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Cumulative Medicines

Medicines Advice Initiative Australia

Addressing the hidden risk of cumulative medicines load to reduce harm

Therapeutic Brief

Key Points

- → **Review all your patients' medicines and consider cumulative toxicity as a cause of symptoms.**
- → **Organise a Home Medicines Review (HMR) or Residential Medication Management Review (RMMR) for all your patients over 65 years who are using 5 or more medicines.**
- → **Recognise the need for deprescribing and consider using available resources including a deprescribing tool.**

Medicines can provide many benefits to treat and prevent health problems, but they come with risks. Medicines that were once helpful when first prescribed, may no longer be helpful or become unsafe.[1]

GPs are faced with an ageing population, increasing comorbidities and treatment options. As specialised co-ordinators of patient care, GPs have a unique but challenging role in our complex health system as they provide skilled and compassionate care that prevents disease and promotes health. Assessing cumulative medicine risk is an action that GPs can take to improve health outcomes for their patients. ›

The greatest predictor of medicine adverse effects occurring is the number of medicines taken

More medicines, more harm

One in four people who are using multiple medicines experience an adverse effect that is directly attributable to one or more of their medicines. Certain medicines are considered to be at higher risk of causing an adverse effect, such as anticholinergics, antipsychotics, diuretics, antidepressants, opioids and non-steroidal anti-inflammatory drugs (NSAIDS).[2] The risk increases if any of the high risk medicines are taken together.

A recent review suggests that 250,000 hospital admissions each year in Australia are related to medicine adverse effects and that two-thirds of these are potentially preventable.[3]

More than half the people over 65 years old who are on multiple medicines are taking at least one potentially inappropriate medicine.[4] Older adults are often more sensitive to medicines and disproportionately experience medicine-related harm.[5] Their altered physiology (relative to younger adults) changes the way medicines are metabolised and excreted. Reduced renal and hepatic function is particularly important because it increases their risk of experiencing an adverse effect.[6]

At the time of a credentialed pharmacist-led Medicines Review, up to 25% of older people are found to be experiencing adverse effects of their medicines and an average of four medicine related problems are detected.[7, 8] ›

Factors contributing to polypharmacy include:

- Addition of medicines to treat temporary symptoms, including over the counter products which may not be reassessed by the primary prescriber.[9]
- Multi-morbidity increases the chance of multiple prescribers for the patient; in some cases, the doctor may be unaware of this.[10, 11]
- Fear of symptom rebound; the doctor may be uncertain of how to reduce dosage and be concerned about hindering continuity of care or losing the patient's trust.[11]
- Lack of advice about deprescribing, including availability of specific guidelines.[12]
- Dealing with a large number of medicines may feel overwhelming. So called 'therapeutic inertia' is common and understandable. Clinicians may feel they have not got enough time or will not be adequately remunerated for their deprescribing effort.[10, 12]

Consider a Medicines Review

GPs are ideally suited to start a conversation with patients about their medicines and, if there is good reason, to consider trialling a reduced dose or ceasing altogether. Deprescribing is a patient-centred and systematic process to taper, reduce or stop[13] the use of potentially inappropriate medicines for people who take multiple medicines. A Medicines Review is a practical way to start this process.

The simplest intervention to organise, and arguably most beneficial to the patient, is a Home Medicines Review (HMR) or Residential Medication Management Review (RMMR) with a credentialed pharmacist (see Medicare benefit items 900, 903, 245 and 249). These are structured evaluations of a patient's medication list that improve the patient's understanding of their medicines, optimise their medicine use and help prevent medication-related problems.

Medicare benefit items 900, 903, 245 and 249

Medicines reviews may improve adherence and reduce adverse effects, risk of falls, cognitive impairment and medication burden.[14]

Referral should list the patient's clinical conditions, medicines (including those that you think may be ceased), relevant lab results and exam findings, and any specific areas of concern.

After the initial interview, the credentialed pharmacist produces an HMR report that outlines their findings. The report aims to improve the referrer's understanding of how the patient is using their medicines and make recommendations that help the referrer and patient develop a medication management plan. Share the report with the patient, carers and other relevant members of the health care team, such as nurses in aged care facilities or other community settings as well as the response you have provided to the pharmacist.

Who should I talk to about a Medicines Review?[15, 16]

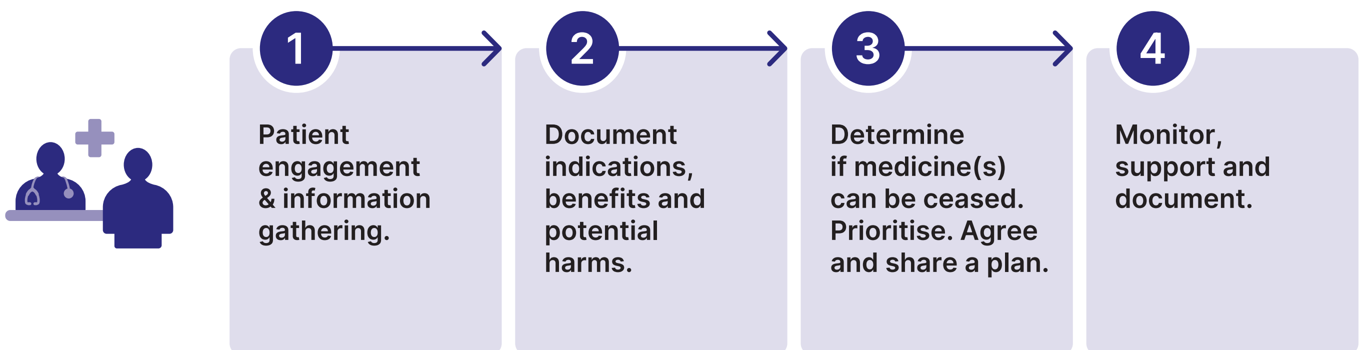
- frail older people, especially those who have a history of falls or who you consider a falls risk
- patients troubled by symptoms that could be linked with medicines
- patients recently discharged from hospital or who have had a significant change in circumstances - for example, new diagnosis of dementia, malignancy
- all patients in aged care facilities, especially on admission[17]
- all patients whose goals of care have significantly changed - for example, life limiting illness.

What should I talk to my patients about?

Talk to your patient about what is important to them - shared decision making is central to successful medication management.[18] Explain that medicines are always worth reviewing especially as circumstances change. Patients tend to have a high level of trust in their GP and are usually happy to have a conversation about their medicines.[19]

A 'patient centred' stepwise approach to deprescribing

Deprescribing can be beneficial and is unlikely to cause harm.[11]
The following stepwise approach may help (adapted from Reeve *et al* (2014),[20] Scottish polypharmacy guidelines 2018[3] and Primary Health Tasmania[16]).



1. Patient engagement and information gathering

The patient is central to the deprescribing process – engage with them and explain that you want to talk about all their medicines. Reassure your patient that in many cases it is possible to safely reduce or stop a medicine and let them know that you will provide support during the process. Gather all relevant information about their medicines including ones they take regularly, as needed and any over the counter products including complementary medicines.[9, 21] Ask them if they are having problems taking any of their medicines. ›

2. Document indications, benefits and potential harms

Establish treatment objectives together. What is important to the patient at this time? Discuss the indications, benefits and potential harms of their medicines. This can help the patient understand the trade-off between potential benefit and adverse effects which assists in clarifying their values, priorities and preferences.

i Identify the necessary or appropriate medicines on the list

Medicines that if stopped would cause serious withdrawal symptoms or worsen existing clinical issues - for example, medicine for epilepsy or arrhythmias.

ii Identify unnecessary or inappropriate medicines on the list

Are there any ineffective medicines? Does the medicine cause more harm than benefit? Was it only ever for a short-term indication? Has the potential benefit been reduced due to changes in the patient's situation and limited life expectancy - for example, statins or antihypertensives?

iii Consider if any of the patient's medicines are causing adverse effects

Always ask the patient if there are any symptoms that are bothering them as the risk of adverse effects may accumulate over time. While some of these effects may be obvious, others more subtle and not recognised or mistaken as symptoms of chronic disease or ageing.[22]

For an online tool to help you visualise the cumulative risk of adverse effects of a patient's medicines visit Veterans' MATES Cumulative Risk Calculator.

This tool has been developed and adapted from the Scottish polypharmacy guidelines[3] 2018 and can be used to see how adjustments to your patients medicines might reduce their risk of cumulative adverse effects.

Cumulative risk calculator

3. Determine if medicine(s) can be ceased. Prioritise. Agree, and share a plan

Does the patient understand what you have discussed? Make sure the decisions made are in line with patient preferences. If the patient is hesitant you may need to negotiate a rate of reduction with which they are comfortable. Provide specific withdrawal plans including tapering schedules as abruptly ceasing medicines could result in rebound symptoms or withdrawal reactions (for example - proton pump inhibitors, antidepressants, opioids, benzodiazepines). Communicate plans to nursing staff if in an aged care setting.

In some cases non-drug approaches could be safer and more effective than medicines – for example, psychological approaches for insomnia or physical therapy for musculoskeletal pain.

Allied health services may be available through MBS funded team care arrangements if your patient has an eligible chronic condition.

Allied health services

4. Monitor, support and document

Monitor for withdrawal reactions. Provide specific supports (pharmacological and non-pharmacological) and action plans to manage symptoms which may worsen as a result of treatment withdrawal. Offer support and follow up. For some patients weekly reviews may be appropriate until they feel more confident.

The GP's experience, clinical judgement, knowledge of the patient and their circumstances is essential in tailoring advice and identifying other additional medication related problems.

Take home messages

→ Identifying and addressing the risk of cumulative medicines load is a collaborative process – work with the patient, family members, carers, pharmacists and nurses in aged care facilities to improve patient outcomes.

→ Use the funded Medicines Review programs that are available to you - think about your patients who are on multiple medicines and organise a Medicines Review if they have not had one recently (within 12 months for HMR, 24 months for RMMR).

→ Deprescribing frameworks and tools are available to support you in your practice.

→ Empowering patients to ask questions will help them feel more confident about their medication management and lead to better health outcomes.[23] Invite your patients to talk to you about the medicines they are taking by asking them about their experiences.

For a list of useful links and reference list, please visit our website MedicinesAdvice.net.au

Medicines Advice Initiative Australia (MAIA)

PROVIDED BY

University of South Australia, Quality Use of Medicines and Pharmacy Research Centre

IN ASSOCIATION WITH

Australian Medicines Handbook (AMH)

Drug and Therapeutics Information Service (DATIS)

Discipline of General Practice, The University of Adelaide

National Aboriginal Community Controlled Health Organisation (NACCHO)

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Supporting quality use of medicines.

Medicines Advice Initiative Australia

Polypharmacy Case Scenario

Albert is a 78-year-old male with multiple comorbidities including ischaemic heart disease (IHD) (coronary artery stenting some years ago), hypertension (last office BP was 118/75), atrial fibrillation (AF), gastro-oesophageal reflux disease (GORD). He has chronic low back and neck pain, depression and is overweight.

Albert has been feeling dizzier and more nauseated recently and has noticed some ankle swelling. His wife Josie states she has seen some bruising on his forearms. She feels he has worsening cognitive decline, is becoming more unsteady on his feet and she is feeling less safe in the car when he drives.

You are Albert's usual GP. He has a cardiologist and is awaiting geriatrician review.

Albert reports taking fish oil for joint pain as he believes it may be 'good for that as well as his heart health and memory.' He has not had any recent episodes of chest pain and has not used his GTN spray for years.

Albert's Mini Mental State Examination (MMSE) score is 23/30. BP measures in clinic today suggest a postural drop; 123/79 sitting and 112/70 standing.

You have decided to refer Albert for a Home Medicines Review (HMR) but want to do a full assessment first by following a stepwise process to help guide your referral to the pharmacist.

Current Medicines

- → diclofenac 50 mg twice a day as needed
- → apixaban 5 mg twice a day
- → aspirin 100 mg daily
- → rosuvastatin 10 mg daily
- → pantoprazole 40 mg daily
- → citalopram 20 mg daily
- → oxazepam 15 mg before bed as needed
- → atenolol 25 mg twice a day
- → amlodipine 5 mg daily
- → irbesartan 150 mg with hydrochlorothiazide 12.5 mg daily
- → glyceryl trinitrate (GTN) spray as needed for chest pain
- → fish oil 1000 mg daily

1. Patient engagement and information gathering.

> I'm sick of taking tablets. My ankles are swollen. I sometimes feel dizzy.

Albert

> I'm having trouble keeping track of his medicines, he is getting more forgetful and has had a couple of minor slips and falls. His arms are looking more bruised.

Josie

- You talk with Albert about how he is taking his medicines at home and how this matches what is documented in your records.
- To identify potential harms, you type Albert's medicines into the cumulative medicine risk tool. You get the following result.

Cumulative risk calculator

Cumulative Risk Calculator

Select medicines below to visualise their cumulative contribution to adverse drug reaction risks. Only medicines contributing to one of the adverse drug reactions below are listed.

glyceryl

- NSAID
  - Diclofenac
- Antithrombotic
  - Apixaban
- PPI
  - Pantoprazole
- SSRI or SNRI
  - Citalopram
- Benzodiazepine
  - Oxazepam
- Beta blocker
  - Atenolol
- CCB (dihydropyridine)
  - Amlodipine
- ACE or ARB
  - Irbesartan
- Nitrate or nicorandil
  - Glyceryl Trinitrate

Cumulative risks and types of adverse drug reactions

Medicine class risk count →

0 1 2 3 4 5

Falls and fracture +2

Renal injury

Bleeding

Heart failure

CNS depression

Constipation

Urinary retention

Serotonin syndrome

Bradycardia

Hyperkalemia

Hypokalemia

Hypoglycaemia

Glaucoma

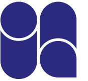
2. Document indications, benefits and potential harms.

- By using the cumulative risk tool, you see that Albert is at risk of experiencing many potential harms including ones that may result in significant morbidity, with medicines contributing to falls risk, renal injury, bleeding risk and constipation.
- You also consider the ongoing management of Albert's chronic conditions:
  - Prevention of complications of AF and IHD are important, but have the goals of care changed given his Albert's increasing frailty and cognitive decline?
  - Assess depression – length of therapy and problems in the past. Current mental state.
  - Hypertension – Albert is feeling dizzy – last BP was quite low, measures in clinic suggest a small postural drop. Reducing antihypertensive medicines may be appropriate.

3. Determine if medicine(s) can be ceased. Prioritise. Agree and share a plan.

There are multiple medicines that could be considered for deprescribing, including:

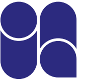
- Fish oil produces a theoretical increased bleeding risk for which there is little strong clinical evidence. There are contradictory findings about its benefit for heart health and memory. The risk is probably low but cessation is worth discussing, especially given Albert's increasing unsteadiness and bruising.
- Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) which increases bleeding risk as well as renal and cardiac problems. Avoid regular or intermittent (PRN) use. There is potential to cease this therapy and consider non-pharmacological interventions for pain such as physiotherapy.



- Amlodipine is a calcium channel blocker that may be contributing to ankle oedema. There is potential to consider ceasing with a plan to check BP soon. Rebound hypertension is unusual after ceasing antihypertensive medicine in elderly people.[1]
- Rosuvastatin is an HMG-CoA reductase inhibitor (statin). Ongoing use of statin will depend on Albert's situation and preferences.
- Aspirin is an antiplatelet and apixaban is a directly acting oral anticoagulant. Bleeding risk significantly increases in patients over 75 years of age on this combination.[1] A cardiology opinion may be warranted given this and the abovementioned concerns with Albert's antihypertensives and statin
- Oxazepam is a benzodiazepine that is known to increases falls risk and confusion. You could plan to cease but you would need to taper slowly to prevent withdrawal effects if Albert has been taking this regularly.
- Pantoprazole is a proton pump inhibitor (PPI). Long-term use of PPIs is rarely indicated and may increase risk of fractures and pneumonia. Reassess the management of Albert's GORD in the context of his reported nausea and step down PPI therapy if it is no longer indicated.[2]
- Citalopram is a selective serotonin reuptake inhibitor (SSRI). This medicine class is accepted as first line in the treatment of depression in older people but can cause hyponatremia and may increase fracture risk.[3] Consider the ongoing need.

Ceasing or reducing medicines needs to be done slowly. In some cases, tapering is required to mitigate the risk of withdrawal effects or relapse. Prioritise medicines and make one change at a time to build confidence in the deprescribing process. This is, especially important if Albert and Josie are feeling reluctant or unsure.

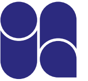
Primary Health Tasmania deprescribing resources



In the boxes below indicate whether you would consider ceasing each medicine, and the priority for cessation, noting that not all medicines should be ceased at the same time.

	Cease?	Priority?	Priority Order	Tapering plan or immediate cessation (stat)	
Medicine	**Yes**	**Yes**	**Order**	**Taper**	**Stat**
Fish Oil	◯	◯		◯	◯
Diclofenac	◯	◯		◯	◯
Amlodipine	◯	◯		◯	◯
Rosuvastatin	◯	◯		◯	◯
Pantoprazole	◯	◯		◯	◯
Apixaban	◯	◯		◯	◯
Aspirin	◯	◯		◯	◯
Oxazepam	◯	◯		◯	◯
Citalopram	◯	◯		◯	◯
Atenolol	◯	◯		◯	◯
Irbesartan	◯	◯		◯	◯
Hydrochlorothiazide	◯	◯		◯	◯

Having developed your prioritised list, re-enter the medicines in the cumulative medicines risk tool to see how Albert's risk of harms has changed. >



You consider ceasing one of the medicines that requires a tapering plan. Complete a tapering schedule for the relevant medicines for this patient by completing the boxes below.

In planning your tapering schedule consider the length of time Albert has been on the medicine, and the risk of withdrawal symptoms, including the likely severity of withdrawal symptoms.

Tapering Schedule Planner

Week/s __________

Dose __________

Week/s __________

Dose __________

Week/s __________

Dose __________

Week/s __________

Dose __________

Hint:

For antidepressants
visit Royal College of Psychiatrist's guidelines

For benzodiazepines
look at the tapering plan on page 11 of this deprescribing handout for patients

For PPIs
look at the tapering plan on page 10 of this Deprescribing handout for patients

Consider the issues you will need to discuss with Albert and Josie to implement the tapering plan successfully.

For inspiration, have a look at the patient handouts developed by the Canadian Deprescribing Network.

Canadian Deprescribing Network patient handouts

4. Monitor, support and document.

- Offer to review Albert's progress in one to two weeks to check any withdrawal symptoms and reassess BP.
- Write a referral for a medicines review to the credentialed pharmacist noting your concerns and ask them to explore if a dose administration aid could be beneficial. Be sure to include information about any plans you have for deprescribing. The pharmacist can help you in determining the priority for deprescribing.

Reviewing your own performance

Find up to four of your own patients who may be at risk of medication related harm. Enter their current medicine list into the cumulative medicines risk tool. Consider the level of cumulative risk from their medicines and if there is opportunity for deprescribing.

If appropriate, refer these patients for a Medicines Review and ask the pharmacist to assist you in developing a deprescribing plan. Provide your patient with a copy of the brochure 'Talking to my GP and pharmacist about my medicines' to explain the Medicines Review process and help them prepare for the review

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