Australian Government
Department of Veterans' Affairs

Veterans' MATES

August 2022

Therapeutic Brief

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Addressing the hidden risk of cumulative medicines load to reduce harm

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 they have a unique and important (but admittedly challenging) role in an increasingly complex health system. Despite these obstacles they provide skilled and compassionate care that prevents disease and promotes health. Assessing cumulative medicine risk is an important role for GPs that can improve health outcomes for their patients.

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

↑ medicines = ↑ risk of cumulative toxicity = ↑ risk of adverse effects

More than half the people over 65 on multiple medicines are taking at least one potentially inappropriate medicine.[2] 25% of patients who are on multiple medicines have adverse effects (AEs) directly attributable to one or more medicines. Certain medicines are considered higher risk e.g. anticholinergics, antipsychotics, diuretics, antidepressants, opioids and non-steroidal anti-inflammatory drugs (NSAIDS).[3] The risk increases if any of the high risk medicines are taken together.

Deprescribing is a patient-centred and systematic process to taper, reduce or stop[4] the use of potentially inappropriate medicines for people who take multiple medicines. A Medicines Review is a practical way to start this process.

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.[5]

250,000
hospital admissions

2/3
potentially preventable

INSIDE

Key points

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

Adverse effects and polypharmacy

Older adults are often more sensitive to medicines and disproportionately experience medicine-related harms.[6] Their altered physiology (relative to younger adults) changes the way medicines are metabolised and excreted, most importantly reduced renal and hepatic function, which increases the risk of AEs.[7]

At the time of an accredited pharmacist-led Medicines Review, up to a quarter of older people are experiencing adverse effects of their medicines and on average four medicine related problems are detected.[8, 9]

Factors contributing to polypharmacy includes:

- Medicines are sometimes added to treat temporary symptoms, this includes over the counter (OTC) products, and may not be reassessed by the primary prescriber.[10]
- Multi-morbidity increases the chance of multiple prescribers for the patient; in some cases the doctor may be unaware of this.[11, 12]
- The doctor may fear symptom rebound and be uncertain how to reduce dosage and be concerned about hindering continuity of care or losing the patient's trust.[12]
- Research indicates that clinicians perceive a lack of advice about deprescribing including availability of specific guidelines.[13]
- Dealing with a large number of medicines may feel overwhelming – so called 'therapeutic inertia' is common and understandable. Clinicians may feel they haven't got enough time or won't be adequately remunerated for their deprescribing effort.[11, 13]

Consider a Medicines Review

Who should I talk to about a Medicines Review?[14, 15]

- 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 e.g. new diagnosis of dementia, malignancy
- all patients in aged care facilities, especially on admission to the facility ("despite RMMRs being a key means for minimising medication-related harm, MBS claims for RMMRs are lodged for only a fraction of residents who enter Residential Aged Care Facilities (RACFs)")[16]
- all patients whose goals of care have significantly changed e.g. 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 deprescribing.[17] 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.[18]

Ask your patient what they understand about their medicines and how they are managing them.

- do they feel they are taking too many medicines?
- are they taking other medicines or supplements that you have not prescribed?
- ask specifically about over the counter (OTC) products or other medicines prescribed by another health professional.

Talk about potential adverse effects. Patients may be experiencing symptoms that could relate to their medicines without realising it.

Reassure your patient that in many cases they could safely reduce or stop a medicine. In some cases non-drug approaches could be safer and more effective e.g. psychological approaches for insomnia or physical therapy for musculoskeletal pain. Allied health services are available through the Department of Veterans' Affairs (DVA) for all Gold Card holders, White Card holders for accepted conditions, or for all via Medicare's chronic disease management items.

Use a 'patient centred' stepwise approach to deprescribing

Deprescribing can be beneficial and is unlikely to cause harm.[12]

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.

The following stepwise approach may help (adapted from Reeve et al (2014),[19] Scottish polypharmacy guidelines 2018[3] and Primary Health Tasmania[15]).

1. Patient engagement and information gathering

The patient is central in any Medicines Review process – engage with them and explain that you want to talk about all their medicines. Reassure them 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.[10, 20] Are they having any problems taking any of their medicines?

2. Document indications, benefits and potential harms

Establish treatment objectives together. What is important to the person at this time? Discuss indications, benefits and potential harms. This can help patients understand the trade-off between potential benefit and adverse effects and help clarify 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, e.g. medicines for epilepsy or arrhythmias.

ii. **Identify unnecessary or inappropriate medicines on the list.**
Are there 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 e.g. statins or antihypertensives.

iii. **Consider if any of the patient's medicines are causing adverse effects.**
The risk of adverse effects may accumulate over time, some of these effects may be obvious, others more subtle and not recognised. Some may be mistaken as symptoms of chronic disease or ageing.[21] Always ask if there are any symptoms that are bothering your patient.

Use the cumulative risk tool included in the prescriber feedback alongside patient feedback to guide you in determining which medicines might require dose reduction or cessation in order to alleviate adverse effects.

A 'patient centred' stepwise approach to deprescribing

1. **Patient engagement and information gathering.**
2. **Document indications, benefits and potential harms.**
3. **Determine if medicine(s) can be ceased. Prioritise. Agree and share a plan.**
4. **Monitor, support and document.**

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

Does the patient and/or carer understand what you have discussed? Make sure the decisions made are in line with patient preferences. Provide specific withdrawal plans including tapering schedules if abruptly ceasing medicines could result in rebound symptoms or withdrawal reactions (e.g. PPI, antidepressant, opioid, benzodiazepines). Communicate plans to nursing staff if in an aged care setting. If the patient is hesitant you may need to negotiate a rate of reduction with which they are comfortable.

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.

For an online calculator to help you determine the cumulative risk of adverse effects of a patient's medicines visit www.veteransmates.net.au/cumulative-risk-calculator

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

The Medicines Review process

The simplest intervention to organise and, arguably most beneficial to the patient, is to organise a Home Medicines Review (HMR) or Residential Medication Management Review (RMMR) with an accredited pharmacist (see Medicare benefit items 900 and 903 www9.health.gov.au/mbs/fullDisplay.cfm?type=item&q=900&qt=item). 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.

Medicine reviews may improve compliance and reduce:[22]

- adverse effects and unnecessary hospital admissions
- risk of falls
- cognitive impairment
- medication burden.

The patient's home is the preferred location for an HMR. However, in response to the COVID-19 pandemic, HMRs may occur via telehealth where a patient meets the eligibility criteria (aged over 70, has a chronic health condition or is immunocompromised).

A 'patient centred' deprescribing process usually generates a significant amount of information to share with an accredited pharmacist. Referral should list the patient's clinical conditions, medicines (including those that you think may be ceased) and any specific areas of concern, for instance, physical symptoms that you think are linked with medicines. After the initial interview, the accredited 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.

Take home messages

For you, the GP

Consider the risk of cumulative medicine load, assess potential adverse effects, and refer for an HMR or RMMR.

- Think about your patients who are on multiple medicines and organise a HMR if they have not had one in the last 12 months.
- The medicines review referral should include the reason for the referral, and all relevant prescribing and clinical history.
- Patient interview must take place within 90 days of the date of the referral to be remunerated under the HMR Program.
- Work with family members, carers, community pharmacists and nurses in aged care facilities to improve patient outcomes.

For your patients

Ask them to think about the medicines they are taking. Do they understand what they are all for? Have any symptoms been bothering them? What are their treatment preferences and overall goals of care?

Empowering patients to ask questions will help them feel more confident about their medication management and lead to better health outcomes.[23]

For the pharmacist

When doing a Medicines Review ask about symptoms using a structured 'body systems' approach. Inquiring about symptoms regardless of their origin is important as patients do not always recognise drug-associated symptoms as such.

For those working in an aged care setting

Liaise with the patient and their family about any possible adverse effects, elicit preferences about medicines, and co-ordinate care with GP and pharmacist. Encourage referral for a RMMR.

Useful deprescribing and polypharmacy links

- Guidelines to reduce and cease specific classes of medicines: www.primaryhealthtas.com.au/resources/deprescribing-resources
- An electronic medicines decision support system which includes the Drug Burden Index (DBI): www.nps.org.au/professionals/anticholinergic-burden/clinical-resources-and-tools
- Deprescribing resources, information for the public and professionals: www.australiandeprescribingnetwork.com.au
- RACGP aged care clinical guide (Silver Book) 5th ED Part A Deprescribing, 2019: www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines/silver-book/part-a/deprescribing
- Scottish guidance provides a 7 step framework to assess medicines and guide to deprescribing (the World Health Organization have adopted a similar approach in its Global Patient Safety Challenge): www.therapeutics.scot.nhs.uk/polypharmacy/
- Canadian resource for patients, the public and health professionals which includes practical videos for clinicians to improve patient engagement: www.deprescribingnetwork.ca
- Another Canadian resource from the Bruyere research institute with resources for patients and clinicians: www.deprescribing.org
- Veterans' MATES deprescribing tools for GPs and pharmacists: www.veteransmates.net.au/tools

For deprescribing in specific clinical situations

- Cognitive decline: cdpc.sydney.edu.au/research/medication-management/deprescribing-guidelines/
- Depression: www.nps.org.au/australian-prescriber/articles/switching-and-stopping-antidepressants
- Palliative care: www.palliaged.com.au/tabid/4432/Default.aspx
- Opioids: www.primaryhealthtas.com.au/wp-content/uploads/2018/09/A-Guide-to-Deprescribing-Opioids-2019.pdf

Full reference list available at: www.veteransmates.net.au

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In association with: Discipline of General Practice, The University of Adelaide | School of Public Health, The University of Adelaide | NPS MedicineWise | Australian Medicines Handbook | Drug and Therapeutics Information Service

Polypharmacy case scenario

Background

78 year old veteran 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.

He has been feeling more dizzy and nauseated recently, and has noticed ankle swelling. His wife has seen more bruising on his forearms, and feels he has worsening cognitive decline, is becoming more unsteady on his feet and is feeling less safe in the car when he drives.

He has a usual GP and a cardiologist and is awaiting geriatrician review.

He 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.

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

You have decided to refer for an 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 (check dose etc).

A 'patient centred' stepwise approach to deprescribing

1. **Patient engagement and information gathering.**
2. **Document indications, benefits and potential harms.**
3. **Determine if medicine(s) can be ceased. Prioritise. Agree and share a plan.**
4. **Monitor, support and document.**

A patient centred stepwise approach

1 Patient engagement and information gathering

Patient

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

Carer

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.

- Check the patient is actually taking the medicines on your list. Are there others they are taking? (including over the counter products and consider intermittent injectable products such as denosumab, B12 or goserelin). Create a full list and recheck with the patient/carer.

2 Document indications, benefits and potential harms

- Prevention of complications of AF and IHD are important, but have the goals of care changed given increasing frailty and cognitive decline?
- Assess depression – length of therapy and problems in the past. Current mental state.
- Hypertension – the patient is feeling dizzy – last BP was quite low, measures in clinic suggest a small postural drop. Reducing antihypertensive medicines may be appropriate.
- There are many potential harms including ones that may result in significant morbidity such as falls and bleeding risk.

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

- 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.
- 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. Cease and consider non-pharmacological interventions for pain such as physiotherapy.
- Amlodipine may be contributing to ankle oedema. Cease with a plan to check BP soon. Rebound hypertension is unusual after ceasing antihypertensive medicine in elderly people.[1]
- Ongoing use of statin will depend on the patient's situation and preferences.
- Aspirin and apixaban – is there an ongoing need for dual anticoagulation? Bleeding risk significantly increases in patients over 75 years of age on this combination.[1]
- A cardiology opinion may be warranted given the above three areas of concern.
- Oxazepam increases falls risk and confusion. Plan to cease but taper slowly to prevent withdrawal effects (see below).
- Proton pump inhibitor (PPI) – reassess need for management of GORD. Long-term use is rarely indicated and may increase risk of fractures and pneumonia. Stepping down PPI therapy is advisable.[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.
- Tapering is important in several of these cases and should mitigate the risk of withdrawal effects. Use simple online guidelines to reduce the benzodiazepine and PPI (see Primary Health Tasmania deprescribing resources **www.primaryhealthtas.com.au/resources/deprescribing-resources/** includes videos to help better understand the process).
- Ceasing or reducing medicines needs to be done slowly, prioritise and make one change at a time to build confidence in the deprescribing process especially if the patient is reluctant or unsure.

4 Monitor, support and document

- Suggest a dose administration aid. Offer to review in one to two weeks to check any withdrawal symptoms and reassess BP.
- Write a referral for an HMR to the accredited pharmacist noting your concerns including reported symptoms, recent falls, postural drop and cognitive decline.

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The hidden risk of cumulative medicines load: reducing adverse effects

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