abrupt cessation may be considered, particularly if the serum level is subtherapeutic. If tapering is preferred, it may be reasonable to reduce the dose by 50% every two weeks until the dose reaches ≤ 62.5 microgram, then cease completely.

Note that in cases of digitalis toxicity, abrupt cessation is necessary and introduce an alternative agent for rate control if indicated. The management of digoxin toxicity is out of the scope of the current guidelines.

GRADE Summary of Findings (SoF) Table

Table 12. Summary of findings for deprescribing digoxin

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
1 [296]	Non-controlled study	31	N/A	0%	
2. Adverse drug withdrawal events (ADWEs)					
5 [294, 296-299]	Non-controlled studies	109	NA	10-56%	
3. Health outcomes					
Physical function					
2 [297, 299]	Non-controlled studies	33	N/A	Exercise tolerance unchanged, 100% [297] Weight gain, 52% [299] Weight loss, 26% [299] Increased pulse, 47% [299] Decreased pulse, 5% [299] Unchanged pulse, 47% [299]	
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*Effect measures are reported as the proportion of individuals with the outcome of interest.

Organic nitrates

Organic nitrates include glyceryl trinitrate*, isosorbide mononitrate*, and isosorbide dinitrate.

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing decisions be made in consultation with the individual and their GP and/or specialist providers to ensure it aligns with their preferences, goals and overall treatment plans. We suggest deprescribing be offered to older people taking long-acting nitrates in combination with beta-blockers or calcium channel blockers for stable coronary heart diseases who have not experienced angina symptoms or have not required short-acting nitrates for at least six months.
Ongoing treatment	
CBR	We suggest short-acting nitrates be offered to people for acute relief should angina symptoms occur.
CBR	If deprescribing is unsuccessful despite one attempt, we suggest maintaining the lowest effective dose; however, we suggest reassessing the need for long-term therapy periodically.
How to deprescribe	
CBR	In general, we suggest tapering the dosage and ensuring that short-acting nitrates are available should symptoms occur. For oral formulations, gradually reduce the dose, such as from 120mg daily to 60mg daily, to 30mg daily, then finally discontinue completely. For transdermal formulations, gradually reduce the dose, such as from 15 mg/24 hours to 10 mg/24 hours, to 5 mg/24 hours, then finally discontinue completely. If symptoms recur, we suggest restarting long-acting nitrates at the previously tolerated dose, delaying further dose reductions by an agreed interval for stabilisation, and planning for a more gradual taper if appropriate.
Monitoring	
CBR	We suggest closely monitoring for blood pressure or recurrence of angina symptoms tailoring the approach to individual factors such as preferences, responses, and tolerance to deprescribing. If in-person visits are impractical, we suggest advising people to report symptom recurrence as needed (e.g. telehealth).

CBR, consensus-based recommendation

Introduction

Long-acting nitrates are commonly used for angina prophylaxis and are effective in increasing exercise capacity in people with stable angina. However, RCTs have not demonstrated a reduction in major adverse cardiac events (MACE) with the use of nitrates [301]. In people with stable angina, long-acting nitrates are typically prescribed to prevent angina attacks [302]. Current guidelines for the management of chronic coronary disease recommend antianginal therapy with either a beta-blocker, calcium channel blockers, or long-acting nitrate for relief of angina or equivalent symptoms [303]. The addition of a long-acting nitrate to a beta blocker or a calcium channel blocker has been shown to improve exercise tolerance and reduce the frequency of angina and use of short-acting nitrate [303].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

For immediate short-term relief of angina, short-acting sublingual nitroglycerin remains the mainstay of treatment. The benefits of long-acting nitrates must be weighed against the potential adverse effects, including headache, orthostatic hypotension, rebound angina, dyspepsia, and peripheral oedema [304].

Deprescribing (de-escalation from combination therapy) may be appropriate in people taking long-acting nitrates in combination with beta-blockers or calcium channel blockers for stable coronary heart diseases who have not experienced angina symptoms or have not required short-acting nitrates for at least six months.

Narrative summary of evidence on deprescribing

We identified one RCT and one non-controlled study related to long-acting nitrates deprescribing from the systematic review and meta-analysis [305, 306].

Overall, the current evidence for deprescribing long-acting nitrates is derived from a single RCT and a single-arm study of small sample sizes and low certainty. Although these studies showed that most participants with stable coronary disease were able to safely discontinue their long-term nitrates without major adverse cardiac events, the evidence is insufficient to inform evidence-based recommendations.

It may be appropriate to closely monitor for the recurrence of angina symptoms (e.g. breathlessness) and blood pressure. Current evidence indicates that most individuals who experience a recurrence of angina symptoms report it within the first month of medication withdrawal. The monitoring approach should be tailored to each individual's needs and circumstances. It may be helpful to provide examples of common symptoms when encouraging individuals to self-monitor and report symptoms. As some symptoms are non-specific, many individuals may not recognise that they could be indicative of a worsening of the condition.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

George 2003 [305] conducted an RCT that reported deprescribing of long-acting nitrates in 80 participants with coronary artery disease who were angina-free and hemodynamically stable. Eight out of 80 participants (10%) in the intervention group had a recurrence of anginal symptoms within the first month of withdrawal, compared with one out of 40 (2.5%) control participants. The mean interval until the recurrence of anginal symptoms was two weeks. All eight participants responded well to the reinitiation of nitrates.

Jackson 2005 [306] reported a before-and-after study of deprescribing long-acting nitrates in 55 men with stable coronary disease and concurrent erectile dysfunction to facilitate the use of phosphodiesterase type five (PDE5) inhibitors. Concomitant beta-blocker or calcium antagonist therapy was continued following nitrate deprescribing. Three participants (5%) restarted their nitrates due to a slight increase in breathlessness. There were no adverse cardiac events or deterioration in subjective exercise ability.

Narrative evidence summary: withdrawal schedules

> Nitrates were discontinued abruptly in the RCT [305] whereas in another study, the nitrate dose was halved for two days and then discontinued if no there was no increase in symptoms [306].

Compared to abrupt cessation, dose tapering is likely more acceptable for most people and practical to determine the lowest effective dose for some people requiring dose reduction rather than complete cessation. Short-acting nitrates should be available for acute relief should angina symptoms occur.

GRADE Summary of Findings (SoF) Table

Table 13. Summary of findings for deprescribing organic nitrates

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
No available evidence					
2. Adverse drug withdrawal events (ADWEs)					
ADWEs					
1 [306]	Non-controlled study	55	N/A	Recurrence of the underlying condition (breathlessness), 5%	
Exacerbation /return of underlying condition					
1 [305]	RCT	80	40	In the first month, eight participants (10%) had a recurrence of anginal symptoms, compared with one control subject (2.5%), OR 4.33 (0.52, 35.92)	
Adverse events					
1 [306]	Non-controlled study	55	N/A	Adverse cardiac events, 0%	
3. Health outcomes					
Physical function					
1 [306]	Non-controlled study	55	N/A	Deterioration in subjective exercise ability, 0% Change in five-item Sexual Health Inventory for Men scores (to assess erectile dysfunction in men) from 7.9 ± 5.15 to 21.8 ± 4.3, indicating an improvement.	
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*Effect measures are reported as either the proportion of individuals with the outcome of interest or both the baseline and endpoint values as mean ± standard deviation.

Antihypertensives

Antihypertensives include:
Agents acting on the renin-angiotensin system:

- Angiotensin-converting enzyme (ACE) inhibitors: Captopril, enalapril, fosinopril, lisinopril, perindopril*, quinapril, ramipril*, trandolapril
- Angiotensin II receptor blockers (ARBs): Candesartan*, irbesartan*, olmesartan*, telmisartan*, valsartan
- Drugs for heart failure: Sacubitril with valsartan*

Beta-blocking agents:

- Heart failure restricted beta-blockers (bisoprolol*, carvedilol, metoprolol succinate, nebivolol*)
- Unrestricted beta-blockers (atenolol*, metoprolol tartrate*, propranolol)

Calcium channel blockers (CCBs):

- Selective CCBs with mainly vascular effects: Amlodipine*, clevidipine, felodipine*, lercanidipine*, nifedipine
- Selective CCBs with direct cardiac effects: Diltiazem*, verapamil*

Diuretics:

- Low-ceiling diuretics, thiazides: Hydrochlorothiazide (alone or with amiloride)
- Low-ceiling diuretics, excluding thiazides: Chlorthalidone, indapamide

Other antihypertensives:

- Antiadrenergic agents, centrally acting: Clonidine, methyldopa, moxonidine*
- Antiadrenergic agents, peripherally acting: Prazosin*
- Agents acting on arteriolar smooth muscle: Diazoxide, hydralazine, minoxidil

Combination drugs used for hypertension:

- Hydrochlorothiazide with amiloride/ candesartan*/ enalapril/ fosinopril/ irbesartan*/ olmesartan (alone or with amlodipine)/ quinapril/ telmisartan*/ valsartan (alone or with amlodipine*) / amlodipine (alone or with valsartan) / olmesartan (alone or with amlodipine)
- Amlodipine with telmisartan*/ perindopril*/ valsartan*/ olmesartan/ hydrochlorothiazide (alone or with valsartan*/ olmesartan)
- Perindopril with indapamide*
- Ramipril with felodipine
- Trandolapril with verapamil
- Lercanidipine with enalapril
- Antihypertensives in combination with lipid-modifying agents: Amlodipine with atorvastatin*

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing decisions be made in consultation with the person and their GP and/or specialist providers to ensure it aligns with their preferences, goals and overall treatment plans. Following shared decision-making, we suggest deprescribing of antihypertensives be offered to older people with: 1. Relative contraindications such as: • Verapamil or diltiazem used in heart failure with reduced ejection fraction in the absence of atrial fibrillation (AF); • Beta-blockers or verapamil/diltiazem use in inappropriate bradycardia (e.g. < 60 beats/minute) or any evidence of atrioventricular block causing symptoms (e.g. exertion fatigue); • Loop/thiazide diuretics used in symptomatic hyponatremia, diabetes mellitus, or gout; • Refractory/persistent hyperkalaemia in people taking ACE inhibitors, ARBs, aldosterone antagonists or potassium-sparing diuretics; or • Combination of ACE inhibitor and ARB (at least one should be deprescribed) 2. Adverse effects potentially outweigh benefits: • Systolic blood pressure (SBP) < 150 mmHg in people aged ≥ 80 years (SBP < 140 mmHg if 75-79 years of age) and diastolic blood pressure (DBP) < 90 mmHg with any of the following: orthostatic syncope/ recurrent falls /moderate-to-severe frailty assessed using validated tools/ life expectancy < 3 years • After a single episode of hyperkalaemia in people taking ACE inhibitors, ARBs, aldosterone antagonists or potassium-sparing diuretics where the symptoms of heart failure or blood pressure can be controlled with other agents.
Ongoing treatment	
CBR	We suggest continuing antihypertensives in people: • Who are robust, including those aged 85 years or older, if well tolerated, with the same target blood pressure as younger people • Taking beta-blockers for the management of AF at the lowest effective dose • Taking ACE inhibitors, ARBs, or beta-blockers for the management of heart failure • Taking ACE inhibitors or ARBs for renoprotection
CBR	If deprescribing is unsuccessful despite two attempts, we suggest maintaining the lowest effective dose; however, we suggest reassessing the need for long-term therapy periodically.
How to deprescribe	
CBR	We suggest tapering beta blockers and centrally acting antihypertensives (e.g. methyldopa, moxonidine and clonidine) as they are more likely to lead to withdrawal symptoms (e.g. headache, palpitations, and tremors) or rebound hypertension when stopped abruptly. In general, we suggest halving the daily dose every two weeks, ensuring individuals remain symptom-free and SBP < 150 mmHg in people 80 years or above (SBP < 140 mmHg if 75-79 years of age) and DBP < 90 mmHg before initiating each tapering. Once half the lowest standard dose formulation is reached, we suggest discontinuing completely and providing advice on lifestyle changes. For other antihypertensive drug classes, we suggest individualising the need for tapering depending on the drug class and the individual's response and tolerance.

CBR	We suggest restarting antihypertensives if SBP is ≥ 150mmHg in people 80 years or above with moderate-to-severe frailty or a history of adverse effects (or SBP ≥ 140 if aged 75-79 years) and DBP is ≥ 90 mm Hg on three consecutive readings over four weeks. If SBP ≥ 180mmHg or DBP ≥ 110mmHg, restart immediately.
CBR	For people taking multiple antihypertensives, we suggest deprescribing one medicine at a time. Priority should be given to antihypertensives with a higher risk of side effects. We suggest the following sequence for deprescribing: 1. Loop diuretics, centrally acting antihypertensives, peripheral vasodilators or alpha-blockers 2. Aldosterone antagonists 3. Beta-blockers, thiazide diuretics 4. Calcium channel blockers 5. ACE inhibitors, ARBs When two antihypertensives have a similar safety profile, the individual's preferences should guide the deprescribing process.
Monitoring	
CBR	We suggest advising people to self-monitor for orthostatic symptoms, angina symptoms, blood pressure, and heart rate at home by using a blood pressure monitor if people can use it correctly and to report unusual symptoms to their healthcare provider as needed. We suggest monitoring other drug-specific adverse drug withdrawal events such as palpitations (verapamil, diltiazem, beta-blockers), prostatism (alpha-blockers), or peripheral oedema and shortness of breath (diuretics).
CBR	We suggest closely monitoring for fall risks and ongoing cardiovascular risk factors, at least monthly for the first six months after deprescribing, followed by monitoring every six months thereafter. However, this should be tailored based on individual factors such as their preferences, responses and tolerance to deprescribing. People at a higher risk of cardiovascular risk factors may require more frequent monitoring. We suggest offering advice on lifestyle optimisation for potentially modifiable cardiovascular risk factors.

CBR, consensus-based recommendation

Note: This section includes evidence from studies that targeted drugs commonly used for hypertension, which includes one or more common drug classes classified under the cardiovascular system. Evidence from studies specifically targeting diuretics is presented separately in the following section.

Introduction

Hypertension is a common condition among older people that is multifactorial (genetic and environmental) and often contributed to by age-related changes in arterial stiffness (especially systolic hypertension) [307]. Elevated blood pressure (BP) is a well-established risk factor for cardiovascular disease and stroke. Stage 2–3 hypertension, defined as systolic blood pressure (SBP) ≥160 mm Hg or diastolic blood pressure (DBP) ≥100 mm Hg, has been associated with an increased risk of all-cause mortality (hazard ratio [HR] 1.23, 95% confidence interval [CI]: 1.10–1.37) [308]. The primary factor driving the reduction in cardiovascular events in both younger and older people with hypertension is the extent of blood pressure reduction, rather than the specific type of antihypertensives (e.g. ACE inhibitors, beta-blockers, CCBs, or diuretics) [309, 310]. The management of hypertension in older people is particularly complex due to multimorbidity, including frailty, orthostatic hypotension, falls, cognitive impairment, and an increased risk of adverse drug events [311].

Low blood pressure (hypotension) can also lead to significant adverse outcomes. A cohort study found that a substantial proportion of older people on antihypertensives experienced low SBP (<120 mmHg), which was associated with increased risks of mortality, acute kidney injury, and

hospitalisation [312]. Additionally, older people with drug-induced postural hypotension, particularly those at a higher risk of falls, may benefit from deprescribing when the potential harms, such as morbidity from hypotension, outweigh the benefits of reduced cardiovascular events and mortality [313]. Screening for orthostatic hypotension both before and after initiating antihypertensives may be beneficial. BP measurements should be taken while the person is supine and then standing, with a two-minute interval between readings. Orthostatic hypotension is diagnosed when there is a drop of at least 20 mmHg in SBP, a drop of at least 10 mmHg in DBP, or the presence of symptoms such as dizziness, suggesting cerebral hypoperfusion. For postprandial hypotension, screening for symptoms such as weakness, fatigue, or dizziness after meals may be beneficial and confirming these with BP measurements.

Identifying people with pseudohypertension is crucial to prevent overdiagnosis and avoid unnecessary treatment. In some cases, blood pressure may be overestimated in older people due to arterial stiffening or calcification, which increases the cuff pressure required to occlude the artery. This discrepancy between cuff-measured and intra-arterial pressure is referred to as pseudohypertension [314]. Pseudohypertension can lead to overdiagnosis or overtreatment, increasing the risk of adverse effects from unnecessary antihypertensive therapy. While the prevalence of pseudohypertension is unclear, it is known to occur more frequently in people over 65 years of age. In people with resistant or refractory hypertension, pseudohypertension should be considered as a possible cause [315, 316]. A cost-effective screening tool for pseudohypertension is Osler's manoeuver, which involves assessing the palpability of the radial or brachial artery distal to the point of occlusion by the sphygmomanometer cuff. If the artery remains palpable despite the cuff's pressure, the test is considered positive, suggesting the possibility of pseudohypertension. Alternatively, an X-ray of the arteries of the upper limb may assist in confirming the diagnosis [314].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

There is currently no consensus among guidelines on the optimal blood pressure target for older people with hypertension. The decision is highly individualised, as the absolute risk reduction depends on a person's baseline cardiovascular risk and their ability to tolerate antihypertensive therapy [311]. A systematic review of guidelines summarised that most guidelines suggest targeting a systolic target of < 150 mmHg, while four other guidelines suggest more intensive treatment with targets below 130 mmHg or even 120 mmHg [317]. For very old and frail people, treatment should align with general guidelines as long as they are able to tolerate antihypertensive therapy. The 2024 European Society of Cardiology Guideline for hypertension management indicates that there is no default need to deprescribe or discontinue antihypertensives in very old and frail people who are tolerating antihypertensives well, but assessment of the appropriateness of therapy should be conducted regularly [318]. The Australian Heart Foundation provides strong recommendations that clinical judgment should guide decisions on the benefit of treatment versus the risk of adverse effects in older people with lower grades of hypertension [319].

Below we summarised the findings from key trials that contributed to the guidelines for hypertension in older people.

> As with other health conditions, older people are underrepresented in the majority of hypertension clinical trials. Of the few studies that specifically focused on older people, the 2008 JATOS study evaluated 4,418 people aged 65–84 years, comparing strict BP control (SBP <140 mmHg) to lenient BP control (SBP 140–160 mmHg) over two years [320]. The study found no significant differences in cardiovascular disease, renal disease, or stroke morbidity and mortality between the two groups with different BP targets.

Similarly, the 2010 VALISH study assessed 3,260 people aged 70–84 years, comparing strict BP control (SBP <140 mmHg) with moderate BP control (SBP 140–150 mmHg) over a mean follow-up period of 2.85 years [321]. No significant differences were observed in stroke (fatal and non-fatal), myocardial infarction, or all-cause mortality between the two groups.

The HYVET study evaluated 3,845 multi-ethnic people aged 80 years or older with a sustained baseline SBP ≥160 mmHg [322]. The study aimed to achieve a BP goal of <150/80 mmHg, focusing on fatal or non-fatal stroke as the primary outcome over a median follow-up of 1.8 years. Participants were randomised to receive either indapamide (with or without perindopril) or a matching placebo. With the target BP of 150/80mmHg in the treatment group, there was a significant reduction in death from stroke, all-cause mortality, and the rate of heart failure compared to the control group. However, there was no significant reduction in the rate of fatal or nonfatal stroke or mortality from cardiovascular causes.

A prospective observational study that explored mortality and cardiovascular outcomes in frail individuals aged 75 years or older reported an association between BP below 130/80 mmHg and increased mortality, while an SBP between 140–160 mmHg was correlated with the lowest all-cause mortality [323].

The 2015 SPRINT trial was a landmark RCT that compared intensive blood pressure control (target SBP < 120 mmHg, n=4678) to standard blood pressure control (< 140mmHg, n = 4683) over a median follow-up period of 3 years [324]. In this study, 28% (2636/9361) of participants were aged 75 years or older, with a mean overall age of 68, and with varying levels of frailty. All participants had a baseline SBP of 130 - 180 mmHg, increased cardiovascular risk but without diabetes mellitus or prior stroke. Increased cardiovascular risk was defined as at least one of the following: clinical or subclinical cardiovascular disease other than stroke, chronic kidney disease (excluding polycystic kidney disease) with an estimated glomerular filtration rate (eGFR) of 20 to <60 mL/min/1.73m^2 of body surface area, the 10-year risk of cardiovascular disease of ≥ 15% on the basis of the Framingham risk score or an age of 75 years or older. During the entire follow-up period, the mean SBP for the intensive control group was 122 mmHg, compared to 135 mm Hg in the standard control group. On average, participants in the intensive group used three blood pressure medicines, while those in the standard group used two. The study reported a clear benefit of intensive treatment targets in reducing heart failure, cardiovascular mortality and all-cause mortality. A post-hoc study further reported people with frailty benefited from intensive blood pressure control similar to the overall group when tolerated, without a significant increase in serious adverse events [325]. However, the higher rate of adverse events (serious adverse events of hypotension, syncope, electrolyte abnormalities, and acute kidney injury or failure) in the intensive control group warrants a cautious approach to antihypertensive drug treatment and careful assessment of the severity of frailty. Furthermore, the effects of intensive blood pressure therapy on chronic kidney disease progression were inconclusive due to the small number of renal events, but as mentioned, the intensive-treatment group had more frequent acute kidney injury or acute renal failure than the standard-treatment group [326]. In terms of cognition, intensive BP control was found to significantly reduce the risk of mild cognitive impairment but no significant difference in the risk of probable dementia [327].

Finally, the 2021 STEP trial included over 9,000 people aged 60 to 80 years with hypertension at high risk of cardiovascular events. The trial concluded that compared to standard BP control (target SBP 130-150mmHg), intensive control (target SBP 110-130mmHg) had a lower incidence of stroke, ACS, decompensated heart failure atrial fibrillation, and cardiovascular death. Most adverse events (including dizziness, syncope, fracture, angioedema, headache, cough, and hives) and adverse renal outcomes did not differ significantly between the two groups, except for

the incidence of hypotension that was significantly increased in the intensive group (3.4% vs 2.6%; P = 0.03) [328].

To identify individuals who are least likely to derive sufficient net benefit from antihypertensives or tolerate intensive blood pressure control, several factors should be considered. These include age, life expectancy (less than three years), frailty, a high predicted risk of serious adverse events, and a history of adverse events such as falls, syncope, hypotension, or acute kidney injury. Age alone should not be the sole criterion for deprescribing, but it can help identify those more likely to benefit from deprescribing. People over 80 years of age with a SBP < 150 mmHg and DBP < 90 mmHg, and those aged 75 to 79 with a SBP < 140 mmHg, should be carefully assessed for potential risk of adverse outcomes, frailty and a history of adverse events or side effects. To assess frailty, healthcare providers should use validated tools such as the 9-point Clinical Frailty Scale [329]. To effectively assess past adverse events or side effects, obtaining an accurate clinical history is crucial. In addition to a history of falls, syncope, and acute kidney injury, people should also be screened for postural or orthostatic hypotension. Orthostatic hypotension and postprandial hypotension are common side effects of antihypertensive medications, with a prevalence of up to 20% in older people with hypertension [328]. These conditions significantly increase the risk of falls, making early identification essential for adjusting antihypertensive therapy.

Deprescribing may be appropriate when the potential benefits of a medicine are outweighed by the risk of harm. This is particularly relevant when precautions are necessary for continued use or when contraindications are present, as the risk of harm may be inherently higher, especially in older people. The following is a non-exhaustive list of situations where these considerations may apply:

Loop and thiazide diuretics can lead to electrolyte imbalances, exacerbate gout, and may elevate blood glucose levels [330].

Similarly, ACE inhibitors, ARBs, aldosterone antagonists, and potassium-sparing diuretics can raise the risk of hyperkalaemia, particularly in individuals with renal impairment [330].

The combination of an ACE inhibitor and an ARB results in an increased risk of adverse outcomes, including vascular events and renal dysfunction, with limited additional benefit for blood pressure control [331-333].

Nondihydropyridine calcium channel blockers (diltiazem and verapamil) are contraindicated in heart failure with reduced ejection fraction (HFrEF) in the absence of AF due to an associated increase in mortality, unless prescribed under specialist supervision [303, 330]. In people with both AF and HFrEF, these agents are also not recommended, as their negative inotropic effects can worsen heart failure [303, 334].

Use of beta-blockers or verapamil/diltiazem is contraindicated in individuals with inappropriate bradycardia (e.g. resting heart rate <60 beats/minute) or symptomatic atrioventricular (AV) block (e.g. exertional fatigue) [330].

People aged 85 years or younger who do not meet the criteria for limited life expectancy (less than three years), frailty, a high predicted risk of serious adverse events, and a history of adverse events such as falls, postural hypotension, syncope, or acute kidney injury should generally be managed according to the guidelines for the younger population [318].

Some antihypertensives may be prescribed for comorbid conditions, such as atrial fibrillation, heart failure, or chronic kidney disease. It may not be appropriate to attempt deprescribing in people taking a beta-blocker for atrial fibrillation, a diuretic for symptomatic heart failure, or ACE inhibitors, ARBs,

or beta-blockers for heart failure. Similarly, people using ACE inhibitors or ARBs for chronic kidney disease may need to continue taking these medicines for renal protection.

If multiple antihypertensives are considered appropriate to deprescribe, they should be deprescribed one at a time. Some antihypertensives, such as beta-blockers, diuretics, and centrally acting antihypertensives, require tapering due to the risk of rebound hypertension or beta-blocker withdrawal syndrome [293]. Healthcare providers should monitor for withdrawal-related side effects, such as accelerated hypertension (BP > 180/110 mmHg), palpitations (following the withdrawal of verapamil, diltiazem, or beta-blockers), or prostatism (following the withdrawal of alpha-blockers). If these symptoms arise, healthcare providers should consider reintroducing the medicines at a lower dose.

The order to deprescribe should generally prioritise those with a higher risk profile, taking into account any comorbidities and mortality data. In the absence of a specific indication for a particular antihypertensive class (e.g. ACE inhibitors and beta-blockers for heart failure), drugs associated with a higher risk of orthostatic hypotension, such as loop diuretics, alpha-blockers and centrally acting antihypertensives should be prioritised for deprescribing. This is then followed by aldosterone antagonists, thiazide diuretics, and beta-blockers due to the potential to cause fatigue and bradycardia [335]. Calcium channel blockers, ACE inhibitors, and ARBs generally have safer profiles and can be considered last for prioritisation [336].

Narrative summary of evidence on deprescribing

We identified 20 studies (eight RCTs and 12 single-arm studies) related to antihypertensives deprescribing from the systematic review and meta-analysis, of which two studies specifically targeted beta-blockers and one study targeting ACE inhibitors [317, 337-357].

Overall, the current evidence for deprescribing antihypertensives is derived from studies with outcomes of low and very low certainty. Most studies had a short follow-up duration, either as a run-in phase or short-term withdrawal and most were single-arm observational studies. Deprescribing antihypertensive medicines appeared to result in only a modest increase in BP in most studies; however, a study suggested that BP may revert to baseline in the longer term. Most studies included people without recent cardiovascular events (stroke or myocardial infarction), and SBP < 150-175 mmHg or DBP < 85-110 mmHg. Deprescribing antihypertensives under these situations appears to be largely safe with close monitoring. An association between deprescribing and increased mortality was reported in one retrospective cohort study, also of very low certainty. There is still currently insufficient evidence to support the development of evidence-based recommendations as most studies lack methodological rigor.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Espeland 1999 investigated lifestyle interventions (weight loss and/or sodium restriction) as a replacement for antihypertensives among older people with hypertension in an RCT (TONE trial) [339]. Participants were included if they were taking one antihypertensive (or single combination regimen, diuretic and nondiuretic) with average SBP and DBP < 145 mmHg and 85 mmHg respectively, or able to step down from two antihypertensives to one and meet the BP eligibility criteria. Participants were excluded if they had a history of heart attack or stroke within the past six months, current angina, congestive heart failure, insulin-dependent diabetes or other severe illnesses. Independent of group assignment in the factorial design, 975 participants were randomised, 886 attempted deprescribing and 774 successfully discontinued their

antihypertensive. There was a total of 57 cardiovascular events that occurred either during or after drug withdrawal.

Juraschek 2022 conducted a further analysis using the data from the TONE trial to investigate the long-term effects of antihypertensive deprescribing on BP and adverse events independent of group assignment [347]. Following deprescribing, SBP increased by 4.6 mmHg ± 11.1 compared to baseline. There were 113 adverse events affecting 95/975 participants (10%) during deprescribing. Among these adverse events, 84 were symptomatic events (light-headedness, dizziness, vertigo) and 29 were clinical events (falls, fracture, syncope).

Moonen 2015 conducted an RCT (DANTE Study Leiden) to discontinue antihypertensives in older people with SBP of < 160 mmHg and mild cognitive impairment (Mini-Mental State Examination, MMSE score of 21 to 27) [350]. People with dementia, a history of serious cardiovascular events (e.g. stroke, transient ischemic attack), coronary reperfusion procedures, or using antihypertensives for reasons other than hypertension (e.g. arrhythmia, heart failure, angina) were excluded. There was no significant difference in cognition at 16 weeks follow-up between the intervention group and control group who continued taking antihypertensives. Further subgroup analysis (Moonen 2016) including people with orthostatic hypotension (n=162) suggested better recovery from orthostatic hypotension in people who discontinued antihypertensive (RR 1.60, 95% CI 1.10 to 2.31; p = 0.01) as per protocol analyses but this was not statistically significant according to intention-to-treat analysis (RR 1.31, 95% CI 0.92 to 1.87; p = 0.13) [358].

Gulla 2018 conducted a post-hoc analysis focusing on antihypertensives [341] using data from a cluster RCT (COSMOS trial) [135] that investigated the effects of a multicomponent intervention including discontinuation of unnecessary medicines on the quality of life of nursing home residents. There was a significant reduction in the number of hospitalisations in the intervention group participants who received medicine reviews aimed at reducing the use of antihypertensive drugs in nursing homes, compared to control group participants who received usual care (OR 0.38, 95% CI 0.19, 0.76). SBP for those who had their antihypertensives deprescribed increased from a baseline of 128 ± 19.5 mmHg to a mean of 134 mmHg at month nine.

Sheppard 2020 conducted an RCT that included 569 participants with an SBP < 150 mmHg who were taking two or more antihypertensives for 12 months or longer with the goal of reducing medicines in people with polypharmacy and multimorbidity (OPTiMISE trial) [353]. The study excluded people with heart failure due to left ventricular systolic dysfunction or recent myocardial infarction or stroke within the past 12 months. BP monitoring was completed at week 4 and treatment was recommenced if the SBP > 150 mmHg or DBP > 90 mmHg for more than a week. Recommendations were provided to the participant's general practitioner to prioritise deprescribing antihypertensive in reverse of the National Institute for Health and Care Excellence treatment algorithm for people aged over 55 [359]. Participants in the intervention group (n=282) who discontinued *one* antihypertensive had a 3.4 mmHg (95% CI 1.0, 5.8) higher mean change in SBP compared with the control group receiving usual care (n=287). More participants in the intervention group experienced at least one serious adverse event compared with the continuation group (4.3% vs 2.4% respectively, OR 1.78, 95% CI 0.69, 4.58). Sheppard 2024 further analysed the four-year follow-up outcomes via manual review of the electronic health records for 554 participants (97% of the original sample size) [360]. Of the 213 participants alive in the intervention group, 109 (51%) were still taking fewer antihypertensives than baseline. There was no significant difference between the two groups in the occurrence of all-cause hospitalisation or mortality (OR 0.78, 95% CI 0.54, 1.15).

Song 2018 conducted a retrospective cohort study to investigate antihypertensive deprescribing in nursing home residents with an index fall and SBP between 80 to 120 mmHg [354]. The study compared recurrent falls, hospitalisations, and mortality between the group whose

antihypertensive medicines were discontinued (n = 239) versus the group who continued taking antihypertensive (n = 1973) in the 30-day follow-up. There was a significantly higher 30-day mortality rate for the discontinuation group (OR 2.64, 95% CI 1.40, 5.00). However, there were no significant differences between the two groups in recurrent falls (OR 0.89, 95% CI 0.62, 1.26) and hospitalisations (OR 1.41, 95% CI 0.99, 2.02). Further stratification by SBP levels indicated that discontinuing antihypertensives was associated with a statistically significantly lower risk of recurrent falls at 30 days among residents with SBP 80 to 100 mmHg (adjusted marginal effect [AME] = -11.4%; p-value < 0.01) but higher mortality risk among residents with SBP 101 to 120 mmHg (AME = 2.1%; p-value = 0.07).

Hajjar 2013 reported short-term (< four weeks) antihypertensive washout in preparation for trial entry in 53 older people with early cognitive impairment or memory impairment without dementia [342]. Blood pressure increased gradually during the tapering process, with an overall increase of 12 mmHg (95% CI 4, 21) in SBP and 6 mmHg (95% CI 1, 11) in DBP.

Alsop 2001 reported discontinuation of cardiovascular medicines in 65 people attending a falls and syncope clinic [337]. Inclusion and exclusion criteria were not specified. Participants were followed up every two to three months depending on the need for ongoing review. At the end of the 30-month follow-up, cardiovascular medicines remained withdrawn in 70% of participants and 78% reported improved symptoms of syncope or pre-syncope.

Ekbom 1994 reported an observational follow-up of a cohort (n=333) of participants previously taking antihypertensives who entered a wash-out phase prior to participation in the STOP-Hypertension study [338]. Participants were excluded if they were taking these antihypertensives for reasons other than hypertension. At the end of five years of follow-up, approximately one in five (20%) participants remained off anti-hypertensive therapy. Recurrent hypertension (n=54), heart failure (n=27) and oedema (n=25) were the main reasons for restarting therapy. Participants who remained off treatment had a lower total mortality risk than the general Swedish population (matched for age and sex) and a lower risk of cardiovascular events than those receiving treatment (19 deaths reported from 30 expected; P < 0.05). However, it should be underlined that the blood pressure of the participants who remained off treatment did not rise enough to prompt the recommencement of antihypertensives. This suggests the possibility that these participants had an inherently low cardiovascular risk.

Fotherby 1994 reported deprescribing in participants who were taking antihypertensives for more than one year with SBP < 175 mmHg and DBP < 100 mmHg [340]. Participants were excluded if they had recent myocardial infarction, stroke, or symptoms of ischaemic heart disease. At 12 months follow-up, 20/74 (27%) remained normotensive without antihypertensive therapy. Among those who were followed up at two years, 13/64 (20%) were normotensive. The majority of participants who required restarting of therapy did so within the first three months of antihypertensive withdrawal.

Hansen 1983 reported a follow-up study of people who had drug washout in preparation for a study investigating the prevalence of secondary hypertension [355]. The study reported that 43/105 participants (41%) with a history of hypertension remained normotensive without treatment at 11 months follow-up.

Lernfelt 1990 included older people who had a BP of < 175/95 mmHg without current cardiovascular diseases in a cohort study [349]. Antihypertensive was withdrawn in 25 participants. At the final follow-up at month 48, eight participants (32%) remained off their antihypertensive and 13 participants (52%) restarted antihypertensive treatment because of increased BP (n=9), AF and heart failure (n=1), myocardial infarction (n=1), shortness of breath

(n=1), or angina (n=1). The remaining four participants (16%) dropped out of the study due to non-cardiovascular reasons.

Nadal 1994 reported an antihypertensive deprescribing before-and-after study in 86 older outpatients attending a hypertension clinic [351]. People were excluded from washout if they had a history of myocardial infarction or stroke in the 12 months prior, insulin-dependent diabetes mellitus, plasma creatinine ≥ 200 mmol/L, and had a SBP ≥ 220 mmHg or DBP ≥ 110 mmHg. Of the 52/86 (60%) participants who remained normotensive after the initial washout, 14/52 (27%) remained without therapy at three years follow-up.

Hassan 2022 investigated deprescribing antihypertensives in older people who used two or more antihypertensives and had at least one adverse drug event (ADE) related to the antihypertensive (dizziness, nocturia, vertigo, headache, imbalance, shortness of breath, and tiredness) [343]. At the end of the 12-month follow-up, antihypertensive drug use was reduced in 11/14 participants (79%). Of these 11 participants, nine (82%) had at least one antihypertensive medicine permanently stopped whereas in two participants (18%), the dose of one antihypertensive drug was halved. All 11 participants had a mean SBP increase of 16 mmHg and a mean DBP increase of eight mmHg. At 12 months follow-up, nine participants (64%) no longer experienced adverse drug events, of whom seven participants had at least one antihypertensive stopped or reduced in dose.

Nelson 2003 conducted a cohort study including 6291 participants who had their antihypertensives discontinued as part of the run-in phase of a larger trial [352]. This study reported that 1228 participants (20%) maintained adequate blood pressure control (mean sitting SBP < 160 mmHg or DBP < 90 mmHg) for 0 to 76 weeks (median of four weeks).

Silva 2024 conducted a subgroup analysis including participants who participated in a larger trial about optimising antihypertensives through seven-day home blood pressure monitoring in older people [357]. The study compared standard care (general practitioner received a home blood pressure monitoring report and decided on deprescribing medications) to study intervention (pharmacist reviews and recommendations). In the intervention group, deprescribing suggestions were provided by the pharmacist to the participants and their general practitioners where appropriate. In the current subgroup study, 72 participants with SBP ≤ 120 mmHg and DBP ≤ 70 mmHg as well as clinical symptoms of hypotension were included (intervention, n = 37; control, n = 35). Compared to control group participants, intervention group participants had a significant reduction in the number of antihypertensives (MD 0.71, 95% CI 0.33, 1.09) on the Day 45 follow-up. Intervention group participants also had a significantly higher in-office SBP (MD 8.06, 95% CI 4.97, 11.15) and DBP (MD 4.49, 95% CI 2.51, 6.47) as well as at-home SBP (MD 7.37, 95% CI 4.42, 10.32) and DBP (MD 4.31, 95% CI 2.53, 6.09). The mean SBP and DBP in the intervention group remained below the target range of 140/90 mmHg after the intervention. There was also a significant reduction in hypotensive symptoms in the intervention group compared with the control group (OR 0.14, 95% CI 0.05, 0.39).

Bogaerts 2024 conducted an RCT trial (DANTON) to investigate the effects of the discontinuation of antihypertensive treatment on neuropsychiatric symptoms and quality of life [356]. Nursing home residents with moderate-to-severe dementia and SBP ≤ 160mmHg were included whereas those with heart failure NYHA-class III to IV, recent cardiovascular events/procedures, or limited life expectancy (< 4 months) were excluded. A total of 205 participants were randomised to discontinuation (n=101) and usual care (n=104). The study was terminated early due to safety concerns and lacking benefits. At the 32-week follow-up, control group participants had fewer neuropsychiatric symptoms measured using the Neuropsychiatric Inventory Nursing Home (NPI-NH) (MD 6.2, 95% CI 1.9, 10.6). However, there was no significant difference between the two groups in terms of quality of life measured using QUALIDEM (MD −3.5, 95%CI –8.1, 1.1), serious

adverse events (OR 1.75, 95% CI 0.95, 3.21), mortality (OR 1.71, 95% CI 0.92, 3.18), SBP (MD 4.9, 95% CI –0.8, 10.6), and DBP (MD 3.3, 95% CI –0.5, 7.2).

Additionally, we identified two studies that specifically targeted beta-blockers and one study targeting ACE inhibitors.

Hearing 1999 included 37 participants who were taking atenolol for at least one year in an RCT [344]. The 23 participants who were randomised to the deprescribing group had their atenolol withdrawn over one week of whom eight participants (35%) remained normotensive.

Jondeau 2009 conducted an RCT to determine whether beta-blockers should be discontinued in people hospitalised for acute heart failure with pulmonary oedema [346]. Inclusion criteria include stable doses of beta-blockers for longer than a month, respiratory rate > 24 min^{-1} during the acute heart failure episode, and left ventricular ejection fraction < 40%. Exclusion criteria were acute ST-elevation myocardial infarction, second or third-degree atrioventricular block, or heart rate lower than 50 min^{-1}. The study found that withholding beta-blockers did not significantly change mortality at month three (OR 0.88, 95% CI 0.27 to 2.85; participants = 147). Participants in the intervention group who stopped beta-blockers at study entry for at least three days were significantly less likely than those in the control group to be taking a beta-blocker at month three (OR 0.38, 95% CI 0.16 to 0.93).

Jiménez-Candil 2005 conducted a before-and-after study to withdraw ACE inhibitors in 20 older people with moderate or severe asymptomatic aortic valve stenosis (considered a relative contraindication to ACE inhibitor therapy) [345]. Participants had previously been taking the ACE inhibitor for at least three months for arterial hypertension. The study found that ACE inhibitor therapy favourably improved stress haemodynamic variables in most hypertensive people with aortic valve stenosis.

Narrative evidence summary: withdrawal schedules

Various methods were used for deprescribing in the included studies. Beta-blockers were more commonly tapered gradually, and it may be appropriate to avoid beta-blocker withdrawal syndrome. There was no direct evidence that any particular method was associated with the greatest benefits and harms. However, compared to abrupt cessation, dose tapering is likely more acceptable and helpful in determining the lowest effective dose for some people requiring dose reduction rather than complete cessation.

In one RCT (DANTE Study Leiden), antihypertensives were either abruptly discontinued or tapered within four weeks according to a study-specific algorithm until a maximum increase of 20 mmHg in SBP, or 180 mmHg in SBP was observed (n=356, low certainty) [350]. Atenolol was gradually tapered over one week (study=1, n=37, very low certainty) [344]. In another RCT (n=569), antihypertensive treatment appeared to be discontinued abruptly with the exception of beta-blocker where gradual tapering was encouraged to minimise rebound adrenergic hypersensitivity [353]. Beta-blocker was abruptly discontinued for at least three days in an RCT conducted in a hospital setting (n=169) [346]. The method of deprescribing was not described in four studies (n=1547, very low certainty) [339, 341, 356, 357].

In the single-arm studies, all very low certainty, the method of deprescribing was not described in seven studies (n=2649) [337, 340, 343, 349, 351, 354, 355], the method was individualised following drug-specific tapering regimens (study=1, n=975) [347], beta-blocker was reduced step-wise over a few days (study=1, n=333) [338], step-wise (i.e. one drug at a time, half doses at weekly intervals to the lowest usual therapeutic dose then cease) (study=1, n=6833) [352], antihypertensives were tapered over three weeks (study=1, n=53) [342], and lastly, withdrawal of

ACE inhibitor was progressive with a daily dose reduction equivalent to 1.25 mg of enalapril (study=1, n=22) [345].

GRADE Summary of Findings (SoF) Table

Table 14. Summary of findings for deprescribing of antihypertensives

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
3 [341, 350, 356]	RCTs	464	421	OR 1.25 (0.83, 1.88)	
1 [346]	RCT **(beta-blocker)**	78	69	OR 0.88 (0.27, 2.85)	
1 [354]	Non-randomised study	239	1973	OR 2.64 (1.40, 5.00)	
3 [338, 340, 349]	Non-controlled studies	2648	N/A	2/25 (8%) [349] 74/333 (22%) [338] 1/78 (1%) [340]	
2. Adverse drug withdrawal events (ADWEs)					
ADWEs, blood pressure					
3 [356, 357, 360]	RCTs	354	369	Deprescribing was associated with a significant change in systolic blood pressure (MD 7.30, 95% CI 4.60, 10.01). Additionally, in one of these studies [357], at-home systolic blood pressure was also reported and deprescribing was associated with a significant change, MD 7.37 (4.42, 10.32).	
2 [356, 357]	RCTs	89	100	Deprescribing was associated with a significant change in diastolic blood pressure (MD 4.24, 95% CI 2.48, 5.99). In one study [357], at-home systolic blood pressure was also reported and deprescribing was associated with a significant change, MD 4.31 (2.53, 6.09).	
1 [344]	RCT **(beta-blocker)**	23	14	This study compared the discontinuation of beta-blocker to continuation at two weeks, eight out of 23 participants (35%) in the intervention group were normotensive following the discontinuation of antihypertensive medicine (OR 15.90, 95% CI 0.84, 301.03).	
9 [338, 342, 343, 345, 347, 349, 351, 355, 361]	Non-controlled studies	2011	N/A	Following the discontinuation of antihypertensive medicines, systolic blood pressure appeared to increase by: 23.8 ± 26.2 mmHg [349] 12 ± 31 mmHg [342] 16 ± 49.2 mmHg [343] 4.59 ± 11.1 mmHg [347] Similarly, diastolic blood pressure appeared to increase by: 9.6 ± 21.4 mmHg [349] 6 ± 18 mmHg [342] 8 ± 27.7 mmHg [343] In three studies, systolic blood pressure at the end of the follow-up was: 151 ± 13.4 mmHg [342]	

				169 ± 15 mmHg [338] 159 ± 12 mmHg [345] Diastolic blood pressure at the end of the follow-up was: 83 ± 8.9 mmHg [342] 88 ± 8 mmHg [338] 80 ± 10 mmHg [345] During the withdrawal of antihypertensives, none of the participants reported two consecutive blood pressure (BP) readings above the threshold and none reported headaches, dizziness, visual changes, or focal weakness during the tapering phase, 0/53 (0%) [342]. A study also reported that 43 out of the 105 participants (41%) with a history of hypertension remained normotensive without treatment at 11 months follow-up [355]. In contrast, in a study of 86 participants, 34 (40%) had their blood pressure rise to the levels contemplated in the study exclusion criteria (systolic BP ≥ 220 mmHg or diastolic BP ≥ 110 mmHg) [351]. Similarly, another study reported 273/503 participants returned to hypertension following the discontinuation of antihypertensive medicine (40%) [361]	
Adverse events/ serious adverse events/ cardiovascular events					
2 [350, 353]	RCTs	481	473	Deprescribing was not associated with a significant change in the proportion of participants with a serious adverse event (OR 1.69, 95% CI, 0.73, 3.91, studies = 2, n = 954). However, in one study, the number of participants experiencing at least one adverse event was significantly higher in the intervention group (OR1.50, 95% CI 1.07, 2.0) [353]. Approximately one-fourth of the adverse events that occurred in the intervention group were considered possibly related to discontinuation of antihypertensive medicine. In this study, adverse drug events were reported by the participant or observed by the investigator during trial follow-up [353].	
4 [338, 339, 349, 351]	Non-controlled studies	1295	N/A	Cardiovascular events 57/886 (6%) [339] 1/25 (4%) [349] 54/333 (16%) [338] 0/52 (0%) [351]	
3. Health outcomes					
Health service use					
2 [341, 350]	RCTs	363	317	Deprescribing was not associated with a significant change in the proportion of participants with an unplanned hospital admission (OR 0.53, 95% CI 0.24, 1.14).	
1 [354]	Non-randomised study	239	1973	OR 1.41 (0.99, 2.02)	
Adverse drug events					
2 [350, 357]	RCTs	123	111	Deprescribing was associated with a significant change in the proportion of participants with hypotension (OR 0.41, 95% CI 0.24, 0.70).	
3 [337, 343, 347]	Non-controlled studies	1054	N/A	In one study, 11 out of 14 participants had their antihypertensive medicine discontinued or lowered during the 12-month follow-up. Adverse drug events (e.g. syncope, dizziness and falls) were reported in five out of 14 participants (36%) [343]. Of the nine participants who did not experience any adverse drug	

				events, seven had their antihypertensive medicine discontinued. In another study, 95 out of all 975 participants (10%) had experienced adverse events (light-headedness, dizziness, vertigo, fall, fracture, syncope) [347]. In one study, 78% of all participants who stopped their cardiovascular medicines reported an improvement in their original symptoms of syncope or pre-syncope at follow-up [337].	
Frailty					
1 [353]	RCT	282	287	Deprescribing was not associated with a significant change in the frailty index (MD -0.01, 95% CI -0.02, 0.00).	
Falls					
1 [354]	Non-randomised study	239	1973	OR 0.89 (0.62, 1.26)	
Exercise tolerance					
1 [345]	Non-controlled study **(ACE inhibitors)**	20	N/A	Following the discontinuation of ACE inhibitors, there was no change in exercise duration [7.0 (2.3) minutes versus 7.0 (4.1) minutes, p = 0.4).	
Neuropsychiatric symptoms					
1 [356]	RCT	101	104	Change in neuropsychiatric inventory nursing home score. A higher score indicates more disruptive behaviour MD 6.2 (95% CI 1.9, 10.6), favouring control group	
4. Cognitive function					
1 [350]	RCT	180	176	Deprescribing was not associated with a significant change in the overall cognition compound score (MD -0.02, 95% CI -0.23, 0.19). A compound score was computed if five out of six tests were available: Stroop interference, Trail Making Test delta, 15-word Verbal Learning Test immediate, 15-word Verbal Learning Test delayed, Visual Association Test, and Letter Digit Substitution Test.	
5. Quality of life (QoL)					
2 [350, 356]	RCTs	281	280	Deprescribing was not associated with a significant change in the quality of life measured using Cantril's Ladder quality-of-life score (MD -0.10, 95% CI -0.35, 0.15) and QUALIDEM (MD -3.5, 95% CI -8.1, 1.1).	

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

Diuretics

Diuretics include:

- Low-ceiling diuretics, thiazides: Hydrochlorothiazide
- Low-ceiling diuretics, excluding thiazides: Chlortalidone, indapamide
- Loop diuretics: Furosemide*, bumetanide
- Aldosterone antagonists and other potassium-sparing agents: Eplerenone, spironolactone*, finerenone
- Combination drugs: amiloride with hydrochlorothiazide

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing decisions be made in consultation with the person and their GP and/or specialist providers (e.g. cardiologist or nephrologist) to ensure it aligns with their preferences, goals and overall treatment plans. Following shared decision-making, we suggest deprescribing of diuretics be offered to older people with: 1. No current indication (i.e. heart failure, renal failure, or hypertension) 2. Adverse effects potentially outweigh benefits (e.g. with urinary incontinence symptoms that significantly affect the quality of life) 3. When the diuretic was prescribed solely for hypertension and the criteria for deprescribing antihypertensive medications as outlined in the antihypertensives section is met 4. A relative contraindication, such as • Potassium-sparing diuretics in people with hyperkalaemia • Loop/thiazide diuretics in people with gout, refractory symptomatic hyponatremia, or diabetes mellitus • Diuretics for drug-induced oedema (e.g. calcium channel blockers)
Ongoing treatment	
CBR	We suggest continuing diuretics in older people taking long-term diuretics for persistently symptomatic fluid overload due to cardiac, renal, or liver failure, despite optimal management being in place.
CBR	We suggest continuing aldosterone antagonists in people with heart failure, especially if reduced ejection fraction (HFrEF), given their benefit in reducing mortality and hospitalisation.
CBR	We suggest continuing finerenone in chronic kidney disease (with albuminuria) in people with type 2 diabetes.
CBR	If deprescribing is unsuccessful despite two attempts, we suggest maintaining the lowest effective dose; however, reassessing the need for long-term therapy periodically.
How to deprescribe	
CBR	We suggest for furosemide: • If daily doses < 40mg, discontinue without tapering • If daily doses amount to 40mg, halve the dose for one week before complete cessation • If daily doses amount to 80mg, halve the dose for two weeks before complete cessation • If daily doses are between 80mg and 160mg, reduce the dose by 40 mg every two weeks until it reaches 40 mg, then discontinue completely. For other diuretics, we suggest tapering the dose with monitoring of fluid status, with daily weight monitoring for potential weight gain following down titration of dosing.

	For combination of thiazide and loop diuretic, we suggest first tapering thiazide diuretic.
CBR	If potassium supplements are being used alongside thiazide or loop diuretics, we suggest adjusting or discontinuing potassium supplements in coordination with any changes to the diuretic therapy. For potassium-sparing diuretics, we suggest reviewing and adjusting other medicines and/or lifestyle factors that affect potassium levels in coordination with any changes to the diuretic therapy.
Monitoring	
CBR	We suggest closely monitoring for blood pressure, signs of exacerbations (e.g. peripheral oedema, signs of heart failure), and changes in body weight weekly during tapering for at least three months following deprescribing. After this initial period, we suggest monthly monitoring for ongoing risk factors for at least three months, followed by monitoring every six months thereafter. If in-person visits are impractical, we suggest advising people to self-monitor blood pressure and body weight at home by using a blood pressure monitor and weighing scales respectively, as well as reporting any significant changes to their healthcare provider as needed. If potassium supplements are being used alongside thiazide or loop diuretics, we suggest monitoring serum potassium levels at one week and two weeks and at least monthly thereafter if the level was outside the normal range when last checked.
CBR	When discontinuing or changing the dose of diuretics, we suggest closely monitoring for changes in serum potassium and renal function (blood urea nitrogen, serum creatinine and eGFR).

CBR, consensus-based recommendation

Introduction

Oedema can arise from other causes, including dependent oedema due to immobility, impaired venous return, venous stasis, and altered vasomotor tone [362]. Although data on the prevalence of oedema are limited, a recent study suggests that approximately 20% of individuals aged 50 and over experience persistent peripheral oedema [363]. Diuretics are frequently prescribed to older people for managing hypertension or fluid retention associated with conditions including heart failure, liver cirrhosis, or renal failure. Loop diuretics (furosemide, bumetanide) are particularly beneficial for acute symptom relief in people with fluid overload due to heart failure [364].

As mentioned in the 'Digoxin/Sotalol' section, the management of heart failure has advanced over the past decade. The 2022 American College of Cardiology/American Heart Association/Heart Failure Society of America guideline for the management of heart failure recommends guideline-directed medical therapy (GDMT) for people with heart failure and reduced ejection fraction (HFrEF) [283]. The GDMT, also known as the "four pillars", includes a renin-angiotensin system inhibitor, a heart-failure specific beta-blocker, a mineralocorticoid receptor antagonist and a sodium-glucose cotransporter 2 inhibitor, as the four main recommended drug treatment regimens for HFrEF. This quadruple therapy is recommended as the regimen for HFrEF due to its demonstrated benefits in reducing morbidity and mortality [284].

Long-term diuretic use has been linked to increased mortality in individuals with heart failure [365]. Diuretics are also among the leading drug classes associated with medicine-related hospital admissions in older people [366]. It is crucial to consider the underlying indication for diuretic use to identify people who may benefit from deprescribing.

The use of diuretics in older people requires careful monitoring as they are more susceptible to electrolyte imbalances (hyponatraemia, hypokalaemia and hyperkalaemia) and orthostatic hypotension [177]. The potential for drug-drug interactions should be emphasised, particularly considering the high prevalence of multimorbidity in the older population and that existing treatment guidelines are often disease-specific [367]. One common concern in the context of diuretics is the 'triple whammy,' which refers to the co-administration of ACE inhibitors or ARBs diuretics, and nonsteroidal anti-inflammatory drugs (NSAIDs). This combination increases the risk of acute kidney injury [368]. Older people with pre-existing renal impairment are particularly vulnerable to the adverse effects of the 'triple whammy'. The New Zealand Health Quality and Safety Commission reported that 3.2% of people aged 65 and over, or approximately 25,000 individuals, were dispensed with this combination within a 90-day period in 2019 [369]. This indicator may be underrepresented as people who purchased and used NSAIDs over the counter were not included in the data.

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

The primary goal of diuretic therapy is to achieve euvolaemia [370]. Once euvolaemia is reached, the necessity for long-term diuretic therapy should be reassessed, especially in asymptomatic or minimally symptomatic individuals, and deprescribing should be considered when appropriate. Prolonged use of diuretics can lead to diuretic resistance and rebound oedema upon discontinuation [371, 372].

Unlike GDMT for heart failure, long-term use of furosemide is associated with increased mortality in older people, and its use should be limited to people with evidence of fluid overload [373]. Despite this, loop diuretics are often overprescribed in older people [374, 375]. Deprescribing should be considered when appropriate criteria are met, such as the suitability of alternative GDMT agents or the absence of a clear indication for continued use. Deprescribing should be prioritised in individuals experiencing known adverse drug effects associated with diuretics, such as hyponatraemia with furosemide and thiazide, and gout with loop or thiazide diuretics. In contrast, individuals taking aldosterone antagonists for heart failure, particularly those with reduced ejection fraction (HFrEF), should likely continue therapy due to strong evidence supporting their role in improving mortality and reducing hospitalisations, independent of their diuretic effect [376].

While the benefits of aldosterone antagonists in heart failure with mildly reduced ejection fraction (HFmrEF) or preserved ejection fraction (HFpEF) are less clear, some evidence suggests that these agents, especially non-steroidal mineralocorticoid receptor antagonist finerenone, may reduce cardiovascular mortality or heart failure-related hospitalisation [377, 378]. Additionally, finerenone has been shown to significantly reduce the progression of chronic kidney disease and cardiovascular events in people with chronic kidney disease and type 2 diabetes [379].

Deprescribing of inappropriate prescribing cascade should be considered. A common example of a prescribing cascade involves lower extremity oedema, which may occur as a side effect of a calcium channel blocker. Rather than discontinuing the causative medicine, a diuretic is often added [230]. If potassium supplements are being used alongside thiazide or loop diuretics, they should also be adjusted in coordination with any changes to the diuretic therapy to avoid the continuation of a 'relic' of prior prescribing.

Deprescribing may also be appropriate when the potential benefits of a medicine are outweighed by the risk of harm. This is particularly relevant when precautions are necessary for continued use or

when contraindications are present, as the risk of harm may be inherently higher, especially in older people.

Loop and thiazide diuretics can lead to electrolyte imbalances, exacerbate gout, and may elevate blood glucose levels [330].

Similarly, potassium-sparing diuretics can raise the risk of hyperkalaemia, particularly in individuals with renal impairment [330].

Loop diuretics account for the retention of up to 25% of filtered sodium and are more potent diuretics than thiazide diuretics [380]. In the context of diuretics used for oedema, when a thiazide and loop diuretic are used in combination, it may be appropriate to first attempt deprescribing the thiazide diuretic as it may associated with a comparatively lower risk of symptom recurrence.

Narrative summary of evidence on deprescribing

We identified seven studies (five RCTs and two before-and-after studies) related to diuretics deprescribing from the systematic review and meta-analysis [381-387].

Overall, the current evidence from available studies is of low and very low certainty. Deprescribing diuretics may lead to peripheral oedema and an increase in blood pressure. In people without a current indication of heart failure or hypertension, the majority were able to stop diuretics without serious adverse events and symptom recurrence. There was also no significant difference in mortality compared to those who continued treatment. However, there is a lack of quality evidence to inform evidence-based recommendations.

It may be appropriate to monitor fluid status (e.g. changes in body weight), serum potassium, renal function (including blood urea nitrogen, serum creatinine, and eGFR), blood pressure, and if applicable, symptoms of heart failure during dose tapering and after discontinuation. When encouraging individuals to self-monitor, it may be helpful to provide concrete examples of symptoms (e.g. swollen ankles) to improve recognition and reporting. Since many symptoms are non-specific, individuals may not realise they could signal the worsening of an underlying condition.

For potassium-sparing diuretics, it may also be necessary to review and adjust other medications and/or lifestyle factors that influence potassium levels, in coordination with any changes to the diuretic regimen.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

De Jonge 1994 randomised 63 people who were taking diuretics for ankle oedema in an RCT to diuretic discontinuation (n=34) or continuation (n=29) [382]. Exclusion criteria were oedema caused by cardiac, hepatic or renal failure, AF, hepatomegaly, or if the diuretics were used for hypertension. Diuretics were withdrawn in 26/34 (76%) participants in the intervention group with eight participants restarting treatment due to symptoms suggestive of heart failure (n=3), hypertension (n=1), being unwell and developed urinary incontinence (n=1), and withdrew consent (n=3). Participants in the intervention group were more likely to report ADWEs, although this was not statistically significant (OR 8.70, 95% CI 0.45, 168.87). The primary outcome was volumetrically determined ankle oedema (oedema index). Oedema appeared to worsen following medicine withdrawal (peaking in the third week), after which it trended towards baseline levels.

Van Kraaij 2000 randomised 32 people with current heart failure with preserved ejection function (HFpEF) to furosemide withdrawal (n=21) or continuation (n=11) [385]. Inclusion criteria were a daily dose of 20-80mg furosemide, two or more prior symptoms (dyspnoea on exertion or at rest, orthopnoea, paroxysmal nocturnal dyspnoea, or peripheral oedema) and one or more prior signs (jugular venous distension, rales, or radiographic pulmonary congestion). Exclusion criteria were SBP > 170 mmHg, DBP > 90 mmHg, persistent AF, symptoms of angina pectoris, overt congestion, or the presence of significant valvular disease. At the three months follow-up, 16/21 (76%) participants did not require recommencement of diuretic therapy. Three participants in the withdrawal group restarted furosemide for ankle oedema, one participant restarted due to hypertension (> 180/100 mmHg) and the reason was not reported for the remaining participant.

Walma 1997 randomised 202 people who had been taking diuretics for at least six months to continuation (n=100) or placebo (n=102) with a six-month follow-up [387]. Participants were excluded if they had hypertension (> 180/100 mmHg), overt heart failure, previous acute decompensated heart failure, hypercalciuria, nephrotic syndrome, glaucoma, taking a daily dose of > 80mg furosemide, or taking fixed combinations of diuretics with beta-blockers or ACE inhibitors, or with alpha-blocker and vasodilators for hypertension. Deprescribing led to a mean increase of 13.5 (95% CI 9.2, 17.8) mmHg in SBP and 4.6 (95% CI 1.9, 7.3) mmHg in DBP. Restarting diuretics was required in 50/102 (49%) participants in the withdrawal group due to the occurrence of symptoms of heart failure or an increase in blood pressure.

Myers 1982 randomised 77 residents in long-term care facilities who had been taking diuretics for more than three months to diuretic continuation (n=39) or placebo (n=38) with a 12-month follow-up [383]. This study excluded people with concurrent digoxin therapy, clinical evidence of hypertension and heart failure. At 12 months, two participants (5%) in the placebo group had to restart their diuretic therapy for hypertension. Participants in the placebo group had a significantly higher final DBP than participants in the continuation group (MD 4.10, 95% CI 3.05 to 5.15). However, participants in the placebo group also had a higher baseline DBP. Ankle oedema did not differ significantly between the two groups (MD 0.30, 95% CI -1.01 to 1.61). At month three, mortality also did not differ significantly between the two groups (OR 3.20, 95 CI% 0.78 to 13.14).

Burr 1977 conducted an RCT that included 106 inpatients who had been taking diuretics for more than a month, without a history of heart failure in the three months prior, nephrotic syndrome, glaucoma or hypertension [381]. The participants were randomised to placebo (n=54) or continuing diuretic therapy (n=52). At 12 months, there was a slight increase in ankle oedema and blood pressure in the placebo group. In the placebo group, 41 (75%) participants remained off their diuretic at 12 months whereas eight (15%) participants restarted diuretic therapy and two (4%) participants dropped out of the trial. Re-commencement of therapy was required in the eight participants due to heart failure (n=4), peripheral oedema (n=2) and bronchopneumonia (n=1). There were three deaths (6%) in the placebo group caused by haemorrhage from gastric ulcer, colon cancer, or bronchopneumonia, compared to one death (2%) in the continuation group caused by myocardial infarction (OR 3.00, 95% CI 0.30 to 29.81).

Straand 1993 conducted a before-and-after study that included 33 community-dwelling, older people who were receiving a stable dose of diuretic for at least six months. Participants were included if there were no signs of hypertensive end organ damage, New York Heart Association functional class III or IV heart failure and BP ≤ 220/110 mmHg. Deprescribing was successful in 18/33 participants (55%), with the remaining 15 participants (45%) restarting treatment due to sudden cardiovascular events (n=4), heart failure (n=2), peripheral oedema (n=3), hypertension (n=3), anxiety (n=2), malignancy (n=1) [384].

Walma 1993 conducted a before-and-after study that included 15 participants who had been using diuretics for at least six months with satisfactory control of blood pressure (<165/95 mmHg), and

free from overt signs of heart failure [386]. Diuretics were discontinued in all 15 participants. At month six, 6/15 (40%) participants remained without diuretic therapy whereas nine participants (60%) restarted diuretic due to congestive heart failure (n=1), hypertension (n=3), bronchial asthma (n=1), ankle oedema (n=2), and subjective complaints (n=2).

In these two before-and-after studies by Straand 1993 and Walma 1993 (n=48), it was reported that 24-53% experienced recurrence of the underlying condition, 9-13% experienced peripheral oedema, 9-20% became hypertensive, and 6-7% had symptoms of congestive heart failure [384, 386]. In the study by Walma 1993, participants were reported to have a mean increase in body weight of 1.2 kg [386] and subjective withdrawal symptoms were reported in 2/15 (13%) participants. In Straand 1993, life-threatening cardiovascular events were reported in 4/33 (12%) participants (two acute heart failure, one myocardial infarction/stroke, one cerebrovascular stroke), of which three out of four cases occurred four months or later after diuretic withdrawal [384].

Narrative evidence summary: withdrawal schedules

Various methods were used for deprescribing in the included studies and there was no direct evidence that any particular method was associated with the greatest benefits and harms. However, compared to abrupt cessation, dose tapering is likely more acceptable and helpful in determining the lowest effective dose for some people requiring dose reduction rather than complete cessation. Tapering, if required, may be undertaken by reducing the dose by 50% every one to two weeks depending on the baseline dose.

In the RCT by Walma 1997, participants with a baseline furosemide dose of 40 mg daily had their dose halved for one week before complete withdrawal; if 80 mg daily, the dose was halved for two weeks (n=202, low certainty) [387]. One RCT (n=32) reported diuretic dose was halved for one week, and then substituted by a placebo; however, the study did not report important or critical outcomes associated with deprescribing [385]. The method of deprescribing was not described in three other RCTs [381-383] and one before-and-after study [384]. In the before-and-after study by Walma 1993, thiazide diuretic and furosemide in daily dosages of <40 mg were stopped abruptly; furosemide daily dosages of 40 mg were halved for one week before stopping completely (n=15, very low certainty) [386].

GRADE Summary of Findings (SoF) Table

Table 15. Summary of findings for deprescribing diuretics

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
2 [381, 383]	RCTs	92	91	OR 3.14 (0.94, 10.47)	
2. Adverse drug withdrawal events (ADWEs)					
Exacerbation/return of underlying condition					
3 [381-383]	RCTs	114	115	In one study, four out of 34 participants in the intervention group experienced exacerbations that would have led to serious adverse events without resuming diuretics (OR 8.70, 95% CI 0.45, 168.87) [382]. In another study, ankle oedema was assessed on a scale of 0-4 (0 = no oedema; 1 = trace; 2 = ankle; 3 = mid-calf; 4 = above mid-calf). Significant ankle oedema was noted in both placebo and diuretic groups, although the placebo group had a greater extent of oedema at the end of follow-up (MD 0.30, 95% CI -1.01, 1.61) [383]. Similarly, ankle oedema increased significantly in the intervention group at 12 weeks (OR 2.55, 95% CI 1.06, 6.11) and there was no significant change in the proportion of participants who had an improvement in oedema (OR 0.38, 95% CI 0.13, 1.09) [381].	
2 [384, 386]	Non-controlled studies	48	N/A	Recurrence of the underlying condition was reported in 8/33 (24%) participants in one study [384] and 8/15 (53%) participants in the other study [386]. In the latter study, 2/15 (13%) had subjective complaints that led to the resumption of diuretics. Peripheral oedema was reported in 3/33 (9%) participants in one study [384] and 2/15 (13%) participants in the other study [386]. Hypertension was reported in 3/33 (9%) participants in one study [384] and 3/15 (20%) participants in the other study [386]. Symptoms of congestive heart failure were reported in 2/33 (6%) participants in one study [384] and 1/15 (7%) participants in the other study [386].	
3. Health outcomes					
Blood pressure, systolic					
3 [381, 383, 387]	RCTs	181	187	MD 9.49 (5.55, 13.43)	
Blood pressure, diastolic					
3 [381, 383, 387]	RCTs	181	186	MD 3.99 (3.04, 4.94)	
Adverse events/ serious adverse events/ cardiovascular events					
1 [384]	Non-controlled study	33	N/A	Sudden cardiovascular events occurred in four out of 33 participants (12%).	
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

Lipid-modifying agents

Lipid-modifying agents include:

- HMG CoA reductase inhibitors (Statins): Atorvastatin*, fluvastatin, pravastatin*, rosuvastatin*, simvastatin*
- Fibrates: Fenofibrate*, gemfibrozil
- Bile acid sequestrants: Colestyramine
- PCSK9 (proprotein convertase subtilisin/kexin type 9) inhibitors: Evolocumab, inclisiran
- Other drugs for dyslipidaemia: Nicotinic acid, ezetimibe*
- Combination lipid-modifying agents: ezetimibe with atorvastatin* or simvastatin* or rosuvastatin*
- Lipid-modifying agents in combination with other drugs: Atorvastatin with amlodipine*

*Common PBS medicines

Type	Recommendation
When to deprescribe	
CBR	Following a shared decision-making discussion in which potential benefits and harms are clearly communicated along with considerations of other individual factors, we suggest deprescribing be offered to older people taking lipid-modifying agents: 1. For primary prevention of cardiovascular diseases (CVD) and cerebrovascular diseases in people aged: • 65-79 with CVD risk < 5% (over five years) • 65-79 with CVD risk between 5% and < 10% (over five years) and, if tested, a coronary artery calcium score of zero and/or no coronary artery disease shown on computed tomography (CT) or invasive coronary angiogram • ≥ 80 where the risk of adverse effects potentially outweighs the benefit 2. For secondary prevention in people aged ≥ 80 years unable to tolerate high-intensity statin, **moderate-intensity** therapy can be considered 3. For primary or secondary prevention in the context of frailty or advanced life-limiting illness (e.g. poor prognosis malignancies) with a life expectancy < 12 months when there are no recent active cardiovascular diseases to reduce risk of adverse effects, reduce medication burden, and improve quality of life 4. With possible adverse effects (e.g. statin-related muscle symptoms such as myalgia, myopathy, rhabdomyolysis)
GPS	Healthcare providers should use the Australian CVD Risk Calculator* to assess cardiovascular risk over the next five years, as it accounts for the specific contexts of the Australian population and healthcare system (https://www.cvdcheck.org.au/calculator) (ungraded good practice statement). *Note that the Australian cardiovascular disease risk calculator is validated for use in people without known CVD aged 30 to 79 years who do not already meet high risk criteria.
GPS	The 'Surprise Question' should be used as a prognostic tool to estimate life expectancy in individuals with advanced disease or progressive life-limiting conditions ("*Would you be surprised if this person were to die in the next 12 months?*") in conjunction with clinical judgement (ungraded good practice statement).
Ongoing treatment	
CBR	We suggest ongoing treatment with statins be considered in people without limited life expectancy: 1. For primary prevention of CVD and cerebrovascular disease • With a high CVD risk ≥ 10% (over 5 years) • With a coronary artery calcium score > 100 • With total cholesterol levels above 7.5mmol/L, independent of their CVD risk

	• With familial hypercholesterolaemia 2. For secondary prevention of CVD and cerebrovascular disease provided this aligns with the individual's goals and preferences, following informed consent.
How to deprescribe	
CBR	We suggest discontinuing lipid-lowering agents without the need for tapering provided it aligns with the individual's wishes and goals.
Monitoring	
CBR	We suggest monitoring lipid concentrations annually.

CBR, consensus-based recommendation; GPS, good practice statement

Introduction

HMG-CoA reductase inhibitors (i.e. statins) are the first-line lipid-modifying therapy for hypercholesterolemia or for CVD prevention in people at a high risk of coronary heart disease, regardless of their cholesterol levels [177]. Other lipid-lowering agents such as ezetimibe and fenofibrate, are also commonly prescribed. Irrespective of the lipid-lowering effects, fenofibrate also plays a role in delaying the progression of diabetic retinopathy and improving glycaemic control in people with diabetes [388].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

Primary prevention

While statins are widely used for primary prevention, evidence supporting their efficacy in individuals aged 80 and older remains limited. However, their use in this age group has increased in recent years [389].

At the time of writing, the follow-up or reporting for both STAREE and PREVENTABLE trials are still ongoing.

The Statins in Reducing Events in the Elderly (STAREE) trial is a double-blind, placebo-controlled RCT evaluating the benefits of statins versus placebo in people aged 70 and older (mean age = 75) for primary prevention [390].

The Pragmatic Evaluation of Events and Benefits of Lipid Lowering in Older Adults (PREVENTABLE) is another double-blind placebo-controlled trial that targeted community-dwelling adults aged > 75 years. The study compares the impact of high-intensity atorvastatin 40mg and placebo on cardiovascular death, hospitalisations for unstable angina, myocardial infarction, heart failure, stroke, or coronary revascularisation [391].

Below is a summary of key clinical trials that have contributed to current guidelines on lipid-lowering therapy in older people.

One of the few RCTs specifically targeting older people is the PROSPER trial, which enrolled 5,804 participants aged 70 to 82 years (mean age 75) with either risk factors for vascular disease (primary prevention) or a history of vascular disease (secondary prevention) [392]. Over a mean follow-up of three years, pravastatin significantly reduced the risk of coronary heart disease in the secondary prevention group. However, no significant benefit was observed for primary prevention.

Complementing this evidence, a 2018 retrospective cohort study using the SIDIAP database included 46,864 individuals aged 75 years and older without clinically established cardiovascular

disease [393]. Participants were followed for a mean of six years, with analyses stratified into two age groups: 75-84 years and ≥85 years. Statin use was not associated with a significant reduction in cardiovascular events, stroke, or all-cause mortality among individuals aged ≥ 85, nor among those aged 75-84 without type 2 diabetes. In contrast, a significant reduction in cardiovascular events and all-cause mortality was observed among participants under 85 years of age with type 2 diabetes.

The HOPE-3 trial, which included participants with a mean age of 65.7 years, demonstrated a significant reduction in cardiovascular events and mortality among individuals at intermediate cardiovascular risk, with a reported number needed to treat (NNT) of 378 per year [35]. Conversely, a post hoc secondary analysis of the ALLHAT-LLT trial, which recruited older people with moderate hyperlipidaemia and hypertension but no baseline atherosclerotic cardiovascular disease, found no significant benefit of statin therapy for primary prevention when initiated after the age of 65 [394].

Systematic reviews and meta-analyses examining statin use in older people (mean age ≥ 70 years) in the context of primary prevention have generally demonstrated a significant reduction in cardiovascular events, although they have not shown a consistent benefit in reducing all-cause mortality [395-397]. Furthermore, a systematic review and meta-analysis that combined both primary and secondary prevention populations reported that the relative reduction in cardiovascular events with lipid-lowering therapy (including statins, PCSK9 inhibitors, and ezetimibe) was consistent between individuals aged ≥75 years and those younger than 75 years [398].

While mortality benefits are often not observed in trials, this may be due to inadequate statistical power, small sample sizes, or low event rates. Individual risk factor assessment is again important. In order to determine which people above the age of 65 would benefit from lipid-lowering agents for primary prevention, the Heart Foundation recommends calculation of cardiovascular risk [399]. In Australia, the Australian Cardiovascular Disease Risk Calculator (Aus CVD Risk Calculator) is a validated tool to estimate five-year cardiovascular risk in people aged 30 to 79 years who do not already meet the high-risk criteria [399]. The guideline provides a conditional recommendation for people with a risk of 10% or more (high risk) to initiate pharmacotherapy including a lipid-lowering agent [399].

In people at intermediate cardiovascular risk (AusCVDrisk 5 to <10%), determining who will benefit from lipid-lowering therapy can be challenging. As discussed in the 'anti-thrombotic agents' section, CAC scoring in addition to clinical risk assessment may provide guidance in pharmacological treatment decisions [257, 258]. While CAC score is not recommended for routine cardiovascular risk screening in the general population, CAC score can be useful in reclassifying individuals at intermediate risk to a lower or higher cardiovascular risk category when treatment decisions are uncertain [399]. CAC is a highly specific marker of atherosclerosis and has strong predictive value for future cardiovascular events [400]. The association between arterial calcification and cardiovascular disease risk is well-established [401]. One study reported a five-year number needed to treat (NNT) with statins of 549 for individuals with a CAC score of zero, compared to 24 for those with a CAC score greater than 100 [400]. In individuals at intermediate cardiovascular risk with a CAC score of zero – or with no evidence of coronary artery disease on CT or invasive coronary angiography – lipid-lowering therapy is generally not required following the reclassification of risk level to low [400]. In contrast, those with a CAC score above 100, or with prior imaging evidence of arterial calcification or atheromatous plaques, are more likely to benefit from lipid-modifying therapy.

In people with familial hypercholesterolaemia and very high cholesterol (i.e. total cholesterol levels > 7.5mmol/L), initiation of lipid-modifying agents is often required, rather than according to calculated absolute AusCVD risk [399]. Refer to disease-specific guidelines for the management guidance.

Secondary prevention
For secondary prevention of cardiovascular and ischemic cerebrovascular disease, strong evidence supports a significant benefit of statins, even in individuals over 75 years of age [402]. The PROSPER study [392] reported an NNT of 23.2 over 3.2 years for secondary prevention [35].

For the secondary prevention of haemorrhagic stroke, a recent systematic review and meta-analysis of RCTs found limited benefits of LDL-C-lowering therapy (statins, ezetimibe, and PCSK9 inhibitors) [403].

For individuals undergoing percutaneous coronary intervention (PCI), long-term statin therapy improves epicardial perfusion post-PCI [404]. A meta-analysis of six RCTs (mean age 58-65 years) showed that post-PCI statin therapy significantly reduced myocardial infarction but had no significant effect on all-cause mortality or revascularisation compared to placebo [405].

In terms of the intensity of statin therapy, high-intensity therapy is recommended for people aged ≤ 75 years with chronic coronary syndrome [303]. Emerging data suggests that people aged over 75 years may also benefit from high-intensity statins [406]. For those unable to tolerate high-intensity statins, moderate-intensity therapy remains beneficial and should be considered [303].

Other considerations
The benefits of statins typically manifest within two to five years [407]. Therefore, individuals with advanced life-limiting illnesses and a prognosis of fewer than 12 months are unlikely to benefit from initiating statins solely for mortality reduction. However, continuation may be warranted if there are other compelling indications. In addition to life expectancy, polypharmacy, treatment burden, functional status, and quality of life are all important considerations for the continuation or discontinuation of statins in older people.

In older people with advanced life-limiting diseases who have no recent active CVD, discontinuation of statins may be considered with the aim of improving quality of life and reducing medication burden. The 'Surprise Question' may be considered a prognosis tool to estimate life expectancy in people with advanced disease or progressive life-limiting conditions within the last year of life. A recent systematic review reported a modest accuracy for predicting mortality across various populations despite limitations and suggested it may be useful as a starting point to identify people who may benefit from an early integration of palliative care [408]. However, it should not be used alone to base clinical decisions.

<u>Narrative summary of evidence on deprescribing</u>
We identified four studies (one RCT, one retrospective cohort study, and two before-and-after studies) related to statins deprescribing from the systematic review and meta-analysis [173, 409-411]. We were unable to identify any direct evidence related to the deprescribing of other lipid-modifying agents (e.g. fibrates, bile acid sequestrants, PCSK9 inhibitors).

Overall, the current evidence for deprescribing statins is derived from studies of very low certainty and varied in terms of indication for use and study setting. Deprescribing statins following intracerebral haemorrhage was associated with a significant increase in mortality in a cohort study, but the outcome is of very low certainty due to methodological limitations. In participants nearing the end of life, there was no evidence of significant harms or benefits associated with deprescribing statins. There was also a lack of evidence for deprescribing drugs for dyslipidaemia other than statins. The evidence at this stage is insufficient to inform evidence-based recommendations.

If lipid-modifying agents are considered appropriate to deprescribe, monitoring of cholesterol concentrations at least annually may be appropriate.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Kutner 2015 randomised 381 participants with advanced life-limiting illness (life expectancy less than 12 months) to statins discontinuation (n=189) or continuation (n=192) [411]. Of all participants, 49% had cancer as their primary diagnosis with life expectancy between one month to one year. Participants were included if they had worsening functional status, no recent active cardiovascular diseases, and were taking statin therapy for at least three months, regardless of whether for primary or secondary prevention. Mortality within 60 days did not differ significantly between the two groups (OR 1.23, 95% CI 0.75 to 1.99). Cardiovascular events (OR 1.22, 95% CI 0.53 to 2.79), overall symptoms (MD -2.5, 95% CI -6.0 to 1.1) and statin-specific side effects (muscle-related pain, weakness, headache, and fever) also did not differ significantly between the two groups (MD -0.20, 95% CI -1.4 to 0.9). There was no significant difference in the quality of life between the two groups (MD 0.18, 95% CI -0.28 to 0.64).

Chung 2018 conducted a retrospective cohort study of 2,468 people following intracerebral haemorrhage [409]. Participants were included if they were using statins for dyslipidaemia in the three months prior and were excluded if they had a cerebrovascular accident within three months of intracerebral haemorrhage. At three years, there was a significantly higher all-cause mortality among people who discontinued statins compared to those who continued statins following intracerebral haemorrhage (12.9% vs. 25.3%; OR 2.29, 95% CI 1.74 to 3.03).

Visser 2021 targeted both statins and PPIs by applying a study-specific evidence-based implicit deprescribing algorithm in nursing home residents [173]. The algorithm considered both primary and secondary prevention indications for statins. In this before-and-after study, 34/66 (52%) of the residents had their PPI and/or statin dosage either successfully reduced or discontinued after three months which were maintained at six months. Of the 13 residents who were using a statin, eight (61%) had their statin completely discontinued and five (39%) continued using their statin.

Korsholm 2024 conducted a before-and-after study that included 98 participants who were taking statins for primary prevention treatment on a stable dosage for a minimum of 12 months [410]. This study reported that discontinuation of statins led to a mean increase in total cholesterol concentrations (from 4.8 ± 0.7 to 6.5 ± 0.9 mmol/L) and low-density lipoprotein cholesterol concentrations (from 2.2 ± 0.5 to 3.9 ± 0.8 mmol/L). However, physical function related to muscle performance improved as shown in a chair stand test (number of repetitions per 30 seconds increased from 15.7 ± 4.3 to 16.3 ± 4.9, p<0.05), 6-minute walking test (distance increased from 544 ± 78 m to 556 ± 80 m, p<0.05), power (increased from 268 ± 100 to 276 ± 102 W, p<0.05), and relative power (increased from 3.6 ± 1.1 to 3.7 ± 1.2 W/kg, p not stated).

Narrative evidence summary: withdrawal schedules

In one before-and-after study, statins were discontinued abruptly (n=98) [410]; however, this study did not report important or critical outcomes associated with deprescribing. The method of deprescribing was not explicitly described in the other three studies (RCT, n=381; retrospective cohort study, n=2468; before-and-after study, n=67) [173, 409, 411].

GRADE Summary of Findings (SoF) Table

Table 16. Summary of findings for deprescribing HMG CoA reductase inhibitors

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
1 [411]	RCT	189	192	OR 1.23 (0.75, 1.99)	
1 [409]	Non-randomised study	708	708	OR 2.29 (1.74, 3.03)	
2. Adverse drug withdrawal events (ADWEs)					
Adverse events/ serious adverse events/ cardiovascular events					
1 [411]	RCT	189	192	OR 1.22 (0.53, 2.79)	
1 [409]	Non-randomised study	708	708	Intracerebral haemorrhage OR 1.23 (0.82, 1.84) Acute ischemic stroke OR 0.75 (0.50, 1.12) Any stroke OR 0.96 (0.71, 1.31)	
3. Health outcomes					
Adverse drug events					
1 [411]	RCT	189	192	There was no significant difference in side effects specific to statin use (muscle-related pain, weakness, headache, and fever) (MD −0.2, 95% CI −1.4, 0.9) measured using the 13-item Edmonton Symptom Assessment System scale. When combined with the nine standard items on the same scale (pain, fatigue, nausea, depression, anxiousness, drowsiness, appetite, well-being, and breathing), the overall symptoms also did not differ significantly (MD –2.5, 95% −6.0, 1.1).	
Cholesterol concentrations					
1 [410]	Non-controlled study	98	N/A	Total cholesterol concentrations increased from 4.8 ± 0.7 to 6.5 ± 0.9 mmol/L. Low-density lipoprotein cholesterol (LDL-C) concentrations increased from 2.2 ± 0.5 to 3.9 ± 0.8 mmol/L.	
Physical function					
1 [410]	Non-controlled study	98	N/A	Physical function improved as follows: Chair stand test, number of reps per 30 seconds increased from 15.7 ± 4.3 to 16.3 ± 4.9, p<0.05. Power (W) increased from 268 ± 100 to 276 ± 102, p<0.05. Relative power (W/kg) increased from 3.6 ± 1.1 to 3.7 ± 1.2, p not stated 6-min walking test increased from 544 ± 78 m to 556 ± 80 m, p<0.05.	
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
1 [411]	RCT	189	192	There was no significant change in the overall quality of life following the deprescribing of statin therapy (MD 0.18, 95% CI -0.28, 0.64) measured using the McGill Quality of Life Questionnaire.	

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

DERMATOLOGICALS

This section includes:

- Corticosteroids (skin)

DERMATOLOGICALS

Corticosteroids (skin)

Corticosteroids for skin use include betamethasone*, clobetasol, clobetasone, desonide, hydrocortisone, methylprednisolone*, mometasone*, and triamcinolone*.

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing decisions be made in consultation with the person, their GP and/or specialist providers (e.g. dermatologist, clinical immunologist) to ensure it aligns with their preferences, goals and overall treatment plans. To minimise potential adverse effects associated with prolonged use, we suggest deprescribing be offered to older people using long-term topical corticosteroids for: 1. No ongoing indication in people who are asymptomatic after uninterrupted treatment using appropriate potency therapy 2. Unclear or unknown indications
Ongoing treatment	
CBR	We suggest: • continuing the topical corticosteroid treatment during flares or at the first signs of a flare until resolution of symptoms; and • minimising exposure to topical corticosteroids by using the lowest potency topical corticosteroid that is effective, or intermittent use of higher potency topical corticosteroid if required; and • continuing the use of moisturisers.
How to deprescribe	
CBR	We suggest discontinuing topical corticosteroids without the need for tapering when the flare is fully resolved (e.g. itch-free, inflammation resolved) without strict time limits, then switch to on-demand or intermittent use for maintenance therapy if needed, following appropriate non-pharmacological management plan (e.g. use of emollient, avoid triggers) and flare management protocol is in place.
Monitoring	
CBR	We suggest advising individuals to report to their healthcare professionals symptoms of recurrence, noting topical corticosteroid withdrawal syndrome (e.g. red or darker burning skin, papulopustular rashes) is rare but more common in people stopping treatment after using for prolonged continuous periods of moderate-to-high potency topical corticosteroids, particularly on sensitive areas (e.g. face).

CBR, consensus-based recommendation

Introduction

Corticosteroids are widely used to treat dermatological conditions such as eczema and psoriasis because of their anti-inflammatory, immunosuppressive, and antiproliferative properties [177].

Narrative summary of evidence on deprescribing

We were unable to identify any direct evidence related to the deprescribing of topical corticosteroids in older people from the systematic review and meta-analysis. Recommendations are provided in this section following a Delphi consensus process.

Justification of recommendations

All topical corticosteroids can induce skin atrophy, and in older people, the risk may be higher [177]. The recommended treatment duration varies depending on the potency of the topical corticosteroids. A study suggests up to three weeks duration for very high potency corticosteroids (e.g. clobetasol propionate 0.05%) and up to 12 weeks for medium to high potency (e.g. betamethasone dipropionate 0.05% ointment) [412]. No time limit was specified for low-potency topical corticosteroids (e.g. hydrocortisone 1%) [412]. Prolonged use of potent corticosteroids may result in severe adverse effects such as periorificial dermatitis, steroid rosacea, pustular psoriasis and rebound flares after stopping treatment [413]. Therefore, in people who are asymptomatic (e.g. skin is completely clear) after uninterrupted treatment using appropriate potency therapy, deprescribing may be appropriate to minimise the adverse effects associated with prolonged use. For body areas prone to recurrent flares, proactive intermittent use of topical corticosteroids two to three times weekly may be considered on the basis of preventing relapses and reducing the need for topical corticosteroids [414].

Ongoing use of emollients is recommended to maintain remission and improve skin conditions [414, 415]. Topical corticosteroids should be resumed at the first signs of a flare and continued until the skin clears, as inadequate treatment increases the risk of recurrence [415].

If considered suitable to deprescribe, topical corticosteroids generally do not require tapering when the flare is fully resolved (e.g. itch-free, inflammation resolved) without strict time limits. Appropriate non-pharmacological management plan (e.g. use of emollient to improve skin conditions and avoid aggravating factors) and flare management protocol should be in place at all times [415].

In some cases, topical corticosteroid withdrawal syndrome, a drug-related skin condition, may occur after discontinuing moderate- to high-potency topical corticosteroids following prolonged continuous use. It is characterised by red or hyperpigmented, burning or stinging skin, papulopustular rashes, and itch [416]. The condition may be caused by a combination of tachyphylaxis, rebound vasodilation, and skin barrier dysfunction [417]. While it most commonly affects sensitive areas such as the face and groin, it can involve any part of the body [416, 417]. Monitoring is important to minimise topical corticosteroid withdrawal syndrome. Healthcare providers should advise individuals to report back any symptoms of recurrence, noting topical corticosteroid withdrawal syndrome (e.g. red or darker burning skin, papulopustular rashes).

GENITO-URINARY SYSTEM

This section includes:

- Estrogens
- Anticholinergics
- Drugs used in benign prostatic hypertrophy (BPH)

Estrogens

Estrogens include estradiol and estriol (common PBS medicines).

Type	Recommendation
When to deprescribe	
CBR	**Systemic Menopausal Hormone Therapy (MHT)** We suggest deprescribing be offered to older women taking MHT (menopausal hormone therapy i.e. estrogen monotherapy or estrogen combined with progestogen) whose menopausal symptoms have resolved or improved over time, provided this aligns with the individual's goals and preferences and following informed consent. **Vaginal MHT** We suggest deprescribing be offered to older women on low-dose vaginal estrogen therapy for genitourinary syndrome of menopause whose symptoms have resolved or improved over time.
Ongoing treatment	
CBR	We suggest continuing MHT in people who experience symptoms recurrence that impact their quality of life and cannot be managed with non-hormonal options. If deprescribing is unsuccessful, we suggest non-hormonal and non-pharmacological therapies (e.g. lifestyle interventions) for genitourinary syndrome of menopause such as moisturisers, lubricants or pelvic floor muscle exercises may be considered as alternative options before considering the reinitiation of MHT. If MHT needs to be resumed, we suggest maintaining the lowest effective dose; however, we suggest reassessing the need for long-term therapy periodically including the possibility of switching to another route of administration (e.g. topical low-dose estrogen intravaginal cream for localised symptoms).
How to deprescribe	
CBR	We suggest stopping MHT abruptly without the need for tapering; however, some patients may prefer gradual tapering by reducing the dose or dosing frequency. For oral formulations, we suggest reducing one dose per week every two to four weeks (e.g. reducing from daily administration to six days a week with one day off for two to four weeks, then to five days a week for two to four weeks, and so on, until discontinuation). For transdermal formulations, we suggest gradually reducing the strength of the patch over three to six months, depending on the available preparations. For gel, cream or pessary formulations, we suggest tapering by reducing the dosing frequency every two to four weeks.
Monitoring	
CBR	We suggest periodic evaluation of patient preferences, symptom control and ongoing benefit-risk profile including fracture risk (e.g. using Fracture Risk Assessment Tool) and if indicated, bone mineral density, as well as consideration for alternative treatments for management of osteoporosis if required.

CBR, consensus-based recommendation

Introduction

Estrogens are widely used as menopausal hormone therapy (MHT) to alleviate menopausal symptoms and prevent bone loss resulting from decreased endogenous estradiol production [177]. However, the decision to use MHT must be carefully balanced against the potential risks, including an increased risk of cardiovascular disease and estrogen-dependent cancers, such as breast cancer, with the risk increasing with prolonged use [177]. The Australasian Menopause Society provides information for healthcare professionals about non-hormonal treatments for menopausal symptoms, along with guidance on other aspects of women's health through midlife health and menopause [418].

Genitourinary Syndrome of Menopause (GSM) refers to atrophic symptoms in the vulvovaginal and bladder-urethral regions resulting from the menopause-related loss of estrogen [419]. GSM affects an estimated 40% to 90% of postmenopausal women and can significantly impact their quality of life [420]. First-line treatment for GSM typically includes non-hormonal moisturisers, lubricants, and pelvic floor muscle exercises. If these measures do not provide sufficient symptom relief, vaginal estrogen therapy or other hormonal treatments may be considered [419]. For moderate-to-severe vaginal atrophy unresponsive to non-hormonal therapy, low-dose vaginal estrogen may be considered if there is no absolute contraindication. In Australia, commonly used formulations include estriol 1 mg/g cream, estriol 500 mcg pessary, and estradiol 10 mcg pessary. Estradiol has a greater effect on systemic estrogen levels and is therefore considered a second-line option [421].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

Vaginal MHT

The standard dosing regimen involves daily application for the first two weeks, followed by maintenance therapy once or twice weekly. Low-dose vaginal estrogen can also be used alongside systemic MHT if atrophic symptoms persist. Long-term use of vaginal MHT is generally considered safe due to minimal systemic absorption; however, evidence from trials beyond one year is limited [422]. The need for continued therapy should be reassessed based on symptom progression and individual preferences. If symptoms have resolved or improved, a trial discontinuation may be appropriate, with the option to restart therapy if needed.

Systemic MHT

The greatest benefits of systemic MHT are observed in women within 10 years of menopause onset and those under 60 years of age [422]. As a result, MHT is generally recommended for a maximum duration of five years and is typically avoided in individuals over the age of 60. However, treatment should be individualised, with dosing adjusted based on symptom response rather than age alone. In some women over 65, continued MHT may be appropriate if the benefits, such as improved quality of life and bone loss prevention, outweigh the risks.

For those with bothersome vasomotor symptoms (e.g. hot flushes and night sweats), non-hormonal and non-pharmacological therapies should be first considered prior to commencing or reinitiating hormonal therapy. If these approaches are ineffective, hormonal use may be considered at the lowest effective dose provided the benefits and risks are carefully considered in perspective for each woman following shared decision-making [421, 422].

Narrative summary of evidence on deprescribing

We identified one study related to estrogen deprescribing from the systematic review and meta-analysis [423]. This study was a comparison of the effect of deprescribing estrogen and placebo on

surrogate outcomes indicative of fracture risks. There is no direct evidence of the benefits or harms related to estrogen deprescribing. The current evidence is of very low certainty and inadequate to inform evidence-based recommendations.

Key study characteristics and results

Gallagher 2002 conducted a five-year 2x2 factorial RCT comparing MHT, calcitriol, MHT with calcitriol, and placebo for three years and the effect of discontinuing therapy for two more years. All participants were women aged over 65 who did not have primary hyperparathyroidism and were not taking bisphosphonates, anticonvulsants, estrogen, fluoride, or thiazide diuretics, in the past six months. After discontinuing therapy at the end of year three, much of the bone density gained during treatment was lost in all three treatment groups, although all treated groups still had a significantly higher total body bone mineral density (BMD) compared to placebo. Compared to the group who were untreated (placebo group), the percentage change in total body BMD from baseline to five years for those who received MHT for the preceding three years before discontinuation was lower (MD 2.89, 95% CI 2.71 to 3.07) as was spinal BMD (MD 2.39, 95% CI 2.02 to 2.76), femoral neck (MD 1.33, 95% CI 0.94 to 1.72), and total hip (MD 1.19, 95% CI 0.84 to 1.54). There was no significant difference between the two groups in BMD of the trochanter (MD -0.11, 95% CI -0.55 to 0.33).

Narrative evidence summary: withdrawal schedules

The method of deprescribing was not described in the study.

There is limited evidence on the safest method for discontinuing MHT. Guidelines suggest up to 50% of women experience symptom recurrence within four to six weeks of discontinuing systemic MHT [421]. An RCT of 81 postmenopausal women on combined estrogen-progestogen therapy compared tapering versus abrupt discontinuation. However, this study was excluded from our systematic review and meta-analysis, as the mean age at inclusion was 58 in the taper-down group and 59 in the abrupt discontinuation group (both under 65). The trial found no significant differences between the two groups in the incidence or severity of hot flashes, quality of life, or the rate of therapy reinitiation [424].

If gradual tapering is preferred, it may be implemented by reducing the dose or dosing frequency [425]. For example:

- For oral formulations, reduce one dose per week every two to four weeks; or
- For transdermal formulations, gradually lower the patch strength over a period of three to six months, depending on the available dosage forms; or
- For gel, cream or pessary formulations, reduce the dosing frequency every two to four weeks.

GRADE Summary of Findings (SoF) Table

Table 17. Summary of findings for deprescribing estrogens

No. of studies	Study design	Number of participants		Effect measure*, comparing hormone replacement therapy withdrawal vs placebo withdrawal	Certainty of evidence (GRADE)
		Depres cribing	Contin uation		
1. Mortality					
No available evidence					
2. Adverse drug withdrawal events (ADWEs)					
ADWEs, bone mineral density					
1 [423]	RCT	56	44	There was no significant difference between the discontinuation and continuation group in bone mineral density of the trochanter (MD -0.11, 95% CI -0.55, 0.33). Those participants who received estrogen replacement therapy for the preceding three years before two years of discontinuation had a lower percentage change in bone mineral density from baseline to five years in total body (MD 2.89, 95% CI 2.71 to 3.07), spinal (MD 2.39, 95% CI 2.02 to 2.76), femoral neck (MD 1.33, 95% CI 0.94 to 1.72), and total hip (MD 1.19, 95% CI 0.84 to 1.54) compared to the group who were untreated (placebo group).	
3. Health outcomes					
No available evidence					
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*For randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals.

Anticholinergics (genitourinary)

Genitourinary anticholinergics include darifenacin, oxybutynin, propantheline, solifenacin, and tolterodine.

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing decisions be made in consultation with the person and their specialist providers to ensure it aligns with their preferences, goals and overall treatment plans. We suggest deprescribing of genitourinary anticholinergics be offered to older people: 1. With cognitive impairment, delirium, dementia and/or a high risk of falls due to the risk of adverse cognitive outcomes and sedation potentially outweigh the benefits of continued use, especially in patients with high anticholinergic burden; or 2. With no clear indication (e.g. no identifiable benefit); or 3. For drug-induced symptoms where the original drug can be suitably reduced, discontinued, or replaced by another drug (e.g. inappropriate prescribing cascade).
Ongoing treatment	
CBR	If multiple attempts at deprescribing are unsuccessful and non-pharmacological interventions or alternative medications with fewer anticholinergic effects are not effective/possible, we suggest continuing the genitourinary anticholinergic at the lowest effective dose; however, the need for long-term therapy should be reassessed periodically.
How to deprescribe	
CBR	Generally, we suggest discontinuing genitourinary anticholinergics without the need for tapering. Tapering may be considered for high-dose therapy, and some individuals may prefer gradual tapering by reducing the dose or dosing frequency per week that the medicine is taken.
GPS	Healthcare providers should consider offering adequate education on lifestyle interventions (e.g. bladder training, pelvic floor exercises, timed toileting) to individuals, as appropriate, in addition to referrals to a continence advisor (ungraded good practice statement).
Monitoring	
CBR	We suggest periodic evaluation of individual preferences, and psychological effects of deprescribing, and advising individuals to report to their healthcare professionals any symptoms of recurrence or disease exacerbation (e.g. any return or worsening of urgency, frequency, incontinence, or nocturia).

CBR, consensus-based recommendation; GPS, good practice statement

Introduction

Overactive bladder is common in older people and presents as urinary frequency, urgency, incontinence, and nocturia [426]. It is twice as prevalent in women as in men [427]. Non-pharmacological management includes symptom diaries, bladder training, intravesical botulinum toxin injections, pelvic floor exercises, and avoiding bladder irritants such as caffeine, alcohol, carbonated beverages, and acidic juices.

Narrative summary of evidence on deprescribing

We identified one study related to deprescribing drugs for urinary frequency and incontinence from the systematic review and meta-analysis [428]. This retrospective, observational, before-and-after study reported a pharmacist-led intervention to reduce the use of urinary anticholinergics in older

people. Appropriateness of urinary anticholinergics was assessed using a clinical decision support software (MedWise) coupled with the pharmacist's clinical judgement (considering the duration of use, presence of side effects and reasonable benefits). At nine months, pharmacist recommendations to deprescribe urinary anticholinergics were accepted by prescribers in 118 out of 187 participants (63%). Among the 118 participants, complete discontinuation was the most common pharmacist recommendation (n = 50), followed by switching to mirabegron (n = 32), and dose reduction (n = 18). By study conclusion, six participants (5%) either had their urinary antimuscarinic dose returned to the baseline or increased. However, it was unclear what the pharmacist recommendations were for these six participants. Anticholinergic exposure, as measured using standardised daily doses reduced from 2.6 ± 2.8 at baseline to 0.9 ± 2.1 at nine months. Overall, this study did not investigate any critical or important outcomes (i.e. mortality, adverse drug withdrawal effects, physical health outcomes, cognitive function, and quality of life). Therefore, recommendations for the deprescribing of drugs for urinary frequency and incontinence are developed based on consensus.

Narrative evidence summary: withdrawal schedules

The approach to deprescribe was individualised – urinary anticholinergics were either completely stopped, switched to mirabegron, or reduced in daily dose.

Justification of recommendations

Urinary anticholinergics, including darifenacin, oxybutynin, propantheline, solifenacin, and tolterodine, are primarily used to manage urge incontinence by reducing bladder muscle contractility and increasing bladder capacity [177]. A Cochrane review found that while these medications offer modest symptom improvement over placebo, they also have a higher incidence of adverse effects, leading to increased discontinuation rates (except for tolterodine) [429]. There is limited evidence to determine the most effective anticholinergic or whether more selective agents (e.g. solifenacin, darifenacin) have fewer side effects. For people unable to tolerate anticholinergics, mirabegron may be an alternative for urinary urge incontinence, though it is currently not subsidised by PBS at the time of writing.

Older people are particularly susceptible to anticholinergic side effects, including urinary retention, blurred vision, dry mouth, constipation, and cognitive impairment [177]. Deprescribing should be considered when an inappropriate prescribing cascade is identified [430]. For instance, oxybutynin is sometimes prescribed after initiating cholinesterase inhibitors (e.g. donepezil) for dementia, which may induce urge incontinence [431]. Additionally, many commonly used medicines, such as diuretics, calcium channel blockers, ACE inhibitors, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, antipsychotics, opioids, and benzodiazepines, can worsen lower urinary tract symptoms (LUTS) [432]. Assessing whether LUTS are a side effect of other medicines before initiating treatment for urinary incontinence is essential to avoid inappropriate prescribing cascades.

Cumulative anticholinergic burden in older people is associated with an increased risk of falls, cognitive decline, and all-cause mortality [433]. Before prescribing medicines with anticholinergic properties, their risks and potential interactions should be carefully assessed. While some medicines are prescribed for their anticholinergic effects, others possess anticholinergic activity unrelated to their primary indication. A comprehensive medication review is crucial for older people receiving multiple medicines with anticholinergic properties. This should include an assessment of the anticholinergic burden using validated tools such as the Drug Burden Index, which quantifies cumulative anticholinergic and sedative drug exposure [434]. Deprescribing may be appropriate for people with cognitive impairment, delirium, dementia and/or a high risk of falls due to the risk of adverse cognitive outcomes and sedation potentially outweigh the benefits of continued use, especially in patients with high anticholinergic burden. In the absence of a clear indication for ongoing treatment, or when the benefits are not identifiable, deprescribing should be considered.

Drugs used in benign prostatic hypertrophy (BPH)

Drugs used in BPH include:

- Alpha-adrenoreceptor antagonists: Alfuzosin, silodosin, tamsulosin
- Testosterone-5-alpha-reductase inhibitors: Dutasteride, finasteride
- Combination drugs for BPH: Dutasteride with tamsulosin*

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing drugs used for benign prostatic hypertrophy (BPH) in people: • Whose symptoms have resolved or improved, such as those who have undergone transurethral resection of the prostate (TURP) or prostatectomy. • With adverse effects or interactions that outweigh the potential benefits (e.g. symptomatic hypotension)
Ongoing treatment	
CBR	We suggest continuing drugs used for BPH in older men with persistent and severe symptoms, with regular assessments to evaluate the need for ongoing therapy. For men who remain on alpha-blockers, we suggest periodic blood pressure monitoring alongside reviews of the long-term necessity of the treatment.
CBR	If deprescribing is unsuccessful despite multiple attempts, we suggest maintaining the lowest effective dose, with periodic reassessment of the need for long-term therapy.
How to deprescribe	
CBR	We suggest deprescribing without the need for tapering; however, some patients may prefer gradual tapering by reducing the dose or dosing frequency per week that the medicine is taken. For individuals who continue to have mild to moderate symptoms, we suggest a trial of lifestyle modifications (e.g. limit fluid intake, limit bladder irritants, maintain a healthy weight) and behavioural strategies (e.g. timed voiding regimens, double-voiding techniques, pelvic floor exercises) before restarting pharmacological treatment.
Monitoring	
CBR	We suggest periodic evaluation of individual preferences and psychological effects of deprescribing, and advising individuals to report to their healthcare professionals any symptoms of recurrence or disease exacerbation (e.g. any return or worsening of urgency, frequency, incontinence, or nocturia) after stopping drugs used for BPH.
GPS	Healthcare professionals should advise individuals to keep a record that they have taken drugs for BPH in the past if receiving eye surgery due to the risk of intraoperative floppy iris syndrome.

CBR, consensus-based recommendation

Introduction

Benign prostatic hyperplasia (BPH) is common in older men, with treatment guided by symptom severity, often assessed using the International Prostate Symptom Score (IPSS). Before initiating BPH treatment, other causes of lower urinary tract symptoms (LUTS), including overactive bladder, urethral stricture, and prostate cancer, should be ruled out. Combination therapy, such as dutasteride with tamsulosin, is commonly preferred when both rapid symptom relief and prostate size reduction are needed, as it lowers the risk of acute urinary retention and surgery [177].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

While selective alpha-blockers including tamsulosin have fewer systemic effects than non-selective alpha-blockers, they can still cause hypotension, which has been linked to a small but significant increase in the risk of falls, fractures, and head trauma in older people [435].

There is limited guidance on the optimal duration of combination therapy or whether selective alpha-blockers can be discontinued in people without worsening urinary symptoms. A small study (n = 7) suggested that changes in pupil diameter during tamsulosin therapy may be reversible in short-term users, with a significant increase in post-dilation pupil diameter observed after 30 days of discontinuation [436]. Selective alpha-blockers may interfere with mydriasis during surgery, increasing the risk of intraoperative floppy iris syndrome [437-439]. Notably, tamsulosin has been strongly associated with serious ophthalmic complications following cataract surgery [440].

For individuals with mild symptoms that do not significantly impact quality of life, lifestyle modifications are recommended as first-line management. These include limiting fluid intake before bedtime, reducing alcohol and caffeine consumption (due to their mild diuretic effects), avoiding bladder irritants (e.g. spicy foods), preventing constipation, and using behavioural strategies such as pelvic floor exercises, double-voiding, and timed voiding. People who have undergone transurethral resection of the prostate (TURP) or prostatectomy generally do not require pharmacological therapy post-surgery [437].

Narrative summary of evidence on deprescribing

We identified one RCT related to deprescribing drugs used in BPH from the systematic review and meta-analysis [441].

Overall, there is no direct evidence of the benefits or harms related to the deprescribing of drugs used in BPH. The only evidence we identified was a comparison of the effect of deprescribing from combination therapy to monotherapy. If discontinuation is considered appropriate, monitoring may involve symptoms indicative of clinical BPH progression (e.g. any return or worsening of urgency, frequency, incontinence, or nocturia). The reported outcomes in the study are of very low certainty and remain insufficient to inform evidence-based recommendations. An accompanying editorial stated that “considering the minor effect of its discontinuation, this study clearly suggests that after a priming period, alpha-blockers might be discontinued”. However, the lack of a placebo control group makes it difficult to attribute the observed outcomes specifically to the removal of alpha-blockers, as opposed to other factors.

Key study characteristics and results

Lin 2014 compared the discontinuation of either drug from the combination therapy consisting of alpha-blocker (doxazosin) and 5-alpha-reductase inhibitor (dutasteride) in men with moderate to severe urinary tract symptoms. During the two-year combination therapy, improvements in symptom scores, urine flow, and prostate measures were observed. These measures appeared to deteriorate in both groups upon commencing monotherapy after receiving combination therapy for two years. At 12 months, deprescribing of either drug was not associated with a significant difference in the clinical BPH progression in terms of International Prostate Symptom Score, maximum flow rate, post-void residual urine volume, the need for surgical resection of the prostate, and overall BPH/ lower urinary tract symptom progression. However, a significantly greater proportion of participants with 5-alpha-reductase inhibitor discontinued had a total prostate volume increased ≥ 20% and resumed the medicine, when compared to the group with alpha-

blocker discontinued. After 12 months, 135/230 (59%) participants continued with monotherapy. Additionally, the study reported that men with larger total prostatic volume (TPV) were significantly more likely to resume combination therapy.

Narrative evidence summary: withdrawal schedules

The method of deprescribing was not specified, but it appears to have involved abrupt discontinuation.

GRADE Summary of Findings (SoF) Table

Table 18. Summary of findings for deprescribing drugs used in benign prostatic hypertrophy (BPH)

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
No available evidence					
2. Adverse drug withdrawal events (ADWEs)					
Exacerbation/return of underlying condition					
1 [441]	RCT	117	113	One RCT compared the discontinuation of either drug from the combination therapy of alpha-blocker and 5-alpha-reductase inhibitor. At 12 months, deprescribing of either drug was not associated with a significant difference in the following: • International Prostate Symptom Score ≥ 4, OR 1.00 (0.55, 1.81) • Maximum flow rate reduced ≥ 2mL/s, OR 1.41 (0.80, 2.48) • Post-void residual urine volume increased by ≥ 50%, OR 0.66 (0.36, 1.20) • Transurethral resection of the prostate, OR 2.23 (0.92, 5.40) • Overall BPH/ lower urinary tract symptom progression, OR 0.67 (0.31, 1.43) However, there was a significantly greater proportion of participants who had a total prostate volume increased by ≥ 20% in the group with their 5-alpha-reductase inhibitor discontinued than in the group with alpha-blocker discontinued (OR 4.73, 95% CI 2.15, 10.42). Additionally, a significantly greater proportion of participants who had their 5-alpha-reductase inhibitor discontinued resumed the medicine compared to the group with alpha-blocker discontinued (OR 2.35, 95% CI 1.37, 4.02). OR > 1 indicates a greater likelihood of the event occurring in the group with 5-alpha-reductase inhibitors discontinued.	
3. Health outcomes					
No available evidence					
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals.

SYSTEMIC HORMONAL PREPARATIONS

excluding sex hormones and insulins

This section includes:

- Prednisone/ Prednisolone
- Levothyroxine
- Teriparatide

SYSTEMIC HORMONAL PREPARATIONS excluding sex hormones and insulins

Prednisone / Prednisolone

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing decisions be made in consultation with the person and their GP and/or specialist providers to ensure it aligns with their preferences, goals and overall treatment plans. We suggest deprescribing be offered to older people taking long-term oral corticosteroids for: • Chronic obstructive pulmonary disease (COPD) as long-term oral corticosteroids are not indicated for this condition; or • Autoinflammatory or autoimmune conditions, once clinical remission or sustained low disease activity has been achieved; or • Polymyalgia rheumatica, after at least 12 months of therapy and lack of signs and symptoms of an active disease.
Ongoing treatment	
CBR	We suggest that ongoing treatment with oral corticosteroids may be necessary for some people with autoimmune diseases who experience a relapse after attempts to deprescribe, despite concurrent use of disease-modifying agents. In such cases, we suggest maintaining long-term oral corticosteroids at the lowest effective dose.
How to deprescribe	
CBR	We suggest individualising the tapering schedule and adjusting the schedule based on individual preferences, overall risk of withdrawal effects, risk of glucocorticoid-induced adrenal insufficiency, risk of relapse, adverse drug effects, disease activity, the initial dose, and duration of use. In general, we suggest reducing the dose by prednisone equivalent of 10-20% per week; however, some people may require very gradual tapering such as 1 mg every four to eight weeks, especially when approaching physiological glucocorticoid dosing.
Monitoring	
CBR	We suggest advising patients to report to their healthcare providers symptoms of potential signs and symptoms of glucocorticoid withdrawal syndrome (e.g. sleep disturbance and mood changes), glucocorticoid-induced adrenal insufficiency (e.g. myalgias, fatigue, and muscle weakness) and recurrence of underlying conditions (e.g. breathlessness for COPD or arthralgias in rheumatoid arthritis). We suggest monthly monitoring of erythrocyte sedimentation rate and C-reactive protein for at least three months, followed by monitoring every six months thereafter. However, this should be tailored based on individual factors such as their preferences, responses and tolerance to deprescribing.

CBR, consensus-based recommendation

Introduction

At pharmacological doses, corticosteroids are widely used for their anti-inflammatory and immunosuppressive effects across various conditions [177]. While corticosteroids offer substantial therapeutic benefits, prolonged systemic corticosteroid use is associated with serious adverse effects, including osteoporosis, hypertension, glaucoma, peptic ulcer disease, increased infection

risk, worsened glycaemic control, and psychiatric disturbances [177]. However, these effects are dose-dependent and less likely to occur at physiological replacement doses [177].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

Older people, particularly those with severe chronic conditions, are frequently prescribed long-term oral corticosteroids. These medications provide rapid symptom relief and help achieve clinical remission, which is a key goal in managing autoimmune or autoinflammatory diseases [177]. Systemic corticosteroids are typically reserved for managing disease flares or as an adjunct therapy to induce remission while awaiting the therapeutic effects of disease-modifying drugs (biologic or synthetic), which have more favourable long-term safety profiles. This process can generally take six to 12 weeks. Once remission or low disease activity is achieved, deprescribing corticosteroids should be considered. A cohort study of older people with inflammatory bowel disease found that 40% were on long-term corticosteroid therapy, despite 24% being in remission or having only mild disease activity [442]. Since long-term corticosteroid use is rarely warranted, especially in respiratory and endocrine conditions, deprescribing should be considered when the disease is stable or in remission [443].

The duration and approach to oral corticosteroid use vary considerably depending on the condition being treated. For instance, polymyalgia rheumatica, a chronic inflammatory condition typically seen in people over the age of 50 years, typically requires treatment with oral corticosteroids for at least 12 months as monotherapy [444]. In some cases, methotrexate can be used as a corticosteroid-sparing agent, while the use of biologic disease-modifying drugs is generally not indicated. A common corticosteroid regimen involves initiating prednisolone at 15 mg daily for four weeks, followed by dose reductions of 2.5 mg every four weeks until reaching 10 mg daily. Subsequently, reductions of 1 mg every four to eight weeks are recommended, depending on the individual's response and tolerability. Regimens lasting less than nine months are generally not advised due to a higher risk of relapse. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are useful for monitoring disease activity but are not specific markers and should be interpreted alongside the individual's symptoms [444]. Current guidelines recommend monthly monitoring of CRP and ESR during the first three months of treatment, followed by monitoring every two to three months thereafter or as clinically indicated [444].

Chronic glucocorticoid therapy (≥ 3-4 weeks) increases the risk of glucocorticoid-induced adrenal insufficiency, which can occur both after discontinuation and during continued use, even at low doses (≤5 mg prednisolone equivalent) [445]. The risk increases with treatment duration (≥ 3-4 weeks) and higher doses (e.g. >15–25 mg hydrocortisone equivalent: 4–6 mg prednisone/prednisolone, 3–5 mg methylprednisolone, 0.25–0.5 mg dexamethasone) [446]. Symptoms of adrenal insufficiency, such as fatigue, malaise, muscle aches, and low energy, often overlap with those of the underlying inflammatory disease, glucocorticoid withdrawal syndrome, or stress events (e.g. infection). The European Society of Endocrinology/Endocrine Society joint guideline suggests considering the total daily glucocorticoid dose when distinguishing adrenal insufficiency from withdrawal symptoms, as higher doses make adrenal insufficiency less likely [446].

We suggest advising patients to report to their healthcare providers symptoms of potential signs and symptoms of glucocorticoid withdrawal syndrome (e.g. sleep disturbance and mood changes) [446], glucocorticoid-induced adrenal insufficiency (e.g. myalgias, fatigue, and muscle weakness) [446] and recurrence of underlying conditions. It may be helpful to provide examples of common symptoms when encouraging individuals to self-monitor and report symptoms. As some symptoms

are non-specific, many individuals may not recognise that they could be indicative of withdrawal syndrome or adrenal insufficiency.

Narrative summary of evidence on deprescribing

We identified five studies (one RCT and four before-and-after studies) related to prednisolone deprescribing from the systematic review and meta-analysis [447-451] and one retrospective cohort study related to glucocorticoid deprescribing in general [452].

Overall, the included studies investigated glucocorticoid use across various diseases. Although an observational study suggested that deprescribing may reduce hospitalisation rates, the certainty of this evidence is very low. There appears to be an increased risk of disease flare-ups in patients with severe conditions (polymyalgia rheumatica and autoimmune pancreatitis). However, the current evidence is inadequate to inform evidence-based recommendations.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Three studies included people with **rheumatoid arthritis**.

- Hirata 2021 conducted a before-and-after study that included 36 who had been receiving a stable regimen of prednisolone and methotrexate for more than six months regardless of disease activities [449]. Participants were excluded if they required a long-term glucocorticoid for extraarticular manifestations (e.g. rheumatoid vasculitis or interstitial lung disease). Prednisolone dose was reduced with an increment of methotrexate dose in all participants. After 24 months, the proportion of people using prednisolone reduced by 86.1% ($p<0.0001$) while the clinical remission rate increased from 25.0% to 38.9%. Serious adverse events were reported in 2/36 (6%) people which were peritoneal cancer and myelodysplastic syndrome.
- Almayali 2023 conducted an extension study that included patients who previously completed a two-year RCT [451]. In the main RCT, participants with inadequate control of rheumatoid arthritis (DAS28-ESR [Rheumatoid arthritis Disease Activity Score with Erythrocyte Sedimentation Rate] ≥2.60) were randomised to two years of 5mg prednisolone daily or placebo. Participants were excluded if they were already receiving glucocorticoid therapy or if they had other uncontrolled conditions. Among the 96 patients who had been receiving prednisolone for two years, tapering of prednisolone after two years of therapy significantly increased disease activity (DAS-28 score increased from 2.88 ± 1.14 to 3.12 ± 1.15, $p=0.04$) and 43/96 (45%) of all participants experienced disease flares during tapering. However, there was a small reduction in signs and symptoms of adrenal insufficiency (1.1 ± 1.2 to 0.8 ± 1.3), indicating that withdrawal of low-dose prednisolone could be safe in certain cohorts.
- Goto 2023 conducted a retrospective cohort study that included 122 patients who discontinued glucocorticoids and 126 patients who continued [452]. Patients were included in the analysis if they had a diagnosis of rheumatoid arthritis and received therapeutic intervention. Those who discontinued their glucocorticoids had a significantly lower rate of infection requiring hospitalisation (OR 0.35, 95% CI 0.18, 0.67).

One study included patients with **chronic obstructive pulmonary disease** (COPD).

- Rice 2000 conducted a blinded placebo-controlled RCT that included 38 men with COPD who had been taking both inhaled beta-agonists and oral prednisolone (> 5mg/day) for at least six months [450]. Participants were included if there had not been any reduction in their prednisolone dose in the past month and if they had a smoking history of at least 20

pack years. Participants were excluded if they had asthma, a history of eosinophilia, a high IgE titer, a strong family history of atopy, or normal or highly (50%) variable spirometry results within the last five years. All eligible participants were randomised to either on-demand dosing (n=18) versus continuation (n=20). At six months, participants in the on-demand group had a significantly lower average daily corticosteroid dose (MD -7.4, 95% CI -12.38, -2.42). However, there were no significant differences between the two groups in terms of the number of participants experiencing at least one exacerbation, exacerbation rate, or number of days until the first exacerbation.

One study included patients with **autoimmune pancreatitis**.

- Hirano 2015 conducted a before-and-after study that included 21 patients with autoimmune pancreatitis who were clinically and serologically stable [448]. All participants who had received prednisolone for at least three years without clinical relapse with immunoglobulin G < 1600 mg/dL in the past year on maintenance dose ≤ 5mg were included. Participants had their low-dose maintenance prednisolone tapered before complete withdrawal. During the follow-up period (range 19 to 48 months), clinical (n=10/21, 48%) and serological (n=5/21, 24%) relapse occurred. There were two malignancies (gastric cancer and tongue cancer) in two patients who survived after surgical resection. HbA_{1c} levels increased significantly, particularly in patients having clinical or serological relapse (6.16 ± 0.57% and 6.68 ± 0.69%, p = 0.0012), which could be attributed to the resumption of prednisolone.

One study included patients with **polymyalgia rheumatica**.

- Esselinckx 1977 conducted a before-and-after study that included 18 patients with polymyalgia rheumatica treated with stable doses of prednisolone [447]. Patients with any signs that correlated with giant cell arteritis were excluded. Two participants (11%) died during the follow-up period, one of a bleeding duodenal ulcer and one of ovarian cancer. All participants experienced a recurrence of the underlying condition. In three participants, the relapse was severe and rapid, so within four days, the original dose of prednisolone had been reinstated. Within one week, 12 (67%) participants had relapsed. Two participants relapsed in week two, and one participant relapsed in week 10. Satisfactory symptomatic control was re-established with the reintroduction of oral prednisolone. After the gradual withdrawal, one participant was maintained on a lower dose, one participant was maintained on a higher dose, and in the other participants, the initial dose was resumed. Although two participants were symptom-free, they were described as having a markedly raised erythrocyte sedimentation rate (ESR) so the oral prednisolone therapy was resumed.

Narrative evidence summary: withdrawal schedules

In the RCT, prednisolone was gradually tapered by 5mg per week in patients with chronic obstructive pulmonary disease (n=38, low certainty) [450].

The method was not described in the retrospective cohort study related to glucocorticoid deprescribing in patients with rheumatoid arthritis (n=248) [452].

For the other four single-arm studies investigating prednisolone deprescribing, the prednisolone dose was:

- Withdrawn abruptly and gradually titrated at a mean rate of 1mg per month over four to five months (study=1, n=18) [447]
- Tapered by 1mg every 8-10 weeks until complete cessation (study=1, n=21), Individualised (study=1, n=36) [448]

- The dose was tapered over 12 weeks, starting with a baseline dose of 5 mg of prednisolone daily. Every two weeks, a 'prednisolone-free' day was added until complete discontinuation by week 13 (study=1, n=96) [451]
- Prednisolone was gradually reduced up to 1 mg per month while at the same time, the methotrexate dose was gradually increased up to 16 mg per week and up to 4 mg per month for folate (study=1, n=36) [449]

There is no universally established tapering strategy for long-term glucocorticoid therapy, making an individualised approach essential [453]. Current guidelines recommend a slower tapering rate as the dose approaches physiological levels (e.g. 4-6 mg prednisone) [446]. As the dose decreases, the risk of adrenal insufficiency rises, necessitating a slower taper to allow recovery of the hypothalamic–pituitary–adrenal axis that leads to increased adrenocorticotropic hormone levels and the eventual restoration of normal adrenal function and cortisol production [454].

GRADE Summary of Findings (SoF) Table

Table 19. Summary of findings for deprescribing glucocorticoids

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
1 [447]	Non-controlled study	18	N/A	2/18 (11%)	
2. Adverse drug withdrawal events (ADWEs)					
Exacerbation/return of underlying condition					
1 [450]	RCT	18	20	Deprescribing was not associated with a significant change in the proportion of participants having at least one exacerbation (OR 1.50, 95% CI 0.35, 6.50), the number of exacerbations (MD 0.20, 95% CI -1.46, 1.86) or the number of days until first exacerbation (MD -7.00, 95% CI -35.94, 21.94).	
4 [447-449, 451]	Non-controlled studies	75	N/A	In one study, recurrence of the underlying condition occurred in all 18 participants after discontinuation of prednisolone [447]. In another study, clinical relapse occurred in 10 out of 21 (48%) participants whereas serological relapse occurred in five out of 21 (24%) participants [448]. Hence, 15 out of 21 (71%) participants had either clinical or serological relapse [448]. One other study reported that the Clinical Disease Activity Index remission rate increased from 25.0% to 38.9% at follow-up [449]. In another study, the Disease Activity Score 28 joints increased from 2.88 ± 1.14 to 3.12 ± 1.15, p=0.04 and disease flares occurred in 45% of all participants [451].	
3. Health outcomes					
Adverse events/ serious adverse events/ cardiovascular events					
2 [448, 449]	Non-controlled studies	57	N/A	Serious adverse events occurred in two out of 36 (6%) participants [449]. Malignancies were detected in two out of 21 (10%) participants [448].	
Adverse drug event					
1 [451]	Non-controlled study	52	N/A	Signs and symptoms of adrenal insufficiency 1.1 ± 1.2 to 0.8 ± 1.3	
Health service use					

1 [452]	Non-randomised study	122	126	Unplanned hospitalisation OR 0.35 (0.18, 0.67)	
Adrenocorticotropic/ cortisol hormone level					
1 [451]	Non-controlled study	23	N/A	Adrenocorticotropic hormone level, 5.8 ± 4.1 pmol/L Cortisol hormone level, 310 ± 166 nmol/L Adrenocorticotropic /cortisol hormone level, 67 ± 40 nmol/L	
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

Levothyroxine

Type	Recommendation
When to deprescribe	
GPS	The target TSH concentration should be individualised for older adults; in general, targeting a reference range of 1-5 mU/L for people aged 65 to 80 years, and 4 to 6 mU/L for people aged 80 years and older (ungraded good practice statement).
CBR	We suggest deprescribing decisions be made in consultation with the person and their GP and/or endocrinologist to ensure it aligns with their preferences, goals and overall treatment plans. To minimise potential adverse effects associated with overtreatment, especially related to cardiovascular events and loss of bone mass in older people, we suggest deprescribing be offered to older people taking long-term levothyroxine: 1. Who are asymptomatic and stable on a low dose (e.g. 25 to 50 microgram); 2. For unclear/unknown indication or no clear evidence of clinical benefit (e.g. subclinical hypothyroidism); or 3. For drug-induced indication where the original drug can be suitably reduced, discontinued, or replaced by another drug e.g. inappropriate prescribing cascade with e.g. ○ Lithium ○ Amiodarone (taking into consideration the possible long half-lives)
Ongoing treatment	
CBR	We suggest continuing long-term levothyroxine for autoimmune conditions (e.g. Hashimoto thyroiditis), radioactive iodine treatment and thyroidectomy where the benefits of continuing treatment potentially outweigh the potential risks, with periodic re-assessment of thyroid function every 6 to 12 months.
CBR	If the serum TSH concentration increases (primary hypothyroidism) or if the free serum T_4 concentration falls below the reference range without an elevated TSH (central hypothyroidism) during deprescribing, we suggest restarting levothyroxine at the previously tolerated dose.
How to deprescribe	
CBR	We suggest reducing the dose by approximately 50% if the baseline TSH concentration is within an acceptable range. After six weeks, if the TSH concentration remains within an acceptable range, discontinue the thyroid therapy completely. After another six weeks, if the TSH concentration remains within an acceptable range, measure the free thyroxine (T_4) level. If the free T_4 concentration is within an acceptable range, there is no need to restart thyroid hormone therapy. After a further six weeks, measure the final TSH concentration.
Monitoring	
CBR	We suggest closely monitoring for potential symptoms of hypothyroidism (e.g. fatigue, weight gain, cold intolerance, poor mental concentration, mood changes) during deprescribing by advising people to report symptoms to their healthcare providers. We suggest reviewing TSH and/or free serum T4 concentrations six weeks after each dose adjustment, as levothyroxine has a long half-life and TSH concentrations take 6-8 weeks to stabilise; however, this review should be tailored to individual factors, such as the patient's preferences, response, and tolerance to deprescribing.

CBR, consensus-based recommendation; GPS, good practice statement

<u>Introduction</u>

Levothyroxine is indicated for hypothyroidism [177]. In frail, older people or those with severe ischemic heart disease, levothyroxine treatment for hypothyroidism, if clinically indicated, should be initiated with smaller doses and under specialist advice, due to the increased risk of cardiovascular

adverse effects [177]. Thyroid dysfunction is associated with metabolic syndrome, contributing to an increased risk of cardiovascular disease, type 2 diabetes, and all-cause mortality [455]. The prevalence of hypothyroidism increases with age [456]. In older people, a higher serum TSH target is generally acceptable for several reasons: thyroid hormone requirements naturally decline with age, normal TSH levels increase (especially after age 80), and older people are more vulnerable to the adverse effects of overtreatment of hypothyroidism, including an increased risk of unrecognised cardiac ischemia [457]. For this reason, Therapeutic Guidelines recommend a target TSH range of 1-5 mU/L for those aged 60 and older and 4–6 mU/L for individuals over 80 [457].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

Many older people who initiate thyroid hormone therapy often continue it for life without dose adjustments for prolonged periods [458]. However, thyroid function changes with age and so does thyroid hormone requirement [456]. In some cases, dose reduction or discontinuation may be appropriate, particularly in asymptomatic individuals with subclinical hypothyroidism, where thyroid hormone levels remain within the normal reference range but serum TSH is mildly elevated [459]. Subclinical hypothyroidism affects between 8-18% of older people, with a higher prevalence in women than men [460]. The management of subclinical hypothyroidism in older people remains a topic of debate. The AMH Aged Care Companion suggests that in asymptomatic older adults with negative antithyroid antibodies, treatment is generally not required, though periodic TSH monitoring is recommended, with a follow-up test in three months. However, individuals with positive antithyroid antibodies and rising TSH levels have a greater risk of progressing to overt hypothyroidism, making antibody testing a useful tool in clinical decision-making [177].

In older people, global fatigue is a common reason for thyroid hormone testing in primary care which often leads to levothyroxine prescription [461, 462]. However, current evidence suggests that thyroid hormone therapy in older people with subclinical hypothyroidism does not significantly improve physical or mental fatigue [463, 464]. Even in individuals with cardiovascular risk factors, a large cohort study found no significant association between levothyroxine use for subclinical hypothyroidism and reduced mortality, major adverse cardiac events, or hospitalisation [465]. A fine balance is required, as both undertreatment and overtreatment of hypothyroidism can increase the risk of cardiovascular events and mortality [466].

It is important to rule out any medicine-related causes to prevent an inappropriate prescribing cascade as medicines such as lithium and amiodarone can cause thyroid dysfunction [467].

Most people with hypothyroidism caused by permanent underlying conditions (e.g. autoimmune conditions including Hashimoto thyroiditis, post-ablative therapy including radioiodine therapy and thyroidectomy) often require lifelong maintenance therapy after the initial treatment [468].

Narrative summary of evidence on deprescribing

We identified one before-and-after study related to levothyroxine deprescribing from the systematic review and meta-analysis [469]. The current evidence for deprescribing levothyroxine is based on a single-arm study. Although one in two participants was able to successfully discontinue their thyroid hormone therapy in the study, the certainty of the evidence is very low certainty due to a very small sample size, lack of a comparison group, and other methodological limitations. The evidence at this stage is insufficient to inform evidence-based recommendations.

If levothyroxine is considered appropriate to deprescribe, closely monitoring for any hypothyroidism symptoms including fatigue, weight gain, cold intolerance, poor mental concentration, and mood changes may be appropriate. It may be helpful to provide examples of common symptoms when encouraging individuals to self-monitor and report symptoms. As some symptoms are non-specific and could be attributed to age-related changes or other health conditions, many individuals may not recognise that they could be indicative of hypothyroidism.

Key study characteristics and results

Coll 2000 included 22 nursing home residents who did not have a record of a previous TSH level > 10 mU/L in a before-and-after study. The study excluded nursing home residents who had a baseline TSH level of > 7 mU/L, who were taking lithium or amiodarone, had a history of thyroid nodule or goitre, or palpable thyroid nodule during a neck examination. Levothyroxine was successfully deprescribed in 11/22 (50%) participants, defined as TSH concentrations remaining ≤ 7mU/L after at least three months without thyroid hormone therapy. One participant (5%) reported potential adverse drug withdrawal effects (increased agitation and restlessness) following deprescribing.

Narrative evidence summary: withdrawal schedules

A deprescribing protocol was used in which thyroxine treatment was approximately halved if TSH concentrations were ≤ 7mU/L at baseline, then discontinued after a month if TSH remained ≤ 7mU/L. For instance:

- 125 mcg daily dose reduced to 75mcg daily
- 75 mcg daily dose reduced to 50 mcg daily

GRADE Summary of Findings (SoF) Table

Table 20. Summary of findings for deprescribing thyroid hormones

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
No available evidence					
2. Adverse drug withdrawal events (ADWEs)					
ADWEs					
1 [469]	Non-controlled study	22	N/A	1 out of 22 participants (5%) had psychiatric symptoms (agitation and restlessness) during deprescribing.	
3. Health outcomes					
No available evidence					
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*Effect measures are reported as the proportion of individuals with the outcome of interest.

Teriparatide

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing decisions be made in consultation with the person and their specialist providers to ensure it aligns with their preferences, goals and overall treatment plans. We suggest deprescribing be offered to older people who have been taking teriparatide for 24 months or longer* due to the limited efficacy and safety data beyond 24 months of continuous treatment or reinitiation of treatment; however, the duration of therapy should be guided by individual factors and informed consent. ** Teriparatide is approved for 24 months lifetime use in Australia with Pharmaceutical Benefits Scheme subsidisation for 18 months per lifetime per person.*
Ongoing treatment	
CBR	For postmenopausal women and men discontinuing teriparatide, we suggest transitioning to bisphosphonate therapy for at least 12 months. If bisphosphonates are contraindicated or not tolerated, alternative antiresorptive therapy should be considered.
How to deprescribe	
CBR	We suggest ceasing teriparatide without the need for tapering.
Monitoring	
CBR	We suggest closely monitoring for fracture risk using the Fracture Risk Assessment Tool and/or bone turnover markers, and the need for restarting therapy for osteoporosis in people not receiving therapy at a high risk of fracture, such as at least monthly for the first six months after deprescribing, followed by monitoring every six months thereafter to maintain the therapeutic relationship while working on lifestyle optimisation to reduce falls and fracture risk through multifactorial approach (e.g. environmental changes, exercise, nutrition). We suggest assessing bone mineral density by using dual-energy X-ray absorptiometry for men and women once after 12 months of discontinuation of therapy.

CBR, consensus-based recommendation

Introduction

Teriparatide, a parathyroid hormone analogue, is used to treat osteoporosis by stimulating bone formation and increasing bone mineral density (BMD) [177]. Teriparatide has been shown to reduce the risk of vertebral and non-vertebral fractures [470]. A 2019 systematic review and meta-analysis also found that teriparatide significantly reduced hip fractures in people with osteoporosis after a median treatment duration of 18 months (range: 6 to 24 months) [471]. Additionally, a 2024 retrospective cohort study reported that the functional benefits of teriparatide may vary by sex, with more pronounced improvements observed in men compared to women [472].

Teriparatide is indicated for individuals with osteoporosis at very high risk of fracture, such as those with a T-score ≤ –3.0 (with or without a history of fragility fracture) or a T-score < –2.5 with a history of fragility fracture. It is also recommended for individuals whose osteoporosis is refractory to antiresorptive therapy [473]. In Australia, teriparatide is approved for a maximum lifetime duration of 24 months, with PBS subsidisation limited to 18 months per person, due to the lack of long-term safety data. While high-dose teriparatide has been associated with an increased risk of osteosarcoma in rats, this risk has not been reported in humans [474]. Caution is advised when using teriparatide in individuals with a history of urolithiasis, as it may exacerbate the condition, and in those with impaired kidney function. Another potential adverse effect is postural hypotension, which can increase the risk of falls in older people. Combination therapy with bisphosphonates or

other antiresorptive agents is not recommended due to insufficient evidence supporting additional fracture risk reduction.

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

Following teriparatide discontinuation, transitioning to an antiresorptive agent, preferably a bisphosphonate, is recommended to maintain the BMD gains with teriparatide. For individuals who cannot tolerate bisphosphonates, denosumab or raloxifene (for females only) can be considered suitable alternatives [473]. The importance of post-teriparatide antiresorptive therapy is supported by multiple studies summarised below.

The 2005 Parathyroid Hormone and Alendronate (PaTH) trial randomised women who had received parathyroid hormone monotherapy for one year to either placebo (n=60) or **alendronate** (n=59) for an additional year [475]. Those who received alendronate experienced greater BMD gains at both the spine and hip compared to those who received no follow-up treatment.

The EUROFORS (EUROpean study of FORSteo) trial further supports the role of antiresorptive therapy in maintaining BMD after teriparatide discontinuation. The study compared continued teriparatide treatment for an additional year versus switching to **raloxifene** or placebo. Women who continued teriparatide for 24 months showed further BMD increases, while those who switched to raloxifene maintained their BMD. In contrast, individuals in the placebo group experienced BMD loss [476].

Additionally, an RCT investigating **denosumab** therapy after teriparatide discontinuation demonstrated benefits in increasing BMD at the spine, femoral neck, and total hip [477].

For those who discontinue teriparatide, it is important to continue close monitoring of fracture risk and the need for restarting therapy for osteoporosis, such as monthly for the first six months. Fracture risk can be monitored using the Fracture Risk Assessment Tool [478] and/or bone turnover markers using dual-energy X-ray absorptiometry (DXA) scan, ideally using the same densitometer for consistency [479].

As part of a multifactorial approach to fall and fracture prevention, it is also essential to address modifiable risk factors through other strategies. These may include nutritional review, environmental modifications and participating in fall prevention exercise programs, which have been shown to significantly reduce fall-related injuries, including fractures [480].

Narrative summary of evidence on deprescribing

We identified one cohort study examining teriparatide deprescribing from the systematic review and meta-analysis [481]. The findings from the study suggest that postmenopausal women may require more urgent initiation of antiresorptive therapy following discontinuation of teriparatide due to more rapid bone loss in the spine, whereas men might be managed more conservatively with observation and closer monitoring. However, the reported outcome is very low in certainty due to a very small sample size and methodological limitations. The evidence at this stage is insufficient to inform evidence-based recommendations.

Key study characteristics and results

This study included 14 postmenopausal women and 17 eugonadal men with lumbar spine or femoral neck BMD T-scores below -2. Participants were provided 400 units of vitamin D daily, with

calcium intake maintained between 1000 to 1200 mg daily through diet and/or supplements. Teriparatide therapy was discontinued after 24 months, in alignment with its approved duration due to safety concerns. At 12 months after discontinuation, there was a greater reduction in bone mass density in women than in men for spinal and trabecular BMD of the lumbar spine. BMD in the femoral neck and total hip remained stable for men.

Narrative evidence summary: withdrawal schedules

The method of deprescribing was not specified in the study, but it appears to have involved abrupt discontinuation.

GRADE Summary of Findings (SoF) Table

Table 21. Summary of findings for deprescribing teriparatide

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
No available evidence					
2. Adverse drug withdrawal events (ADWEs)					
No available evidence					
3. Health outcomes					
Bone mass density (BMD)					
1 [481]	Non-controlled study	31	N/A	12 months after deprescribing: **Spinal BMD:** Women: Reduced by 0.07 ± 0.04 g/cm^2 (7.1 ± 3.8%) Men: 0.04 ± 0.04 g/cm^2 (4.1 ± 3.5%) (P < 0.001 versus baseline in both men and women) **Trabecular BMD:** Women: Reduced by 21.6 ± 14.3 mg/cm^3 (17.0 ± 8.9%) Men: 15.4 ± 13.0 mg/cm^3 (11.1 ± 12.2%) in men (P < 0.001 versus baseline for both) **Total hip BMD:** Women: Reduced by 3.8 ± 3.9% (P < 0.05 vs. baseline) Men: Remained stable **Femoral neck BMD:** Women: Reduced by 3.1 ± 4.3% (P < 0.05 vs. baseline) Men: Remained stable	
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*Effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

MUSCULOSKELETAL SYSTEM

This section includes:

- Anti-inflammatory and antirheumatic products, non-steroids (NSAIDs)
- Anti-gout preparations
- Calcium & Vitamin D
- Denosumab/ Bisphosphonates

MUSCULOSKELETAL SYSTEM

Anti-inflammatory and antirheumatic products, non-steroids

Non-steroidal anti-inflammatory and antirheumatic products include:

- Acetic acid derivatives and related substances: Diclofenac, indomethacin, ketorolac
- Oxicams: Meloxicam*, piroxicam
- Propionic acid derivatives: Ibuprofen, ketoprofen, naproxen
- Fenamates: Mefenamic acid
- Coxibs: Celecoxib*, etoricoxib, parecoxib

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	Given the risk of gastrointestinal complications (e.g. severe esophagitis gastrointestinal ulcer, bleeding, perforation) as well as cardiovascular and renal adverse effects, we suggest deprescribing be offered to older people taking long-term NSAIDs.
Ongoing treatment	
CBR	If deprescribing is unsuccessful despite multiple attempts, we suggest maintaining the lowest effective dose; however, we suggest only continuing NSAIDs in older people if the benefits of pain relief and improved function significantly outweigh the risks of gastrointestinal, cardiovascular, or renal adverse effects, particularly when: • Alternative pain management strategies are less effective or unavailable; and • The potential benefits and risks have been clearly communicated to the person; and • There is appropriate monitoring of renal function and other risk factors, with periodic reassessment of the possibility of deprescribing.
CBR	We suggest referral to other healthcare providers as needed for further evaluation and management, and/or considering safer alternatives for symptoms. Instead of oral NSAIDs, we suggest a judicious trial of intermittent or on-demand use of topical NSAIDs or other topical treatments for superficial localised painful conditions (e.g. knee osteoarthritis) for a short period, with monitoring of possible adverse effects and discontinuing use if not effective. If symptoms are persistent, we suggest adequate investigation and differential diagnoses and appropriate non-pharmacological therapies have been considered.
How to deprescribe	
CBR	We suggest individualised deprescribing based on the individual's preference. In general, we suggest discontinuing NSAIDs without the need for tapering; however, some people may prefer a gradual dose reduction of 25%-50% every one to two weeks. Once half the lowest standard dose formulation is reached, we suggest ceasing completely and switching to on-demand or intermittent use of NSAIDs at the lowest effective dose as well as providing advice for alternative pain management strategies (e.g. cognitive behavioural therapy, manual therapy, massages) and lifestyle interventions (e.g. exercise, weight management) if applicable.

	If symptoms recur during tapering, we suggest restarting therapy at approximately 50-75% of the previously tolerated dose and delaying further dose reductions by an agreed interval for stabilisation.
Monitoring	
CBR	We suggest advising patients to report to their healthcare professionals any symptoms of pain, changes in function or quality of life.

CBR, consensus-based recommendation

Introduction

According to the ATC classification system, non-steroidal anti-inflammatory and antirheumatic products include NSAIDs. While NSAIDs are commonly used to manage pain and inflammation, their use requires careful monitoring, particularly in older people, who are at increased risk of adverse effects such as heart failure, gastrointestinal ulceration, and acute kidney injury [177].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

The evidence supporting long-term NSAID use is limited [482-485]. Prolonged use should generally be avoided, as the risks, including gastrointestinal, renal, and cardiovascular complications, often outweigh the benefits in terms of pain relief and functional improvement [486]. Deprescribing should be considered for all individuals taking NSAIDs once symptoms have improved or remained stable for a sustained period [487]. For chronic inflammatory conditions such as rheumatoid arthritis and ankylosing spondylitis, long-term NSAID therapy may be necessary. However, regular monitoring and re-evaluation are essential, with consideration given to optimising other maintenance therapies (e.g. disease-modifying antirheumatic drugs [DMARDs]) or incorporating non-pharmacological management strategies [487]. Referrals to other healthcare providers as needed for further evaluation and pain management, and/or considering safer alternatives for symptoms.

Instead of oral NSAIDs, a judicious trial of intermittent or on-demand use of topical treatments (topical NSAIDs or topical capsaicin) for a short period may be considered for superficial localised painful conditions if appropriate, with monitoring of possible adverse effects and discontinuing use if not effective [488]. Topical NSAIDs or topical capsaicin may relieve pain associated with knee osteoarthritis [489, 490].

Strategies to manage chronic pain are multi-dimensional. Alternative pain management strategies (e.g. cognitive behavioural therapy, manual therapy, massages) and lifestyle interventions (e.g. exercise, weight management) if applicable may be considered to limit the use of NSAIDs [491].

Narrative summary of evidence on deprescribing

We identified one before-and-after study and one retrospective cohort study related to NSAID deprescribing from the systematic review and meta-analysis [492, 493]. Overall, some evidence suggests that deprescribing NSAIDs in individuals at increased risk of gastrointestinal or cardiovascular events may reduce gastrointestinal adverse events and hospitalisations, without leading to pain exacerbations. However, these findings are based on evidence of very low certainty due to methodological limitations. At present, the available evidence is insufficient to inform evidence-based recommendations. If discontinuation is considered appropriate, close monitoring of changes in symptoms, functions, and quality of life, is necessary.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

O'Mahony 2021 reported a before-and-after study that included 51 primary care patients who had been taking long-term NSAIDs for at least three months [492]. Pharmacist-led educational interventions were delivered to healthcare providers to encourage NSAID deprescribing where appropriate. Upon re-audit at approximately three months, the intervention led to a 37% reduction in regular NSAID use. However, the study did not investigate the effects of deprescribing on patient-important outcomes such as mortality, adverse drug withdrawal effects, physical health outcomes, cognitive function, or quality of life.

Rashid 2020 reported a retrospective cohort study involving a pharmacist-led NSAID deprescribing program [493]. This study included 2,155 people who had been taking NSAIDs at least 270 days in the past 12 months and met at least one of the following criteria: gastrointestinal bleeding or disorders, cardiovascular diseases, end-stage renal disease, current usage of an anticoagulant or prednisone >10 mg per day or an equivalent systemic corticosteroid measured over the previous 12 months. A total of 431 people who received the deprescribing intervention were included in the analysis, matched by 1,724 people in the usual care. Compared to the usual care group, participants who had their NSAIDs deprescribed had significantly reduced gastrointestinal bleed events (OR 0.59, 95% CI 0.35, 0.99), pain exacerbations (OR 0.58, 95% CI 0.39, 0.86), and unplanned hospitalisations (OR 0.53, 95% CI 0.33, 0.84). However, there was no significant difference between the two groups for acute kidney injury (OR 0.58, 95% CI 0.30, 1.13) and emergency department visits (OR 0.69, 95% CI 0.42, 1.14).

Narrative evidence summary: withdrawal schedules

In the retrospective cohort study, deprescribing was based on the current drug regimen, individual preference, and lifestyle following shared decision-making with the individuals. In general, a dose reduction of 25% to 50% or discontinuation of the NSAID is initially recommended [493]. The method of deprescribing was not described in the before-and-after study [492].

GRADE Summary of Findings (SoF) Table

Table 22. Summary of findings for deprescribing non-steroidal anti-inflammatory drugs (NSAIDs)

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
No available evidence					
2. Adverse drug withdrawal events (ADWEs)					
Exacerbation /return of underlying condition					
1 [493]	Non-randomised study	342	1463	At least one pain exacerbation OR 0.58 (0.39, 0.86)	
3. Health outcomes					
Adverse drug events					
1 [493]	Non-randomised study	431	1724	Gastrointestinal bleeding events OR 0.59 (0.35, 0.99) Acute kidney injury OR 0.58 (0.30, 1.13)	
Health service use					
1 [493]	Non-randomised study	431	1724	Unplanned hospitalisation OR 0.53 (0.33, 0.84) At least one emergency department visit OR 0.69 (0.42, 1.14)	
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*Effect measures are reported as ratio measures (odds ratio, OR) along with 95% confidence intervals.

Anti-gout preparations include:

- Preparations inhibiting uric acid production: Allopurinol*, febuxostat
- Preparations increasing uric acid excretion: Probenecid
- Preparations with no effect on uric acid metabolism: Colchicine*

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing be offered to older people taking long-term **urate-lowering therapy** who have been in clinical remission for at least a year, with a normal serum uric acid concentration (< 0.36 mmol/L for non-tophaceous gout, or < 6 mg/dL), no tophi, no flares, when the risks of adverse drug events, drug-drug interactions, and treatment burden outweigh the benefits of preventing gout reoccurrence.
CBR	We suggest deprescribing be offered to older people taking long-term **colchicine** for prophylaxis of gout flares, except when initiating urate-lowering treatment for a short period of time (typically six months or more until no further attacks and the target serum uric acid concentration has been achieved).
Ongoing treatment	
CBR	We suggest continuing long-term urate-lowering therapy with tophi.
CBR	We suggest continuing long-term anti-gout preparations for evidence-based indications other than gout (e.g. colchicine used for pericarditis) for the appropriate duration of use, as the benefits of continued use likely outweigh the risks, under specialist care.
How to deprescribe	
CBR	In general, we suggest halving the daily dose every two weeks, ensuring individuals remain symptom-free before initiating each tapering. Once half the lowest standard dose formulation is reached, we suggest ceasing completely.
Monitoring	
CBR	We suggest closely monitoring for serum uric acid concentrations, renal function, and gout flares every two weeks for at least a month following deprescribing if practical. After this initial period, we suggest monthly monitoring for at least three months, followed by monitoring every six months thereafter. However, this should be tailored based on individual factors such as their preferences, responses and tolerance to deprescribing. If in-person visits are impractical, we suggest advising people to report symptom recurrence as needed. We suggest providing education on how to manage an acute gout attack.
CBR	We suggest the periodic assessment of cardiovascular risks and the appropriate management of comorbidities in people with gout and/or hyperuricaemia, including offering lifestyle modification advice where appropriate to modify cardiovascular risk factors.

CBR, consensus-based recommendation

Introduction

Gout

Gout is the most prevalent form of inflammatory arthritis, caused by the accumulation of monosodium urate crystals in the joints, triggering an intensely painful immune response [494]. It is typically an acute, self-limiting condition that primarily affects the lower limb joints [495]. While

hyperuricaemia is the strongest risk factor for gout, other factors such as age and sex also play a role, with gout being more common in men and increasing in prevalence with age [496]. Dietary intake of purine-rich foods, including meat, seafood, alcohol, and fructose-sweetened beverages, can contribute to hyperuricaemia [495]. However, a recent cohort study of adults without kidney disease or gout who were not taking urate-lowering or diuretic medications found that dietary factors had a minimal impact on serum uric acid concentrations compared to genetic factors [497]. Similarly, a previous Mendelian randomisation study found no causal relationship between increased alcohol consumption and the development of hyperuricaemia or gout [498]. Despite this, gout is frequently associated with comorbidities such as hypertension, diabetes, dyslipidaemia, chronic kidney disease, and obesity, which may benefit from lifestyle modifications. However, implementing these changes can be challenging for older people due to factors such as reduced appetite, altered food preferences, declining physical function, difficulty preparing meals, and financial constraints [499].

Serum uric acid

Elevated serum uric acid concentrations have been linked to chronic kidney disease and cardiovascular conditions, including hypertension, atrial fibrillation, heart failure, coronary artery disease, and cardiovascular mortality [500]. A recent cohort study found that men with gout who were not regularly dispensed allopurinol with serum uric acid concentration above the treatment target of 0.36 mmol/L had a significantly increased risk of cardiovascular disease [501]. However, the causal relationship between serum uric acid concentration and cardiovascular disease remains uncertain [500], and there is no clear evidence that lowering serum uric acid reduces major adverse cardiovascular events, all-cause mortality, or kidney failure [502].

Utilisation of urate-lowering therapy and colchicine

Long-term urate-lowering therapy (ULT) is recommended for all individuals with a confirmed diagnosis of gout, alongside the management of comorbidities [494]. Allopurinol is considered the first-line ULT, but febuxostat (a xanthine oxidase inhibitor) or probenecid may be prescribed if allopurinol is contraindicated or poorly tolerated [494]. Colchicine is commonly used to treat acute gout attacks and as prophylaxis to prevent flares when initiating or adjusting ULT [494]. When used prophylactically, colchicine should be continued until gout flares cease and target serum uric acid concentrations are achieved, which may take six months or longer [494].

Narrative summary of evidence on deprescribing

We were unable to identify any direct evidence related to the deprescribing of anti-gout preparations in older people from the systematic review and meta-analysis. Recommendations are provided in this section following a Delphi consensus process.

Justification of recommendations

The 2020 American College of Rheumatology (ACR) guideline conditionally recommends continuing ULT indefinitely if it is well-tolerated and not burdensome, based on very low-certainty evidence that most individuals in long-term clinical remission with controlled serum uric acid concentration experienced gout flares within five years of ULT discontinuation [503]. In many cases, the benefits of lifelong ULT in maintaining target serum uric acid concentration generally outweigh the risks of recurrent gout, which can impair quality of life and physical function as well as lead to long-term joint damage. Evidence specifically addressing ULT discontinuation in older people is lacking. A systematic review of younger adults (aged 42-60 years) found that gout recurrence following ULT discontinuation was high, ranging from 36% to 81%, with a recurrence timeframe of approximately one to 4.5 years.

Deprescribing decisions should be guided by a thorough assessment of factors such as changes in risk factors and concurrent medications that influence serum uric acid concentration (e.g. diuretics) [504]. In certain situations, ULT dose reduction or discontinuation may be appropriate, particularly for individuals at low risk of gout recurrence. If deprescribing is considered appropriate, evidence suggests that lower serum uric acid concentrations before and after deprescribing are associated with a reduced risk of recurrence [503, 505]. Maintaining a normal serum uric acid concentration (below 0.36 mmol/L in non-tophaceous gout or < 6 mg/dL) and remaining free of tophi or flares likely contributes to a lower risk of gout recurrence. For those who have achieved clinical remission for at least a year, or who have improved modifiable risk factors for hyperuricaemia (e.g. diet, change in concurrent medicines) and maintained a normal serum uric acid concentration, deprescribing may be considered when the potential harms of continued therapy, such as adverse drug events, drug-drug interactions, or treatment burden, outweigh the benefits of ongoing prevention of gout recurrence.

For people using anti-gout preparations for other long-term indications, continuation or discontinuation considerations may include an assessment of indications, duration of use, benefit-risk profile, goals of care as well as individual values and preferences.

The tapering approach and monitoring are based on pharmacological rationale and clinical experience, considering the possible gout recurrence associated with sudden changes in extracellular uric acid concentration [506]. Additionally, gout is associated with an increased risk of cardiovascular mortality [507]. Therefore, periodic assessment of cardiovascular risks is important, along with the appropriate management of comorbidities in people with gout and/or hyperuricaemia. Lifestyle modification advice should be offered to individuals where appropriate to modify cardiovascular risk factors.

Calcium and Vitamin D (including calcitriol and colecalciferol).

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	**Calcium supplementation** We suggest deprescribing calcium supplementation be offered to community-dwelling people* with a daily calcium dietary intake of > 1,300 mg.* ** Ongoing treatment recommended for people living in a residential aged care service*
CBR	**Vitamin D supplementation** Given the limited evidence to support the routine use of vitamin D supplementation, we suggest deprescribing be offered to community-dwelling people* with optimal serum vitamin D concentrations (≥ 50 nmol/L) who are not at risk of vitamin D deficiency or fractures.* ** Ongoing treatment recommended for people living in a residential aged care service*
Ongoing treatment	
CBR	**Calcium supplementation** We suggest continuing calcium supplementation in older people for long-term indications such as calcium used as a phosphate-lowering therapy in people with chronic kidney disease.
CBR	**Vitamin D supplementation** We suggest continuing vitamin D supplementation, at optimal dosage, for long-term indications (e.g. calcitriol for the management of mineral and bone disease in chronic kidney disease, regardless of measured vitamin D levels).
How to deprescribe	
CBR	We suggest discontinuing calcium and vitamin D without the need for tapering.
Monitoring	
CBR	We suggest periodic monitoring for changes in dietary intake and/or sunlight exposure (taking into consideration seasonal changes) while working on potentially modifiable risk factors to reduce fall and fracture risk through other approaches (e.g. environmental changes, exercise).

CBR, consensus-based recommendation

Introduction

Calcium

Calcium and vitamin D supplementation are widely used among older people to support bone health and prevent osteoporosis and fractures. While the optimal daily calcium requirement is not firmly established, most guidelines recommend a dietary intake of 1,000 to 1,300 mg per day [508, 509]. If dietary intake meets these requirements, supplementation is generally unnecessary. However, many individuals overestimate their daily calcium intake [510], making it important to evaluate actual intake, particularly in those with low bone mineral density. A practical tool for this assessment is an online calcium calculator, such as the International Osteoporosis Foundation Calcium Calculator (https://www.osteoporosis.foundation/educational-hub/topic/calcium-calculator) [508].

Vitamin D

Vitamin D plays a crucial role in calcium homeostasis, bone mineralisation, and various physiological functions, including immune system support [511]. In Australia, sunlight (ultraviolet) exposure is the primary source of vitamin D [512]. The amount of ultraviolet exposure required for adequate vitamin D synthesis depends on skin type, extent of skin exposure, and environmental factors such as geographic location, season, time of day, and cloud cover [511]. Generally, exposing approximately 15% of the body's surface (e.g. hands, face, and arms) for around 10 minutes in the mid-morning or mid-afternoon on most days during summer is sufficient to maintain adequate vitamin D levels. Although sunscreen has been shown to block vitamin D synthesis in laboratory settings, its impact on vitamin D levels in real-world conditions appears minimal [509].

Vitamin D Production and Dietary Sources

Older people have a reduced ability to synthesise vitamin D due to age-related declines in skin capacity and metabolic changes [513]. They may require longer sun exposure to achieve the same level of vitamin D production as younger individuals. However, factors such as skin cancer concerns, limited mobility, being housebound, or residing in a residential aged care service can restrict sun exposure. In such cases, dietary sources, such as fatty fish (e.g. salmon), eggs, meats, and fortified dairy products can help maintain vitamin D levels [508, 509]. However, most individuals obtain less than 10% of their vitamin D requirements from diet alone [514], making supplementation necessary for some people.

Indicator of vitamin D status

Serum 25-hydroxyvitamin D (25[OH]D) is the standard biomarker for assessing vitamin D status, though optimal concentrations vary across guidelines [515]. Both low and excessively high 25(OH)D levels have been linked to adverse health outcomes, including cardiovascular diseases and tuberculosis [516]. Additionally, variability in analytical methods can affect the accuracy of 25(OH)D measurements [517].

Vitamin D deficiency is typically defined as a serum 25(OH)D concentration below 30 nmol/L, while levels between 30–50 nmol/L are considered insufficient. Healthy Bones Australia recommends maintaining a concentration of at least 50 nmol/L year-round [518]. Overscreening for vitamin D deficiency in healthy older people has led to concerns about unnecessary testing and overtreatment [519].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

For frail older people living in residential aged care services, current guidelines recommend ongoing calcium and vitamin D supplementation, along with adequate protein intake, to prevent fracture [480]. If discontinuation of calcium and/or vitamin D is deemed appropriate, periodic monitoring of dietary intake and sunlight exposure (taking into consideration seasonal variation) is important to promptly detect any potential deficiency [480]. As part of a holistic approach to fall and fracture prevention, it is also essential to address modifiable risk factors through other strategies. These may include environmental modifications and participating in fall prevention exercise programs, which have been shown to significantly reduce fall-related injuries, including fractures [480].

Calcium

Calcium is generally well-tolerated, but excessive doses may increase the risk of renal calculi, constipation, and abdominal bloating [520]. Some studies have suggested a potential link between calcium supplementation and an increased risk of myocardial infarction (MI) and stroke, though the evidence remains inconclusive [521, 522]. Calcium supplementation alone has not been shown to significantly reduce the risk of fractures of any type [523, 524]. However, in older people living in a residential aged care service, combined calcium and vitamin D supplementation has demonstrated a reduction in fracture risk [525]. Calcium supplementation is recommended when daily dietary calcium intake is below 1,300 mg [526]. If supplementation is necessary, doses of 250-600 mg of elemental calcium daily are generally recommended, depending on dietary intake [509]. Other long-term indications that may require ongoing treatment include the use of calcium as a phosphate-lowering therapy for individuals with hyperphosphatemia and chronic kidney disease if appropriate [527]. However, its use requires caution due to the risk of hypercalcaemia [528].

Vitamin D

For individuals undergoing antiresorptive therapy for osteoporosis, vitamin D supplementation is recommended if serum 25(OH)D levels fall below 50 nmol/L. Most guidelines suggest daily doses of 600-800 IU of vitamin D for the general older population, with higher doses required for those with moderate-to-severe deficiency [508, 509]. Other long-term indications that may require ongoing treatment include the use of calcitriol for the management of mineral and bone disease in chronic kidney disease if appropriate, regardless of measured vitamin D levels [527]. However, its use requires caution due to the risk of [528].

Given the lack of clear evidence supporting the routine use of vitamin D supplementation in relatively healthy, community-dwelling older people, supplementation is generally not recommended for individuals with 25(OH)D levels between 30–50 nmol/L. In fact, high doses of vitamin D (e.g. > 60,000 IU monthly or > 1,000-4,000 IU daily) have been associated with an increased risk of falls in older adults [529, 530].

A 2018 systematic review and meta-analysis of 81 RCTs found that vitamin D supplementation alone did not significantly reduce the risk of falls or fractures, or improve bone mineral density [531]. This was consistent across both high and low doses of vitamin D supplementation, with most studies conducted in community-dwelling individuals.

In contrast, a Cochrane review found that vitamin D supplementation significantly reduced the rate of falls in residential aged care settings, though it did not lower the overall risk of falling [532].

The 2024 VITAL (VITamin D and OmegA-3 TriaL), a double-blind, placebo-controlled study, examined the effects of daily supplementation with 2,000 IU of vitamin D or omega-3 fatty acids

(460 mg eicosapentaenoic acid and 380 mg docosahexaenoic acid) on physical performance in healthy adults (mean age 65) [533]. Participants with a history of cancer (except nonmelanoma skin cancer), cardiovascular disease, hypercalcemia, parathyroid disorders, renal failure, severe liver disease, sarcoidosis, or other serious conditions were excluded. The mean baseline 25(OH)D level was 28 ng/mL. At two years, there were no significant differences between the supplementation and placebo groups in physical performance measures, including strength, balance, and walking speed. Similar findings were reported in the 2020 DO-HEALTH RCT, which included older participants (mean age = 75) with lower baseline 25(OH)D levels (mean = 22 ng/mL) [534].

Narrative summary of deprescribing evidence

We identified one RCT related to calcium and vitamin D deprescribing [535], one RCT related to calcitriol deprescribing [423], and one prospective cohort study related to calcium deprescribing [536] from the systematic review and meta-analysis.

Overall, there are some reports that there may be a decline in BMD following discontinuation of calcium and/or vitamin D, especially in women. However, these reported outcomes are of very low to low certainty and are surrogate outcomes indicative of fracture risks. It is difficult to interpret the effects of deprescribing in the absence of a true active group for comparison. The evidence is of very low certainty and inadequate to inform evidence-based recommendations.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Dawson-Hughes 2000 reported follow-up results from a two-year study extended from a three-year RCT of calcium and vitamin D supplementation (as 500mg of elemental calcium and 700 units of vitamin D) [535]. This study included 295 men (n=128) and women (n=167) who had completed the original RCT. Participants were excluded from the main trial if they had hyperparathyroidism, concurrent therapy with a bisphosphonate, calcitonin, estrogen, tamoxifen, or testosterone in the past six months, therapy with fluoride in the last two years, femoral neck BMD T-scores below -2, or dietary calcium intake > 1500 mg per day. The study sought to determine whether gains in BMD induced by calcium and vitamin D supplementation persist after discontinuation. In men, benefits gained from calcium and vitamin D from supplementation in spinal and femoral neck BMD were lost after discontinuation but small benefits in total-body BMD remained. In women, there were no lasting benefits in BMD. There was no significant difference between the group who discontinued calcium and vitamin D supplementation and the group who discontinued placebo in terms of non-vertebral fractures (5 vs 9; OR 1.84, 95% CI 0.60, 5.62).

Gallagher 2002 conducted a five-year 2x2 factorial RCT comparing MHT, calcitriol, MHT with calcitriol, or placebo for three years and the effect of discontinuing therapy for two more years [423]. All participants were women aged over 65 who did not have primary hyperparathyroidism and were not taking bisphosphonates, anticonvulsants, estrogen, fluoride, or thiazide diuretics, in the past six months. After discontinuing therapy at the end of year three, much of the bone density gained during treatment was lost in all three treatment groups, although all treated groups still had a significantly higher total body bone mineral density (BMD) compared to placebo. Compared to the group who were untreated (placebo group), those who took calcitriol for the preceding three years before two years discontinuation had a significantly lower percentage change from baseline to five years in the BMD for the total body (MD 1.31, 95% CI 1.14, 1.48; study = 1), spine (MD 0.89, 95% CI 0.55, 1.23), total hip (MD 1.04, 95% CI 0.73, 1.35) compared to the group who were chronically untreated, but significantly higher percentage change in the BMD for femoral neck (MD

-0.34, 95% CI -0.65 to -0.03). However, there was no significant difference in the percentage change for trochanter BMD (MD 0.27, 95% CI -0.12, 0.66) between the two groups.

Radford 2014 reported follow-up five-year results from a study extended from a five-year RCT of calcium supplementation [536]. All participants included in the original RCT were females who were at least five years post-menopause with a normal lumbar spine BMD for their age. The RCT excluded women who were receiving treatment for osteoporosis with serum vitamin D levels <25 nmol/L. The current follow-up study included a selected subset of 194 participants who were randomised to receive calcium for five years in the original RCT and did not take bone-active medicines post-trial. After five years following the discontinuation of calcium, there were no persisting benefits of calcium on BMD at the spine, femoral neck or total body. In addition, the adverse effects of calcium supplements on cardiovascular risk also did not persist after discontinuation.

Narrative evidence summary: withdrawal schedules

In the prospective cohort study, calcium was discontinued abruptly [536]. The method of deprescribing was not described in two RCTs [423, 535].

GRADE Summary of Findings (SoF) Table

Table 23. Summary of findings for deprescribing calcium and/or vitamin D

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
1 [536]	Non-randomised study	739	732	OR 0.83 (0.63, 1.08)	
2. Adverse drug withdrawal events (ADWEs)					
ADWEs, bone mineral density					
2 [423, 535]	RCTs	204	191	Two years following the discontinuation of calcium and vitamin D supplements, supplement-induced increases in spinal and femoral neck BMD were lost but small benefits in total body BMD remained for men (MD 1.59, 95% CI 1.45, 1.73). In women, there were no lasting benefits in total-body BMD (MD -0.14, 95% CI -0.29, 0.01) or at any bone site [535]. In another study, participants who took calcitriol for the preceding three years before two years discontinuation had a significantly lower percentage change from baseline to five years in the BMD for total body (MD 1.31, 95% CI 1.14 to 1.48; study = 1, n = 100), spine (MD 0.89, 95% CI 0.55 to 1.23), total hip (MD 1.04, 95% CI 0.73 to 1.35) compared to the group who were chronically untreated, but significantly higher percentage change in the BMD for femoral neck (MD -0.34, 95% CI -0.65 to -0.03) [423]. However, there was no significant difference in the percentage change for trochanter BMD (MD 0.27, 95% CI -0.12 to 0.66) between the two groups [423].	
ADWEs, fractures					
1 [535]	RCT	148	147	Non-vertebral fractures OR 1.84 (0.60, 5.62)	
1 [536]	Non-randomised study	739	732	There was no significant difference in the incidence of total fracture (OR 1.12, 95% CI 0.90, 1.40), osteoporotic fracture (OR 1.20, 95% CI 0.95, 1.52), and hip fracture (OR 0.71, 95% CI 0.44, 1.13) between those who took calcium versus placebo for the entire follow-up period (10 years). However, there was a significantly higher incidence of forearm fracture (OR 1.65, 95% CI 1.13, 2.41) and vertebral fracture (OR 1.96, 95% CI 1.18, 3.24) in those who took placebo compared to calcium.	
3. Health outcomes					
Adverse events/ serious adverse events/ cardiovascular events					
1 [536]	Non-randomised study	739	732	Stroke OR 0.96 (0.69, 1.34) Myocardial infarct OR 0.96 (0.67, 1.36)	
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

Denosumab/ Bisphosphonates

Denosumab* and bisphosphonates (include alendronate, risedronate*, zoledronic acid).

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	**Bisphosphonates** We suggest deprescribing be offered to older people who: • Develop contraindications during therapy, such as achalasia, Barrett's oesophagus, oesophageal scleroderma, certain gastric bypass procedures (e.g. Roux-en-Y), or chronic kidney disease (estimated glomerular filtration rate, eGFR <30 mL/min/1.73m^2) • Experience adverse effects, including GORD or an inability to remain upright for 30 minutes after administration, increasing the risk of oesophageal irritation • Sustain an atypical femur fracture during therapy • Have a life expectancy of less than one year, unless bisphosphonates are essential (e.g. cancer management or secondary prevention in people at high risk of future fractures during their lifetime).
CBR	**Bisphosphonates** We suggest offering a "drug holiday" to older people receiving long-term bisphosphonate treatment (5–10 years) who have no history of vertebral fractures, particularly those with a T-score ≥ –2.5, as the risk of rare but serious adverse events (e.g. atypical femoral fracture) may outweigh the benefits of continued treatment.
CBR	**Denosumab** We suggest deprescribing be offered to older people: • Experience denosumab-related side effects that impact quality of life (e.g. arthralgia, myalgia); or • With advanced chronic kidney disease or are receiving dialysis due to the risk of severe hypocalcaemia; or • Sustain an atypical femur fracture during therapy.
Ongoing treatment	
CBR	**Bisphosphonates** We suggest continuing bisphosphonate therapy beyond 5–10 years in people with a T-score < –2.5 and/or a history of fragility fracture. For people who have discontinued bisphosphonates or are on a "drug holiday", we suggest consideration of restarting bisphosphonates if: • Bone loss of ≥ 5% occurs, particularly at the hip • The person sustains a fracture following minimal trauma • The person has completed 3 to 5 years of a drug holiday, showed improvement during their initial treatment, and had no prior fractures.
CBR	**Denosumab** We suggest continuing denosumab in older people likely to derive a net benefit and have no significant adverse effects, even beyond 10 years, due to the increased risk of vertebral fractures after discontinuation.
How to deprescribe	
CBR	**Bisphosphonates** We suggest ceasing bisphosphonates without the need for tapering.

	Seek expert advice for antiresorptive therapy in the context of chronic kidney and end-stage kidney disease.
CBR	**Denosumab** We suggest transitioning to bisphosphonate therapy either 2 months before the next scheduled denosumab dose or at the time of the due dose and continuing for at least 12 months, due to the increased risk of rebound vertebral fractures following denosumab discontinuation or delayed administration.
Monitoring	
CBR	We suggest closely monitoring for fracture risk using the Fracture Risk Assessment Tool and/or bone turnover markers, and the need for restarting therapy for osteoporosis in people not receiving therapy at a high risk of fracture, such as at least monthly for the first six months after deprescribing, followed by monitoring every six months thereafter to maintain the therapeutic relationship while working on lifestyle optimisation to reduce falls and fracture risk through multifactorial approach (e.g. environmental changes, exercise, nutrition).
CBR	We suggest monitoring requirements and monitoring intervals for C-terminal telopeptide (CTX) and procollagen type 1 N propeptide (P1NP) be guided by specialists.
CBR	We suggest assessing bone mineral density (BMD) with dual-energy X-ray absorptiometry (DXA) for men and women once, after 12 months of discontinuation of therapy, if clinically appropriate and feasible. For people receiving antiresorptive treatment, we suggest monitoring BMD with DXA every two to five years when clinically appropriate, to evaluate treatment efficacy and the need for continued therapy, using the same instrument when possible. We suggest further assessment if BMD decreases by ≥ 5% at any major site or if a fracture occurs.
CBR	For people receiving denosumab, we suggest the optimal timing for elective invasive dental procedures is immediately before the next scheduled dose. We suggest against withholding the next scheduled dose due to the risk of rebound fractures. We suggest a comprehensive dental review before initiating or reinitiating antiresorptive therapy due to the potential risk of medication-related osteonecrosis of the jaw.

CBR, consensus-based recommendation

Introduction

Bisphosphonates and denosumab are indicated for the treatment of postmenopausal osteoporosis to prevent fractures and associated morbidity in people with low bone mineral density (BMD) or a history of fracture [177]. In addition to pharmacological treatment, optimising bone health should include non-pharmacological strategies. These include ensuring a daily intake of at least 1,300 mg of calcium and 800 units of vitamin D, engaging in weight-bearing exercise for at least 30 minutes on most days of the week, smoking cessation for smokers, and limiting alcohol intake to two standard drinks per day [537].

Bone-modifying agents, including bisphosphonates and denosumab, are also used in the management of bone metastases but should not be relied upon solely for pain relief, as their analgesic effect is modest [538].

Mineral and bone disorders are common complications of chronic kidney disease (CKD), particularly in individuals with stage 3a CKD or more advanced disease (eGFR <60 mL/min/1.73m^2), due to disruptions in mineral metabolism [528]. Management becomes increasingly complex in advanced CKD (stages 4-5), where specialist guidance on antiresorptive therapy is crucial.

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

1. Mineral and bone disorders

The evidence supporting bisphosphonate use in advanced CKD is limited. As bisphosphonates are renally cleared, they are contraindicated in severe CKD due to potential nephrotoxicity, which has been reported particularly with pamidronate and zoledronic acid, whereas ibandronate appears to have a safer renal profile [539]. Unlike bisphosphonates, denosumab is not renally cleared and can be used in CKD. However, its use in advanced CKD requires caution due to the increased risk of hypocalcaemia (discussed further below).

2. Fracture prevention

2a) Bisphosphonates

Oral bisphosphonates are considered first-line treatment for most individuals at high risk of fractures. However, they are contraindicated in people with gastrointestinal conditions such as achalasia, Barrett's oesophagus, or oesophageal scleroderma; certain gastric bypass procedures (e.g. Roux-en-Y); and CKD with an eGFR < 30 mL/min/1.73m². While bisphosphonates are well-documented in preventing fractures in postmenopausal women with osteoporosis, it remains unclear which subgroups with varying fracture risk derive the most benefit from treatment [540]. Additionally, a 2023 systematic review found that most osteoporosis guidelines provide limited guidance for healthcare providers, patients, and caregivers in making individualised deprescribing decisions for bisphosphonates [541].

- **Duration of therapy**

  Guidelines typically recommend reviewing bisphosphonate therapy after three to five years to assess the need for continued treatment [542]. A recent meta-analysis found that among postmenopausal women with osteoporosis, the estimated time to prevent one nonvertebral fracture per 100 women was 12.4 months (absolute risk reduction [ARR] = 0.010), while the time to prevent one hip fracture was 20.3 months (ARR = 0.005) and 12.1 months for clinical vertebral fractures (ARR = 0.005) [543]. However, this analysis excluded trials involving individuals at higher absolute fracture risk (e.g. secondary prevention of osteoporosis). For patients with limited life expectancy (<12 months) receiving bisphosphonates for primary osteoporosis prevention and at low risk of future fractures, deprescribing may be appropriate.

- **Adverse effects and risk-benefit considerations**

  The risk of medication-related osteonecrosis of the jaw (MRONJ) and atypical femoral fractures (AFF), increases with treatment duration of bisphosphonate for osteoporosis though these events remain rare [480]. Most MRONJ cases occur in cancer patients receiving antiresorptive therapy for malignancy-related skeletal events, with incidence rates 100 times lower among those using bisphosphonates for osteoporosis [480]. Considerations on MRONJ risk are summarised in the section below.

  There is no consensus on whether bisphosphonates should be discontinued following MRONJ in people with cancer who may benefit from pain control or skeletal event prevention. However, temporary discontinuation may be reasonable until resolution or stable improvement is observed.

  For AFF, the risk increases with more than five years of bisphosphonate use, but the absolute risk remains low (3.5 to 50 cases per 100,000 person-years) and declines after

discontinuation [544, 545]. If an AFF occurs, bisphosphonate therapy should be ceased. Conversely, osteoporotic hip fractures are associated with a three-fold increase in 12-month mortality in older people [546], making it essential to balance these risks against the benefits of fracture prevention when considering continued treatment. As with all therapeutic decisions, management should be individualised.

- **Long-term bisphosphonate use**
  The Fracture Intervention Trial Long-Term Extension (FLEX) trial found that extending alendronate therapy to 10 years did not significantly reduce the risk of nonvertebral fractures compared to a five-year regimen [547]. However, prolonged use was associated with a lower risk of clinical vertebral fractures, though it did not affect morphometric vertebral fracture risk, regardless of baseline vertebral fracture status. Additionally, a post hoc analysis of the FLEX trial found that alendronate significantly reduced nonvertebral fracture risk in women with a baseline T-score ≤ -2.5 but not in those with a T-score between -2 and -2.5 or > -2 [548]. Australian guidelines recommend continuing bisphosphonate therapy for five to 10 years in postmenopausal women and men over 50 with osteoporosis who have a T-score < -2.5 and/or a history of osteoporotic fractures [480].

2b) Denosumab

Denosumab is commonly used to treat postmenopausal osteoporosis in older women at high risk of minimal trauma fractures by suppressing bone turnover [177]. Its efficacy and safety in men with osteoporosis are less clear, with bisphosphonates typically being the first-line treatment [177]. Denosumab is administered via subcutaneous injection every six months, making it a potentially suitable option for individuals with high pill burden or compliance challenges who require long-term osteoporosis treatment [549]. It may also be considered for patients who experience treatment failure with bisphosphonate.

- **Safety considerations**
  Common side effects of denosumab include arthralgia, myalgia (ranging from transient to several months post-injection), hypercholesterolemia, cystitis, and flatulence. A significant concern is severe hypocalcaemia, particularly in individuals with advanced CKD. Among those with an eGFR <15 mL/min/1.73 m² or on dialysis, the incidence of mild and severe hypocalcaemia is 24% and 15%, respectively [550]. Hypocalcaemia typically occurs within four weeks post-injection [551], and in severe cases, it can lead to serious complications, including severe weakness, tetany, prolonged QT interval requiring hospitalisation, or life-threatening cardiac arrhythmias [552]. In January 2024, the FDA issued a black box warning for denosumab due to the increased risk of severe hypocalcaemia in individuals with advanced CKD or on dialysis [553]. Kidney function and baseline serum calcium should be assessed before initiating treatment, as they strongly predict the risk of hypocalcaemia.

- **Treatment discontinuation and rebound effects**
  Unlike bisphosphonates, denosumab does not provide a sustained benefit after discontinuation [177]. An RCT of denosumab that included 256 postmenopausal women (mean age 59 years) reported a temporary increase in bone resorption markers after denosumab discontinuation before returning to baseline by 48 months, indicating a hyper-resorptive state, suggesting a temporary hyper-resorptive state [554]. Although BMD declined following discontinuation, it remained higher in the denosumab-treated group than in the placebo group. However, clinical outcomes such as fracture risk remain unclear. A cohort study found that delaying or discontinuing denosumab doses by ≥ 16 weeks was associated with a higher risk of vertebral fractures (HR 3.91, 95% CI 1.62–9.45) compared to on-time dosing (within four weeks of the scheduled injection) [555].

- **Duration of therapy**
  Denosumab, like bisphosphonates, has been linked to MRONJ and AFF, though these adverse effects are rare for denosumab [556]. Long-term safety data beyond 10 years are limited, but there are no formal restrictions on treatment duration [557]. The benefits of denosumab are not sustained after discontinuation, so drug holidays are not recommended. Given the increased risk of rebound vertebral fractures, ongoing treatment beyond 10 years may be considered for high-risk individuals with regular monitoring [558]. However, this decision should be discussed with the individual before initiating therapy, ensuring informed consent is adequately obtained.

  If discontinuation is necessary, an alternative therapy should be initiated to prevent rapid BMD loss and fractures. Sequential treatment with bisphosphonates, particularly alendronate, is preferred and should commence six months after the final denosumab dose [559]. This should continue for at least 12 months to minimise the risk of vertebral fracture associated with denosumab discontinuation. However, the cumulative risk of MRONJ and AFF with prolonged use of denosumab for osteoporosis remains uncertain and future studies should investigate long-term management strategies.

3. Monitoring responses

Individuals initiating antiresorptive therapy should undergo a dual-energy X-ray absorptiometry (DXA) scan within one to two years, ideally using the same densitometer for consistency [479]. Treatment is considered effective if BMD remains stable or increases compared to prior scans. A change in BMD is only statistically significant if it exceeds the least significant change (LSC) for the specific densitometer used. If the LSC is unavailable, a threshold difference of ≥ 5% has been suggested [560]. For individuals with stable or improving BMD, subsequent DXA scans may be spaced out over two to five years. However, BMD stability does not always correlate with fracture risk reduction. Some patients may require more aggressive treatment despite maintaining a stable BMD.

For those receiving therapy for at least 12 months, a significant BMD decrease (≥ LSC) or a new fragility fracture should prompt further evaluation. In such cases, adherence, malabsorption, calcium and vitamin D intake, and potential secondary causes of osteoporosis should be assessed. Bone turnover markers (e.g. C-terminal telopeptide [CTX] and procollagen type 1 N-terminal propeptide [P1NP]) may be useful in specialist settings to differentiate non-adherence from malabsorption. Suppressed bone turnover markers indicate adequate medication adherence and absorption [560]. Patients with new fragility fractures or T-scores ≤ -2.5 may require a transition to anabolic therapy.

For those who discontinue antiresorptive therapy, it is important to continue close monitoring of fracture risk and the need for restarting therapy for osteoporosis, such as monthly for the first six months. Fracture risk can be monitored using the Fracture Risk Assessment Tool [478] and/or bone turnover markers as mentioned above.

As part of a multifactorial approach to fall and fracture prevention, it is also essential to address modifiable risk factors through other strategies. These may include nutritional review, environmental modifications and participating in fall prevention exercise programs, which have been shown to significantly reduce fall-related injuries, including fractures [480].

4. Preventive measures for MRONJ in people on antiresorptive medicines

Both bisphosphonates and denosumab are associated with MRONJ, a rare but serious condition [561]. A retrospective cohort study found that comprehensive dental care significantly reduces

MRONJ risk [561]. Preventative dental care includes dental evaluation before initiating antiresorptive or antiangiogenic drugs and limiting invasive dental procedures during treatment. High-risk individuals (e.g. those on high-dose therapy, receiving treatment for more than three years, or with existing MRONJ risk factors) may require more frequent dental monitoring and prophylactic treatment [562].

For individuals taking bisphosphonates for osteoporosis, there is no clear evidence supporting a "drug holiday" for the purposes of minimising MRONJ risk prior to invasive dental procedures [563].

For individuals taking denosumab for osteoporosis, it is considered appropriate to perform invasive dental procedures four weeks after the last denosumab dose [563]. Guidelines suggest invasive dental procedures in patients on denosumab should ideally be undertaken just prior to the next six-monthly injection because the in vivo effect on bone suppression will be waning [480]. However, it may be reasonable to schedule invasive dental procedures no later than six weeks before the next due denosumab administration to allow adequate healing of the extraction socket [563].

For individuals receiving bisphosphonates or denosumab for cancer or skeletal fracture prevention, decisions regarding discontinuation due to dental procedures or MRONJ development should be individualised and made in consultation with the oncology team [563].

Narrative summary of evidence on deprescribing

We identified six studies (two RCTs, two before-and-after studies, and two prospective cohort studies) related to bisphosphonate deprescribing (alendronate, risedronate, pamidronate, zoledronic acid) from the systematic review and meta-analysis; however, no studies related to denosumab deprescribing [547, 564-568].

Overall, there are reports that discontinuation of bisphosphonates may lead to loss of BMD gains while on treatment, although BMD at some body sites remained higher than baseline. Additionally, in postmenopausal women who had a history of vertebral fractures and low femoral neck BMD, discontinuation of bisphosphonates (alendronate, risedronate, zoledronic acid) after three to five years of treatment may lead to an increased risk of vertebral fractures. However, such a significant difference was not observed in non-vertebral fractures. These results support a legacy effect of bisphosphonates up to five years after ceasing therapy. For people with a T-score ≥ –2.5 and no prior vertebral fractures, deprescribing of alendronate may be considered after five years without a significant increase in their risk of non-vertebral fracture. However, the reported outcomes in the studies included are of low and very low certainty. Several extension studies lacked a true active group for direct comparison. There is a lack of evidence for newer therapy such as romosozumab and a lack of evidence for discontinuing bisphosphonate therapy for osteoporosis treatment in men. For instance, romosozumab as a newer bisphosphonate promotes both bone formation and suppresses bone resorption. All in all, the evidence at this stage is inadequate to inform evidence-based recommendations.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Black 2006 conducted a study that extended from an original placebo-controlled RCT that examined the effects of alendronate on BMD and fracture risk in postmenopausal women with low femoral neck BMD (< 0.68 g/cm^2) [547]. The current study included a subset of participants who were randomised to receive alendronate in the original RCT (mean of five years of alendronate treatment). Participants were excluded from this study if their total hip BMD was less than 0.515 g/cm^2 (T score < −3.5) or lower than at the baseline of the original RCT. Concomitant use of hormone therapy or raloxifene was permitted. All participants were offered oral calcium (500 mg) and vitamin D (250 units). All eligible participants were randomised to stop alendronate (n=437) or continue alendronate for another five years (n=662). At five years, there was no significant difference between the two groups in terms of mortality (OR 1.54, 95% CI 0.80, 2.94), non-vertebral fractures (OR 1.01, 95% CI 0.74, 1.37), or adverse drug events (OR 1.11, 95% CI 0.75, 1.63). However, the continuation group had significantly more favourable BMD changes (i.e. either higher gain or lower reduction in BMD) for total body (MD 1.28, 95% 1.25, 1.31), trochanter (MD 3.17, 95% 3.14, 3.20), lumbar spine (MD 3.74, 95% CI 3.71, 3.77), femoral neck (MD 1.94, 95% CI 1.91, 1.97), and total hip (MD 2.36, 95% CI 2.33, 2.39). Additionally, there was a significantly increased risk of clinical vertebral fractures among people who discontinued alendronate compared with those who continued (OR 2.24, 95% CI 1.17, 4.30).

Black 2012 conducted a study that extended from an original placebo-controlled three-year RCT that examined the effects of zoledronic acid on reducing vertebral fracture and hip fracture in postmenopausal women either with femoral neck BMD T score ≤ −2.5, or ≤ −1.5 with evidence of two or more mild vertebral fractures or one moderate vertebral fracture [564]. Concomitant use of hormone therapy, raloxifene, calcitonin, tibolone, or tamoxifen was permitted. All participants received oral calcium (1000 to 1500 mg) and vitamin D (400 to 1200 units). The current study included a subset of participants who were randomised to receive zoledronic acid in the original

RCT. All eligible participants were randomised to stop zoledronic acid (n=617) or continue zoledronic acid for another three years (n=616). At three years, there was no significant change in mortality (OR 0.68, 95% CI 0.37, 1.25), adverse drug events (OR 0.95, 95% CI 0.66, 1.38), or percentage change in BMD for spine (MD 2.03, 95% CI 0.76, 3.30), femoral neck (MD 1.04, 95% CI 0.43, 1.65), and total hip (MD 1.22, 95% CI 0.75, 1.69). However, there was a significantly increased risk of clinical vertebral fractures in people who discontinued zoledronic acid compared with those who continued (OR 2.14, 95% CI 1.12, 4.09).

Da Silva 2011 conducted a prospective cohort study that included postmenopausal women with osteoporosis who had been taking alendronate for at least five years and had their treatment discontinued (n=40) and those who had been taking alendronate for at least one year and continued treatment (n=25) [565]. All participants received vitamin D 1000 units daily during the study and those with a low calcium intake (not defined) received calcium supplementation in a dose sufficient to achieve 1000 mg/daily. At 12 months, there was no significant difference between the two groups in terms of non-vertebral fractures (OR 1.94, 95% CI 0.08, 49.40) or the proportion of participants with a clinically significant BMD loss in the femoral neck (OR 7.20, 95% CI 0.84, 61.38). However, significantly more participants who discontinued alendronate had clinically significant BMD loss in the spine (OR 10.67, 1.43, 100.39). The study considered BMD losses of ≥ 2.8% in the lumbar spine and ≥ 4.2% in the femur as clinically significant.

Eastell 2011 conducted a prospective cohort study that included 61 postmenopausal women with osteoporosis who had previously received risedronate for either two years (n=30) or seven years (n=31) in an RCT [566]. All participants enrolled in the original RCT were at least five years post-menopausal and had at least two vertebral fractures at baseline. The current study excluded those who used calcitonin, calcitriol or vitamin D supplements in the past month, anabolic steroids, estrogen, estrogen-related drugs or progestogen in the past three months, or bisphosphonates, fluoride or subcutaneous estrogen implant in the past six months. All participants received 1000 mg elemental calcium supplementation daily and those who required vitamin D supplementation received up to 500 units daily. Risedronate was discontinued in all participants. At 12 months, participants who had only two years of prior risedronate use had a significantly lower mean percentage change in BMD of the lumbar spine (MD 7.82, 95% CI 6.44, 9.20) and femoral neck (MD 4.33, 95% CI 2.90, 5.76) compared to those with seven years prior use. There was no significant difference between the two groups in terms of non-vertebral fractures (OR 0.33, 95% 0.01, 8.51) or adverse drug events (OR 1.24, 95% CI 0.45, 3.41).

Watts 2008 conducted a before-and-after study as a follow-up to an original placebo-controlled three-year RCT that examined the effects of risedronate on vertebral and nonvertebral fractures in postmenopausal women with osteoporosis [568]. Participants enrolled in the original RCT were at least five years post-menopausal and had at least two vertebral fractures at baseline or one vertebral fracture with low spinal BMD (T score ≤ −2). All participants received 1000 mg elemental calcium supplementation daily and those who required vitamin D supplementation received up to 500 units daily. In the current study, those who were randomised to receive risedronate (n=398) or placebo (n=361) in the original RCT stopped therapy. Concomitant calcium and/or vitamin D were permitted if the baseline levels were low. At 12 months, the participants who had risedronate discontinued had a significantly higher percentage change in BMD of trochanter (MD 3.08, 95% CI 2.06, 4.10), lumbar spine (MD 2.60, 95% CI 1.56, 3.64), and femoral neck (MD 2.32, 95% CI 1.40, 3.24). There was no significant difference in non-vertebral fractures between the two groups (OR 0.96, 95% CI 0.49, 1.85) but participants who had previously received risedronate for three years had a significantly reduced odds of vertebral fracture (OR 0.53, 95% CI 0.32, 0.89).

Orr-Walker 1997 conducted a before-and-after study as a follow-up to an original placebo-controlled two-year RCT (plus a one-year open-label period) that examined the effects of pamidronate on BMD and vertebral fractures in postmenopausal women with osteoporosis [567].

Participants enrolled in the original RCT had at least one vertebral fracture at baseline, and people with concurrent use of hormone replacement therapy or had treatment with sodium fluoride, calcitonin, anabolic steroids or bisphosphonate in the past six months were excluded. All enrolled participants received 1000 mg elemental calcium supplementation daily. At 12 months after pamidronate discontinuation, there was a non-significant reduction in total body BMD (-0.3 ± 0.7%, p = 0.7) compared to the original trial's inception. However, BMD at other body sites remained higher than baseline; lumbar spine (7.1 ± 1.1%, p < 0.0001) and femoral trochanter (4.5 ± 1.8%, p < 0.03), femoral neck (2.2 ± 1.3%, p not stated), ward's triangle (0.1 ± 2.5%, p not stated).

Narrative evidence summary: withdrawal schedules

The method of deprescribing was not specified in all studies, but it appears to have involved abrupt discontinuation.

GRADE Summary of Findings (SoF) Table

Table 24. Summary of findings for deprescribing drugs affecting bone structure and mineralisation

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
2 [547, 564]	RCTs	1053	1275	OR 1.02 (0.46, 2.26)	
2. Adverse drug withdrawal events (ADWEs)					
No available evidence					
3. Health outcomes					
Vertebral fractures					
2 [547, 564]	RCTs	923	1131	OR 2.19 (1.38, 3.46)	
1 [568]	Non-randomised study	361	398	Compared to untreated participants, participants who had previously received risedronate for three years had significantly reduced odds of vertebral fracture (OR 0.53, 95% CI 0.32, 0.89).	
Non-vertebral fractures					
1 [547]	RCT	437	662	OR 1.01 (0.74, 1.37)	
3 [565, 566, 568]	Non-randomised studies	468	417	OR 0.94 (0.50, 1.78)	
Bone mass density (BMD)					
2 [547, 564]	RCTs	898	1094	Percentage change in bone mass density • Spine (MD 3.01, 95% CI 1.35, 4.67, studies = 2) • Femoral neck (MD 1.54, 95% CI 0.67, 2.42, studies = 2) • Trochanter (MD 3.17, 95% CI 3.14, 3.20, study = 1) • Total hip (MD 1.82, 95% CI 0.70, 2.93, studies = 2)	
2 [566, 568]	Non-randomised studies	301	327	Percentage change in bone mass density • Spine (MD 5.19, 95% CI 0.07, 10.30) • Femoral neck (MD 3.25, 95% 1.28, 5.21) • Trochanter (MD 3.08, 95% CI 2.06, 4.10)	
1 [567]	Non-controlled study	22	N/A	Percentage change in bone mass density from baseline to 1 year after discontinuation • Total body, -0.3 ± 0.7%, p = 0.7 • Lumbar spine, 7.1 ± 1.1%, p < 0.0001 • Femoral neck, 2.2 ± 1.3%, p not stated • Ward's triangle, 0.1 ± 2.5%, p not stated • Trochanter, 4.5 ± 1.8%, p < 0.03	
Adverse drug events					
2 [547, 564]	RCTs	1053	1275	OR 1.03 (0.79, 1.34)	
1 [566]	Non-randomised study	30	31	OR 1.24 (0.45, 3.41)	

4. Cognitive function
No available evidence
5. Quality of life (QoL)
No available evidence

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

NERVOUS SYSTEM

This section includes:

- Analgesics
- Antiepileptics
- Levodopa
- Antipsychotics
- Benzodiazepine anxiolytics
- Hypnotics and sedatives
- Antidepressants
- Anti-dementia medicines

NERVOUS SYSTEM

Analgesics

Analgesics include:

- Opioids: Alfentanil, buprenorphine*, codeine, aspirin with codeine, ibuprofen with codeine, paracetamol with codeine*, fentanyl, hydromorphone, methadone, morphine, oxycodone*, oxycodone with naloxone*, pethidine, remifentanil, tapentadol*, tramadol*, tramadol with paracetamol
- Other analgesics and antipyretics: Aspirin, paracetamol*, paracetamol with ibuprofen, cannabinoid
- Gabapentinoids: pregabalin*, gabapentin

*Common PBS medicine

Note: Please refer to the antiepileptics section for antiepileptics used for neuropathic pain.

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing be offered to older people taking opioid or non-opioid analgesics with: 1. No ongoing indication or benefits (e.g. long-term opioid for chronic non-cancer pain with little benefit in pain relief or improving function) 2. Presence of obvious contraindication (e.g. recurrent falls) 3. Adverse effects or interactions outweigh the potential benefits (e.g. significant drug-drug interactions, cognitive impairment, sedation, respiratory depression, falls, osteoporosis, constipation, and immunosuppression) 4. Symptoms resolved and unlikely to recur or symptoms stable (e.g. pain related to an acute injury that has healed, or chronic pain that is controlled with non-pharmacological measures)
Ongoing treatment	
CBR	If deprescribing is unsuccessful despite multiple attempts, we suggest maintaining the lowest effective dose; however, we suggest reassessing the need for long-term therapy at least annually. We suggest appropriate non-pharmacological therapies and/or safer alternatives be considered and offered.
GPS	*For older people using opioid analgesics to manage cancer-related pain in the palliative stage, healthcare providers should consider seeking input from palliative care providers (ungraded good practice statement).* ***---- proposed for deletion (although the Guideline Development Group reached consensus (>75% agreement), qualitative feedback indicated that this GPS may not be feasible in certain settings, such as residential aged care facilities. As a result, it is proposed for deletion from the final version of the guidelines.)***
How to deprescribe	
CBR	**Non-opioids (excluding paracetamol)** We suggest individualising the tapering schedule and adjusting it according to the individual's response to establish the lowest effective dose if therapy continuation becomes necessary. In general, we suggest reducing the non-opioid analgesic dose gradually every 2-4 weeks. Once completely ceased, we suggest switching to on-demand or intermittent use of non-opioid analgesics at the lowest effective dose.

	Non-opioid (paracetamol) We suggest tapering may not be needed for paracetamol. However, tapering may be required to establish the lowest effective dose if therapy continuation becomes necessary.
GPS	**Opioids (ungraded good practice statements)** For people taking opioids for < 12 months, we suggest gradually reducing by 5-10% of the morphine equivalent dose or 10-25% of the opioid dose every **week**. If symptoms recur, return to the previously tolerated dose until symptoms resolve and plan for a more gradual taper For people taking opioids for 12 months or more, We suggest gradually reducing by 5-10% of the morphine equivalent dose or 10-25% of the opioid dose every **month**. If symptoms recur, return to the previously tolerated dose until symptoms resolve and plan for a more gradual taper. We suggest advising people of the increased susceptibility to opioid overdose or opioid poisoning during dose tapering due to a change in opioid tolerance, and that extra caution is required, especially if returning to doses prior to deprescribing.
GPS	**Opioids and non-opioids** Healthcare providers should consider offering non-pharmacological interventions (e.g. pain management services, walking programs), referrals to relevant allied health professionals, and psychological support as part of the management plan, as appropriate (ungraded good practice statement).
Monitoring	
CBR	We suggest closely monitoring for pain, functional status, and quality of life every two weeks until at least four weeks after the medicine is fully ceased if practical. After this initial period, we suggest monthly monitoring for at least three months, followed by monitoring every six months thereafter to maintain therapeutic relationships with the individuals. This should be tailored based on individual factors such as their preferences, responses and tolerance to deprescribing. If in-person visits are impractical, we suggest advising people to report symptoms as needed.
GPS	Healthcare providers should use validated assessment tools to evaluate changes in pain severity, functional status, and quality of life (ungraded good practice statement).

CBR, consensus-based recommendation; GPS, good practice statement

Note: Evidence for deprescribing of NSAIDs is covered separately in the musculoskeletal system section.

Introduction

Chronic pain affects approximately one in five (20%) Australians aged 65 to 74 [569]. The most common cause of chronic pain-related hospitalisations is musculoskeletal and connective tissue disorders (e.g. osteoarthritis and lower back pain), accounting for 40% of admissions [569].

Non-pharmacological interventions for pain management encompass a range of psychological and physical techniques. For some people, non-pharmacological approaches can be as effective as standalone treatments for mild pain, or used in conjunction with pharmacological therapies to enhance pain relief in cases of moderate to severe pain. A 2024 systematic review and meta-analysis of 25 trials found that non-pharmacological interventions significantly reduced pain intensity, pain interference, depressive symptoms, and catastrophising beliefs while improving physical health [570]. In particular, older people who incorporated psychological approaches and physical activity had a small but statistically significant effect on improving pain interference.

Non-opioids
For mild to moderate nociceptive pain, paracetamol and NSAIDs are often recommended as first-line pharmacological treatments in people without contraindications [571]. NSAIDs are particularly effective for pain with an inflammatory component but may be unsuitable for people with renal impairment, cardiovascular disease, or gastrointestinal complications.

Opioids
For severe pain, opioids may be indicated, either alone or in combination with other analgesics such as paracetamol and NSAIDs. A multimodal analgesic approach reduces individual drug dosages, thereby minimising side effects [571]. Opioids are primarily used for severe acute pain or chronic cancer pain [571], with limited evidence supporting their long-term use (≥ 12 weeks) for chronic non-malignant pain in older people due to poor efficacy and an unfavourable side effect profile [572]. It is essential to clearly communicate the risks and benefits to individuals prior to any changes in therapy, enabling informed consent and shared decision-making. Regular monitoring is crucial, and clinical practice guidelines recommend planning for deprescribing at the time of opioid initiation [573].

Justification of recommendations
Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

Common side effects related to opioids include nausea, vomiting, constipation, orthostatic hypotension, and dizziness [177]. Opioids also contribute to anticholinergic burden which is associated with cognitive impairment, sedation, and respiratory depression in older people [177]. Opioids may increase the risk of falls, fall injuries, and fractures [574] as well as the risk of infection due to their potential immunosuppressive effects [575]. Older people typically require lower opioid doses, with dose requirements decreasing progressively with age [177]. However, tolerance can develop, leading to escalating doses. Long-term high-dose opioid use can exacerbate pain through nociceptive sensitisation [576]. Deprescribing may be appropriate when the risks of harm with continuation outweigh the benefits and in people where opioids offer little benefit in pain relief or improving function or those experiencing recurrent falls caused by opioid-induced sedation, orthostatic hypotension and dizziness [577]. If pain related to an acute injury has resolved or chronic pain is well managed by other non-pharmacological measures, it may be appropriate to offer deprescribing to individuals to minimise the potential substantial harm related to long-term opioid use. Individual's goals of care, values and preferences are important considerations in the shared decision-making process. If opioids are used for the management of complex and/or refractory pain, cancer-related pain or chronic cancer-survivor pain, referral for specialist input is necessary (e.g. pain and/or palliative care specialists if relevant).

Opioids
Discontinuing opioids is complex and requires clinical expertise and patient engagement. Motivational interviewing is recommended at each visit to encourage patient participation. Educating patients about the risks of long-term opioid use enhances their readiness for discontinuation. Several online resources, such as the NPS MedicineWise Lowering Your Opioid Dose consumer guide, can aid in patient education [578].

Before tapering, healthcare providers and patients should collaboratively develop a discontinuation plan, outlining goals, tapering steps, and review intervals. Ideally, opioid discontinuation should be accompanied by non-opioid medications and non-pharmacological therapies (e.g. acupuncture, massage, physiotherapy, osteopathy) where relevant. A 2019 meta-analysis found that mind-body therapies provided moderate pain relief and reduced opioid use, although the overall evidence remains limited [579].

Opioid substitution for tapering is generally not encouraged, except in cases where transdermal formulations necessitate gradual withdrawal. Two tapering strategies are commonly recommended [177, 580, 581]:

- Fast tapering (for use <1 year): Reduce the opioid dose by 10–25% per week
- Slow tapering (for use >1 year): Reduce the opioid dose by 10–25% per month

For individuals using both immediate-release and extended-release opioids, deprescribing long-acting opioids first is generally recommended. If tapering leads to withdrawal symptoms or worsening pain, a temporary pause is advised to reassess goals and consider adjunct non-opioid analgesics. Referral to a pain or addiction specialist may be necessary [580].

Opioid withdrawal may present with nausea, vomiting, sweating, diarrhoea, anxiety, myalgia, and irritability [177, 580]. Routine pharmacological management to prevent withdrawal symptoms is generally not recommended but rather, attempting slower tapering strategies to reduce the risk of adverse drug withdrawal events. However, for individuals with severe symptoms, clonidine (0.1–0.2 mg every six hours) may be considered [580], with careful monitoring for bradycardia and hypotension [571, 581].

Withdrawal-associated hyperalgesia (increased sensitivity to pain) may occur but is usually temporary [581]. If withdrawal-associated hyperalgesia occurs during opioid tapering, individuals should be reassured that the heightened pain is likely short-lived and that, over time, reducing or stopping opioids often leads to improved pain management and overall well-being.

There is also an increased susceptibility to opioid-related harms (e.g. opioid overdose or poisoning) during dose tapering due to a change in opioid tolerance or increased sensitivity [582]. Therefore, extra caution is required, especially if returning to doses prior to deprescribing.

Non-opioids

Please refer to the antiepileptics section for antiepileptics used for neuropathic pain. For other non-opioids analgesics, tapering is generally not required; however, some people may prefer gradual tapering such as reducing the dose evert two to four weeks or at an even slower rate. The approach to deprescribe should be individualised with the speed of tapering be guided by the individuals. Tapering may also be helpful to establish the lowest effective dose if therapy continuation becomes necessary.

Narrative summary of evidence on deprescribing

We identified one RCT related to tramadol deprescribing [583] from the systematic review and meta-analysis [583].

Overall, the current evidence is derived from a single RCT focused on tramadol and is of very low certainty due to methodological limitations, including a small sample size and short follow-up duration. A significantly higher proportion of participants in the discontinuation group reported insufficient pain relief compared to those who continued tramadol but adverse drug events were more frequently reported in the tramadol group. This highlights a trade-off between pain control and treatment-related harms. Deprescribing may still be appropriate in people who are at higher risk of adverse effects, especially when alternative non-opioid strategies are available or pain is well-controlled. However, the evidence is inadequate to inform evidence-based recommendations. There is also a lack of evidence on deprescribing non-opioid analgesics such as paracetamol. If deprescribing is considered appropriate, it may be appropriate to closely monitor for changes in pain, functional status, and quality of life.

Key study characteristics and results

Kawai 2022 conducted an RCT that included patients with chronic knee osteoarthritis pain for at least three months [583]. Prior to the four-week double-blind period comparing tramadol discontinuation and continuation, all participants entered an open-label, tramadol dose-escalation period of one to three weeks (100 to 300 mg daily). Eligible participants were randomised to continue tramadol or switched to a placebo for four weeks (double-blind period). Eligible participants were those with 1) an improvement in Numeric Rating Scale (NRS) for pain of ≥ 2 points dose escalation period compared to baseline, 2) a difference of ≤ 2 points between the minimum and maximum NRS value in the three days prior to randomisation, and 3) dose compliance rate of ≥70%. Concomitant use of NSAIDs (for osteoarthritis), aspirin (as antithrombotic medicine), and prochlorperazine (as an antiemetic) were permitted as long as the dose was kept the same as pre-trial. Rescue analgesics were not permitted. Four weeks after randomisation, there were considerably more participants in the placebo group who reported inadequate analgesic coverage compared with the tramadol group (25/81 vs. 12/78; OR 2.46, 95% CI 1.13, 5.33). However, adverse drug events were more frequent in the tramadol group than placebo (20/78 vs. 11/81; OR 0.46, 95% CI 0.20, 1.03), with the most common complaints being nausea, vomiting, constipation, somnolence, and dizziness.

Narrative evidence summary: withdrawal schedules

The method of deprescribing was not described in the study, but it appears to have involved abrupt discontinuation by using a placebo [583].

GRADE Summary of Findings (SoF) Table

Table 25. Summary of findings for deprescribing analgesics

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
No available evidence					
2. Adverse drug withdrawal events (ADWEs)					
ADWEs					
1 [583]	RCT	81	78	Inadequate analgesic effect OR 2.46 (95% CI, 1.13, 5.33)	
3. Health outcomes					
Adverse drug events					
1 [583]	RCT	81	78	Adverse drug events related to opioids included nausea, vomiting, constipation, somnolence, and dizziness OR 0.46 (95% CI 0.20, 1.03)	
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
No available evidence					

*Effect measures are reported as a ratio measure (odds ratio, OR) along with 95% confidence intervals.

Antiepileptics

Antiepileptics include:

- Barbiturates and derivatives: Phenobarbital, primidone
- Hydantoin derivatives: Phenytoin
- Succinimide derivatives: Ethosuximide
- Benzodiazepine derivatives: Clonazepam, nitrazepam
- Carboxamide derivatives: Carbamazepine, oxcarbazepine, rufinamide
- Fatty acid derivatives: Valproate, vigabatrin, tiagabine
- Other antiepileptics: Brivaracetam, cannabidiol, gabapentin, lacosamide, lamotrigine, levetiracetam, perampanel, stiripentol, sulthiame, topiramate, zonisamide

Note: Please refer to the sedative hypnotics section for benzodiazepine derivatives used as sedative hypnotics (flunitrazepam, midazolam, nitrazepam, temazepam) and anxiolytics section for benzodiazepine derivatives used as anxiolytics (alprazolam, bromazepam, clobazam, diazepam, lorazepam, oxazepam).

Type	Recommendation
When to deprescribe	
CBR	**Epilepsy indication** We suggest deprescribing decisions be made in consultation with the individual and their neurologist to ensure it aligns with their preferences, goals and overall treatment plans. We suggest deprescribing can be considered if preferred by the individual, provided they have been seizure-free for at least two years, and the risks (e.g. seizure recurrence implications such as driving license implications) and benefits (e.g. reduced adverse effects, interactions or treatment burden) are clearly communicated following an individualised risk assessment, and individual values, preferences, and goals are considered.
CBR	**Non-epilepsy indications** We suggest deprescribing be offered to older people taking antiepileptics for non-epilepsy indications (e.g. neuropathic pain or behavioural and psychological symptoms of dementia) when there is no evidence of therapeutic benefit after a reasonable trial at an optimal dose (e.g. ≥ two to three months) or when the treatment is poorly tolerated.
GPS	**Epilepsy and non-epilepsy indication** Deprescribing decisions should be made in consultation with the individual and their neurologist to ensure alignment with the individual's preferences, goals, and overall treatment plan (ungraded good practice statement).
Ongoing treatment	
CBR	**Epilepsy indication** We suggest continuing antiepileptics for the indication of epilepsy for a minimum of two years without a seizure, or longer (as every additional year of seizure freedom reduces the risk of seizure recurrence), balanced by the individualised risk-benefit assessment.
CBR	**Non-epilepsy indication** We suggest continuing antiepileptics for non-epileptic indications (e.g. primidone for essential tremor) when the benefit clearly outweighs the risk.
How to deprescribe	
CBR	For all indications, we suggest individualising the tapering schedule and adjusting it according to the individual's response.
CBR	**Epilepsy indication** For epilepsy, we suggest reducing the dose of antiepileptics by 10-25% monthly, with close monitoring for breakthrough seizures. If seizure activity occurs, we suggest returning to the previous effective dose. However, we suggest the speed of tapering be

	guided by the person by taking into considerations other factors such as driving implications.
CBR	**Non-epilepsy indications** In general, we suggest reducing the dose gradually by 25% of the previous dose every week initially. If there is any indication of symptom recurrence (e.g. anxiety, restlessness, pain) or if used for longer than a month consider tapering more gradually (up to 6 months may be preferred for a barbiturate or clonazepam).
Monitoring	
CBR	**Epilepsy and non-epilepsy indication** We suggest closely monitoring for symptom recurrence (e.g. seizure recurrence or changes in psychological symptoms for non-epilepsy indications) and whether other concurrent medicines require adjustments due to changes in drug-drug interactions when tapering antiepileptics. Monitoring should ideally occur every one to two weeks following each dose adjustment until at least four weeks after the medicine is fully ceased if practical. After this initial period, we suggest monthly monitoring for at least three months, followed by monitoring every six months thereafter. However, this should be tailored based on individual factors such as their preferences, responses and tolerance to deprescribing. If in-person visits are impractical, we suggest advising people to report symptoms and/or any appearance of new symptoms as needed.
GPS	**Epilepsy indication** For individuals with epilepsy, healthcare providers should ensure a seizure action plan is in place in case breakthrough seizures occur and encourage individuals to track any seizure activities (ungraded good practice statement).

CBR, consensus-based recommendation; GPS, good practice statement

Introduction

Epilepsy and seizures are more common in older adults than in younger individuals [584]. Some of the most common risk factors for new-onset epilepsy in older people include neurological conditions such as cerebrovascular disease (e.g. stroke) and dementia [584]. Antiepileptic medicines are effective in managing epilepsy for approximately two-thirds of individuals [585], but they can also cause significant adverse effects [586]. Studies reported that up to 90% of people taking antiepileptics experience adverse effects, including dizziness, sedation, cognitive impairment, and neuropsychiatric symptoms [586, 587]. The primary goal of treatment is to induce remission while minimising side effects.

There is insufficient evidence to support their routine prophylactic use of seizures in conditions such as traumatic brain injury, subarachnoid haemorrhage, brain tumours, and post-stroke [588]. A study on valproic acid found that using it for more than three months after a stroke did not significantly reduce the risk of late-onset seizures [589]. Importantly, individuals who discontinued valproic acid within three months did not have a higher risk of late seizures compared to those who continued treatment beyond three months [589]

Apart from epilepsy, certain antiepileptics are prescribed for other indications including neuropathic pain, bipolar disorder, or migraine prevention. In the context of neuropathic pain, a 2017 randomised, double-blind, placebo-controlled trial of pregabalin found no significant difference in leg pain severity associated with sciatica between the pregabalin and placebo groups [590]. Given the potential for side effects, deprescribing should be considered when antiepileptics provide little or no apparent benefit, particularly if individuals experience adverse effects such as dizziness.

Justification of recommendations

Non-epilepsy indications

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

When there is clear risk-benefit balance for the use of antiepileptics, it may be appropriate to continue therapy with regular monitoring in place. For instance, primidone is also indicated for the management of essential tremor [591].

Epilepsy indication

When seizures have been well-controlled for several years, some individuals may wish to discontinue antiepileptic medications. However, this decision requires a thorough discussion of the associated risks and benefits. Discontinuation is a complex process that should involve consultation with a neurologist, who can assess factors that increase the likelihood of successful withdrawal. These factors include monotherapy, the absence of epileptiform abnormalities on electroencephalogram prior to withdrawal, a long seizure-free period, and no history of focal seizures [586, 592]. Additionally, developmental delay, the duration of epilepsy before remission, age at onset of seizures, and a history of febrile seizures also play crucial roles in the decision-making process [593].

The potential benefits of discontinuation should be weighed against the risk of seizure recurrence, which ranges from 30% to 50%, depending on the individual's condition and risk factors [588]. For those who have been seizure-free for at least two years, deprescribing may be considered, particularly in those at low risk [594]. Each additional year of seizure freedom further reduces the likelihood of seizure recurrence [593, 595], suggesting that a longer seizure-free period is preferable before initiating withdrawal. However, this must be balanced against the long-term adverse effects of continued antiepileptic use. While the two-year threshold is commonly referenced, it is an arbitrary threshold; the risk of recurrence continues to decrease with each additional seizure-free year [593]. Lamberink et al. developed nomograms based on a systematic review and individual participant data meta-analysis, which can assist in determining the optimal timing for deprescribing in individual patients [593].

Apart from the risk of seizure recurrence, the decision to stop antiepileptics should take into account the type of epilepsy, seizure history as well as personal and social factors important to the person (e.g. relationships, driving, and employment) given potentially devastating consequences of recurrent seizures [596]. In Australia, under the driver licensing authority standards for driving a private vehicle, a person should not drive a vehicle while their antiepileptic dose is being tapered and for three months after the final dose [597]. However, there are two exceptions to this restriction: 1) the dose reduction is due only to the presence of current dose-related side effects and is unlikely to affect seizure control; or 2) the dose reduction is required, after an increase due to a temporary situation, to a dose that was effective before the increase [597]. The risks and implications of seizure recurrence versus the benefits of discontinuing therapy should be communicated to the person to ensure informed consent and shared decision-making. If deprescribing is considered appropriate in the context of epilepsy, gradual dose reduction should be individual with close monitoring for breakthrough seizures. The speed of tapering should be guided by the person by taking into consideration other factors such as driving implications. A slow tapering (such as by 10-25% monthly over several months) allows for monitoring and identifying the minimal effective dose in case of seizure recurrence, but it prolongs the non-driving period for the person may have significant personal impacts [586].

Drug interactions should also be considered, as some antiepileptics, especially older agents like phenytoin and carbamazepine, can alter the metabolism of other medicines through enzyme induction [598].

Narrative summary of evidence on deprescribing

We identified one RCT related to carbamazepine deprescribing from the systematic review and meta-analysis [599] and one before-and-after study related to gabapentinoid deprescribing [600]; however, no evidence related to the withdrawal of antiepileptics in people treated for epilepsy.

There is currently insufficient evidence to guide deprescribing of antiepileptics in people with epilepsy. Existing data come from one RCT and one before-and-after study in older adults using antiepileptics for non-epilepsy indications (e.g. behavioural and psychological symptoms of dementia, neuropathic pain). Both studies are of very low certainty due to small sample sizes and short follow-up. While these studies suggest that deprescribing may be feasible and not associated with harm in these non-epilepsy contexts, the evidence is too limited to support formal recommendations. If deprescribing is considered appropriate, close monitoring of symptom recurrence should be undertaken as well as a review of concurrent medicines that require adjustments due to changes in drug-drug interactions when tapering antiepileptics.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Tariot 1999 evaluated the washout of carbamazepine administered for behavioural and psychological symptoms of dementia (BPSD) versus placebo. Participants were included if they had a diagnosis of dementia and exhibited agitation for at least two weeks with a Brief Psychiatric Rating Scale (BPRS) score of ≥ three for tension, hostility, uncooperativeness, or excitement. The study assessed BPSD using the BPRS which is an 18-item scale with higher scores indicating greater psychiatric disturbance. At the end of the three-week washout period, there was no significant difference in BPRS scores between the two groups (MD 0.60, 95% CI -4.94, 6.14). Similarly, there was no significant difference between the two groups for aggression (MD 0.10, 95% CI -3.23, 3.43), total behaviour rating scale of dementia (MD -5.20, 95% CI -17.36, 6.96), and physical self-maintenance scale (MD -1.70, 95% CI -4.42, 1.02). There was also no significant difference in cognition at the end of the washout period (MD -0.70, 95% CI -2.96 to 1.56).

Gingras 2024 conducted a before-and-after study involving inpatients aged 60 years and older who were receiving a gabapentinoid at the time of hospitalisation [600]. Patients were excluded if they had a known seizure disorder, a life expectancy of less than three months, or a major neurocognitive disorder. Patients initially enrolled in the study received usual care (n=80), while another 80 patients in the intervention period were provided with a direct-to-consumer educational brochure with information on gabapentinoids, non-pharmacological alternatives, and a proposed deprescribing algorithm. During the same intervention period, ward clinicians attended monthly educational sessions on gabapentinoids. Most participants were prescribed pregabalin (133/160, 83%), while the remainder received gabapentin (27/160, 17%), primarily for pain and/or osteoarthritis. Among the 142 participants who completed the study, there were no significant differences between the intervention and control groups in gabapentinoid discontinuation or ongoing tapering (OR 0.41, 95% CI 0.16, 1.07), concurrent pain medication doses (OR 0.15, 95% CI 0.02, 1.32), or initiation of new pain medications (OR 1.24, 95% CI 0.50, 3.09) at eight weeks post-discharge. Similarly, no significant differences were observed in global physical health (MD -0.80, 95% CI -3.0, 1.3), pain intensity (MD -2.5, 95% CI -5.8, 0.8), or cognition (MD 1.8, 95% CI -1.1, 4.7), as assessed using the Patient-Reported Outcomes Measurement Information System (PROMIS) questionnaires.

Narrative evidence summary: withdrawal schedules

The method of deprescribing was not described in the two studies.

For non-epilepsy indications, the dose of antiepileptics may be gradually reduced (e.g. by 25% of the previous dose every week) as it may be helpful to determine the minimal effective dose in case of symptom recurrence. In people who have been taking antiepileptics for longer than four weeks, especially for barbiturates and benzodiazepines, it may be reasonable to consider tapering more gradually over several months to minimise the risk of adverse drug withdrawal events [601].

GRADE Summary of Findings (SoF) Table

Table 26. Summary of findings for deprescribing antiepileptics

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
No available evidence					
2. Adverse drug withdrawal events (ADWEs)					
1 [600]	Non-randomised study	71	71	Physical health, measured using Patient-Reported Outcomes Measurement Information System (PROMIS) MD -0.80 (95% CI -3.0, 1.3) Pain intensity, measured using PROMIS MD -2.5 (95% CI -5.8, 0.8)	
3. Health outcomes					
Physical function					
1 [599]	RCT	22	23	At the end of the washout period, there was no significant difference between the group previously taking placebo and the group previously taking carbamazepine for behavioural and psychological symptoms of dementia in the Physical Self-Maintenance Scale (MD -1.70, 95% CI -4.42, 1.02).	
Behavioural and psychological symptoms					
1 [599]	RCT	22	23	Aggression MD 0.10 (95% CI -3.23, 3.43) Total behaviour rating scale of dementia MD -5.20 (95% CI -17.36, 6.96) Total Brief Psychiatric Rating Scale (BPRS) score MD 0.60 (95% CI -4.94, 6.14)	
4. Cognitive function					
1 [599]	RCT	22	23	Washout of carbamazepine administered for behavioural and psychological symptoms of dementia (BPSD) versus placebo, MD -0.70 (95% CI -2.96, 1.56)	
1 [600]	Non-randomised study	71	71	Cognitive functions, measured using PROMIS MD 1.8 (95% CI -1.1, 4.7)	
5. Quality of life (QoL)					
No available evidence					

*Effect measures are reported as a difference measure (mean difference, MD) along with 95% confidence intervals.

Levodopa

This section includes:

- Levodopa with benserazide or carbidopa*
- Levodopa with carbidopa and entacapone

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing decisions be made in consultation with the individual, their carer/family members, and their GP and/or specialist providers to ensure it aligns with their preferences, goals and overall treatment plans. We suggest deprescribing be offered to older people taking levodopa when: • There has been no clinically meaningful improvement in motor symptoms or functional outcomes after at least three months of uninterrupted therapy at an optimal dose; or • Non-motor side effects intolerable; or • The overall adverse impact of non-motor side effects outweighs the treatment benefits.
Ongoing treatment	
CBR	We suggest continuing levodopa if the benefits (e.g. motor or non-motor) clearly outweigh the potential risks (e.g. fall risk, orthostatic hypotension and sedation); however, we suggest reassessing the need for long-term therapy periodically and monitoring for emerging risks and benefits.
How to deprescribe	
CBR	We suggest levodopa may be ceased abruptly (e.g. when there is a need to rapidly assess levodopa responsiveness or in the presence of significant toxicity) or gradually tapered by reducing the dose by one tablet or 100 mg every two weeks until it is fully withdrawn (e.g. for people on high baseline daily doses), ensuring individuals remain symptom-free before initiating each tapering.
Monitoring	
CBR	We suggest closely monitoring for worsening motor (e.g. tremors, bradykinesia, rigidity) and non-motor symptoms (e.g. mood changes, cognitive decline) such as every one to two weeks.

CBR, consensus-based recommendation

Introduction

Parkinson's disease

Levodopa is the most effective and commonly used treatment for the motor symptoms of Parkinson's disease. However, its dosage often requires careful adjustment based on the individual's condition and response. The prescribed dose must balance treatment benefits (both motor and non-motor) against potential dose-limiting side effects. This balance becomes increasingly complex in advanced Parkinson's disease and in older people with comorbidities such as dementia. Levodopa-induced complications, including increasing dyskinesia duration, more disabling dyskinesia as well as longer, more sudden and unpredictable OFF periods, had significant adverse impacts on the quality of life of people with Parkinson's disease [602].

Restless legs syndrome (RLS)

Levodopa may be prescribed with a dopamine decarboxylase inhibitor as needed to treat intermittent RLS symptoms (i.e. symptoms occurring less than once or twice a week). It is not

recommended as a chronic treatment due to the high risk of tolerance and augmentation. Augmentation is a serious adverse event described as the "onset of RLS symptoms earlier in the day after an evening dose of medication, the spread of symptoms to the arms, paradoxical worsening of symptoms with dose increase, and shorter effect of each dose of medication" [603, 604].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

Although levodopa can reduce fall risks in some people by addressing specific gait issues, levodopa may induce or worsen orthostatic hypotension in more than half of people which in turn increases fall risks [605, 606]. Additionally, levodopa may cause sedation and daytime somnolence, thereby increasing the risk of falls [607, 608].

Given the potential risks associated with long-term use of levodopa, deprescribing may be considered appropriate if side effects are intolerable or there has been no clinically meaningful improvement. In contrast, for people who continue to receive meaningful therapeutic benefits, and the risks are tolerable, levodopa should be continued with periodic monitoring for emerging risks and benefits.

Narrative summary of evidence on deprescribing

We identified two studies (one RCT and one before-and-after study) related to levodopa deprescribing [609, 610].

Overall, the current evidence of outcomes arises from only two studies of very small sample sizes and are of low and very low certainty due to methodological limitations. The evidence at this stage is inadequate to inform evidence-based recommendations.

If levodopa is considered appropriate to deprescribe, it may be appropriate to closely monitor for worsening motor (e.g. tremors, bradykinesia, rigidity) and non-motor symptoms (e.g. mood changes, cognitive decline).

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Tse 2008 conducted an RCT that included 11 nursing home residents who are currently treated with levodopa and not taking any other medicines for Parkinson's disease for the past 30 days [610]. Participants were included if they had advanced Parkinsonism (presence of bradykinesia and at least one of the following: rest tremor, rigidity, or postural instability) and dementia (MMSE < 19). Participants with current or past treatment with antipsychotics, stroke, or history of central nervous system structural lesions were excluded. Residents were randomised to levodopa continuation (n=5) or discontinuation (n=6). At week four, there was no significant difference between the two groups in terms of cognition (MD 3.20, 95% CI -7.80, 14.20) or motor and non-motor symptoms evaluated using the Unified Parkinson's Disease Rating Scale (MD -11.99, 95% CI -39.98, 16.00).

Hauser 2000 conducted a before-and-after study that included 31 community-dwelling older people with early Parkinson's disease (Hoehn and Yahr stage one to three) who previously participated in RCT to determine the effects of selegiline, levodopa, and bromocriptine on the

progression of Parkinson's Disease [609]. Participants were included if they had at least two of three cardinal features of Parkinson's Disease (bradycardia, rigidity, resting tremor) and participants with a history of exposure to neuroleptic medicines were excluded. Comparing day one to day 15, discontinuation of levodopa/carbidopa and bromocriptine led to a reduction in the total Unified Parkinson's Disease Rating Scale scores (± standard error) by 7.4 ± 1.5 (p <0.0001) in all participants. During deprescribing, none of the participants reported complications other than worsening Parkinsonian symptoms.

Narrative evidence summary: withdrawal schedules

In the RCT, the levodopa dose was tapered by one tablet (or 100 mg) every three days until completely withdrawn (low certainty; n=11) [610]. The method of deprescribing was not described in the before-and-after study (very low certainty; n=31) [609].

Levodopa may be gradually tapered by reducing the dose by one tablet or 100 mg over several weeks, particularly for people on high baseline daily doses. However, when there is a need to rapidly assess levodopa responsiveness or in the presence of significant toxicity, it may be more appropriate to cease levodopa abruptly without the need for tapering.

GRADE Summary of Findings (SoF) Table

Table 27. Summary of findings for deprescribing levodopa

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
No available evidence					
2. Adverse drug withdrawal events (ADWEs)					
1 [610]	RCT	5	3	Severity and progression of Parkinson's disease, measured by Unified Parkinson's Disease Rating Scale (UPDRS) MD -11.99 (95% CI -39.98, 16.00)	
1 [609]	Non-controlled study	31	N/A	Adverse drug withdrawal effects (other than recurrent of the underlying symptoms), 0% Change in UPDRS at 15 days where higher scores indicate a greater symptom severity, -7.4 ± 1.5, p<0.0001	
3. Health outcomes					
No available evidence					
4. Cognitive function					
1 [610]	RCT	6	5	Cognition, measured by Mini-Mental State Examination Mean 3.20 (-7.80, 14.20)	
5. Quality of life (QoL)					
No available evidence					

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

Antipsychotics

Antipsychotics include amisulpride, aripiprazole, asenapine, brexpiprazole, cariprazine, chlorpromazine, clozapine, droperidol, flupentixol, haloperidol, lurasidone, olanzapine, paliperidone, periciazine, quetiapine, risperidone, trifluoperazine, ziprasidone, zuclopenthixol.

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing be offered to older people who are taking antipsychotics when: • There is no clear indication, that a contraindication exists, or prescribing is inappropriate (e.g. use for vocal disruption or conditions other than primary psychotic illness). • Adverse effects or drug interactions outweigh potential benefits (e.g. Parkinson's disease or Lewy body dementia without psychotic symptoms, risk of QT prolongation, history of stroke, extrapyramidal side effects, recurrent falls, or significant weight gain). • Used for the management of behavioural and psychological symptoms of dementia (BPSD) beyond 12 weeks, if symptoms have resolved, are unlikely to recur, or remain stable.
Ongoing treatment	
CBR	**BPSD** If deprescribing is unsuccessful despite multiple attempts and non-pharmacological options have been considered, we suggest maintaining the lowest effective dose, provided this aligns with the individual preferences, goals and overall treatment plans, and that the benefit clearly outweighs the harm and that potential underlying causes for BPSD (e.g. pain, constipation, depression) have been considered and/or addressed. However, we suggest reassessing the need for long-term therapy periodically at least every three to six months or more frequently if symptoms change and additional monitoring for cardiometabolic risks in people using antipsychotics (weight, blood pressure, lipids, diabetes screening, cardiovascular risk calculation).
How to deprescribe	
CBR	We suggest individualising the tapering schedule and adjusting it according to the individual's response. In general, we suggest reducing the dose by 25% to 50% every one to four weeks, ensuring the absence of withdrawal symptoms and/or symptoms indicative of relapse before initiating further tapering. Once half the lowest standard dose formulation is reached, we suggest ceasing completely. However, smaller dose reductions may be appropriate or preferred by some individuals, particularly as lower doses are approached.
GPS	Healthcare providers should consider and offer adequate non-pharmacological management options such as psychosocial practices, structured care protocols, and sensory practices during and after deprescribing (ungraded good practice statement).
GPS	Healthcare providers should consider and offer appropriate management strategies to the individual's families and care providers (e.g. verbal de-escalation, psychological intervention, increased staff-to-patient ratio, increased staff training in behaviour management (ungraded good practice statement).
Monitoring	
CBR	We suggest closely monitoring for individual responses and tolerance to antipsychotic tapering, paying specific attention to changes in psychological withdrawal effects (e.g. agitation, hallucinations, anxiety) and physical withdrawal symptoms (e.g. dyskinesia), function, and quality of life every one to two weeks following each dose adjustment until at least four weeks after the medicine is fully ceased if practical. After this initial period,

	we suggest monthly monitoring for at least three months, followed by monitoring every six months thereafter. However, this should be tailored based on individual factors such as their preferences, responses and tolerance to deprescribing. If in-person visits are impractical, we suggest advising people to report symptoms as needed.
GPS	Healthcare providers should use validated assessment tools to evaluate changes in neuropsychiatric symptoms, functional status, and quality of life (e.g. Neuropsychiatric Inventory for neuropsychiatric symptoms, Functional Status Questionnaire for functional status, and EQ-5D for health-related quality of life) (ungraded good practice statement).

CBR, consensus-based recommendation; GPS, good practice statement

Introduction

Antipsychotics are primarily used to treat psychotic disorders, such as schizophrenia and bipolar disorder, by alleviating symptoms like hallucinations, delusions, and abnormal behaviours/thoughts [177]. Their sedative and tranquillising effects can also help manage severe aggression and behavioural disturbances [177]. As a result, they are sometimes prescribed off-label in older adults for conditions such as behavioural and psychological symptoms of dementia (BPSD), insomnia, and anxiety disorders [611]. However, antipsychotic use for non-psychotic conditions should generally be avoided due to significant adverse effects, some of which are severe and potentially irreversible. In older people with dementia, antipsychotic use is particularly concerning, as it is associated with an increased risk of mortality and cerebrovascular events [612].

Antipsychotics are sometimes used to manage severe agitation, aggression, or psychotic symptoms in dementia, but they pose a high risk of serious side effects and offer only modest symptom relief [613]. BPSD encompasses agitation, aggression, hallucinations, delusions, depression, wandering, disinhibition, and vocal disruptions (e.g. calling out and screaming) [614]. These symptoms can be distressing for both the individual and their caregivers. While BPSD typically occurs or worsens with dementia progression, underlying factors such as physical pain, constipation, fatigue, or loneliness can also precipitate BPSD and should be assessed as part of the management plan [615].

A 2016 systematic review found that atypical antipsychotics, such as risperidone, olanzapine, and aripiprazole, provided limited improvements, while quetiapine was less effective. Typical antipsychotics showed similar modest benefits [616]. Importantly, any potential benefits should be observed shortly after initiation, as a lack of response within two weeks suggests further improvement is unlikely [617]. Some symptom resolution may occur naturally over time, which can overstate the perceived effectiveness of antipsychotics [613].

Non-pharmacological interventions are recommended as first-line treatments for BPSD [618-620]. These include psychosocial therapies (e.g. validation therapy, reminiscence therapy, music therapy), structured care approaches (e.g. bathing, oral care routines), and sensory interventions (e.g. aromatherapy, massage, bright light therapy, pet therapy) [621]. When BPSD symptoms are particularly distressing or pose a safety risk, the Monash Clinical Practice Guidelines suggest short-term risperidone at the lowest effective dose for acute behavioural disturbances [622]. However, atypical antipsychotics are not recommended for symptoms such as vocal disruptions, wandering, or disinhibition due to their risks and lack of proven benefit [622].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

Antipsychotics can cause orthostatic hypotension, confusion, anticholinergic effects (e.g. constipation, dry mouth, dry eyes), and extrapyramidal side effects (e.g. dystonia, akathisia, parkinsonism, tardive dyskinesia) [623]. Long-term use is associated with metabolic complications, including weight gain, diabetes, metabolic syndrome, and QT prolongation. Older people, particularly women, have an increased risk of tardive dyskinesia, which may persist even after discontinuation [177]. The use of antipsychotics in dementia increases the risk of all-cause mortality and stroke risk [624, 625].

Given these risks, deprescribing should be considered in cases where antipsychotics are prescribed inappropriately or where the indication is no longer relevant [623]. Factors such as adverse effects, drug interactions, high drug burden index (DBI), poor adherence, or patient preference should prompt discussions between healthcare providers and patients about deprescribing opportunities [623]. DBI is a pharmacological measure used to quantify an individual's exposure to medicines with anticholinergic and sedative properties, including antipsychotics [434]. A high DBI is associated with an increased risk of falls, cognitive decline, and reduced physical function [626].

When antipsychotic therapy is identified as suitable for deprescribing, the tapering plan should be individualised, ensuring the absence of physical or neuropsychiatric withdrawal symptoms before initiating further tapering. The general approach of tapering a long-term antipsychotic used for BPSD involves approximately reducing the dose by 25 to 50% every one to two weeks until the lowest practical dose is reached, then after one to two weeks, stop the antipsychotic [627]. Slower tapering may be necessary for people with a high baseline dose or those with a history of severe symptoms [627]. The Maudsley deprescribing guidelines recommend a hyperbolic tapering strategy, using progressively smaller dose reductions at lower doses, to reduce withdrawal risks and relapse [43]. This method may be preferred by some individuals seeking a gradual transition off antipsychotics.

Narrative summary of evidence on deprescribing

We identified 18 studies (eight RCTs, one prospective cohort study, and nine before-and-after studies) related to antipsychotic deprescribing from the systematic review and meta-analysis [628-643].

Overall, the current evidence for deprescribing antipsychotics is derived from studies of low and very low certainty with a focus on people with cognitive impairment using antipsychotics for BPSD, especially in nursing home residents. There was no evidence for deprescribing for psychotic disorders except for one study that investigated drug-induced psychosis in people with idiopathic Parkinson's disease [637]. It was also difficult to interpret the findings given the potential confounding factors related to the use of concomitant psychoactive drugs, including antidepressants, benzodiazepines, and sedative hypnotics. The majority of the studies have very short follow-up periods (one to 12 months) so it may be possible that severe and persistent withdrawal syndromes, if occurred, were not captured. There was also a lack of clear differentiation between withdrawal effects and relapse of the initial condition in many studies. The evidence at this stage is insufficient to inform evidence-based recommendations.

If antipsychotics are considered appropriate to deprescribe, closely monitoring for psychological withdrawal effects (e.g. agitation, hallucinations, anxiety) and physical withdrawal symptoms (e.g. dyskinesia), function, and quality of life may be appropriate.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Ruths 2008 randomised 55 nursing home residents with dementia taking antipsychotics for BPSD to the placebo group (n=27) or continuation (n=28) [639]. Participants were included if they were taking either haloperidol, risperidone, or olanzapine for at least three months, and were excluded if it was prescribed primarily for a major psychotic disorder or if they had an intellectual disability. Standing orders for concomitant psychoactive medicines (e.g. antidepressants, hypnotics, and anxiolytics) were permitted during the study. At week four, 23/27 participants (85%) in the intervention group remained off antipsychotics. There was no significant difference between the two groups in terms of mortality (OR 3.38, 95% CI 0.33, 34.65), neuropsychiatric symptoms (MD 3.00, 95% CI 0.16, 5.84), or behavioural deterioration (OR 2.16, 95% CI 0.18, 25.32). In an earlier sub-analysis (Ruths 2004) involving an actigraphy assessment in 30 participants, discontinuation of antipsychotics significantly reduced sleep efficiency (sleep time was 54 minutes shorter in the placebo group; p=0.029) [644].

Van Reekum 2002 randomised 33 nursing home residents with dementia who were taking a stable dosage of antipsychotics for at least six months to discontinuation (n=17) or continuation (n=16) [642]. Participants were excluded if they had delirium, a history of schizophrenia, behavioural symptoms that were disturbing to caregivers in the past two weeks or were using antipsychotics for treating nausea only. On-demand use of 0.5 to 1.0mg lorazepam was permitted for agitation during the study. At six months, there was no significant difference between the two groups in terms of mortality (OR 0.44, 95% CI 0.04, 5.36) or behavioural deterioration leading to study withdrawal (OR 1.33, 95% CI 0.25, 7.17).

Bridges-Parlet 1997 randomised 36 nursing home residents with possible or probable Alzheimer's disease who were taking a stable dosage of antipsychotics for at least three months to discontinuation (n=22) or continuation (n=14) [633]. Participants were included if they had a history of physically aggressive behaviour and were excluded if they were using antipsychotics primarily for a psychiatric disorder or had an intellectual disability. Concomitant use of antidepressants was permitted during the study if the medicine doses had been stable. At week four, there was no significant difference between the two groups in terms of agitation (OR 13.54, 95% CI 0.16, 79.29) or the number of physically aggressive behaviour episodes (MD -3.23, 95% CI -8.19, 1.73).

Devanand 2011 randomised 20 outpatients with Alzheimer's disease who previously responded to haloperidol treatment to discontinuation (n=10) or continuation (n=10) [645]. Participants were included if they were diagnosed with dementia and probable Alzheimer's disease and had current symptoms of psychosis (i.e. presence of delusions and/or hallucinations) or agitation/aggression. Participants were excluded if they were diagnosed with a psychotic disorder, had delirium, alcohol or substance abuse or dependence in the past 12 months, had stroke, other dementia type, or movement disorders. Concomitant psychotropic medicines were not permitted during the study. Discontinuation of haloperidol was associated with an increased risk of relapse (8/10 [80%] on placebo relapsed compared to 4/10 [40%] on haloperidol). Relapse was defined as at least 50% worsening from psychotic or agitation/aggression symptoms and score on the Clinical Global Impressions Scale.

Devanand 2012 randomised 110 outpatients with Alzheimer's disease who previously responded to risperidone treatment to the placebo group for 32 weeks (n=40), or continuing risperidone for 32 weeks (n=32), or continuing risperidone for 16 weeks before taking placebo for 16 weeks (n=38) [636]. Participants were excluded if they had a history of stroke, transient ischemic attack, or uncontrolled AF. Stable doses of concomitant psychotropic medicines (e.g. anxiolytics, hypnotics, and antidepressants) were permitted during the study. On-demand lorazepam at 1 mg or less per day was permitted. At 32 weeks, there was no significant difference in mortality (OR 0.38, 95% CI 0.03, 4.44) between the group that continued with risperidone and the group that took a placebo for 32 weeks. At 16 weeks, the placebo group (n=40) had an increased risk of

relapse of psychosis or agitation compared with the two groups who had continued taking risperidone for 16 weeks (n=70) (OR 3.07, 95% CI 1.37, 6.86).

Ballard 2004 randomised 100 nursing home residents with possible or probable Alzheimer's disease who had been taking antipsychotics for longer than three months with no severe behavioural disturbances to discontinuation (n=46) or continuation (n=54) [631]. At week four, there was no significant difference in mortality (OR 1.19, 95% CI 0.23, 6.18), neuropsychiatric symptoms measured using the Neuropsychiatric Index (NPI) (MD 3.0, 95% CI -3.69, 9.69), or quality of life (MD -0.53, 95% CI -1.42, 0.36) between the two groups.

In a subsequent larger RCT (n=165), Ballard 2008 included nursing home residents with possible or probable Alzheimer's disease who were taking thioridazine, chlorpromazine, haloperidol, trifluoperazine or risperidone for three months or longer for BPSD [630]. Participants were randomised to discontinuation (n=82) or continuation (n=83). At 12 months, there was no significant difference between the two groups in the neuropsychiatric symptoms using the NPI, extrapyramidal symptoms, severity of Parkinson's disease measured using the modified unified Parkinson's disease rating scale, activities of daily living measured using the Bristol ADL, cognition measured using the standardised Mini-Mental State Examination or using the Severe Impairment Battery (SIB). However, there was a significant decline in verbal fluency, measured using the Verbal Fluency Task, among people who continued their antipsychotics (MD -3.80, 95% CI -6.91, -0.69). In the longer-term follow-up of up to 54 months, Ballard 2009 reported deprescribing was associated with reduced mortality (OR 0.51, 95% CI 0.28, 0.96) [646].

Cohen Mansfield 1999 reported a double-blind crossover RCT that included 58 nursing home residents who were taking either haloperidol, thioridazine or lorazepam (antipsychotics or benzodiazepines) for agitation [635]. Participants were excluded if they were taking other antipsychotics or anxiolytics concurrently (except for low-dose trazodone hydrochloride for sleep), had uncontrolled blood glucose, or had a diagnosis of major affective disorder of schizophrenia. There were no significant differences between the discontinuation and continuation period in terms of psychiatric symptoms measured using the Brief Psychiatric Rating Scale, physical aggression measured using the Cohen-Mansfield Agitation Inventory, global clinical status measured using the Clinical Global Impression Scale, or cognition measured using the Mini-Mental Status Exam.

Somani 1996 conducted a non-randomised study that included 57 nursing home residents with dementia who had been taking antipsychotics for at least three months for BPSD [640]. Participants who were diagnosed with movement disorders, or schizophrenia, or were using beta-blockers or long-acting benzodiazepines concurrently were excluded. In the study, 17 participants had their antipsychotics gradually discontinued, 18 participants had dose changes, and 22 participants had continued taking their antipsychotics. There were no significant differences between the control group (n=22) and the intervention group/dose change group (n=35) in terms of falls, dyskinesias measured using the Dyskinesia Identification System Condensed User Scale Instrument, or disease exacerbation. However, compared to the control group, the intervention group/dose change group had a significantly higher incidence of withdrawal dyskinesia (9 vs. 0, OR 32.14, 95% CI 1.67, 617.16) and behavioural relapse (11 vs. 0, OR 21.12, 95% CI 1.18, 379.52). Behavioural relapse was defined as an increase in target behaviours after dose reduction that necessitated a return to at least the baseline dose.

Thapa 1994 reported a prospective cohort study using an educational program to reduce antipsychotic prescribing in nursing homes [641]. A total of 271 nursing home residents who were receiving antipsychotics at baseline were included in this cohort study (discontinuation group, n=64; continuation group, n=207). There were no significant differences between the two groups in terms of involuntary movements measured using the Abnormal Involuntary Movement Scale, behavioural problems, measured using the Nursing Home Behaviour Problem Scale, depression

measured using the Geriatric Depression Scale, activities of daily living, measured using the Lawton's Physical Self-Maintenance Scale, and cognition measured using the Mini-Mental State Examination. However, discontinuation of antipsychotics was associated with a significant reduction in observer-rated psychiatric symptoms measured using a modified Brief Psychiatric Rating Scale with a higher score indicating more severe symptoms (MD -0.36, -0.59, -0.13).

Azermai 2013 conducted a before-and-after study to abruptly discontinue antipsychotics in 40 inpatients with dementia or cognitive impairment who had been using antipsychotics for at least a month explicitly for BPSD [628]. The majority (n=31, 78%) remained off antipsychotics after one month, with an improvement in neuropsychiatric symptoms measured using NPI (-5.7, p=0.003, lower score indicates less severe symptoms) although mild withdrawal symptoms (e.g. physical symptoms such as nausea, vomiting, diarrhoea and psychological symptoms such as agitation, insomnia, anxiety, hallucinations) were observed in 72% of the participants [628].

Brodaty 2018 reported a before-and-after study in which an antipsychotic deprescribing protocol was implemented in 23 nursing homes [634]. At 12 months, there was a substantial reduction in the number of participants prescribed antipsychotics (reduced by 81.7%, 95% CI 72.4, 89.0). Compared to the pre-intervention period, discontinuation of antipsychotics did not lead to a statistically significant difference in BPSD, falls, hospitalisations, or cognition.

Fernandez 2005 reported a before-and-after study that discontinued clozapine or quetiapine in six community-dwelling people with idiopathic Parkinson's disease and no ongoing psychosis [637]. Participants were included if they were currently taking antipsychotics for at least 6 months, had a history of drug-induced psychosis, and were excluded in the presence of dementia with Lewy bodies. Concomitant medicines for Parkinson's disease remained stable throughout the study. Five of the six participants (83%) reported psychosis episodes two weeks to two months following the end of each tapering period. However, there was no change in the Parkinson's Disease motor severity measured using the Unified Parkinson's Disease Rating Scale (44.5 vs. 43.8, p=0.36).

Horwitz 1995 conducted a before-and-after study to compare the discontinuation of antipsychotics among nursing home residents with dementia based on clinical judgment and mandate [638]. Deprescribing by mandate was more likely to fail compared with discontinuing at the discretion of physicians (50% vs 5%). Among residents who restarted antipsychotics, the most common reasons were increased verbal and physical aggression. Antipsychotic withdrawal did not lead to an improvement in neurological performance, functional status, or cognition.

Bach 2017 conducted a before-and-after study that involved a pharmacist-led chart review of antipsychotic use in 20 nursing home residents with dementia [629]. Residents with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder, mood disorders (e.g. bipolar disorder), Tourette's disorder, or Huntington's disease were excluded. In the study, the most common indication for antipsychotic use was verbal or physical aggression (35%), followed by resisting care (30%), agitation and restlessness (15%), verbal outbursts (10%), wandering (5%), and hallucinations (5%). Overall, antipsychotic use was reduced from 28 residents (21%) to 19 residents (14%) in the nursing home throughout the seven months.

Bravo-Jose 2019 conducted a before-and-after study that targeted the use of antipsychotic drugs in 35 nursing home residents with dementia and behavioural disturbances [647]. Residents were included if they met one or more of the following criteria: 1) stable for six months, 2) without treatment modification for more than a year, 3) severe side effects to antipsychotics, 4) receiving a typical antipsychotic, 5) receiving two or more antipsychotics, or 6) advanced functional impairment and advanced dementia. Participants were excluded if they were using antipsychotics for delusions, or hallucinations, or previously had a psychiatric condition. Antipsychotics were successfully deprescribed in 28/35 (80%) participants living in long-term care institutions and

reduced to the lowest effective dose in seven participants (20%). Deprescribing of antipsychotics did not lead to significant changes in neuropsychiatric symptoms measured using NPI (12.9 ± 12.8 to 13.8 ± 16.7, p=0.124).

Westbury 2018 conducted a before-and-after study using a multi-component intervention to reduce the use of antipsychotics and benzodiazepines in aged care facilities [643]. Participants who were receiving respite or end-stage palliative care and those who were prescribed antipsychotics or benzodiazepines for severe psychiatric disorders were excluded. At six months, 39% who were prescribed antipsychotics or benzodiazepines had their dose either reduced or ceased. There was no significant change in BPSD, social withdrawal, quality of life, agitation, or aggression following the discontinuation of antipsychotics.

Bergh and Engedal 2008 conducted a before-and-after study that included 23 nursing home residents with Alzheimer's disease or vascular dementia who had been taking antidepressants or antipsychotics for three months or longer [632]. Deprescribing was implemented for antidepressants (n=11) or antipsychotics (n=12). Participants were excluded if they had a severe psychiatric disorder or diabetes mellitus. At 24 weeks, discontinuation of antipsychotics was not associated with a significant change in cognition measured using Severe Impairment Battery (49.9 ± 35.2 to 60.3 ± 19.5), neuropsychiatric symptoms measured using NPI (33.4 ± 23.9 to 32.0 ± 30.9), depression symptoms measured using Cornell's Depression Scale (7.6 ± 5.8 to 6.7 ± 6.4) or both motor and non-motor symptoms measured using Unified Parkinson Disease Rating Scale (3.9 ± 2.8 to 2.8 ± 1.6).

Narrative evidence summary: withdrawal schedules

Various methods were used for deprescribing in the included studies and tapering was the most common method. While there was no direct evidence that any particular method was associated with the greatest benefits and harms, dose tapering is likely more acceptable than abrupt cessation and helpful in determining the lowest effective dose for some people requiring dose reduction rather than complete cessation.

In two RCTs, the dose was halved for the first week, then quartered of the original dose in the second week, then ceased in the third week (n=53, very low certainty) [642, 645]. For people on 2 or 3mg haloperidol daily, 1mg was given for two weeks, then ceased. People on 0.5 to 1 mg ceased haloperidol abruptly (study=1, n=20, very low certainty) [645]. Antipsychotics were ceased abruptly in two studies (n=66, very low certainty) [633, 644], among which one study stated the dose was halved for one week before complete discontinuation if people were taking daily dose > 50mg chlorpromazine equivalent (n=30) [633]. In one RCT, antipsychotics were tapered for three weeks before complete discontinuation (n=58, very low certainty) [635] whereas in another study dose was tapered over one week (n=11, very low certainty) [632]. The method of deprescribing was not described in the other three RCTs (n=375, n not stated in one study) [630, 631, 636].

In non-randomised controlled trials (all very low certainty), antipsychotics were tapered at a rate of 25% of the daily dose each month for four months (based upon the availability of suitable dosage forms) with a goal of discontinuation after a maximum of four months (study=1, n=57) [640] whereas method was not described in another study (study=1, n=271) [641].

In one non-controlled trial (very low certainty), antipsychotics were ceased abruptly (n=40) [628] and the method was not described in two studies (n=136) [638, 643]. Antipsychotics were gradually tapered in other non-controlled trials, as summarised below:

- Individualised titration schedule over two to eight weeks (study=1,n=6) [637]
- Gradual dose reduction (study=1,n=20) [629]
- Gradual tapering according to a deprescribing guideline (study=1,n=35) [647]

- The dose was halved every two weeks until after two weeks on the minimum dose, then ceased completely (study=, n=139) [634]

GRADE Summary of Findings (SoF) Table

Table 28. Summary of findings for deprescribing antipsychotics

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
5 [630, 631, 636, 642, 644]	RCTs	212	213	OR 0.62 (0.37, 1.05)	
1 [628]	Non-controlled study	40	N/A	2/40 (5%)	
2. Adverse drug withdrawal events (ADWEs)					
Exacerbation/return of underlying condition					
4 [633, 636, 642, 644]	RCTs	106	128	At least one exacerbation/ return of the underlying condition OR 2.62 (1.33, 5.16)	
1 [640]	Non-randomised study	35	22	Exacerbation/ return of the underlying condition OR 21.12 (1.18, 379.52)	
1 [637]	Non-controlled study	6	N/A	Recurrence of the underlying condition of psychosis in people with comorbid dementia and Parkinson's disease while continuing levodopa therapy 83%	
ADWEs					
1 [640]	Non-randomised study	35	22	Withdrawal dyskinesia OR 32.14 (1.67, 617.16)	
1 [628]	Non-controlled study	40	N/A	Mild adverse drug withdrawal effect after abrupt withdrawal 72% • Physical adverse drug withdrawal symptoms (e.g. nausea, emesis, diarrhoea, vertigo, altered appetite, dyskinesia, parageusia) 15% • Psychological adverse drug withdrawal symptoms (e.g. agitation, insomnia, anxiety, hallucinations) 67%	
3. Health outcomes					
Physical function					
1 [630]	RCT	52	54	Activities of daily living (ADL), measured using the Bristol ADL MD -1.60 (-4.68, 1.48)	
1 [641]	Non-randomised study	64	207	Activities of daily living, measured using Lawton's Physical Self-Maintenance Scale. Higher scores indicate greater abilities. MD -0.02 (-0.48, 0.44)	
Clinical Global Impression Scale					
1 [635]	RCTs **(typical antipsychotics and**	35	35	Clinical Global Impression Scale with a higher score indicates more severe illness MD 0.18 (-0.19, 0.55)	

	benzodiazepines)				
Health service use					
1 [634]	Non-controlled study	93	N/A	When considering only participants who had their antipsychotics deprescribed, -10%, p=0.14	
Falls					
1 [640]	Non-randomised study	35	22	Number of participants who fell at least once OR 0.42 (0.13, 1.29)	
1 [634]	Non-controlled study	93	N/A	When considering only participants who had their antipsychotics deprescribed, were mobile and completed the study, there were no significant differences in falls (reduced from 56.3% to 42.4%, p=0.32). The proportion of participants who fell at least once reduced from 54.2% to 44.7% from pre- to post-intervention (p not stated).	
Movement disorders					
1 [630]	RCT	83	83	Extrapyramidal symptoms OR 1.00 (0.54, 1.84) Modified unified Parkinson's disease rating scale (8-point scale) MD 0.00 (-1.33, 1.33)	
2 [640, 641]	Non-randomised studies	99	229	Involuntary movements, measured using the Abnormal Involuntary Movement Scale (AIMS) MD 2.37 (-1.57, 6.31) [641] Dyskinesias, measured using the Dyskinesia Identification System Condensed User Scale (DISCUS) Instrument MD 0.10 (-1.35, 1.55) [640]	
2 [632, 637]	Non-controlled studies	18	N/A	Change in Parkinson's Disease severity (measured using the Unified Parkinson's Disease Rating Scale) 44.5 vs. 43.8; p=0.36 [637] Severity and progression of Parkinson's disease, measured using the Unified Parkinson's Disease Rating Scale (UPDRS) 3.9 ± 2.8 to 2.8 ± 1.6, p not stated [632]	
Behavioural and psychological symptoms					
5 [630, 631, 633, 635, 644]	RCTs	164	155	Deprescribing of antipsychotics was not associated with a significant change in the number of episodes of physically aggressive behaviour in one week (MD -3.23, 95% CI -8.19, 1.73, study = 1, n =36) [633], neuropsychiatric symptoms measured using the Neuropsychiatric Inventory-Nursing Home (MD -1.50, 95% CI -6.13, 3.13, study = 1, n = 82) [631], daytime psychiatric symptoms measured using the Brief Psychiatric Rating Scale (MD -0.20, 95% CI -0.48, 0.08, study = 1, n = 70) [635], or physical aggression measured using the Cohen-Mansfield Agitation Inventory (MD 0.05, 95% CI -0.17, 0.27, study = 1, n = 70) [635]. However, the Neuropsychiatric Inventory score increased significantly in a meta-analysis of three studies (MD 2.61, 95% CI 0.39, 4.84, studies = 3, n = 213), with a higher score indicating more severe symptoms [630, 631, 644].	
1 [641]	Non-randomised study	64	207	Deprescribing of antipsychotics was not associated with a significant change in behavioural problems measured using the Nursing Home Behaviour Problem Scale (MD -1.26, 95% CI -4.08, 1.56) or depression measured using the Geriatric Depression Scale (MD 1.24, 95% CI	

				-1.77, 4.25). However, psychiatric symptoms appeared to be improved when assessed using the Brief Psychiatric Rating Scale (MD -0.36, 95% CI -0.59, -0.13).	
5 [628, 632, 634, 643, 647]	Non-controlled studies	254	N/A	In one study, the mean difference in Neuropsychiatric Index (NPI) score from baseline to endpoint for those who were successfully deprescribed was -5.7 (p = 0.003, n = 31) whereas for those who were not successfully deprescribed, the mean difference was -3.5 (p = 0.345, n = 6) [628]. Similarly, the total NPI-NH score improved by -1.0 points (p=0.58, n = 93) in one study [634], and in another study, it improved from 33.4 ± 23.9 to 32.0 ± 30.9 (n = 12, p not stated) [632]. In contrast, one study reported a slight increase in NPI score from 12.9 ± 12.8 at baseline to 13.8 ± 16.7 at six months (p = 0.124, n = 35) [647]. For each 10 % reduction in the chlorpromazine daily dose equivalent, behavioural and psychological symptoms improved by 0.13 points (p = 0.782, study = 1, n = 83) on a Neuropsychiatric Inventory-Nursing Home version (NPI-NH) scale, agitation/aggression improved by 0.73 points (p = 0.210, study = 1, n = 83) on a total Cohen-Mansfield Agitation Inventory scale, and social withdrawal improved by 0.16 points (p = 0.192, study = 1, n = 83) on a Multidimensional Observation Scale for Elderly Subjects-withdrawal subscale (MOSES-withdrawal subscale) [643]. Similarly, in a study by Brodaty 2018, agitation/aggression improved by 1.7 points (p = 0.37, study = 1, n = 93) on a total Cohen-Mansfield Agitation Inventory scale. However, social withdrawal worsened by 0.27 points (p = 0.52, study = 1, n = 93) on a Multidimensional Observation Scale for Elderly Subjects-withdrawal subscale (MOSES-withdrawal subscale) [634]. In a study by Bergh and Engedel 2008, depression improved after 24 weeks of deprescribing of antipsychotics when assessed using the Cornell score (from 7.6 ± 5.8 to 6.7 ± 6.4, n = 12, p not stated) [632].	
4. Cognitive function					
2 [630, 635]	RCTs	79	75	In a study, deprescribing of either antipsychotics or benzodiazepine (haloperidol, thioridazine, lorazepam) was not associated with a significant change in cognition measured using the standardised Mini-Mental State Examination (MD -0.80, 95% CI -2.47, 0.87), verbal fluency in receptive language (MD -0.20, 95% CI-1.07, 0.67) and expressive language (MD -0.80, 95% CI -1.79, 0.19) measured using the Sheffield Test for Acquired Language Disorders (STALD) as well as Severe Impairment Battery score (MD 2.00, 95% CI -4.81, 8.81) [630]. However, verbal fluency measured using the Verbal Fluency Task deteriorated (MD -3.80, 95% CI -6.91, -0.69) [630]. In another cross-over RCT, deprescribing of antipsychotics was not associated with a significant change in cognition measured using Mini-Mental Status Exam (MD 1.60, 95% CI -0.28, 3.48) [635].	

1 [641]	Non-randomised study	64	207	Cognition, measured using the Mini-Mental State Examination MD 0.04 (-2.09, 2.17) [641]	
2 [632, 634]	Non-controlled studies	105	N/A	Two studies reported contradicting results. In one study, cognition deteriorated by 0.22 points (p = 0.56, n = 93) on the Psychogeriatric Assessment-Cognitive Impairment Scale (PAS-CIS) when not on regular antipsychotics [634]. In another study, cognition improved from 49.9 ± 35.2 to 60.3 ± 19.5 (n = 12, p not stated) when evaluated using the Severe Impairment Battery after 24 weeks [632].	
5. Quality of life (QoL)					
1 [631]	RCT	36	46	Deprescribing of antipsychotics was not associated with a significant change in well-being (MD -0.53, 95% CI -1.42, 0.36) evaluated using the Dementia Care Mapping (DCM) tool.	
1 [643]	Non-controlled study	83	N/A	For each 10 % reduction in the chlorpromazine daily dose equivalent, quality of life deteriorated by 0.01 points (p = 0.124) on an Assessment of Quality of Life-4D (AqoL-4D) utility-scale [643].	

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

Benzodiazepine anxiolytics

Benzodiazepine derivatives used as anxiolytics include alprazolam, bromazepam, clobazam, diazepam*, lorazepam, oxazepam.
*Common PBS medicine

Note: Please refer to the antiepileptics section for benzodiazepine derivatives used as antiepileptics (clonazepam, nitrazepam) and sedative hypnotics section for benzodiazepine derivatives used as sedative hypnotics (flunitrazepam, midazolam, nitrazepam, temazepam).

Type	Recommendation
When to deprescribe	
CBR	Given the risk of dependence and other potential harm (e.g. falls, dependence, sedation) generally outweighs the potential benefits, we suggest deprescribing be offered to older people taking long-term (beyond four weeks) benzodiazepines, except in special circumstances, including but not limited to significant alcohol withdrawal or palliative care.
Ongoing treatment	
CBR	If deprescribing is unsuccessful despite multiple attempts with considerations for non-pharmacological options (e.g. action plan for recurrence of anxiety symptoms), intermittent or “as-required” dosing, we suggest maintaining the lowest effective dose; however, we suggest reassessing the need for long-term therapy periodically.
How to deprescribe	
CBR	We suggest individualising the tapering schedule and adjusting it according to the individual's response. In general, we suggest reducing the dose by 25% to 50% every one to four weeks, ensuring the absence of withdrawal symptoms and/or symptoms indicative of relapse before initiating further tapering. Once half the lowest standard dose formulation is reached, we suggest ceasing completely. However, smaller dose reductions may be appropriate or preferred by some individuals, particularly as lower doses are approached.
GPS	Healthcare providers should consider and offer adequate non-pharmacological management options (e.g. psychological interventions for psychiatric disorders such as cognitive-behavioural therapy and relaxation techniques) during and after deprescribing (ungraded good practice statement).
GPS	Healthcare providers should consider and offer appropriate management strategies to the individual’s families and care providers (e.g. verbal de-escalation, psychological intervention, increased staff-to-patient ratio, increased staff training in behaviour management (ungraded good practice statement).
Monitoring	
CBR	We suggest closely monitoring for changes in anxiety symptoms, changes in psychological or physical health status, and quality of life every one to two weeks following each dose adjustment until at least four weeks after the medicine is fully ceased if practical. After this initial period, we suggest monthly monitoring for at least three months, followed by monitoring every six months thereafter. However, this should be tailored based on individual factors such as their preferences, responses and tolerance to deprescribing. If in-person visits are impractical, we suggest advising people to report symptoms as needed during monitoring.

CBR, consensus-based recommendation; GPS, good practice statement

Note: Benzodiazepines used as anxiolytics will be the focus of this section. Benzodiazepines used for insomnia are discussed in the following section.

Introduction

Benzodiazepines are prescribed for a wide range of conditions, with the choice of benzodiazepines depending on the desired duration of action. Long-acting benzodiazepines, such as diazepam, are used for short-term management of anxiety and agitation, typically in severe or treatment-resistant cases [177]. In contrast, temazepam, with its rapid onset and short half-life, is preferred for short-term treatment of insomnia [177]. Benzodiazepines are also used in managing alcohol withdrawal, mania/hypomania, epilepsy, acute seizures, restless legs syndrome, agitation in inpatient settings, musculoskeletal disorders, and palliative care [177].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

In practice, benzodiazepines are most commonly prescribed for insomnia and anxiety disorders. While they can provide symptom relief, they are not recommended as first-line treatment for anxiety, particularly in older people, due to limited evidence of long-term benefits and a high risk of harm [648]. Prolonged use is associated with physical and psychological dependence, tolerance, and misuse [177]. Older people are particularly vulnerable to adverse effects of benzodiazepines, including oversedation, falls, confusion, impaired memory, and respiratory depression [648]. Despite these risks, long-term benzodiazepine use remains prevalent in older people [649].

Given the risk of potential harm and dependence with long-term use (e.g. beyond four weeks) generally outweigh the benefits, deprescribing should generally be considered in older people [650]. However, there may be special circumstances where the benefits could potentially outweigh the risks (e.g. palliative care, alcohol withdrawal management). If psychological and behavioural interventions are proven ineffective, trial on-demand or intermittent use of benzodiazepines at the lowest effective dose may be considered if appropriate. The limitations of benzodiazepines, potential benefits, and harms should be thoroughly communicated to the patient so they can make an informed decision about their treatment choice.

When benzodiazepine therapy is identified as suitable for deprescribing, the tapering plan should be individualised, ensuring the absence of physical or neuropsychiatric withdrawal symptoms before initiating further tapering. The common general approach to tapering involves approximately reducing the dose by 25% of the original dose every 1 to 4 weeks [627]. A slower taper may be necessary for the final dose reductions or if withdrawal symptoms arise [627]. The Maudsley deprescribing guidelines recommend a hyperbolic tapering strategy for psychotropic medications, including benzodiazepines, to minimize relapse and withdrawal effects [43]. This strategy involves progressively smaller dose reductions at lower doses, which may be preferred by some individuals.

Narrative summary of evidence on deprescribing

We identified 16 studies (five RCTs, two cohort studies, and nine before-and-after studies) related to anxiolytic deprescribing from the systematic review and meta-analysis [635, 643, 651-663].

Overall, the current evidence for benzodiazepine deprescribing is derived from studies of low and very low certainty. While deprescribing was shown to lead to a significant improvement in daily functioning in an RCT and improved memory in a cohort study, these outcomes are low and very low in certainty respectively. Single-arm studies suggest that approximately three to eight people in every ten were able to either reduce the dose or discontinue their benzodiazepine completely. Common withdrawal symptoms were anxiety and insomnia. There is no direct evidence indicating that the duration of withdrawal symptoms varies between the different types of benzodiazepines. Furthermore, the evidence to date is from studies with small sample sizes and generally have serious methodological limitations. The majority of the studies have very short follow-up periods

(one to 12 months) so it may be possible that severe and persistent withdrawal syndromes, if occurred, were not captured. There was also a lack of clear differentiation between withdrawal effects and relapse of the initial condition in many studies. The evidence at this stage is insufficient to inform evidence-based recommendations.

If benzodiazepines are considered appropriate to deprescribe, closely monitoring for any withdrawal symptoms and/or symptoms indicative of relapse, including worsening in anxiety symptoms, changes in psychological or physical health status, and quality of life may be appropriate.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Habraken 1997 randomised 55 nursing residents who had been taking stable doses of benzodiazepines for more than 12 months to discontinuation (n=27) or continuation (n=28). Participants were excluded if they had dementia, serious psychological problems, or had a recent psycho-traumatic experience (e.g. hospitalisation, death of a relative). At 12 months, it was reported that daily functioning (measured using the Geriatrics Behavioural Observational scale) had significantly improved for participants who discontinued benzodiazepines compared to those who continued (MD -7.60, 95% CI -14.28, -0.92). However, there was no significant difference in mortality at 12 months (OR 0.10, 95% CI 0.01 to 1.93).

Cohen Mansfield 1999 reported a double-blind crossover RCT that included 58 nursing home residents who were taking either haloperidol, thioridazine or lorazepam (antipsychotics or benzodiazepines) for agitation [635]. Participants were excluded if they were taking other antipsychotics or anxiolytics concurrently (except for low-dose trazodone hydrochloride for sleep), had uncontrolled blood glucose, or had a diagnosis of major affective disorder of schizophrenia. There were no significant differences between the discontinuation and continuation period in terms of psychiatric symptoms measured using the Brief Psychiatric Rating Scale, global clinical status measured using the Clinical Global Impression Scale, or cognition measured using the Mini-Mental Status Exam.

Navy 2018 reported an RCT that included 346 community-dwelling patients who were taking alprazolam for at least 90 days in the previous 12 months [660]. In this educational outreach study, 153 patients were randomised to receive a deprescribing educational letter (intervention group) and 173 patients received usual care (control group). At month six, there were no significant differences between the two groups in terms of alprazolam discontinued (OR 0.57, 95% CI 0.27, 1.17) or achieved >50% alprazolam dose reduction (OR 1.21, 95% CI 0.58, 2.55).

Gnjidic 2019 randomised 42 inpatients who were prescribed at least one benzodiazepine to a control group (usual care) or an educational intervention where a patient-empowerment booklet was provided (n=20) during hospitalisation [656]. The study revealed a similar proportion of participants had discussed with their doctor or pharmacist about stopping the benzodiazepine (33% in intervention vs 36% in control). Among the 22 participants discharged on benzodiazepine, 6/11 (55%) intervention group participants and 7/11 (64%) control group participants discontinued benzodiazepines one month following discharge (OR 1.46, 95% CI 0.26 to 8.05).

Tannenbaum 2014 conducted a cluster RCT that involved direct-to-consumer education and tapering intervention [662]. The study randomised 303 community-dwelling patients who were taking at least five active medicines (one being a benzodiazepine for at least three consecutive months) to the intervention group (n=148) and control group consisting of usual care (n=155). Participants who had a severe mental illness, or dementia, or who were taking antipsychotics were

excluded. At six months, complete discontinuation was achieved in 40/148 participants (27%) receiving the patient empowerment intervention and a stepwise tapering protocol compared with 7/155 (5%) participants in the control group (OR 0.13, 95% CI 0.06, 0.30).

Salzman 1992 conducted a prospective cohort study that included 25 nursing home residents who were taking benzodiazepines and complained of mild forgetfulness [661]. Participants with moderate-to-severe dementia were excluded. In 13 residents, benzodiazepines were deemed clinically appropriate to deprescribe by the healthcare providers whereas benzodiazepines were continued in 12 residents. Compared to the continuation group, participants who discontinued benzodiazepines had a significant memory improvement (measured using WAIS-R digit span test, MD -1.90, 95% CI -3.40, -0.40) at two to three weeks follow-up. At 12 months, 10 participants were available for follow-up interviews and only 4/10 (40%) restarted on a different benzodiazepine for insomnia, daytime agitation, or behavioural control.

Del Giorno 2018 reported a before-and-after study that involved prescription monitoring, benchmarking, and educational interventions to reduce benzodiazepine prescriptions among internal medicine inpatients [654]. The study revealed a 1.70% reduction in the monthly initiation of new benzodiazepine prescriptions ($p<0.001$) during the 18-month intervention period.

Benzodiazepines were either completely withdrawn or reduced in dose in 35-85% of participants in the following seven single-arm studies [643, 651-653, 655, 658, 659].

Mendes 2018 reported two studies (one retrospective cohort study and one before-and-after study) using a direct-to-consumer educational brochure to reduce the use of benzodiazepines[659]. In the retrospective cohort study, it was reported that participants who received an educational brochure had a higher likelihood of benzodiazepine deprescribing was more likely within 24 months (OR 0.70, 95% CI 0.61 to 0.81). Of the 3,896 veterans who received educational brochures in the before-and-after study, benzodiazepine dose was reduced in 1,847 (47%), tapered and then discontinued in 458 (12%), and discontinued immediately without tapering in 455 (12%). The remaining 607 veterans (15%) had a dose increase and 529 (14%) remained on the same dose.

Da Silva 2022 conducted a before-and-after study that included 35 primary care patients who had been taking clonazepam for at least three months [653]. Following an educational intervention involving the patients and the primary care physicians, of the 27 who were available for follow-up after 10 weeks, 22 (81%) had their dose successfully reduced (n=16) or withdrawn completely (n=6).

Westbury 2018 conducted a before-and-after study using a multi-component intervention to reduce the use of antipsychotics and benzodiazepines in aged care facilities [643]. Participants who were receiving respite or end-stage palliative care and those who were prescribed antipsychotics or benzodiazepines for severe psychiatric disorders were excluded. At six months, 39% who were prescribed antipsychotics or benzodiazepines had their dose either reduced or ceased. There was a significant reduction in the mean diazepam equivalent dose at four months (5.1 ± 5.5 mg to 4.3 ± 6.1, $p<0.001$) and six months (1.4 ± 5.6 mg to 1.1 ± 8.4, $p<0.001$). However, there was no significant change in BPSD, social withdrawal, quality of life, agitation or aggression following the discontinuation of benzodiazepine.

Javelot 2018 reported a before-and-after study that included 31 nursing home residents who were treated with one or more benzodiazepines without the diagnosis of alcoholism and epilepsy [658]. At month six, benzodiazepines were completely withdrawn in 11/31 (35%) residents, and the

mean number of falls per resident was significantly reduced from 2.3 ± 0.6 to 0.5 ± 0.2 (p = 0.01) among these 11 residents.

Fernandes 2022 conducted a before-and-after study that included 66 primary care patients who were using benzodiazepines daily use for at least three months with benzodiazepine dependence [655]. The study reported 38/66 (59%) participants successfully discontinued their benzodiazepine. Of these participants, 31/38 (82%) had at least one withdrawal symptom during deprescribing (most frequently insomnia and anxiety). Of the 39 who had at least an 80% reduction in the initial dose and were available for follow-up at 12 months, 33 (85%) maintained the state.

Chae 2024 reported a before-and-after study that included a patient educational outreach program targeting primary care patients who were prescribed at least one long-term benzodiazepine [652]. Patients with a single prescription for less than 15 tablets were excluded. Among the 25 patients who initiated a deprescribing discussion with their primary care physician, seven (28%) had their benzodiazepine discontinued and nine (36%) had a dose reduction.

Carr 2019 conducted a before-and-after study that included inpatients who were taking one or more regular benzodiazepines on hospital admission [651]. Patients with severe anxiety were excluded, although this was not formally assessed. Of the 11 patients who initiated benzodiazepine deprescribing, 6 (55%) had their benzodiazepines ceased completely, whereas the remaining five patients (45%) had a dose reduction of greater than 50%. Among the 11 patients, six (55%) experienced at least one withdrawal symptom including anxiety and sleep problems.

Allary 2024 reported the long-term effects of benzodiazepine and Z-drugs discontinuation among 45 participants enrolled in a previous RCT with available follow-up data at 12 months [663]. Participants were included in the original RCT if they had taken a benzodiazepine or Z-drug for the past two years and were wanting to stop. Participants were excluded if they were experiencing a crisis (e.g. suicidal ideation), having an alcohol or drug dependence disorder, or other indications for use (e.g. epilepsy). At 12 months after discontinuation, depressive symptoms intensity measured using the Beck Depression Inventory–II reduced with reduced use of benzodiazepine or Z-drug (unstandardised regression coefficient, 0.879, p < .01). However, there was no statistically significant association between the change of benzodiazepine or Z-drug use and worry intensity measured using the Penn State Worry Questionnaire or sleep quality measured using the Pittsburgh Sleep Quality Index.

Narrative evidence summary: withdrawal schedules

Various methods were used for deprescribing in the included studies and tapering was the most common method. While there was no direct evidence that any particular method was associated with the greatest benefits and harms, dose tapering is likely more acceptable than abrupt cessation and helpful in determining the lowest effective dose for some patients requiring dose reduction rather than complete cessation. Deprescribing benzodiazepines can be particularly challenging, especially among long-term users, those taking higher doses or high-potency benzodiazepines due to the risk of withdrawal symptoms. We acknowledge that the duration of successful tapering can vary substantially between individuals. While one single-arm study of a very small sample size (n=64) switched to diazepam (a long-acting benzodiazepine) prior to initiating gradual tapering, the evidence is very low in certainty and therefore, does not support its effectiveness in improving cessation success rates or reducing the incidence and severity of withdrawal symptoms.

Benzodiazepine was reduced by 25% per week for the first three weeks, then 12.5% reduction for the final two weeks (study=1, n=55, low certainty) [657], titrated over 21 weeks (study=1, n=303, low certainty) [662]. In drug-specific studies, alprazolam was tapered based on an individualised alprazolam tapering plan (n=314, very low certainty) [660] whereas lorazepam was tapered over

three weeks before complete withdrawal (n=58, very low certainty) [635]. The method was not described in one study (n=42) [656].

For the two cohort studies (very low certainty), benzodiazepines were gradually tapering over two weeks based on individual response in one study (n=25) whereas in another study (n=2632) benzodiazepines were either tapered for up to 12 weeks or ceased abruptly [659].

In the nine non-controlled trials (all very low certainty), benzodiazepines were gradually tapered in other non-controlled trials, as summarised below, with the method not described in two studies (n=45,715) [643, 654]:

- Individualised (study=1, n=12) [651]
- All benzodiazepines switched to diazepam prior to initiating gradual tapering (study=1, n=64) [655]
- Initial dose reduced by 25% in the first week, then continue reducing over four to ten weeks (study=1, n=31) [658]
- Tapering plan based on previously published clinical guidelines (study=1, n=25) [652]
- Dose reduced by 25% every two weeks (study=1, n=129) [653]
- Either tapered for up to 12 weeks or ceased abruptly (n=3,896) [659]
- Gradual dose reduction for up to 16 weeks (study=1, n=45 very low certainty) [663]

GRADE Summary of Findings (SoF) Table

Table 29. Summary of findings for deprescribing benzodiazepine derivatives used as anxiolytics

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
1 [657]	RCT	27	28	OR 0.10 (0.01 to 1.93)	
2. Adverse drug withdrawal events (ADWEs)					
ADWEs					
2 [651, 655]	Non-controlled studies	77	N/A	At least one withdrawal symptoms: • 6/11 (55%), presented as worsening anxiety symptoms and withdrawal symptoms [651] • 31/66 (47%), presented as insomnia and anxiety [655]	
3. Health outcomes					
Behavioural and psychological symptoms					
1 [635]	RCT **(typical antipsychotics and benzodiazepine)**	35	35	Brief Psychiatric Rating Scale (daytime) where a higher score indicates more severe psychiatrically impairment MD -0.20 (-0.48, 0.08) Physical aggression, measured using the Cohen-Mansfield Agitation Inventory (daytime) where a higher score indicates more pronounced agitation MD 0.05 (-0.17, 0.27)	
1 [643]	Non-controlled study	118	N/A	For each 10 % reduction in the diazepam daily dose equivalent, behavioural and psychological symptoms improved by 0.38 points (p=0.153) on a Neuropsychiatric Inventory-Nursing Home version (NPI-NH) scale, agitation/aggression improved by 0.49 points (p=0.078) on a total Cohen-Mansfield Agitation Inventory scale, and social withdrawal worsened by 0.04 points (p=0.590) on a Multidimensional Observation Scale for Elderly Subjects-withdrawal subscale (MOSES-withdrawal subscale).	

Physical function					
1 [657]	RCT	15	18	Change in daily functioning, measured using the Geriatrics Behavioural Observational Scale where a higher score indicates better functioning MD -7.60 (-14.28, -0.92)	
Clinical Global Impression Scale					
1 [635]	RCT **(typical antipsychotics and benzodiazepine)**	35	35	Clinical Global Impression Scale where a higher score indicates more severe illness MD 0.18 (-0.19, 0.55)	
Falls					
1 [658]	Non-controlled study	11	N/A	Change in the number of falls 2.3 ± 0.6 vs. 0.5 ± 0.2, p = 0.01	
Sleep quality					
1 [663]	Non-controlled study	45	N/A	Unstandardised regression coefficient 0.208 (a non-statistically significant improvement in sleep quality associated with reduced benzodiazepine or Z-drug use[#]	
Depressive symptoms					
1 [663]	Non-controlled study	45	N/A	0.879, p < .01 (Unstandardised regression coefficient, p-value) which translates to reduced depressive symptoms with reduced benzodiazepine or Z-drug use[#]	
Worry intensity					
1 [663]	Non-controlled study	45	N/A	Unstandardised regression coefficient 0.312 (a non-statistically significant improvement in worry intensity associated with reduced benzodiazepine or Z-drug use[#]	
4. Cognitive function					
1 [635]	RCT **(typical antipsychotics and benzodiazepine)**	35	35	Cognition, measured using Mini-Mental Status Exam MD 1.60 (-0.28, 3.48)	
1 [661]	Non-randomised study	13	12	Memory, measured using WAIS-R digit span test MD -1.90 (-3.40, -0.40)	
5. Quality of life (QoL)					
No available evidence					

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

[#]Association between a change in benzodiazepine and Z-drug use and the reported outcome

Benzodiazepine derivatives used as sedative hypnotics include:

- Benzodiazepine derivatives: Flunitrazepam, midazolam, nitrazepam, temazepam*
- Benzodiazepine related drugs: Zopiclone, zolpidem
- Melatonin receptor agonists: Melatonin
- Other hypnotics and sedatives: Suvorexant, lemborexant

*Common PBS medicine

Note: Please refer to the antiepileptics section for benzodiazepine derivatives used as antiepileptics (clonazepam, nitrazepam) and anxiolytics section for benzodiazepine derivatives used as anxiolytics (alprazolam, bromazepam, clobazam, diazepam, lorazepam, oxazepam).

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing be offered to older people taking long-term (beyond four weeks) benzodiazepines for insomnia as the risk of dependence and other potential harm (e.g. falls, fractures, impaired cognition) generally outweighs the potential benefits, except in special circumstances (e.g. palliative care).
Ongoing treatment	
CBR	Given the harms of long-term use are likely to outweigh the benefits in most cases, we generally suggest against the use of long-term benzodiazepines for insomnia in older people and trial on-demand or intermittent use at the lowest effective dose in addition to appropriate investigation to identify and subsequently treat a cause. If symptoms are chronic and persistent, we suggest considering appropriate non-pharmacological therapies and/or safer alternatives for symptoms, provided this aligns with the individual's goals and preferences, following informed consent.
How to deprescribe	
CBR	We suggest individualising the tapering schedule and adjusting it according to the individual's response. In general, we suggest reducing the dose by 25% to 50% every one to four weeks, ensuring the absence of withdrawal symptoms or reduced sleep quality before initiating further tapering. Once half the lowest standard dose formulation is reached, we suggest ceasing completely. However, smaller dose reductions may be appropriate or preferred by some individuals, particularly as lower doses are approached.
GPS	Healthcare providers should consider and offer adequate non-pharmacological management options (e.g. good sleep practices) as appropriate (ungraded good practice statement).
Monitoring	
CBR	We suggest closely monitoring for withdrawal symptoms and/or symptoms indicative of relapse, including worsening sleep quality, changes in psychological or physical health status (e.g. anxiety, and agitation) and quality of life every one to two weeks following each dose adjustment until at least four weeks after the medicine is fully ceased if practical. After this initial period, we suggest monthly monitoring for at least three months, followed by monitoring every six months thereafter. However, this should be tailored based on individual factors such as their preferences, responses and tolerance to deprescribing. If in-person visits are impractical, we suggest advising people to report symptoms as needed.

CBR, consensus-based recommendation; GPS, good practice statement

Introduction

The optimal sleep requirement for older people is approximately the same as for younger people, which is seven to eight hours per night [650]. Sleep disturbances are prevalent in older people and may be exacerbated by common comorbidities such as dementia, depression, anxiety, and chronic pain [664]. When an older person presents with sleep complaints, taking a sleep history and assessing their sleep patterns are crucial, as some may experience a natural shift in sleep schedule, leading to earlier bedtimes and early morning awakenings [665].

Despite the first-line therapy being psychological and behavioural interventions, chronic use of sedative-hypnotics for sleep disruptions is common among older people. Community-dwelling older people are six times more likely than younger people to be prescribed long-term benzodiazepines, with women at higher risk than men [666]. Insomnia is the most frequent indication for benzodiazepines and other sedative-hypnotics in this population [667].

Sleep disruptions, including insomnia, can be distressing for a person and can have important consequences [668]. Longitudinal studies found an association between sleep complaints and depression, falls, cognitive impairment, and compromised physical performance in older people [669-671].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

Sedative-hypnotics, including benzodiazepines, are indicated only for short-term use up to two to four weeks at the lowest effective dose, yet long-term use remains a growing concern [672]. The prevalence of use continues to rise among older people, with the highest increase seen in those aged 85 years and older [673]. Chronic use has been associated with an increased risk of osteoporotic fractures [674], falls, and cognitive impairment [675].

Appropriate non-pharmacological therapies and/or safer alternatives for the management of sleeping complaints should be offered to individuals at all times as pharmacological treatment should not be the sole treatment for insomnia [650].

Given the risk of potential harm and dependence with long-term use (e.g. beyond four weeks) generally outweigh the benefits, deprescribing should generally be considered in older people [650]. However, there may be special circumstances where the benefits could potentially outweigh the risks (e.g. palliative care). If psychological and behavioural interventions are proven ineffective, trial on-demand or intermittent use of sedative hypnotics at the lowest effective dose may be considered if appropriate in addition to appropriate investigation to identify and subsequently treat a cause if symptoms are chronic and persistent. The limitations of sedative hypnotics, potential benefits, and harms should be thoroughly communicated to the patient so they can make an informed decision about their treatment choice.

When deprescribing sedative-hypnotics, the tapering plan should be individualised, ensuring withdrawal symptoms are managed before further dose reductions. A common approach involves reducing the dose by approximately 25% every 1 to 4 weeks [650]. A slower taper may be necessary for final dose reductions or if withdrawal symptoms occur [650]. The Maudsley deprescribing guidelines recommend a hyperbolic tapering strategy for psychotropic medications, including benzodiazepines, to minimise relapse and withdrawal effects [43]. This strategy involves progressively smaller reductions at lower doses, offering a gradual approach that may be preferred by some individuals.

Narrative summary of evidence on deprescribing

We identified 19 studies (six RCTs, two cohort studies and 11 before-and-after studies) related to sedative hypnotic deprescribing from the systematic review and meta-analysis [652, 663, 676-692].

Overall, the current evidence for sedative hypnotic deprescribing is derived from studies with low and very low certainty outcomes. While deprescribing was shown to lead to a significant reduction in the number of hospitalisations and some (not all) sleep measures in RCTs, these outcomes are low and very low in certainty. The evidence to date is from studies with small sample sizes and generally have serious methodological limitations. In many studies, targeted sedative hypnotics also include Z drugs, sedating antihistamines, and certain antidepressants (e.g. mirtazapine). It was challenging to interpret study results considering the substantial differences in efficacy, safety, and risk profiles unique to each drug class. The majority of the studies had a very short follow-up duration (< 12 months) and it may be possible that severe and persistent withdrawal syndromes, if occurred, were not captured. The evidence at this stage remains insufficient to inform evidence-based recommendations.

If sedative hypnotics are considered appropriate to deprescribe, closely monitoring for any withdrawal symptoms and/or symptoms indicative of relapse, including worsening sleep quality, changes in psychological or physical health status (e.g. anxiety, and agitation) and quality of life may be appropriate.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Curran 2003 randomised 104 long-term benzodiazepine users (daily use for at least six months) to immediate tapering (n=45), or to commence tapering after 12 weeks (n=38) [677]. A third group (n=21) who did not wish to discontinue their benzodiazepine served as a control group. All participants were followed for 52 weeks. Participants were excluded if they had dementia, a history of seizures, or current major psychiatric disorders. Other daytime benzodiazepines and psychoactive medicines were permitted during the study. At 12 weeks, mortality was not significantly different between the discontinuation group and control group (OR 0.29, 95% CI 0.01 to 7.32; participants = 104). Similarly, there was no significant difference between the two groups at 12 weeks in terms of ADWEs measured using the Benzodiazepine Withdrawal Scale Questionnaire (BWSQ) (MD 1.50, 95% CI -6.09 to 9.09), depression measured using the Geriatric Depression Scale (MD 0.30, 95% CI -0.85 to 1.45), or quality of life measured using the Short-form 36 (MD 0.00, 95% CI -12.97 to 12.97). Medicine withdrawal was frequently successful (80%), without any adverse effects on sleep (raw data not provided).

Petrovic 2002 randomised 40 inpatients who had been taking benzodiazepines for at least three months to placebo (n=20) or 1 mg lormetazepam (n=20) [683]. After one week, all participants had either the placebo or lormetazepam discontinued. At 30 days, there was no significant difference in the number of participants who had their benzodiazepine completely discontinued between the group with abrupt discontinuation and the group with temporary substitution (OR 0.25, 95% CI 0.06, 1.02). There was also no significant difference between the two groups in the return of underlying symptoms, in this case worsening of sleep (OR 0.21, 95% CI 0.02, 2.08).

Kuntz 2019 randomised 150 people who had two or three Z-drugs prescriptions dispensed in 2016 to receive educational information only (n=50), educational information and pharmacist consultation (n=49), and usual care (n=50) [681]. Participants were excluded if they received less than seven doses of medicines, or were using antipsychotics, cholinesterase inhibitors or memantine. At six months, participants who were provided with evidence-based information about

Z-drugs (with or without a follow-up pharmacist consultation) were significantly more likely to discontinue Z-drugs than those who received usual care (OR 0.28, 95% CI 0.13, 0.59). Additionally, intervention group participants also had a significantly lower number of Z-drugs dispensed (MD -0.90, 95% -1.44, -0.36) and a significantly lower number of hospitalisations following discontinuation of Z-drugs (MD -0.10, 95% CI -0.16, -0.04) but there was no change in the number of emergency department visits (MD 0.00, 95% CI -0.17, 0.17).

Tham 1989 randomised 36 inpatients who had been taking temazepam 10mg at night for at least a month to abrupt discontinuation (n=15) to gradual withdrawal (n=16) [687]. Participants who were randomised to abrupt discontinuation received a placebo for ten nights whereas the other group received temazepam 5mg for the first four nights, then 2 mg for the next four nights, then placebo for the last two nights. There was no significant difference in the mean hours of sleep between the two groups during the ten-night study period (MD 0.00, 95% CI -0.83, 0.83).

Tabloski 1998 randomised 20 women who had been using long-term sedative hypnotics (diphenhydramine, lorazepam, flurazepam, nortriptyline, triazolam) at least five nights a week for at least six months to gradual tapering then complete withdrawal (n=10) or continuation (n=10) [686]. Participants were excluded if they were taking other centrally acting drugs such as antidepressants, antihistamines for allergies, beta-blockers, narcotic drugs, and neuroleptic medicines. After two weeks of complete withdrawal, there was no significant difference between the two groups in the number of wakings (defined as the number of bouts of wakefulness per hour of sleep) (MD 0.30, 95% CI -0.54, 1.14). Control group participants reported significantly longer hours of sleep (MD 1.43, 95% CI 0.88, 1.97) and sleep duration (MD 28.00, 95% CI 14.90, 41.10). However, participants who had discontinued sedative hypnotics reported a significantly shorter sleep latency (MD -13.70 minutes, 95% CI -26.95, -0.45) and wakefulness after sleep onset (MD -28.50, 95% CI -45.60, -11.40).

Fung 2024 included participants who had used lorazepam, alprazolam, clonazepam, temazepam, and/or zolpidem for insomnia at least two nights per week for at least three months [691]. Participants were randomised to either masked taper plus cognitive behavioural therapy (CBT) (n=92) or standard CBT plus unmasked tapering (n=96). Participants in both arms received the deprescribing intervention to have their benzodiazepines discontinued using two different mechanisms for tapering to investigate potential placebo effects with a masked taper strategy. Benzodiazepines were gradually tapered by approximately 25% per week over nine weeks. In some cases, two benzodiazepines were tapered simultaneously. At six months, 116 out of 176 (66%) participants with complete follow-up data had their benzodiazepines discontinued, which translates to 64/87 (74%) in the masked taper group and 52/89 (58%) in the unmasked group. Both groups of participants had an improvement in the severity of insomnia symptoms, measured using the Insomnia Severity Index (lower scores indicate lower severity of insomnia). In the masked taper group, the difference in scores from baseline to 6 months was MD −6.41, 95% CI −7.87, −4.95. In the unmasked taper group, the score difference from baseline to 6 months was MD −6.57, 95% CI −8.00, −5.14. Three participants (2%) had falls that led to discontinuation of the intervention or hospitalisation/emergency department presentation (two participants in the masked taper group and one in the unmasked group).

Gardner 2024 compared two direct-to-patient education interventions (YAWNS-1 and YAWNS-2 packages) with usual care on the use of benzodiazepines and Z-drugs for insomnia in community-dwelling individuals [692]. Individuals were included if they took benzodiazepines and Z-drugs for at least three nights a week for three or more months of insomnia, and were excluded if they resided in a residential care, took other prescription sedatives for insomnia, a score of less than 10 on the mini-Montreal Cognitive Assessment or had any other indications for using benzodiazepines and Z-drugs (e.g. seizure, spasticity related to a spinal injury). We compared intervention group participants (YAWNS-1 or YAWNS-2 combined, n= 378) with usual care (n =

187). At six months, the proportion of participants discontinuing was higher in the intervention groups (YAWNS-1 or YAWNS-2) compared with the usual care group (OR 0.27, 95% CI 0.15, 0.48). However, there was no significant difference in dose reduction at six months between the intervention groups and the control group (OR 0.70, 95% CI 0.42, 1.15). Among participants who stopped their original sedative hypnotics (n=136), there was no significant difference between the intervention groups and the control group in the occurrence of adverse drug withdrawal events (OR 1.58, 95% CI 0.54, 4.66). The most common withdrawal symptoms were insomnia (40/136, 29%), anxiety (12/136, 9%), other mental health effects (4/136, 3%), and physical withdrawal symptoms (7/136, 5%). Withdrawal symptoms lasted for more than four weeks for 13 participants (10%). Withdrawal symptoms were rated as severe in 10 participants (7%).

Allary 2024 reported the long-term effects of benzodiazepine and Z-drugs discontinuation among 45 participants enrolled in a previous RCT with available follow-up data at 12 months [663]. Participants were included in the original RCT if they had taken a benzodiazepine or Z-drug for the past two years and were wanting to stop. Participants were excluded if they were experiencing a crisis (e.g. suicidal ideation), having an alcohol or drug dependence disorder, or other indications for use (e.g. epilepsy). At 12 months after discontinuation, depressive symptoms intensity measured using the Beck Depression Inventory–II reduced with reduced use of benzodiazepine or Z-drug (unstandardised regression coefficient, 0.879, $p < .01$). However, there was no statistically significant association between the change of benzodiazepine or Z-drug use and worry intensity measured using the Penn State Worry Questionnaire or sleep quality measured using the Pittsburgh Sleep Quality Index.

Kosto 2023 reported a cohort study that included inpatients who had been taking benzodiazepines or Z-drugs for insomnia for at least three months [680]. The study compared study quality between patients who received usual care (n=114) and patients who had received explanations and recommendations for deprescribing with (n=55) or without a tapering schedule (n=46). Participants were excluded if they were using the sedative hypnotic as part of the treatment for a psychiatric disorder, had dementia, took more than one sedative hypnotic, or were taking a narcotic drug. After three months, there was no significant change in sleep quality measured using the Pittsburgh Sleep Quality Index (PSQI) between the group who received usual care and the groups who received the educational intervention (MD -3.30, 95% CI -5.09, -1.51).

Puustinen 2014 conducted a cohort study that included 92 primary care patients who had been taking benzodiazepines (temazepam, zopiclone, zolpidem) for at least one month for a primary diagnosis of insomnia [684]. Participants were excluded if they were taking antipsychotics or antiepileptics concurrently, had a history of, active alcohol or drug abuse, severe psychiatric disorder, severe neurological disease, or smoked more than ten cigarettes daily. While their benzodiazepine dose was gradually tapered over four weeks, participants were provided with either melatonin 2 mg (n=46) or placebo (n=46) at night. At six months, among the 89 available for follow-up, 34 (38%) were no longer taking benzodiazepines and 44 (49%) were reduced to on-demand use.

Van der Linden 2023 conducted a before-and-after study that included 173 people admitted to the geriatric ward who were taking regular hypnotics (benzodiazepines and Z-drugs) for insomnia, anxiety or an undefined reason [689]. Participants were excluded if they were using multiple benzodiazepines and Z-drugs or had severe psychiatric or neurological disease. One month after hospital discharge, there was no significant difference between the pre-intervention and post-intervention period in terms of sleep quality measured using PSQI (MD -0.17, 95% CI -1.27, 0.93), delirium (OR 1.14, 95% CI 0.44, 2.96), or the number of participants who fell at least once (OR 0.86, 95% CI 0.31, 2.38).

Chae 2024 reported a before-and-after study that included a patient educational outreach program targeting primary care patients who were prescribed at least one long-term benzodiazepine [652]. Patients with a single prescription for less than 15 tablets were excluded. Among the 25 patients who initiated a deprescribing discussion with their primary care physician, seven (28%) had their benzodiazepine discontinued and nine (36%) had a dose reduction.

Bourgeois 2014 reported a before-and-after study that included 38 nursing home residents who had been using benzodiazepines or Z-drugs daily for at least three months for insomnia [676]. Participants who used benzodiazepine during the day for anxiety, or sedative antidepressants (trazodone, amitriptyline, mirtazapine) were excluded. After two months, 25 residents completely discontinued their benzodiazepines or Z-drugs, seven had a dose reduction, and six restarted the medicine. At month eight, one of the 25 residents restarted the medicine, one resident died, and one additional resident discontinued their benzodiazepines or Z-drugs. Compared to baseline, there was no significant difference in ADWEs measured using BWSQ (3.9 ± 2.8 to 4.1 ± 2.6, p = 0.865) or quality of life measured using EQ-5D (0.439 to 0.456, p = 0.879) after discontinuation.

Fixen 2022 conducted a before-and-after study that included 93 primary care patients who had filled a prescription for a sedative hypnotic (benzodiazepine or nonbenzodiazepine sedative-hypnotic such as zolpidem, zaleplon, eszopiclone) in the past 12 months [678]. Patients were excluded if they had dementia with behavioural symptoms or anxiety disorders but were not prescribed any other medicines for anxiety. All patients received an educational information packet about deprescribing, and their primary care providers received educational intervention from clinical pharmacists. Among the 37 participants who discontinued the medicine, 28 (76%) were prescribed the medicine for symptoms of insomnia. The other indications were anxiety, insomnia and anxiety, muscle spasms, essential tremors, and fear of flying. Anxiety was reported in 7/37 participants (19%) who discontinued the medicine.

Gemelli 2016 reported a before-and-after study that included 36 nursing home residents who had been taking sedative hypnotics (benzodiazepines, Z-drugs, sedating antihistamine, mirtazapine, melatonin, trazodone) for extended durations with a confirmed insomnia diagnosis [679]. Participants were excluded if they had a seizure diagnosis. In the study, pharmacist recommendations to discontinue or taper the sedative hypnotic were accepted by 19/36 (53%) residents.

Lui 2021 conducted a before-and-after study that included 111 primary care patients who had been referred by their physicians to the pharmacist to deprescribe benzodiazepines and/or Z-drugs [682]. In the study, 36 (32%) discontinued their sedative hypnotics and 36 (32%) had a dose reduction of 50% or more. Among the 36 patients who discontinued completely, 26 (72%) remained off the medicines at six months.

Wilson 2018 conducted a before-and-after study that included 50 inpatients who had been taking sedative use (benzodiazepines and Z-drugs) at least weekly in the past month and at least three doses in the week before the hospital admission [690]. All 50 patients received an educational brochure to encourage the conversation about deprescribing with the medical team. At 30 days after hospital discharge, 32/50 (64%) who received the intervention had their sedatives deprescribed.

Ragan 2021 conducted a before-and-after study to reduce sedative hypnotic prescribing in older veterans [685]. The study reported that academic detailing led to a significant reduction in the prescribing of benzodiazepines (-23%, p<0.001) and benzodiazepine receptor agonists (-15%, p<0.001) but an increase in the use of alternative medicines for insomnia (+23%, p<0.001) which included melatonin, trazodone, and mirtazapine.

Tsunoda 2010 conducted a before-and-after study that included 30 nursing home residents who received at least one benzodiazepine hypnotic (brotizolam, flunitrazepam, etizolam, quazepam, estazolam, nitrazepam, flurazepam, diazepam) without a history of substance abuse within the past six months [688]. The included residents had a psychiatric diagnosis of schizophrenia (n=12), primary insomnia (n=9), dementia (n=7), and bipolar disorder (n=2). Four participants dropped out of the study due to insomnia. Among the 26 participants who discontinued their benzodiazepine, there was a significant improvement in the body stability (ability to maintain and control or resist changes in equilibrium) and a recovery in cognitive function during daytime. Body stability was assessed by measuring the range and the total length of the trunk motion by varying the resistance applied, both with eyes open and closed with feet together, with a shorter length indicating better stability.

Narrative evidence summary: withdrawal schedules

Various methods were used for deprescribing in the included studies and tapering was the most common method. While there was no direct evidence that any particular method was associated with the greatest benefits and harms, dose tapering is likely more acceptable than abrupt cessation and helpful in determining the lowest effective dose for some people requiring dose reduction rather than complete cessation.

In an RCT, Z-drug discontinuation was personalised based on a telephone consultation with a pharmacist (n=149, low certainty) [681]. In other RCTs, the dose titration regimen was individualised based on the original dose and benzodiazepine to minimise the risk of withdrawal (study=1, n=138, low certainty) [677], the dose for sedative hypnotics was halved every week until completely ceased (study=1, n=20, very low certainty) [686]. A study targeted benzodiazepines compared abrupt discontinuation to titration for a week using 1mg lormetazepam, which was less than half the average daily benzodiazepine dose (n=40, very low certainty) [683]. No significant difference in outcome was reported in the study. Similarly, in a study targeted temazepam, abrupt discontinuation was compared with gradual withdrawal over ten days and no significant difference in outcome was reported (study=1, n=36, very low certainty) [687]. The method was not described in one RCT (n=565, very low certainty) [692].

In the two cohort studies, the study that targeted both benzodiazepines and Z-drugs stated a drug-specific tapering schedule was followed (n=215, very low certainty) [680] whereas another study that targeted only benzodiazepines stated benzodiazepines were gradually withdrawn over four weeks and supplemented either melatonin 2 mg or placebo (n=89) [684]. The latter study did not report any critical or important outcomes. In another before-and-after study, tapering was either based on a standardised tapering regimen, abrupt discontinuation, or “any attempt” (study=1, n=173, very low certainty) [689].

In the single-arm before-and-after studies, withdrawal schedules were summarised below, with the method not described in three studies (n=357, n unstated in one study) [678, 685, 690]:

- 25% reduction either every one or two weeks (study=1, n=38, very low certainty) [676]
- Weekly reduction of 25% of the regular daily dose from baseline each week for three weeks (study=1, n=30, very low certainty) [688]
- Gradual dose reduction (studies=2, n=249, very low certainty) [663, 691]

The following single-arm before-and-after studies did not report any critical or important outcomes:

- Individualised (study=1, n=111) [682]
- Gradual dose reductions or abrupt discontinuation (study=1, n=36) [679]
- Tapering plan based on previously published clinical guidelines (study=1, n=25) [652]

GRADE Summary of Findings (SoF) Table

Table 30. Summary of findings for deprescribing hypnotics and sedatives

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
1 [677]	RCT	55	49	OR 0.29 (0.01 to 7.32)	
1 [676]	Non-controlled study	38	N/A	This study investigated the deprescribing of benzodiazepines and Z-drugs (most commonly lormetazepam and lorazepam). Death at eight months was 1/38 (3%).	
2. Adverse drug withdrawal events (ADWEs)					
ADWEs					
3 [677, 683, 692]	RCTs	453	256	There was no significant association between the deprescribing of sedative hypnotics and the number of participants who experienced at least one exacerbation (OR 0.21, 95% CI 0.02. 2.08) [683], ADWEs (OR 1.58, 95% CI 0.54, 4.66) [692], or ADWEs measured using the Benzodiazepine Withdrawal Symptom Questionnaire (BWSQ) (MD 1.50, 95% CI -6.09, 9.09) [677].	
5 [663, 676, 678, 688, 691]	Non-controlled studies	281	N/A	In one study, the Benzodiazepine Withdrawal Symptom Questionnaire score increased non-significantly from 3.9 ± 2.8 to 4.1 ± 2.6, p = 0.865 after discontinuation, with higher scores indicating more withdrawal symptoms and the maximum score is 40 [676]. Fixen 2022 investigated deprescribing of benzodiazepines or non-benzodiazepine sedative hypnotics. Among the 37 participants who discontinued the medication, 76% were prescribed the medication for symptoms of insomnia. The other indications were anxiety, insomnia and anxiety, muscle spasms, essential tremors, and fear of flying. Adverse drug withdrawal events, specifically anxiety were reported by 7 out of 37 participants who discontinued the medication (19%) [678]. Recurrence of the underlying condition, specifically insomnia occurred in 4 out of 30 (13%) participants [688]. Insomnia Severity Index, with lower scores indicate lower severity of insomnia [691] • Masked taper group: Difference from baseline to 6 months, −6.41, 95% CI −7.87 to −4.95 (P < .001) • Unmasked taper group: Difference from baseline to 6 months, −6.57, 95%CI −8.00 to −5.14 (P < .001) [691] Unstandardised regression coefficient 0.208 (a non-statistically significant improvement in sleep quality associated with reduced benzodiazepine or Z-drug use#	

3. Health outcomes					
Health service use					
1 [693]	RCT	99	50	Deprescribing led to a significant reduction in the number of hospitalisations per participant in the intervention group (MD -0.10, 95% CI -0.16, -0.04) but there was no change in the rate of emergency room presentation (MD 0.00, 95% CI -0.17, 0.17).	
Sleep					
2 [686, 687]	RCT	46	41	Deprescribing of sedative hypnotics (diphenhydramine, lorazepam, flurazepam, nortriptyline, triazolam) was not associated with a significant difference in the number of wakes (MD 0.30, 95% CI -0.54, 1.14) [686]. The intervention group had a significantly reduced sleep latency (MD -13.70 minutes, 95% CI -26.95, -0.45), and reduced wakefulness after sleep onset (MD -28.50, 95% CI -45.60, -11.40). Control group participants reported longer total sleep time in hours (MD 1.43, 95% CI 0.88, 1.97) and sleep duration (MD 28.00, 95% CI 14.90, 41.10) [686]. Deprescribing of temazepam was not associated with a significant change in the total sleep time in hours (MD 0.00, 95% CI -0.83, 0.83) [687].	
2 [680, 689]	Non-randomised study	132	210	Change in Pittsburgh Sleep Quality Index MD -1.65 (-4.72, 1.41)	
Behavioural and psychological symptoms					
1 [677]	RCT	48	43	Depression, measured using the Geriatric Depression Scale MD 0.30 (-0.85, 1.45)	
Body stability					
1 [688]	Non-controlled study	26	N/A	Change from baseline to endpoint • Total length of the trunk motion with eyes closed, -1.5cm, p=0.002 • Range of the trunk motion with both eyes open, -0.02cm, p=0.046 • Range of the trunk motion with both eyes closed, -1.51cm, p=0.01	
Falls					
1 [689]	Non-randomised study	77	96	OR 0.86 (0.31, 2.38)	
1 [691]	Non-controlled study	176	N/A	Falls that led to the discontinuation of the intervention or hospitalisation/emergency department presentation 3/176 (2%) [691]	
Delirium					
1 [689]	Non-randomised study	77	96	OR 1.14 (0.44, 2.96)	
Depressive symptoms					
1 [663]	Non-controlled study	45	N/A	0.879, p < .01 (Unstandardised regression coefficient, p-value) which translates to reduced depressive symptoms with reduced benzodiazepine or Z-drug use#	
Worry intensity					
1 [663]	Non-controlled study	45	N/A	Unstandardised regression coefficient 0.312 (a non-statistically significant improvement in worry intensity associated with reduced benzodiazepine or Z-drug use#	

4. Cognitive function					
1 [688]	Non-controlled study	26	N/A	Cognitive function (Repeatable Battery for the Assessment of Neuropsychological Status score where a higher score indicates a better cognitive function) • Immediate memory, +10.3, p<0.001 • Visuospatial, +6.1, p=0.036 • Language, +5.2, p=0.007 • Attention, +13.8, p<0.001 • Delayed memory, +7.8, p=0.015 • Total scale index score, +8.8, p<0.001 Central fatigue (measured using the critical flicker fusion test where a lower score is associated with higher levels of central fatigue), +2.1, p<0.001	
5. Quality of life (QoL)					
1 [677]	RCT	48	43	Quality of life, measured using the Short Form-36 MD 0.00 (-12.97, 12.97)	
1 [676]	Non-controlled study	38	N/A	Quality of life measured with the EuroQol-5D increased non-significantly from 0.439 to 0.456, p = 0.879 after discontinuation, with higher scores indicating better health.	

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

#Association between a change in benzodiazepine and Z-drug use and the reported outcome

Antidepressants

Antidepressants include:

- Non-selective monoamine oxidase inhibitors (tricyclic antidepressants): Amitriptyline*, clomipramine, dosulepin, doxepin, imipramine, nortriptyline
- Selective serotonin reuptake inhibitors, SSRIs: Citalopram*, escitalopram*, fluoxetine, fluvoxamine, paroxetine, sertraline*
- Serotonin and norepinephrine reuptake inhibitors, SNRIs: Desvenlafaxine*, duloxetine*, venlafaxine*
- Monoamine oxidase inhibitors, non-selective: Phenelzine, tranylcypromine
- Monoamine oxidase A inhibitors: Moclobemide
- Other antidepressants: Agomelatine, mianserin, mirtazapine*, reboxetine, vortioxetine

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing be offered to older people taking antidepressants for major depressive disorder: 1. Who have achieved symptomatic remission or clinical stability for 6 to 12 months with uninterrupted treatment after appropriate assessment; or 2. When the indication for continued use is unclear or unknown (e.g. no benefit has been derived).
Ongoing treatment	
CBR	If deprescribing is unsuccessful despite multiple attempts, taking into account the possibility of withdrawal effects rather than recurrence of symptoms, we suggest maintaining the lowest effective dose; however, we suggest reassessing the need for long-term therapy periodically.
How to deprescribe	
CBR	We suggest individualising the tapering schedule and adjusting it according to the individual's response. In general, we suggest reducing the dose by 25% to 50% every one to four weeks (taking into consideration the half-life of the antidepressant), ensuring the absence of physical or neuropsychiatric withdrawal symptoms before initiating further tapering. Once half the lowest standard dose formulation is reached for another one to four weeks, we suggest ceasing completely if no sign of reoccurrence of symptoms. However, smaller dose reductions may be appropriate or preferred by some individuals, particularly as lower doses are approached.
GPS	Healthcare providers should consider and offer adequate non-pharmacological management options (e.g. psychological interventions for psychiatric disorders such as cognitive-behavioural therapy) to individuals and their families or carers as appropriate (ungraded good practice statement).
Monitoring	
CBR	We suggest closely monitoring for worsening neuropsychiatric symptoms (e.g. increased anxiety, agitation, depressive symptoms) and cognition which could be short-lived or protracted, severe or mild, in addition to monitoring changes in psychological or physical health status, and quality of life every one to two weeks following each dose adjustment until at least four weeks after the medicine is fully ceased if practical (recognising the possibility of withdrawal effects rather than recurrence of symptoms). After this initial period, we suggest monthly monitoring for at least three months, followed by monitoring every six months thereafter. However, this should be tailored based on individual factors such as their preferences, responses and tolerance to deprescribing.

	If in-person visits are impractical, we suggest advising people to report symptoms as needed.

CBR, consensus-based recommendation; GPS, good practice statement

Introduction

Clinical depression is common in older people and should not be mistaken as a normal part of ageing. Poor mental health is particularly prevalent among those in residential aged care, where 87% have at least one mental health or behavioural condition, and 49% are diagnosed with mood disorders, including depression [50]. Psychotherapies such as Cognitive Behavioural Therapy (CBT) are effective in reducing depressive symptoms in older adults [694].

When antidepressant therapy is indicated, SSRIs and SNRIs are generally preferred in older people due to their lower risk of adverse effects and relative safety in overdose compared to tricyclic antidepressants (TCAs) [695]. However, all antidepressants have potential risks, including hyponatremia, falls, and gastrointestinal bleeding [177]. The optimal duration of therapy and the criteria for discontinuation remain unclear in the literature [696].

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

A systematic review and meta-analysis examined the risk of relapse after discontinuing antidepressants in individuals with major depressive disorder who had achieved remission [697]. The participants in the meta-analysis had a mean age of 43 years (n = 8,890), younger than the target population for this guideline. Those who continued antidepressants for six months had a significantly lower relapse rate compared to those who switched to a placebo. Similarly, a pooled analysis of 45 RCTs found that relapse risk was minimal when antidepressants were continued for at least four to six months after stabilisation [698]. These findings support maintaining antidepressant therapy for at least six months following remission, aligning with the 2023 Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines, which recommend continuing antidepressants for six to 12 months post-remission to prevent recurrence [699].

In people who have achieved symptomatic remission or clinical stability for six to 12 months with uninterrupted treatment after appropriate assessment, offering to attempt deprescribing may be appropriate. Besides, in people where no benefit has been derived from antidepressants, deprescribing should be considered given the unfavourable benefit-risk profile.

Long-term antidepressant use should be regularly reassessed, particularly when initiated for behavioural and psychological symptoms of dementia (BPSD). Ongoing monitoring should consider the indication, effectiveness, tolerability, and iatrogenic risks [50].

When deprescribing antidepressants, the tapering plan should be individualised to minimise withdrawal symptoms and the risk of relapse. A general approach involves reducing the dose by approximately 25% every one to four weeks, with a slower taper for final dose reductions or if discontinuation symptoms arise [627]. Slower tapering could be an appropriate suggestion, especially for people at risk of withdrawal symptoms while tapering (e.g. those who have previously experienced withdrawal symptoms when they have missed a dose), if problematic discontinuation symptoms occur, or when approaching the final dose reduction [627, 700]. In practice, the tapering approach will also depend on the half-life of the antidepressant and its metabolism. Antidepressants with long half-life (e.g. fluoxetine) can be discontinued by staggering the days of use, whereas those with shorter half-life may require more judicious daily dose reduction [701].

The 2024 Maudsley deprescribing guidelines recommend a non-linear, hyperbolic tapering strategy for psychotropic medications, including antidepressants, to minimise the risk of relapse and withdrawal symptoms [43]. This approach involves progressively smaller reductions at lower doses and is based on recent findings of the relationship between the dose and the serotonin receptor occupancy [702]. For example, a suggested tapering schedule for citalopram (20 mg, 9.1 mg, 5.4 mg, 3.4 mg, 2.3 mg, 1.5 mg, 0.8 mg, 0.4 mg) approximates 10% reductions in serotonin receptor occupancy with each citalopram dose reduction. The hyperbolic tapering strategy offers a gradual approach that may be preferred by some individuals. Implementing a slower or hyperbolic tapering regimen may require access to liquid formulations or compounded preparations to achieve the small, precise dose reductions necessary. While these considerations are important for individualised care and may reflect patient preferences, they may also present practical challenges in some settings. Notably, no studies were identified that directly evaluated the impact of these formulation requirements on the feasibility or uptake of antidepressant tapering strategies.

At the time of this guideline's development, the reporting of the RELEASE (REdressing Long-tErm Antidepressant uSE in general practice) trial is ongoing [703]. This study evaluates the effectiveness of multi-strategy interventions for the safe discontinuation of long-term antidepressants. It is likely that future guideline recommendations will evolve as new evidence emerges.

Narrative summary of evidence on deprescribing

From the systematic review and meta-analysis, we identified four studies related to SSRI deprescribing (two RCTs, two before-and-after studies), one before-and-after study related to deprescribing nortriptyline/phenelzine (with or without adjunctive lithium) and two studies related to deprescribing lithium augmentation for depression (one RCT, one case-control study) [632, 704-709].

Overall, the current evidence for antidepressant deprescribing is derived from studies of low and very low certainty. While deprescribing was shown to lead to a significant deterioration in neuropsychiatric symptoms in an RCT, this outcome is of very low certainty. The evidence to date is derived from studies of small sample sizes and generally have serious methodological limitations. The studies targeting SSRIs were all conducted in nursing home settings and had a very short follow-up duration (6-12 months). It may be possible that severe and persistent withdrawal syndromes, if occurred, were not captured. It was uncertain whether the reported outcomes were applicable to other settings. There was also a lack of clear differentiation between withdrawal effects and relapse of the initial condition in many studies. The evidence at this stage remains insufficient to inform evidence-based recommendations.

If antidepressants are considered appropriate to deprescribe, closely monitoring for any worsening of neuropsychiatric symptoms (e.g. increased anxiety, agitation, or depressive symptoms), as well as changes in psychological or physical health, quality of life, and cognitive function may be appropriate. It is also important to recognise that withdrawal effects from some antidepressants can be severe and, in some cases, protracted [43]. Withdrawal effects should be distinguished from a recurrence of the underlying depressive symptoms to minimise unnecessary reinitiation of antidepressants.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Bergh 2012 conducted a double-blind RCT that randomised 128 nursing home residents to discontinuation (n=63) or continuation (n=65) [704]. Residents were included if they had been

taking either escitalopram, citalopram, sertraline, or paroxetine for at least three months, or had Alzheimer's disease, dementia or vascular dementia, and neuropsychiatric symptoms. They were excluded if they had a history of a depressive disorder or schizophrenia. Among the 81 participants who completed the 25-week follow-up (35 intervention, 46 control), discontinuation of antidepressants was not associated with a significant deterioration in the Cornell scale of depression in dementia (MD 1.61, 95% CI −0.39, 3.61). There was no significant difference between the two groups in terms of mortality, body weight, number of falls, self-care ability, physical function measured using the Unified Parkinson's Disease Rating Scale, cognition measured using the Severe Impairment Battery, quality of life measured using the Qualify of Life in Alzheimer's Disease scale, the amount of rescue medicine used (measured in oxazepam mg/day over 21 days), or the total number of psychotropic medicines used by participants. However, neuropsychiatric symptoms measured using NPI were more pronounced in the intervention group than in the control group (MD 7.80, 95% CI 1.10 to 14.50).

Ulfvarson 2003 randomised 70 nursing home residents to discontinuation (n=35) or continuation (n=35) [709]. Residents were included if they had been taking an SSRI (sertraline, citalopram) for at least six months without any documented indication or symptoms of depression or anxiety disorder. Additionally, they had to score 12 or less on the Montgomery-Asberg Depression Rating Scale score to be included. Residents with dementia or a history of depression were excluded. Among the 52 participants who completed six months of follow-up, there were no significant differences between the two groups in terms of mortality, depressive symptoms measured using the Montgomery-Asberg Depression Rating Scale (MADRS), functioning measured using the global assessment of functioning, symptoms of depression and side effects to SSRIs (on a 0-100 point scale, where a higher score indicates greater side effects of depression or SSRIs), or symptoms of common side effects to sertraline and citalopram (on a 0-52 point scale, where a higher score indicates worse symptoms). Quality of life measured using the Health Index was significantly lower in the intervention group than in the control group (MD 1.72, 95% CI 0.11 to 3.33).

Lindström 2007 conducted a before-and-after study that included 119 nursing home residents who had been taking SSRIs for at least 12 months [708]. Residents were excluded if they were using SSRIs for indications other than depression there was a long-term indication, current depressive symptoms, or they had two or more episodes of depression in the past two years. Deprescribing was successful in 63/119 (53%) participants and was reported to be more likely in residents with a low to moderate MADRS score (0-19) prior to deprescribing.

Bergh and Engedal 2008 conducted a before-and-after study that included 23 nursing home residents with Alzheimer's disease or vascular dementia who had been taking antidepressants or antipsychotics for three months or longer [632]. Deprescribing was implemented for antidepressants (n=11) or antipsychotics (n=12). Participants were excluded if they had a severe psychiatric disorder or diabetes mellitus. At 24 weeks, discontinuation of antidepressants was associated with non-statistically significant improvement in BPSD measured using the Neuropsychiatric Inventory (29.2 ± 20.2 to 17.3 ± 21.4), depression measured using Cornell's Depression Scale (6.9 ± 4.5 to 3.3 ± 3.4) and movement disorders measured using the Unified Parkinson Disease Rating Scale (6.4 ± 4.2 to 4.5 ± 3.4). However, cognition, measured using the Severe Impairment Battery, appeared to deteriorate after antidepressant withdrawal (50.1 ± 22.5 to 28.0 ± 20.3).

Flint 1999 conducted a before-and-after study that included 21 patients who were taking nortriptyline (with or without adjunctive lithium) or phenelzine and had not experienced a relapse or depression recurrence for the past two years [706]. Patients with a concurrent axis I diagnosis, history of schizophrenia, schizoaffective disorder, paranoid disorder, dementia, or any neurological disorder were excluded. Deprescribing was successful in 9/21 (43%) participants. Of

the 12 participants who had depression recurrence, 11 (92%) restarted their antidepressants. Reintroduction of antidepressants alone led to improvements for 10/11 participants (91%) who responded in a mean (SD) of 4.5 ± 1.8 weeks.

The following two studies reported deprescribing lithium augmentation therapy for major depressive episodes (with or without psychotic features).

Fahy 2001 reported a case-control study that included 21 patients who were on lithium augmentation but subsequently discontinued [705]. Antidepressant medicines were continued during the observation period. The study reported that 11/21 (52%) had a recurrence of depression, of whom 9/11 (82%) had responded to the reintroduction of lithium and 2/11 (18%) responded to another antidepressant.

Hardy 1997 randomised 12 older people with unipolar depression to receive continued lithium augmentation (n=6) or matching placebo (n=6) [707]. Participants were included if they had not experienced depressive symptoms for at least 12 months while on a stable dose of lithium augmentation, scored <20 on Geriatric Depression Rating Scale and scored <15 on MADRS. Participants were excluded if they had dementia or suicidal tendencies. There was no significant difference between the two groups in terms of depression recurrence (OR 1.00, 95% CI 0.09, 11.03) and thyroid stimulating hormone levels (MD 0.56, 95% CI -0.08, 1.20). Among the six participants who received a placebo, two (33%) reported a recurrence of depression at seven and 92 weeks respectively, without any apparent changes in life stresses and were relatively resistant to reinstitution of lithium augmentation therapy. Comparatively, 2/6 participants (33%) who continued lithium augmentation also reported a recurrence of depression immediately after a stressful life event at 46 and 61 weeks respectively. Control group participants who continued to receive lithium over the two years appeared to have a significantly higher serum creatinine level compared to participants who received a placebo (MD 13.30, 95% CI 0.47, 26.13).

Narrative evidence summary: withdrawal schedules

Various methods were used for deprescribing in the included studies and tapering was the most common method. While there was no direct evidence that any particular method was associated with the greatest benefits and harms, dose tapering is likely more acceptable than abrupt cessation and helpful in determining the lowest effective dose for some patients requiring dose reduction rather than complete cessation.

In the two RCTs targeting SSRIs, the dose was halved for a few days before complete withdrawal (n=70, very low certainty evidence) [709] whereas the method was not described in the other RCT (n=128, very low certainty evidence) [704]. In the two before-and-after studies targeting SSRIs, the dose was tapered gradually over six to eight weeks before complete withdrawal (n=119, did not report critical/important outcomes) [708] whereas in another study dose was tapered over one week (n=11, very low certainty evidence) [632]. Nortriptyline and phenelzine were tapered over eight weeks (n=21, very low certainty evidence) [706].

In the RCT targeting lithium augmentation, the dose was reduced by 150 mg daily each week until completely replaced with a matching placebo (n=12, low certainty evidence) [707]. In the case-control study, lithium augmentation was tapered gradually over a period of two to 12 weeks (n=21, very low certainty evidence) [705].

GRADE Summary of Findings (SoF) Table

Table 31. Summary of findings for deprescribing antidepressants

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
2 [704, 709]	RCTs (SSRIs)	98	100	OR 1.13 (0.47, 2.69)	
2. Adverse drug withdrawal events (ADWEs)					
ADWEs					
2 [704, 709]	RCTs (SSRIs)	56	73	Deprescribing of selective serotonin reuptake inhibitors (SSRIs) was not associated with a significant change in the severity of depression measured using Cornell Scale for Depression in Dementia (MD 1.61, 95% CI -0.39, 3.61) [704] or Montgomery-Asberg depression rating scale (MD -0.80, 95% CI -2.87, 1.27) [709].	
1 [707]	RCT (Lithium augmentation)	6	6	OR 1.00 (0.09, 11.03)	
2 [632, 706]	Non-controlled studies	32	N/A	Recurrence of major depression was reported in 12 out of 21 participants (57%). Eleven participants agreed to restart their antidepressant and 10 out of them (92%) responded to reintroduction of the antidepressant. The average time taken to respond to the re-introduction of antidepressants was 4.5 ± 1.8 weeks [706]. In another study, the severity of depression reduced after 24 weeks of antidepressant discontinuation when measured using Cornell's depression scale (from 6.9 ± 4.5 to 3.3 ± 3.4) [632].	
Exacerbation/return of underlying condition					
1 [705]	Non-controlled study (Lithium augmentation)	21	NA	11/21 (52.4%) relapsed	
3. Health outcomes					
Adverse drug events					
1 [709]	RCT (SSRIs)	25	27	Deprescribing of SSRIs was not associated with a significant change in the side effects of SSRIs (MD 3.13, 95% CI -0.33, 6.59), or symptoms of side effects of SSRI drug treatments (on a 0–52 point scale) (MD 1.40, 95% CI -0.55, 3.34).	
Movement disorders					
1 [704]	RCT (SSRIs)	35	46	Severity and progression of Parkinson's disease, measured using the Unified Parkinson's Disease Rating Scale (UPDRS) MD -0.13 (-1.70, 1.44)	
1 [632]	Non-controlled study (SSRIs)	11	N/A	The severity of movement disorders reduced after 24 weeks of antidepressant discontinuation when measured using the Unified Parkinson's Disease Rating Scale (6.4 ± 4.2 to 4.5 ± 3.4; non-statistically significant).	
Falls					

1 [704]	RCT (SSRIs)	35	45	Change in the number of falls per day MD 0.00 (-0.01, 0.01)	
Physical function					
2 [704, 709]	RCTs (SSRIs)	45	58	Lawton and Brody's physical self-maintenance scale MD -0.35 (-2.77, 2.07) [704] Global assessment of functioning MD -3.42 (-7.74, 0.90) [709]	
Behavioural and psychological symptoms					
1 [704]	RCT (SSRIs)	35	46	Neuropsychiatric inventory, total score MD 7.80 (1.10, 14.50)	
1 [632]	Non-controlled study (SSRIs)	11	N/A	Neuropsychiatric inventory 29.2 ± 20.2 to 17.3 ± 21.4; non-statistically significant	
4. Cognitive function					
1 [704]	RCT (SSRIs)	23	37	Cognition, measured using the Severe Impairment Battery (higher scores indicating less impairment) MD -5.38 (-19.35, 8.59)	
1 [632]	Non-controlled study (SSRIs)	11	N/A	Cognition deteriorated after 24 weeks of antidepressant discontinuation when measured using the Severe Impairment Battery (from 50.1 ± 22.5 to 28.0 ± 20.3; non-statistically significant).	
5. Quality of life (QoL)					
2 [704, 709]	RCTs (SSRIs)	45	58	When using the Health Index as a measure, control group participants who continued using their selective serotonin reuptake inhibitors (SSRIs) reported improved health-related quality of life at six months whereas intervention group participants reported a deterioration (MD 1.72, 95% CI 0.11, 3.33) [709]. In another study that used the quality of life-Alzheimer's disease scale, deprescribing was not associated with a significant change when it was rated by the carer (MD -0.78, 95% CI -3.42, 1.86) or the patient (MD 3.07, 95% CI -0.50, 6.64) [704] at six months.	

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

Anti-dementia medicines

Anti-dementia medicines include:

- Cholinesterase inhibitors: Donepezil*, galantamine, rivastigmine
- Other medicines: Memantine

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing be offered to older people taking cholinesterase inhibitors for the cognitive symptoms of dementia: • For dementias other than Alzheimer's disease, dementia of Parkinson's disease, Lewy body dementia, or vascular dementia, due to limited evidence for efficacy; • For Alzheimer's disease, mixed dementia, dementia of Parkinson's disease, Lewy body dementia, or vascular dementia, if treatment has continued for more than 12 months without clear benefit or if dementia has progressed to the late stage; or • In the presence of significant side effects that impact their quality of life.
Ongoing treatment	
CBR	If deprescribing is unsuccessful despite multiple attempts, we suggest maintaining the lowest effective dose; however, we suggest reassessing the need for long-term therapy periodically.
How to deprescribe	
CBR	We suggest individualising the tapering schedule and adjusting it according to the individual's response. In general, we suggest halving the daily dose every four weeks, ensuring the absence of withdrawal symptoms or worsening of global, cognitive, functional, or neuropsychiatric outcomes before initiating further tapering. Once half the lowest standard dose formulation is reached, we suggest ceasing completely.
CBR	For people on combination therapy of cholinesterase inhibitors and medicines with anticholinergic properties, we suggest first considering the deprescribing of anticholinergics due to the potential adverse effects on cognitive function. Tapering of anticholinergics can generally follow the same approach as cholinesterase inhibitors tapering; however, we suggest individualising the tapering schedule and adjusting it as needed according to the individual's response. The dose for concomitant cholinesterase inhibitors may also need to be adjusted due to the reduction in opposing mechanisms of action following the dose reduction of anticholinergics.
GPS	Healthcare providers should consider and offer adequate non-pharmacological management options to individuals and their families, care providers(e.g. verbal de-escalation, psychological intervention, engaging individuals in meaningful activities, increased staff-to-patient ratio, increased staff training in behaviour management) as appropriate to manage challenging behaviours in dementia (ungraded good practice statement).
Monitoring	
CBR	We suggest closely monitoring individuals for withdrawal symptoms or symptoms of disease exacerbation (e.g. worsening neuropsychiatric symptoms including agitation and apathy, cognitive decline, worsening behavioural symptoms, reduced ability in activities of daily living) every one to two weeks following each dose adjustment until at least four weeks after the medicine is fully ceased if practical. After this initial period, we suggest monthly monitoring for at least three months, followed by monitoring every six months thereafter. However, this should be tailored based on individual factors such as their preferences, responses and tolerance to deprescribing.

	If in-person visits are impractical, we suggest advising people to report symptoms and/or any appearance of new symptoms as needed.
GPS	Healthcare providers should provide clear guidance to care providers on recognising withdrawal symptoms and symptoms of disease exacerbation, enabling them to seek timely medical advice (ungraded good practice statement).
GPS	Healthcare providers should use validated assessment tools to evaluate changes in cognitive function, neuropsychiatric symptoms, functional status, and quality of life (e.g. Psychogeriatric Assessment Scales for cognitive function, Neuropsychiatric Inventory for neuropsychiatric symptoms, Functional Status Questionnaire for functional status, and EQ-5D for health-related quality of life) (ungraded good practice statement).

CBR, consensus-based recommendation; GPS, good practice statement

Introduction

The Australian Institute of Health and Welfare reported a 24% increase in the prescription rates of dementia-specific medications for Australians aged 30 and over from 2013-2014 to 2022-2024, with a greater increase in men than women [710].

Cholinesterase inhibitors and memantine are symptomatic treatments for dementia, with current evidence suggesting their efficacy is modest and unlikely to modify disease progression [711]. The continuation of treatment with these anti-dementia medicines should be based on a demonstrable, clinically meaningful response, such as improvements in quality of life, cognitive function, and/or behavioural symptoms [710].

A systematic review that included two RCTs focusing on cholinesterase inhibitors pharmacotherapy for Alzheimer's disease found modest but significant cognitive improvements in individuals with moderate to severe functional impairments who received cholinesterase inhibitors and these medicines were generally well tolerated [712]. However, the efficacy of long-term cholinesterase inhibitors beyond 12 months remains uncertain. Cholinesterase inhibitors may cause side effects, which older people are particularly susceptible to. Common side effects include dizziness, drowsiness, depression, sleep disturbances (e.g. insomnia, vivid dreams), and gastrointestinal issues (e.g. diarrhoea, anorexia, abdominal pain, dyspepsia) [601]. It is essential to assess these adverse effects carefully and weigh the potential benefits against the risks in the decision about discontinuing or continuing treatment.

The 2019 evidence-based clinical practice guideline for deprescribing cholinesterase inhibitors and memantine recognises the limited availability of high-quality, generalisable studies to inform deprescribing decisions [37]. Similarly, a 2021 Cochrane systematic review of six trials highlighted the lack of evidence to guide decisions about discontinuing or continuing cholinesterase inhibitors and/or memantine, particularly for dementia types other than Alzheimer's disease [713].

The 2025 Korean Dementia Association clinical practice guidelines for dementia provide the following recommendations regarding the use of cholinesterase inhibitors and memantine [714]. The use of cholinesterase inhibitors is strongly recommended for Alzheimer’s disease and Lewy body dementia due to their efficacy in improving cognitive function, activities of daily living, and dementia severity (moderate certainty). For vascular dementia and Parkinson’s disease dementia, the use of cholinesterase inhibitors is conditionally recommended (moderate certainty). For moderate to severe Alzheimer’s disease, the use of memantine is strongly recommended (moderate certainty).

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

Given the potential risks associated with long-term use of cholinesterase inhibitors, deprescribing should be considered if side effects are intolerable or if there has been no clinically meaningful improvement. In contrast, for people who continue to receive meaningful therapeutic benefits with tolerable risks, cholinesterase inhibitors may be continued with periodic monitoring for emerging risks and benefits.

Given the lack of evidence for cholinesterase inhibitors in dementias other than Alzheimer's disease, dementia of Parkinson's disease, Lewy body dementia, or vascular dementia, deprescribing may be considered appropriate and should be offered to individuals currently taking cholinesterase inhibitors for indications other than these.

Narrative summary of evidence on deprescribing

We identified seven studies related to the deprescribing of cholinesterase inhibitors (four RCTs and three before-and-after studies) from the systematic review and meta-analysis [715-720].

Overall, all studies included participants with varying severity of dementia and different types of dementia (Alzheimer's disease, DLB, and/or PDD) in people living in different settings (community or long-term care facilities). None of the reported outcomes reached statistical significance except for a significant worsening in BPSD for PDD in a single-arm study. However, this study is of very low certainty due to a very small sample size, lacking a concurrent control group, a very short follow-up duration after withdrawal (six weeks), and other methodological limitations. In addition, dementia is a progressive disease which makes it challenging to clearly differentiate between natural disease progression and withdrawal effects after stopping cholinesterase inhibitors. The current evidence is insufficient to inform evidence-based recommendations.

If deprescribing cholinesterase inhibitors are considered appropriate, it may be appropriate to closely monitor for withdrawal symptoms or symptoms of disease exacerbation (e.g. worsening neuropsychiatric symptoms including agitation and apathy, cognitive decline, worsening behavioural symptoms, reduced ability in activities of daily living).

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

Gaudig 2011 reported two different study designs comparing the continuation and discontinuation of galantamine for six weeks in patients with mild to moderate **Alzheimer's disease** [716]. Participants were excluded if they had symptoms of other conditions that might contribute to dementia or cognitive impairment resulting from brain injury. In study one, a before-and-after study, participants in the control group who continued with galantamine had a significant improvement in cognition measured using the Alzheimer's Disease Assessment Scale-Cognitive scales (MD 2.50, 95% CI 1.18, 3.82) at the end of six weeks follow-up. There was no significant difference between the two groups in terms of mortality (OR 0.51, 95% CI 0.02, 12.66), adverse drug events (OR 0.99, 95% CI 0.66, 1.47), or serious adverse events (OR 0.82, 95% CI 0.05, 13.58). Similar outcomes were reported in study 2, an RCT, where there was no significant difference in adverse drug events (OR 0.61, 95% 0.24, 1.58), serious adverse events (OR 0.73, 95% CI 0.29, 1.86), or cognition (MD 1.60, 95% CI -1.15, 4.35) at the end of six weeks follow-up.

Scarpini 2011 randomised 139 patients with mild to moderate (MMSE score of 11 to 24) **Alzheimer's disease** who had been taking galantamine for 12 months to continuation (n=76) or discontinuation (n=63) [720]. Participants were excluded if they had another neurodegenerative disorder other than Alzheimer's Disease, a history of previous cerebral infarction, or had used acetylcholinesterase inhibitors in the past three months. Other cholinesterase inhibitors

(donepezil, tacrine, rivastigmine), nootropics, antidepressants, mood stabilisers, and anticholinergics were not permitted during the trial. At 24 months, there were no significant differences between the two groups in terms of mortality (OR 0.47, 95% CI 0.09, 2.49), adverse drug events (OR 0.71, 95% CI 0.34, 1.48), and serious adverse events (OR 0.40, 95% CI 0.12, 1.33).

Herrmann 2016 randomised 40 residents of long-term care facilities with moderate to severe **Alzheimer's disease** (MMSE ≤ 15) who had been taking cholinesterase inhibitors for at least two years to continuation (n=21) versus discontinuation (n=19) [717]. Participants were included if there had been no changes to their dose in the past three months and excluded if they had dementia other than Alzheimer's dementia or were using transdermal rivastigmine. Concomitant psychotropics were permitted during the trial as long as they had been taking a stable dose for at least a month. After two months, there were no significant differences between the two groups in clinical exacerbation (OR 3.75, 95% CI 0.36, 39.59), neuropsychiatric symptoms measured using NPI-NH (MD -4.70, 95% CI -11.53, 2.13), global clinical status measured using the Clinical Global Impression Scale (MD 0.20, 95% CI -0.08, 0.48) or agitation measured using the Cohen-Mansfield Agitation Inventory score (MD 2.80, 95% CI -3.01, 8.61). Similarly, there was no difference in activities of daily living measured using the Alzheimer's Disease Cooperative Study-Activities of Daily Living modified for severe Alzheimer's Disease (MD 0.10, 95% CI -2.14, 2.34), Apathy Evaluation Scale score (MD 1.50, 95% CI -2.65, 5.65), cognition measured using standardised MMSE (MD -1.70, 95% CI -3.91, 0.51), or quality of life measured using the Quality of Life in Late Stage Dementia (MD -0.40, 95% CI -3.12, 2.32).

Moo 2021 randomised 62 primary care patients with **dementia associated with Parkinson's disease** who had been taking cholinesterase inhibitors for at least 12 months to continuation (n=36) versus discontinuation (n=26) [719]. The severity of dementia at baseline was unclear. At six weeks, there were no significant differences between the two groups in activities of daily living measured using the Alzheimer's Disease Cooperative Study-Activities of Daily Living (MD 2.02, 95% CI -16.32, 20.36) or cognition measured using the Six-Item Screener (MD 0.28, 95% CI -0.59, 1.15).

Garcia-Garcia 2022 conducted a before-and-after study that included institutionalised patients with severe **dementia** who had been taking cholinesterase inhibitors for at least 12 months [715]. Cholinesterase was discontinued if 1) cognition and/or function significantly worsened over the past six months, 2) there had been no improvement, stabilisation or reduction in the rate of decline at any time during the treatment, or 3) dementia was severe/end-stage (dependence in most activities of daily living, inability to respond to the environment and/or limited life expectancy). Participants with underlying psychiatric disorders or a disability that could affect cognitive and/or functional assessment were excluded. Cholinesterase inhibitors were deemed suitable to be discontinued in 23 participants. Compared to baseline, after three months of discontinuation, there were no significant differences in cognition measured using MMSE (p = 0.441) and the Reisberg's Global Deterioration Scale (p = 0.976), BPSD measured using the NPI (p = 0.882), or activities of daily living measured using the Barthel index (p = 0.08).

Minette 2003 evaluated the impact of abrupt discontinuation of donepezil in eight participants with **probable dementia with Lewy bodies (DLB)** and 11 participants with **Parkinson's disease who subsequently developed dementia (PDD)** [718]. Participants were excluded if they had a severe gastrointestinal, renal or liver disease, a history of cardiac bradyarrhythmia, asthma, bladder outflow obstruction, a recent history of cerebrovascular disease, or if they were taking cholinergic, anticholinergic, NSAID or neuroleptics. At baseline, participants with DLB had a mean MMSE score of 15.3 whereas participants with PDD had a mean MMSE score of 18.2, indicating moderate cognitive impairment. All participants received up to 10mg of donepezil daily for 20 weeks prior to a six-week withdrawal period. After withdrawal, both groups of participants had no

significant changes in cognition measured using Mini-Mental State Examination or BPSD measured using NPI when compared to baseline. However, when compared to the treatment period at week 20, participants with PDD showed a significant worsening in BPSD measured using NPI after withdrawal (Z = -2.6, p = 0.008) whereas both groups of participants showed a significant worsening in cognition after withdrawal (p not stated).

Narrative evidence summary: withdrawal schedules

Various methods were used for deprescribing in the included studies and tapering across several weeks was the most common method. While there was no direct evidence that any particular method was associated with the greatest benefits and harms, dose tapering is likely more acceptable than abrupt cessation and helpful in determining the lowest effective dose for some patients requiring dose reduction rather than complete cessation. The tapering approach should be individualised with the speed adjusted according to the individual's response and preferences.

In people receiving both cholinesterase inhibitors and medicines with anticholinergic properties concurrently, it may be appropriate to first consider withdrawing the anticholinergic medicine, given its potential to impair cognitive function and contribute to a potentially inappropriate prescribing cascade with cholinesterase inhibitors.

In the two RCTs, one RCT tapered cholinesterase inhibitors for two weeks before the complete withdrawal (n=40, moderate certainty) [717] whereas the other RCT halved the dose for three weeks (n=62, very low certainty) [719]. The method of deprescribing was not described in the other two RCTs (n=257, very low certainty) [716, 720].

In the two before-and-after studies, the cholinesterase inhibitors dose was halved every week through available formulations to the lowest available dose before complete withdrawal in one study (n=23, very low certainty) [715], and the method was not described in the other study (n=723, very low certainty) [716].

In the single-arm study, donepezil was discontinued abruptly (n=19, very low certainty) [718].

GRADE Summary of Findings (SoF) Table

Table 32. Summary of findings for deprescribing anti-dementia medicines

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
2 [716, 720]	RCTs	261	382	OR 0.48 (0.11, 2.10)	
2. Adverse drug withdrawal events (ADWEs)					
Exacerbation/return of underlying condition					
1 [717]	RCT	21	19	OR 3.75 (0.36, 39.59)	
3. Health outcomes					
Adverse drug events					
2 [716, 720]	RCTs	102	108	OR 0.67 (0.38, 1.20)	
1 [716]	Non-randomised study	198	202	OR 0.99 (0.66, 1.47)	
Serious adverse event					

2 [716, 720]	RCTs	102	108	OR 0.44 (0.15, 1.32)	
1 [716]	Non-randomised study	198	202	OR 0.73 (0.29, 1.86)	
Clinical Global Impressions of Change					
1 [717]	RCT	21	19	MD 0.20 (-0.08, 0.48)	
Agitation					
1 [717]	RCT	21	19	MD 2.80 (-3.01, 8.61)	
Apathy					
1 [717]	RCT	21	19	MD 1.50 (-2.65, 5.65)	
Neuropsychiatric symptoms					
1 [717]	RCT	21	19	MD -4.70 (-11.53, 2.13)	
1 [718]	Non-controlled study	24	N/A	Neuropsychiatric Index after six weeks in participants living with Dementia from Parkinson's Disease Worsening, 2.6, p=0.008	
Activities of Daily Living					
2 [717, 719]	RCTs	45	57	MD 0.13 (-2.10, 2.36)	
4. Cognitive function					
2 [717, 719]	RCTs	47	55	Change in cognition, measured by standardised Mini-Mental State Examination (MMSE), MD -1.70 (-3.91, 0.51) Change in cognition, measured by Six-item Screener, MD 0.28 (-0.59, 1.15)	
1 [718]	Non-controlled study	24	N/A	Mean difference in baseline and withdrawal MMSE scores: • Participants living with Dementia with Lewy Bodies, 1.1 (95% CI -3.1 – 0.9), p = 0.229 • Participants living with Dementia from Parkinson's Disease, 1.1 (95% CI -0.8 – 2.9), p = 0.221	
5. Quality of life (QoL)					
1 [717]	RCT	18	15	Change in quality of life, measured by Quality of Life in Late Stage of Dementia score (QUALID) MD -0.40 (-3.12, 2.32)	

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

RESPIRATORY SYSTEM

This section includes:

- Medicines for obstructive airway diseases

Medicines for obstructive airway diseases

Medicines for obstructive airway diseases include:

- Beta$_2$ agonists: Salbutamol, terbutaline, formoterol, indacaterol, olodaterol, salmeterol, vilanterol
- Inhaled anticholinergics: Ipratropium, aclidinium, glycopyrronium, tiotropium*, umeclidinium
- Inhaled corticosteroids: Beclomethasone, budesonide, ciclesonide, fluticasone furoate, fluticasone propionate
- Xanthines: Aminophylline, theophylline
- Dual combination therapy (LAMA/ LABA)
    - Tiotropium/ olodaterol
    - Aclidinium/ formoterol
    - Indacaterol/ glycopyrronium
    - Umeclidinium/ vilanterol
- Dual combination therapy (ICS/ LABA)
    - Fluticasone propionate/ salmeterol*
    - Fluticasone propionate/ formoterol
    - Budesonide/ formoterol*
    - Beclometasone/ formoterol
    - Mometasone/ indacaterol
    - Fluticasone furoate/ vilanterol
- Triple therapy (ICS/ LAMA/ LABA)
    - Fluticasone furoate/ umeclidinium/ vilanterol*
    - Beclometasone/ glycopyrronium/ formoterol
    - Budesonide/ glycopyrronium/ formoterol

*Common PBS medicine

Type	Recommendation
When to deprescribe in COPD	
CBR	Given the risk of adverse effects associated with prolonged ICS treatment potentially outweighing the benefits in people at low risk of COPD exacerbation, we suggest deprescribing of inhaled corticosteroids (ICS) be offered to older people who have been using triple therapy (long-acting muscarinic antagonist + long-acting beta$_2$-agonist + ICS) for stable chronic obstructive pulmonary disease (COPD) **without** a severe exacerbation requiring hospitalisation, or less than two moderate exacerbations in the past 12 months.
Ongoing treatment in COPD	
CBR	We suggest continuing maintenance therapy as appropriate with a long-acting bronchodilator(s) (e.g. long-acting muscarinic antagonist, long-acting beta$_2$ agonist), either as monotherapy or in combination depending on symptomatic response.
How to deprescribe in COPD	
CBR	We suggest individualised deprescribing based on the individual's preference. In general, we suggest discontinuing ICS without the need for tapering; however, some people may prefer a gradual stepwise reduction.
GPS	Healthcare providers should regularly check inhaler techniques and adherence, especially if symptoms remain persistent (ungraded good practice statement).

GPS	In severe disease, consideration should be given to which inhaler is used (i.e. insufficient airflow to utilise a dry powder Ellipta device vs. a jet Respimat device) (ungraded good practice statement).
GPS	Healthcare providers should consider and offer adequate education on lifestyle interventions (e.g. smoking cessation, nutrition, alcohol, physical activity) to individuals as appropriate (ungraded good practice statement).
GPS	Pulmonary rehabilitation should be offered to all people with COPD and may result in significant quality of life and symptom improvements to offset any anxiety around deprescribing (ungraded good practice statement).
Monitoring in COPD	
CBR	We suggest monitoring lung function using a spirometry test three to six months after deprescribing, or sooner if clinical deterioration.
CBR	We suggest closely monitoring for changes in symptoms and quality of life every six weeks for the first six months after deprescribing, then monitoring for exacerbation frequency every six months thereafter, with cough and shortness of breath most likely for the first three months of withdrawal.

CBR, consensus-based recommendation; GPS, good practice statement

Introduction

Chronic Obstructive Pulmonary Disease (COPD)

ICS, in combination with a long-acting bronchodilator, are widely used in the treatment of COPD. ICS can reduce respiratory exacerbation frequency in patients with severe COPD or concomitant asthma and may improve quality of life in those with forced expiratory volume (FEV1) <50% [177, 721]. Guidelines recommend adding ICS to long-acting bronchodilators ("triple therapy") in patients with a severe exacerbation (requiring hospitalisation) or at least two moderate exacerbations in the previous 12 months, and significant symptoms despite LAMA+LABA therapy [177, 722, 723].

Asthma

> This guideline does not include recommendations for deprescribing in the context of adult asthma management, as the evidence identified for deprescribing is limited to COPD and the therapy adjustment strategies for asthma management in adults (i.e. stepping up or stepping down therapy) is part of standard practice. Healthcare providers are encouraged to refer to existing clinical resources, including but not limited to the Australian Asthma Handbook, Therapeutic Guidelines, and the Global Initiative for Asthma (GINA) guidance, as appropriate [724-726].

Inhaled short-acting beta$_2$ agonists (salbutamol, terbutaline) or budesonide with formoterol is used when required for acute symptomatic relief in asthma, whereas inhaled corticosteroids (ICS) form the cornerstone of preventive treatment. Most individuals with asthma require ICS as maintenance therapy, as they improve lung function and quality of life while reducing airway hyper-responsiveness, inflammation, exacerbation frequency and severity, and the risk of asthma-related death [177]. The role of theophyllines is limited in the management of obstructive pulmonary diseases due to the narrow therapeutic range and possible severe adverse effects including on the cardiovascular system [727].

Many patients remain on the same asthma medicines for years, often at higher-than-necessary doses for symptom control. Current evidence of the dose-response relationship of ICS in adult asthma showed that 80-90% of the maximum achievable efficacy of ICS are obtained in adult asthma with a standard daily dose (defined as 200-250 µg/day of fluticasone propionate or equivalent) across the spectrum of severity [728]. Higher ICS doses result in an increased risk of systemic adverse effects with limited additional benefits [728]. A cohort study found that many individuals were prescribed medium to high doses of ICS, either alone or in combination with add-on therapies such as long-acting β-agonists (LABAs), leukotriene receptor antagonists, theophylline,

or long-acting muscarinic antagonists [729]. Notably, half of these patients had neither a reliever prescription nor an exacerbation in the preceding year.

The management of asthma is introduced in a stepwise manner and the stepping-down approach is standard practice [724-726, 730]. Current guidelines recommend stepping down to the minimum effective dose or discontinuing ICS therapy once good asthma control has been achieved for two to three months in adults [177, 730]. In people with severe asthma (defined as asthma that remains uncontrolled despite adherence to optimised treatment and management of contributing factors, or that worsens when high-dose therapy is reduced [731]), any dose reduction should ideally be undertaken in consultation with a respiratory specialist [730].

Overlap of asthma and COPD

People with overlapping of asthma and COPD typically have more rapid disease progression, high symptom burden, worse quality of life, and more frequent and severe exacerbations than those with either condition alone [723]. Specialist input is required for managing asthma-COPD overlap due to limited evidence and varying management approaches.

Justification of recommendations

Refer to the narrative evidence summary, the GRADE Summary of Findings table below, and the Technical Report for a complete presentation of the deprescribing evidence based on the GRADE framework (including other factors considered in developing the recommendations).

ICS are often overprescribed in COPD and are not recommended for people with mild disease or those at low risk of exacerbations. Guidelines recommend adding ICS to long-acting bronchodilators ("triple therapy") in patients with a severe exacerbation (requiring hospitalisation) or at least two moderate exacerbations in the previous 12 months, and significant symptoms despite LAMA+LABA therapy [177, 722, 723]. The use of ICS is associated with an increased risk of pneumonia, cataracts, osteoporosis, oral candidiasis, and potentially impaired glucose tolerance [177, 721]. At high doses (e.g. beclomethasone dipropionate 1000–2250 mcg/day), older people may also be at risk of skin thinning and bruising [177]. The decision to use ICS must be carefully balanced against the potential risks, with the risk increases with prolonged use. If there is no clear indication or demonstrated benefit, deprescribing ICS may be safe, provided long-acting bronchodilator therapy, such as a LABA, a long-acting muscarinic antagonist (LAMA), or both, is maintained [721].

Narrative summary of evidence on deprescribing

We identified seven studies (two double-blind RCTs, one cross-over RCT, two before-and-after studies, and two prospective cohort studies) related to the deprescribing of ICS or tiotropium in people with COPD from the systematic review and meta-analysis [732-738].

Overall, the evidence supporting deprescribing is of low and very low certainty, and only for people with COPD who were either current or ex-smokers. No evidence was found for other medicines used in the management of asthma. One cohort study reported an increased risk of exacerbation in people who discontinued ICS compared with those who had never been treated with ICS; however, this finding had very low certainty due to methodological limitations. Most studies indicated that deprescribing ICS in patients with stable COPD, who had not experienced a recent exacerbation (e.g. within the last 12 months), was safe and did not lead to COPD exacerbations. However, there is a lack of quality evidence to inform evidence-based recommendations. If ICS discontinuation is considered appropriate, close, periodic monitoring of lung function (e.g. spirometry), as well as monitoring changes in symptoms and quality of life, is necessary. Monitoring could be undertaken every six weeks for the first six months after deprescribing, followed by monitoring exacerbation frequency every six months thereafter. It may be helpful to provide examples of common symptoms when encouraging individuals to self-monitor and report symptoms to their healthcare providers. As

some symptoms are non-specific, many people may not recognise that they could be indicative of a disease exacerbation.

Key study characteristics and results

A narrative summary of each study is provided below, highlighting key characteristics and main findings.

O'Brien 2001 conducted a double-blind cross-over RCT that randomised 24 men using inhaled beclomethasone dipropionate with stable but severe irreversible airflow obstruction to deprescribing (placebo inhaler) or continued therapy with a six-week follow-up [736]. All 24 participants were either current or ex-smokers. There was no significant difference in the mean percentage change in the forced vital capacity (FVC) between the baseline and the placebo period (-3.60%, 95% CI -8.87, 1.67) and between baseline and the treatment period (3.23%, 95% CI -3.08, 9.55). There was a significant reduction in the mean percentage change in FEV_1 between the baseline and the placebo period (-6.28%, 95% CI -12.04, -0.52) but no significant difference between the baseline and the treatment period (5.03%, 95% CI -3.89, 13.95). Comparing placebo and treatment periods, there were also no significant differences in COPD exacerbations, exercise-induced dyspnea measured using the T Borg scale assessment of dyspnoea, distance walked during the 6-minute walk test, fatigue, emotional function and mastery measured using the Chronic Respiratory Disease Questionnaire.

Choudhury 2007 randomised 260 primary care patients with COPD to either a placebo group (n=132) or an active group, 500mcg fluticasone propionate twice daily (n=128), in a double-blind RCT [734]. To be eligible, participants must have a history of smoking and have been using an ICS regularly (> three days a week) for at least six months. Those with a chronic active lung disease or lung cancer were excluded. There was no significant difference in the frequency of exacerbations in the placebo group compared to the active group receiving ICS (MD 0.21, 95% CI -0.47 to 0.89). Three COPD-related deaths occurred in the active group (OR 0.14, 95% CI 0.01 to 2.65). At 12 months, there were no significant differences in adverse drug effects associated with ICS (sore throat, oral thrush, hoarseness of voice, skin bruising, skin thinning) and quality of life (measured using EuroQol 5-D total and visual analogue scale) between the two groups.

Borrill 2009 randomised 14 participants with moderate COPD without a recent history of exacerbation to the continuation of ICS/LABA combination therapy (n = 5) or placebo inhaler (n=9) [733]. Participants were included if their postbronchodilator FEV_1 was between 50 to 80% of the predicted value, FEV_1/FVC ratio was < 70%, they were using a stable dose of 500 to 1,000 mcg fluticasone propionate per day, salmeterol 100 mcg per day, and are current or ex-smokers. Participants were excluded if they had a history of more than one COPD exacerbation in the 12 months prior that requiring oral corticosteroids or a history of COPD exacerbation requiring ICU admission or intubation. At six weeks, there was an increase in airway neutrophils (16.5%, p = 0.03) indicating increased airway inflammation and a significant decrease in FEV_1 (0.35 L, p = 0.017) in the placebo group. However, there was no significant difference in the frequency of exacerbations (4/5 intervention vs 0/9 control; OR 9.00, 95% CI 0.38, 210.39) between the two groups.

Jarad 1999 conducted an open-label prospective cohort study that compared COPD who withdrew regular ICS (n=160) with COPD patients who were naïve to ICS (n=112) [735]. Participants were included if they were clinically stable for at least 3 months before study entry. Participants in the regular ICS group were using a median daily dose of 800 mcg (range 50-2400) as either beclomethasone dipropionate or budesonide). Their ICS were withdrawn over one week. In the following seven weeks, exacerbations appeared to be more common among participants who had

withdrawn ICS (38%) compared to those who had never been treated (6%), although there were multiple potential confounding factors.

Patel 2022 conducted a cohort study that included 11,093 patients with COPD who were using ICS for 12 months or more and withdrew at least once during the study period [737]. During the period without ICS, exacerbations, COPD-related hospitalisation, pneumonia or pneumonia episodes were 31%, 11%, 13%, and 7% respectively. Among patients who were prescribed long-acting bronchodilator maintenance therapy during the ICS withdrawal period, 2965/3849 (77%) received a long-acting muscarinic antagonist (LAMA) monotherapy. In comparison to patients receiving monotherapy of either LAMA or LABA, those who were receiving fixed doses of dual LAMA/LABA therapy on average were able to remain without ICS for longer.

Steeves 2024 conducted a retrospective cohort study involving 75 patients with COPD who had been prescribed a stable dose of ICS for at least one year that was subsequently discontinued during the study observation period [738]. The majority of patients were using budesonide/formoterol as their ICS inhaler, with one patient receiving mometasone monotherapy. Most participants (57/75, 75%) were on a medium ICS dose, defined as 400–800 mcg of budesonide or 440 mcg of mometasone, while the remaining patients were on a low dose (200–400 mcg of budesonide or 110–220 mcg of mometasone). Patients were excluded if they had concurrent asthma, used multiple ICS inhalers or nebulisers, or had significant oral steroid use (≥ 5 mg prednisone per day or equivalent for > six weeks) within 12 months of ICS discontinuation. Those with a congestive heart failure exacerbation in the two years prior to ICS discontinuation, a COVID-19 infection up to one year before or six months after ICS discontinuation, or a severe COPD exacerbation requiring hospitalisation within two years prior to ICS discontinuation were also excluded. The study found that within 12 months of ICS discontinuation, five patients (7%) experienced a COPD exacerbation requiring an emergency department visit or hospitalisation, with a mean time to event of approximately six months.

In addition to ICS deprescribing, we identified one study related to tiotropium deprescribing. Adams 2009 conducted a 3-week post-hoc evaluation that included 713 participants previously involved in an RCT [732]. All participants had clinically stable COPD, smoking history, FEV_1 of at least 65% of predicted normal values, and at least 70% FVC. Participants were excluded if their total blood eosinophil count was >600 cells/mm^3, needed daytime supplemental oxygen regularly, or were taking the equivalent of 10 mg prednisone or more daily in the last month. In this post-hoc study, participants either had their tiotropium discontinued (n=445) or placebo discontinued (n=268). After three weeks, there were no significant differences between the two groups in Transition Dyspnea Index Focal score, peak expiratory flow rate, and quality of life.

Narrative evidence summary: withdrawal schedules

Different methods were used for deprescribing in the included studies and there was no direct evidence that any particular method was associated with the greatest benefits and harms. Either method is likely to be acceptable to patients. Given the relatively low rates of COPD exacerbations requiring an emergency department visit or hospitalisation following ICS discontinuation, abrupt discontinuation may be a suitable option for most patients who are unlikely to benefit from continued use. However, individual preferences and factors should be considered as part of the shared decision-making.

ICS were abruptly ceased in one RCT (n= 260, low certainty) [734], withdrawn over one week based on the participant's own discretion in another RCT (n=272, very low certainty) [735], and the method was not described in the other four studies (n=12052) [731-733, 736]. In Steeves 2024, the majority of patients (66/75, 88%) discontinued ICS abruptly, while nine (12%) underwent a gradual taper using various tapering regimens [738]. All five COPD exacerbations requiring an emergency department visit or hospitalisation following ICS discontinuation occurred in patients

who discontinued abruptly. However, due to the low event rate and small sample size, statistical significance could not be determined.

GRADE Summary of Findings (SoF) Table

Table 33. Summary of findings for deprescribing medicines for chronic obstructive airway diseases (COPD)

No. of studies	Study design	Number of participants		Effect measure*	Certainty of evidence (GRADE)
		Deprescribing	Continuation		
1. Mortality					
1 [734]	RCT	132	128	OR 0.14 (0.01, 2.65)	
2. Adverse drug withdrawal events (ADWEs)					
Exacerbation/return of underlying condition					
3 [733, 734, 736]	RCTs	319	261	Deprescribing of inhaled corticosteroids (ICS) in people with COPD was not associated with a significant increase in the frequency of exacerbation (MD 0.21, 95% CI -0.47, 0.89, n = 260) [734]. In two studies, withdrawal of ICS (either alone or with a long-acting beta agonist) also was not associated with a significant increase in the number of participants having at least one exacerbation (OR 8.14, 95% CI 0.91, 72.87, n = 48) [733, 736]. There was no significant change in the T Borg scale assessment of dyspnoea following the withdrawal of inhaled steroids (MD 0.85, 95% CI -0.45, 2.15, n = 30) [736].	
1 [735]	Non-randomised study	160	112	One study reported a higher risk of exacerbation in participants who had their ICS discontinued compared with participants who were chronically untreated with ICS (OR 9.00, 95% CI 3.93, 20.62, n = 272) [735].	
1 [737]	Non-controlled study	11093	N/A	31% of the participants reported an exacerbation event and 13% had primary care recorded pneumonia episodes.	
3. Health outcomes					
Respiratory measures					
1 [736]	RCT	15	15	There was no significant change in mean forced expiratory volume during the placebo and ICS treatment periods (MD 0.02, 95% CI -0.51, 0.55).	
1 [732]	Non-randomised study	264	432	At the end of the 3-week follow-up, when compared to the placebo-discontinuation group, participants who had their tiotropium discontinued had a lower Transition Dyspnoea Index focal score (indicating more dyspnoea) (MD -0.19, 95% CI -0.70, 0.32, n = 696), lower morning Peak Expiratory Flow Rate (MD -0.20, 95% CI -17.47, 17.07, n = 488), and lower evening Peak Expiratory Flow Rate (MD -2.05, 95% CI -20.28, 16.18, n = 409). However, none of these were significant.	
Exercise tolerance					
1 [736]	RCT	7	7	There was no significant change in distance during the 6-min walk test during the placebo and ICS treatment periods (MD 36.00, 95% CI -398.50, 470.50) in feet.	
Fatigue					
1 [736]	RCT	15	15	There was no significant change in the symptoms of fatigue assessed using the Chronic Respiratory Disease Questionnaire during the placebo and ICS treatment periods (MD 1.40, 95% CI -2.07, 4.87).	
Health service use					

2 [737, 738]	Non-controlled studies	11168	N/A	During the ICS-free period, 11% of the participants had a COPD-related hospitalisation and 7% experienced hospitalised pneumonia episodes [737]. In another study, 7% experienced a COPD exacerbation requiring an emergency department visit or hospitalisation within 12 months of ICS discontinuation [738].	
4. Cognitive function					
No available evidence					
5. Quality of life (QoL)					
1 [736]	RCT	15	15	There was no significant change in emotional function (MD 1.80, 95% CI -3.12, 6.72) and mastery (MD 0.90, 95% CI -2.08, 3.88) assessed using the Chronic Respiratory Disease Questionnaire during the placebo and ICS treatment periods.	
1 [732]	Non-randomised study	263	438	When compared to the placebo group, participants who had their tiotropium discontinued for three weeks reported greater improvement in the St George's Respiratory Questionnaire total score (MD -1.69, 95% CI -3.51, 0.13) although not significant. Although not significant, the placebo group had a slight deterioration in the St George's Respiratory Questionnaire impact score but participants who had their tiotropium discontinued had an improvement (MD -1.12, 95% CI -3.24, 1.00).	

*For randomised or non-randomised controlled studies, effect measures are reported as either a ratio measure (odds ratio, OR) or a difference measure (mean difference, MD), accompanied by 95% confidence intervals. For single-arm studies, effect measures are reported as either the proportion of individuals with the outcome of interest, endpoint values as mean ± standard deviation, both the baseline and endpoint values as mean ± standard deviation, or the mean differences with corresponding p-values.

SENSORY ORGANS

This section includes:

- Corticosteroids, plain (eye)
- Antiglaucoma preparations and miotics
- Ocular lubricants (other ophthalmologicals)

Corticosteroids, plain (eye)

Ophthalmic anti-inflammatory agents include corticosteroids such as dexamethasone*, fluorometholone*, hydrocortisone, and prednisolone (alone or in combination with phenylephrine).

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing decisions be made in consultation with the person and their treating ophthalmologist and/or optometrist to ensure it aligns with their preferences, goals and overall treatment plans. We suggest deprescribing be offered to older people using ophthalmic corticosteroids for over 6 to 8 weeks whose symptoms have resolved or are stable and are unlikely to recur (e.g. after post-operative healing).
Ongoing treatment	
CBR	We suggest continuing ophthalmic corticosteroids in older people who have chronic steroid-responsive sight-threatening ophthalmic diseases (e.g. uveitis or chronic cystoid macular oedema) or who have previous corneal transplants or glaucoma incisional surgery to prevent corneal graft rejection and manage wound healing, with treatment and duration guided by the treating ophthalmologist and regular monitoring to balance benefits and risks.
How to deprescribe	
CBR	We suggest tapering ophthalmic corticosteroids in proportion to the duration of use and clinical indication. Short-term use (< 3 weeks) at usual doses generally does not require tapering. For treatment lasting three weeks or more, we suggest a gradual reduction in dosing frequency each week. If used for more than three months or in refractory disease, tapering should be even slower, by reducing frequency every two to four weeks. Tapering should be carried out by reducing the frequency of use rather than the number of drops, as patients should only instil one drop at a time. If rebound of inflammation or symptoms occur, return to approximately 75% of the previously tolerated dose until symptoms resolve and plan for a more gradual taper with the patient.
Monitoring	
CBR	We suggest close monitoring by the treating ophthalmologist for rebound intraocular inflammation or symptom recurrence for two to four weeks after discontinuing ophthalmic corticosteroids, with longer monitoring for those with refractory disease or prolonged use. Beyond this period, ongoing monitoring should be determined using shared decision-making based on the severity of their condition and/or symptoms. We suggest advising patients to inform their healthcare providers of any concerning symptoms.

CBR, consensus-based recommendation

Introduction

Ophthalmic corticosteroids are effective in managing selected allergic and non-infectious ocular inflammatory conditions, including postoperative inflammation [177]. As with other steroids, ophthalmic corticosteroids suppress the immune system and may increase the risk and the severity of an infection or delay healing [177].

Narrative summary of evidence on deprescribing

We were unable to identify any direct evidence related to the deprescribing of ophthalmic corticosteroids in older people from the systematic review and meta-analysis. Recommendations are provided in this section following a Delphi consensus process.

Justification of recommendations

For older people using ophthalmic corticosteroids for over six to eight weeks whose symptoms have resolved or are stable and are unlikely to recur (e.g. after post-operative healing), deprescribing should be considered. Chronic use of ophthalmic corticosteroids may lead to a greater risk of cataracts and glaucoma [177]. For chronic ocular inflammatory conditions (e.g. uveitis or chronic cystoid macular oedema), steroid-sparing immunosuppressive agents may be considered for maintenance therapy. If ongoing ophthalmic corticosteroids are considered appropriate for people with chronic steroid-responsive sight-threatening ophthalmic diseases or those who have previous corneal transplants or glaucoma incisional surgery to prevent corneal graft rejection and manage wound healing, treatment and duration of ophthalmic corticosteroids should be guided by the treating ophthalmologist and regular monitoring (including optometry review) to balance benefits and risks.

For conditions such as allergic conjunctivitis, initial management should include minimising allergen exposure, therapy with oral antihistamines or intranasal corticosteroids (effective for nasal obstruction and also reduce ocular symptoms), saline eye drops, eye washes [739]. Anti-inflammatory eye drops such as corticosteroids should only be used to treat allergic conjunctivitis under specialist advice [739]. If ophthalmic corticosteroids are used, close supervision by a specialist should be in place with plans for transition to non-corticosteroid treatments once acute symptoms have improved, including medicines with antihistamine and/or mast cell stabilising properties.

The tapering and monitoring approach is based on pharmacological rationale and clinical experience, considering the likelihood of rebound intraocular inflammation or symptom recurrence. The requirement for tapering ophthalmic corticosteroids generally depends on the duration of use and clinical indication. For short-term use (< three weeks) at usual doses for indications where rebound inflammation or symptom recurrence are unlikely generally does not require tapering. For treatment lasting three weeks or more, a gradual reduction in dosing frequency should be undertaken each week. If used for more than three months or in refractory disease, tapering should be even slower. Close monitoring of symptoms should be undertaken after discontinuing ophthalmic corticosteroids, with longer monitoring for those with refractory disease or prolonged use.

Antiglaucoma preparations and miotics

Antiglaucoma preparations and miotics include:

- Sympathomimetics in glaucoma therapy: Brimonidine, apraclonidine
- Parasympathomimetics: Pilocarpine
- Carbonic anhydrase inhibitors: Acetazolamide, brinzolamide, dorzolamide
- Beta blocking agents: Betaxolol, timolol
- Prostaglandin analogues: Bimatoprost, latanoprost*, tafluprost, travoprost
- Combination antiglaucoma preparations: Brinzolamide with brimonidine, timolol with bimatoprost*/ travoprost/ latanoprost/ brimonidine/ brinzolamide, dorzolamide

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing be offered to older people who are taking anti-glaucoma preparations where the extent of glaucoma progression after treatment discontinuation is unlikely to impact the quality of life in their lifetime. We suggest deprescribing decisions be made in consultation with the patient and their prescriber (ophthalmologist or optometrist) to ensure it aligns with their preferences, goals and overall treatment plans.
How to deprescribe	
CBR	We suggest ceasing anti-glaucoma preparations without the need for tapering.
Monitoring	
CBR	We suggest closely monitoring for signs of glaucoma progression and intraocular pressure for two to eight weeks after discontinuing the medicine, then 3 to 6 monthly in the first year. Thereafter can be extended to 6-12 monthly based on the severity of glaucoma and patient preferences. We suggest advising patients to inform their healthcare providers of any concerning symptoms in between appointments.

CBR, consensus-based recommendation

Introduction

Antiglaucoma preparations and miotics are indicated for glaucoma and ocular hypertension. Glaucoma is a chronic disease that causes visual field loss which can have a significant impact on the quality of life of patients with glaucoma [740]. Glaucoma can occur at any age but is more common in older people and is one of the most common causes of visual impairment in older Australians [741].

Narrative summary of evidence on deprescribing

We were unable to identify any direct evidence related to the deprescribing of antiglaucoma preparations and miotics in older people from the systematic review and meta-analysis. Recommendations are provided in this section following a Delphi consensus process.

Justification of recommendations

Although the treatment for glaucoma is usually life-long, national guidelines recommend regular review and monitoring to assess the appropriateness of therapy based on life expectancy and severity of the condition [742]. Specifically, the suitability of deprescribing glaucoma eye drops should be evaluated in individuals for whom the progression of glaucoma is unlikely to significantly impact their quality of life, considering their life expectancy [740].

While topical glaucoma medications have long been the cornerstone of treatment, alternative options, such as selective laser trabeculoplasty, may also be considered for glaucoma management [743]. In some cases, these minimally invasive surgical and laser interventions may be more favourable due to benefits such as consistent intraocular pressure control, cost-effectiveness, reduced reliance on patient adherence, prevention of disease progression, and improved quality of life [743].

The tapering and monitoring approach is based on pharmacological rationale and clinical experience. Anti-glaucoma preparations can generally be ceased without the need for tapering. The typical washout period for prostaglandin analogues varies between two to eight weeks [744]. During this period, signs of glaucoma progression and intraocular pressure should be closely monitored, with follow-up assessments becoming less frequent based on the severity of the glaucoma and the patient's preferences. For instance, every three to six months in the first year and can be extended to every six to 12 months if appropriate.

Ocular lubricants (other ophthalmologicals)

Ocular lubricants include the following:

- Carbomer 980
- Carmellose (alone or with glycerin)
- Carmellose with glycerin and polysorbate 80/ sodium hyaluronate
- Hypromellose (alone or with carbomer 980/ dextran 70)
- Hydroxypropyl guar with macrogol 400 and propylene glycol
- Hydroxypropyl guar with macrogol 400, propylene glycol and sorbitol/ sodium hyaluronate
- Hydroxypropyl guar with mineral oil, propylene glycol and sorbitol
- Liquid paraffin + glycerol + tyloxapol + poloxamer-188 + trometamol hydrochloride + trometamol + cetalkonium chloride (Cationorm®)*
- Macrogol 400 with sodium hyaluronate/ propylene glycol
- Polyvinyl alcohol (alone or with povidone)
- Paraffin (alone or with lanolin)
- Perfluorohexyloctane
- Phospholipid liposomes
- Retinol palmitate with paraffin and lanolin
- Sodium hyaluronate

*Common PBS medicine

Type	Recommendation
When to deprescribe	
CBR	We suggest deprescribing be offered to older people taking long-term ocular lubricants whose symptoms have resolved or are stable and are unlikely to recur, particularly if an avoidable or modifiable risk factor (e.g. drug-induced dry eyes) has been addressed.
Ongoing treatment	
CBR	We suggest continuing long-term ocular lubricants (preservative-free if possible) at the lowest effective dose and with appropriate formulations, particularly if other non-pharmacological strategies are less effective, environmental triggers cannot be avoided (e.g. living conditions), or if patients have concurrent ocular conditions/taking concomitant medicines which are known to cause dry/irritated eyes.
How to deprescribe	
CBR	We suggest gradually tapering doses before ceasing if more than daily administration (e.g. twice or three times daily), then switching to “as required” use at the lowest effective dose as well as providing advice for alternative management strategies, provided this aligns with the individual's goals and preferences, following informed consent.
Monitoring	
CBR	We suggest ongoing monitoring for any ocular symptoms such as dry eyes, redness, and discomfort in the eyes for three to six months after deprescribing by advising patients to report to their healthcare providers any concerning symptoms in between appointments. If symptoms are persistent, we suggest adequate investigation (including administration technique) and differential diagnoses and considering appropriate non-pharmacological therapies.

CBR, consensus-based recommendation

Introduction

There is a wide range of ocular lubricants as listed above. Dry eye is a common problem affecting many and is especially common in older people [745]. Tear production diminishes with increasing age [745]. Ocular lubricants are prescribed for patients experiencing symptoms of dry eyes or vision fluctuations associated with a compromised tear film.

Narrative summary of evidence on deprescribing

We were unable to identify any direct evidence related to the deprescribing of ocular lubricants in older people from the systematic review and meta-analysis. Recommendations are provided in this section following a Delphi consensus process.

Justification of recommendations

It is important to rule out any medicine-related causes to prevent an inappropriate prescribing cascade. Many medicines commonly used by older people possess anticholinergic effects that may contribute to or aggravate dry eyes (e.g. antihistamines, antimuscarinics and certain antidepressants) [746]. People with glaucoma often experience coexisting dry eyes or ocular surface disease, as some antiglaucoma medications can disrupt tear film homeostasis [747]. Exploring alternative treatment options or adjusting current medication regimens may help manage or alleviate dry eyes without the need for additional therapies. Adjunctive strategies include conservative measures, such as warm compresses, lid massage, and lid hygiene with over-the-counter wipes or cleansing foams.

If non-pharmacological strategies prove ineffective and environmental triggers or aggravating factors (e.g. living conditions, concurrent ocular conditions, or concomitant medications) cannot be modified or avoided, continued use of ocular lubricants may be appropriate. Preservative-free formulations should be considered, especially for individuals with chronic ocular diseases or those experiencing adverse effects, to reduce the risk of damage to the conjunctiva and cornea [185].

Gradual tapering of doses may be helpful in determining the minimal dose required to manage symptoms if complete cessation is not possible. Individuals should be encouraged to self-monitor and report ocular symptoms such as dryness, redness, and discomfort to their healthcare professionals. If symptoms persist, a thorough investigation (including a review of administration techniques) and differential diagnoses should be considered, rather than assuming deprescribing failure, along with consideration of appropriate non-pharmacological therapies.

Glossary of Terms

Term	Definition
Adverse drug events	Any form of harm or injury resulting from the use of a drug.
Adverse drug withdrawal events	A subset of adverse drug events that refers to a clinical set of symptoms or signs that occur during or after the discontinuation of a medicine.
Adverse effects	Unwanted, harmful effects resulting from a medicine or intervention.
AGREE (Appraisal of Guidelines for Research & Evaluation) instrument	A critical appraisal tool used to assess the methodological rigour and transparency of clinical practice guidelines.
Anatomical Therapeutic Chemical (ATC) Classification System	A system used to classify drugs based on their anatomical, therapeutic, and chemical properties.
Autonomy (in healthcare)	A person's right to make informed decisions about their own medical care, free from undue influence and coercion.
Benefits (of an intervention)	Positive and desirable outcomes or effects expected or resulting from an intervention (including a test or treatment).
Bioavailability (of a medicine)	The extent and rate at which the active moiety (drug or metabolite) enters the systemic circulation and is able to access the site of action.
Carer	A person (including family members, friends or neighbours) who provides assistance to someone who needs help with the tasks of daily living.
Chronic	Long-lasting or ongoing
Clinical practice guidelines	Systematically developed statements that include recommendations intended to assist practitioners and/or patients in making decisions about appropriate care in specific circumstances.
Cognition	Related to mental processes such as thinking, understanding, learning, and memory.
Common medicines	For the purposes of this guideline, 'common medicines' refer to the top 100 medicines, as determined based on prescription dispensing volume or the number of unique individuals dispensed on the Pharmaceutical Benefits Scheme in the 2023 calendar year.
Comorbidity	The presence of one or more additional health conditions co-occurring with a primary condition.
Confidence interval (in statistics)	A statistical range that estimates the uncertainty around a measurement. When reported as 95% CI, it represents the range of values within which the true population parameter is expected to lie 95% of the time, if the same study were repeated under the same conditions.
Consensus-based recommendation	A recommendation based on available evidence, clinical expertise, and consumer/expert opinion, and formulated using a structured Delphi consensus process, after a systematic review of the evidence found insufficient quality evidence on which to base a recommendation.
Consumer	A person who uses or is a potential user of healthcare services, including patients, their family members, carers, and other individuals who are part of a patient's support network

Control group	The group that does not receive the treatment or intervention being tested (typically used as a comparison in a study).
Delphi	A research method that typically involves multiple rounds of surveys or questionnaires to gather expert opinions and achieve consensus on a specific topic. In the current guideline, consensus is defined as at least 75% agreement on each statement.
Deprescribing	Deprescribing is a person-centred process of tapering, stopping, discontinuing, or withdrawing one or more medicines that are considered inappropriate or no longer beneficial to improve outcomes.
Evidence-based recommendation	An evidence-based recommendation, according to the GRADE approach, is a clinical or policy recommendation that is concise, clear, actionable, and informed by a systematic and transparent assessment of the available research evidence, taking into account the balance between the benefits and risks of, individual's values and preferences, resource use, costs, acceptability, the feasibility of implementation, and health equity indicators.
Exacerbation	A worsening or flare-up of a disease or condition.
Frail	A state of increased vulnerability due to reduced physiological reserve across multiple physiological systems.
General practitioner	A General Practitioner (GP) is a medical doctor with a core responsibility to provide comprehensive, continuous care across a wide range of health conditions. Most GPs work in primary care settings, where they play a central role in coordinating healthcare, referring patients to specialists when necessary, and delivering ongoing management of chronic conditions, preventive care, and health education.
Geriatric 5Ms	A framework that includes: Mind, Mobility, Medicines, Multicomplexity, and what Matters most.
Good practice statement	A statement formulated using a structured Delphi consensus process, on a subject outside the scope of the systematic review, that is intended to support the guideline recommendations or implementation in practice.
GRADE (Grading of Recommendations, Assessment, Development and Evaluation) framework	A systematic framework commonly used in guideline developments to assess the certainty of evidence and determine the strength of recommendations in healthcare guidelines.
Harms (of a test or treatment)	Negative and undesirable outcomes or effects expected or resulting from an intervention (including a test or treatment).
Hazard ratio	A ratio of the rate at which one group experiences an outcome to the rate at which another group experiences an outcome of interest over time.
Healthcare professional	A person trained to deliver healthcare services.
Hyperbolic tapering	Hyperbolic tapering is a dose reduction strategy for certain medicines in which medicine doses are decreased in progressively smaller increments to achieve a linear reduction of receptor occupancy to minimise withdrawal symptoms.
Informed consent (in healthcare)	The Australian Commission on Safety and Quality in Health Care defines informed consent as a person's voluntary decision to agree to a healthcare treatment, procedure or other intervention that is made:

	1) following the provision of accurate and relevant information about the healthcare intervention and alternative options available; and 2) with adequate knowledge and understanding of the benefits and material risks of the proposed intervention relevant to the person who would be having the treatment, procedure or other intervention.
Intermittent	Occurring at irregular intervals; not continuous.
Life expectancy	An estimate of the average number of years a person can expect to live.
Mean difference	A measure that quantifies the difference between the mean (i.e. average) values of two groups.
Medication adherence	The extent to which consumers take prescribed medicine in line with the agreed plan with the prescriber
Medication compliance	The extent to which consumers take their prescribed medicines exactly as instructed by the prescriber.
Monitoring	The process of observing and checking the progress or quality of a patient's condition or therapy.
MRONJ	Medication-related osteonecrosis of the jaw, a rare but serious side effect of certain medicines.
Multimodal	The use of more than one method or approach in treatment or care.
Multimorbidity	The presence of two or more chronic health conditions.
Odds ratio	A ratio of the odds of the event occurring in one group versus another group.
Off-label	The use of a medicine for a condition or population not specifically approved by regulatory authorities.
Older people	People aged 65 years and older
Over-prescribing	The prescribing of medicines that are inappropriate, no longer necessary, or where the potential harms outweigh the benefits.
Palliative care	Palliative care is a specialised medical care for anyone living with a life-limiting illness, such as cancer or advanced stages of dementia, as well as their carers or family members. It involves multidimensional aspects and main goal is to prevent or ease suffering and improve the quality of life.
Person-centred care	Care that respects and responds to the preferences, needs and values of the individual and/or their family members or carers.
Pharmaceutical Benefits Scheme	An Australian government subsidy program that subsidises the cost of medicines for eligible individuals.
Polypharmacy	The concurrent use of multiple medicines, typically defined as five or more, to treat one or more conditions.
Potentially inappropriate medicines	Medicines where the potential risks of harm or harmful interactions outweigh the expected benefits
Preference-sensitive decisions	Decisions where multiple options are available, and individual values, preferences, and priorities play a crucial role in determining the most suitable option.
Pro re nata	A Latin term meaning "as needed"; typically refers to medicines not taken on a fixed schedule.
Randomised controlled trial	A prospective study design that evaluates the effectiveness of an intervention or treatment by randomly assigning participants to different groups. This approach allows for the examination of cause-and-effect relationships between the intervention and specific outcomes.

Relative risk	A measure that compares the probability of an event occurring in one group versus the probability of that event occurring in another group, often used to assess the effect of an exposure or treatment.
Risk-benefit profile	The profile of the expected benefits and potential harms of a treatment or intervention.
Side effects	Unwanted, harmful effects resulting from a medicine or intervention.
Specialist provider	A healthcare professional with advanced training in a particular area of medicine.
Steroid-sparing	An alternative approach with the aim to reduce or avoid the use of corticosteroids.
Systematic review	A rigorous research method used to systematically identify, select, appraise, and synthesise evidence from relevant studies on a specific topic using a predefined and structured approach. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies.
Tapering	The gradual dose reduction of a medicine, typically to minimise or avoid withdrawal symptoms or adverse effects.
Titration	Adjusting the dose of a medicine, typically with the aim to achieve the desired effect with minimal side effects.
Trade-off	A compromise between benefits and risks or competing outcomes.
Under-prescribing	The omission of a medicine that is clinically indicated for the treatment or prevention of a condition or a disease, without a valid justification (also known as prescribing omissions).
Vulnerable	At increased susceptibility to the risk of harm due to physical, social, economic, and environmental factors or processes.

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