Deprescribing in older people

SUMMARY
Deprescribing is the process of discontinuing drugs that are either potentially harmful or no longer required.
It can be achieved in older people and may be associated with improved health outcomes without long-term adverse effects.
The risk of drug withdrawal effects can often be mitigated by carefully monitoring and gradually tapering the dose.
Deprescribing should ideally be a shared decision-making process between the patient and the prescriber.

Introduction
Why deprescribe? Older people living with multiple chronic diseases often have a high risk of adverse health events which can be modified by medicines. For these people, the quality use of medicines includes starting new drugs, adjusting doses and discontinuing those that are no longer beneficial. Despite the great potential benefit they can derive from medicines, these patients are at high risk of experiencing medicine-related harm. Using more drugs than is clinically indicated can increase this risk.
Polypharmacy, defined as the concomitant use of five or more medicines, is associated with an increased risk of adverse outcomes such as hospital admissions, falls and premature mortality. It is also expensive for patients. The number of older Australians affected has increased by over 50% since 2006 to nearly one million. This rising prevalence and the associated concerns about poorer health outcomes have led to increasing attention on inappropriate polypharmacy.
Deprescribing addresses the harms associated with inappropriate polypharmacy. It is a patient-centred process involving the discontinuation of one or more drugs that are potentially harmful or no longer required.

Is deprescribing safe?
Many drugs are indicated to delay mortality so prescribers may be reluctant to discontinue them. Despite this concern, a systematic review of deprescribing found no change in mortality overall in randomised studies (odds ratio (OR) 0.82, 95% confidence interval (CI) 0.61–1.11). However, mortality was significantly decreased in non-randomised studies (OR 0.32, 95% CI 0.17–0.60). The review also found that patient-specific interventions significantly reduced mortality in randomised studies, but generalised educational interventions aimed at upskilling practitioners to alter prescribing behaviour did not change mortality. This evidence indicates that reducing polypharmacy may be achieved without perceivable adverse impacts on mortality and with clinically important benefits for some patients. Other reviews have investigated the impact of deprescribing in specific drug classes and specific settings (such as aged-care facilities and hospitals). This research generally suggested that deprescribing is safe.

What are some prompts to consider deprescribing?
Medicines should be reviewed regularly to ensure that each drug is effective for that individual and therapy remains consistent with their care goals. Treatment should also be underpinned by a current and valid diagnosis. A significant event like a fall, or an admission to hospital or a residential care facility, should prompt a thorough medicine review. A review should also be triggered by increasing frailty or a decline in either their cognitive function or ability to manage activities of daily living.

Falls
Older people are at a significantly increased risk of falls. This is exacerbated by both polypharmacy and certain drugs such as psychotropics, cardiovascular drugs and anticholinergics. A New Zealand study found that deprescribing sedative and anticholinergic drugs significantly reduced the number of falls each person experienced. Providing older people with written information supporting discontinuation has been shown to be an effective strategy to improve sedative discontinuation. Although our systematic review suggested that deprescribing does not alter the risk of having a first fall, it reduces the number of
Managing preventive medicines can be challenging in the context of life-limiting illness or frailty. For example, although at least 15% of older Australians live with diabetes, little evidence is available on the effects of discontinuing drugs for diabetes. A recent review identified only two low-quality controlled studies of deprescribing these drugs. Tight glycaemic control (glycated haemoglobin (HbA1c) <7%) may be appropriate in those who have sufficient life expectancy to benefit from the reduced risk of microvascular complications. However, for frail older people, intensive therapy increases the risk of hypoglycaemia without a mortality benefit. De-intensification of therapy is therefore often appropriate. In both studies, there was no significant difference in HbA1c between the group that discontinued diabetes drugs and those that continued.

**Approaches to safe deprescribing**

Drugs may sometimes be discontinued in older people with limited or no adverse effects. In other cases, the symptoms of the underlying condition may reappear or withdrawal effects may occur. A review did not find significant harms when antihypertensives, benzodiazepines and psychotropics were discontinued in older people. The risk of harm can be mitigated by gradually tapering medicines and carefully monitoring for withdrawal effects. It is often not possible to tell if a condition is a current problem while symptom-relieving drugs are used (e.g. proton pump inhibitors to manage reflux, or analgesics to manage pain). For these drugs, discontinuation should be trialled rather than considered definitive. If symptoms recur, restarting the medicine at a lower dose may be sufficient to manage this.

**Reappearance of the original disease or symptoms**

Many older people are prescribed antihypertensives to reduce their risk of cardiovascular events. This needs to be carefully balanced with the potential for harms (e.g. dizziness, falls). A study of frail older people found that deprescribing antihypertensives resulted in an immediate increase in blood pressure, although this reverted to baseline within nine months. Another study found that systolic blood pressure increased by 7 mmHg (95% CI 3–12) after discontinuing antihypertensives. Blood pressure should be routinely monitored during the first year after deprescribing to identify increases that may occur. For symptom management, proton pump inhibitors are recommended for 2–8 weeks, yet they are...
 commonly continued for prolonged periods.\(^{10}\) Stopping them may result in rebound hyperacidity, or lack of symptom control,\(^{10}\) especially during the first two weeks. A study that deprescribed proton pump inhibitors during hospital admissions found that 57% were still discontinued after three months.\(^{25}\) Tapering the dose may reduce the risk of rebound symptoms, particularly if the initial dose is high. Proton pump inhibitors, H\(_2\) antagonists or antacids (e.g. Mylanta) can be used as needed to relieve rebound symptoms.

The fracture risk in people with osteoporosis may be reduced using denosumab or bisphosphonates. Bisphosphonates can be discontinued after 3–6 years in many people without altering fracture risk.\(^{5,26}\) For example, a six-year study of zoledronic acid suggested treatment could be stopped after six annual infusions, with treatment effects maintained for at least three years.\(^{26}\) Unlike bisphosphonates, denosumab is not incorporated into the bone matrix so the effect on bone resorption is not maintained after treatment is discontinued. Discontinuing denosumab therefore results in rapid bone loss and the fracture risk reverts to baseline levels.\(^{23,24}\) Periodic monitoring may identify changes in bone mineral density after a bisphosphonate has been discontinued.

### Withdrawal symptoms

Discontinuing drugs can result in withdrawal symptoms. People taking long-term benzodiazepines are likely to be physiologically dependent. A withdrawal syndrome can include anxiety,
### Table 1 Summary of systematic reviews of deprescribing (continued)

| Analysis type | Mortality | Impact on health outcomes | Falls |
|---------------|-----------|----------------------------|-------|
| Narrative summary | 60 days: 23.8% intervention vs 20.3% control (p=0.36) 12 months: 26% intervention vs 40% control (p=0.16) | One RCT: 7.1 intervention vs 6.9 control (p=0.04) One RCT: 1.0 intervention vs 1.0 control (p=0.94) | Rate of falls over 12 months: fell from 1.3 to 0.8 (p=0.006) in intervention group vs 1.4 to 1.3 (p=0.66) in control group Proportion of people falling at least once: 0.6 intervention vs 0.7 control (p=0.40) |
| Meta-analysis | OR 0.90 (95% CI 0.82–0.99) Medication review-directed deprescribing: OR 0.74 (95% CI 0.65–0.84) | N/A | No significant change in the number of residents who had a fall Medication review-directed deprescribing reduced number of people who fell (OR 0.76, 95% CI 0.62–0.93) |
| Narrative summary | No significant change in mortality reported (values not stated) | No significant difference at 6 months in self-reported QOL QOL using EQ-5D: 0.358 intervention vs 0.294 control (p=0.008) | Rate of falls per 1000 person years: 1.5±8.3 intervention vs 10.6±25.4 control group (p<0.004) |
| Meta-analysis | Randomised trials: OR 0.82 (95% CI 0.61–1.11) Patient-specific interventions: OR 0.62 (95% CI 0.43–0.88) | No significant changes in QOL reported | Risk of experiencing at least one fall: OR 0.65 (95% CI 0.40–1.05) Rate of falls in participants who did fall: mean difference 0.11 (95% CI -0.21–0.02) |
| Meta-analysis | OR 1.02 (95% CI 0.84–1.23) | N/A | N/A |
| Meta-analysis | N/A | N/A | N/A |
| Narrative summary | RR 0.73 (95% CI 0.29–1.87) | N/A | N/A |

* Reported as mean ± SD unless otherwise stated # Higher scores represent increased quality of life

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irritability, insomnia and myoclonic jerks. One study demonstrated that 38% of people reported withdrawal symptoms when discontinuing benzodiazepines and Z-drugs (zopiclone and zolpidem). This highlights the importance of slowly tapering medicines to minimise withdrawal symptoms. This also increases the likelihood of the medicine being successfully deprescribed.

**Enablers and barriers to deprescribing for patients**

It is important to involve patients and their carers in the decision to discontinue medicines when possible. Most older people are willing to stop one or more drugs if their doctor says they can. A person may be reluctant to do this if they believe a drug is still necessary or that they may derive future benefit from it. Patients may be concerned about relapse or withdrawal symptoms, but are more willing to have a medicine deprescribed if they know they can restart it if required. Inadequate time with the prescriber to discuss discontinuation, and lack of guidance on how to stop a medicine (e.g. is tapering needed, what monitoring and follow-up will occur), is another barrier. This highlights the importance of providing additional information about the risks and benefits of medicine use to facilitate an older person’s willingness to deprescribe. For example, those who received a brochure that described harms from Z-drugs and suggested alternative options were significantly more likely to discontinue the medicine than those who received usual care.

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An A3 single-page version of this table is available online.
Tools to support deprescribing decisions

There are many tools to assist clinicians to deprescribe medicines in older people. Implicit tools such as the deprescribing algorithm (Table 2) outline approaches for reviewing an older person’s medicine list to identify targets for deprescribing. These tools require application by a health professional. Explicit tools provide criteria-based guidance on how to approach the deprescribing of specific drugs – an example of medicine-specific guidelines is shown in Table 3.

Referring an older person for a Home Medicines Review or a Residential Medication Management Review by a pharmacist can assist the process. The pharmacist can help to identify targets for deprescribing and develop a plan for tapering doses. Deprescribing advice from pharmacists has been shown to reduce inappropriate prescribing in older people. It is important to ensure that medicine changes are communicated with the older person’s community pharmacist so they can assist in implementing the change. This is particularly important if the pharmacist prepares a dose administration aid for the older person.

After identifying deprescribing targets, it is necessary to consider the order in which to deprescribe medicines. Often it is useful to deprescribe medicines with limited noticeable withdrawal effects first to reassure the person that the process is tolerable (Table 4).

It is usually advisable to limit deprescribing to just 1–3 medicines at a time. However, it is important to make sure they do not have overlapping indications so it is clear which medicine is responsible if withdrawal effects occur.

| Criteria | Examples |
|----------|----------|
| 1. Is the medicine inappropriately prescribed? | Empagliflozin in renal impairment, Laxatives in patients with diarrhoea, Mineral supplements in patients with no documented deficiency |
| 2. Is the medicine having any adverse effects or interactions? | Symptomatic postural hypotension in a patient taking multiple antihypertensives – discontinuing antihypertensive drugs in older people with orthostatic hypotension increases the probability of recovery. |
| 3. Is the medicine intended for symptom relief and symptoms are stable or resolved? | Inhaled corticosteroid in a patient with stable chronic obstructive pulmonary disease – ‘real-life’ study observed that withdrawal of inhaled corticosteroids is possible with no increased risk of exacerbations in patients with stable chronic obstructive pulmonary disease. |
| 4. Is the medicine intended to prevent future events? | Prolonged dual antiplatelet therapy after percutaneous coronary intervention – continuing clopidogrel-based dual antiplatelet therapy beyond six months after percutaneous coronary intervention in older people increases bleeding risk without significantly preventing ischaemic events. |

Source: reference 35

| Link | Organisation | Description |
|------|--------------|-------------|
| www.primaryhealthtas.com.au/resources/deprescribing-resources | Primary Health Tasmania | Deprescribing guidelines for commonly used medicines (e.g. benzodiazepines, aspirin, statins) |
| http://www.match-d.com.au | WA Centre for Health and Ageing, University of Western Australia | Medication appropriateness tool for comorbid health conditions in dementia |
| http://www.nswtag.org.au/deprescribing-tools | NSW Therapeutic Advisory Group | Deprescribing guidelines for commonly used medicines in older adults (e.g. proton pump inhibitors, long-term opioid analgesics) |
| https://deprescribing.org/resources | Bruyère Research Institute | Deprescribing guidelines and algorithms for commonly used medicines (e.g. antihyperglycaemics) |

It is important to ensure that medicine changes are communicated with the older person’s community pharmacist so they can assist in implementing the change. This is particularly important if the pharmacist prepares a dose administration aid for the older person.
In the deprescribing process, the potential benefits and risks of continuing and discontinuing medicines are considered for the individual. Deprescribing to reduce polypharmacy can be achieved with potential benefits for mortality, quality of life and cognition. While some medicines can be deprescribed without noticeable effects, others are associated with predictable drug withdrawal symptoms. These medicines require more careful deliberation, tapering and monitoring if they are to be discontinued. Deprescribing medicines that are no longer indicated reduces the risk of drug-related harm and is an essential part of the quality use of medicines.

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Table 4

| Reason for considering discontinuation of the drug | Risk of withdrawal event or symptom recurrence |
|--------------------------------------------------|-----------------------------------------------|
| Inappropriate medicines | Antihypertensives | Likely – taper dose before stopping |
| No symptomatic benefit from continued therapy | Analgesics, inhaled, topical or oral corticosteroids, diuretics, antiemetics, oral and topical oestrogens, anti-reflux drugs, anxiotytics, hypnotics, levodopa, nasal decongestants, nitrates | |
| Possible symptomatic benefit from continued therapy | Iron supplements, herbal remedies, cough suppressants, digoxin, prophylactic antibiotics, antiglaucoma drugs | Less likely – stop drug without dose tapering |
| Antispasmodics, anticholinergic antihistamines, short-acting calcium channel blockers, muscle relaxants, diprydamole, nitrofurantoin, oxybutinin, amiodarone | Statins, potassium supplements, mineral supplements, vitamins, bisphosphonates, other anti-diabetic drugs, strontium | |

Source: references 38-45
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