Polypharmacy in older people

When should you deprescribe?

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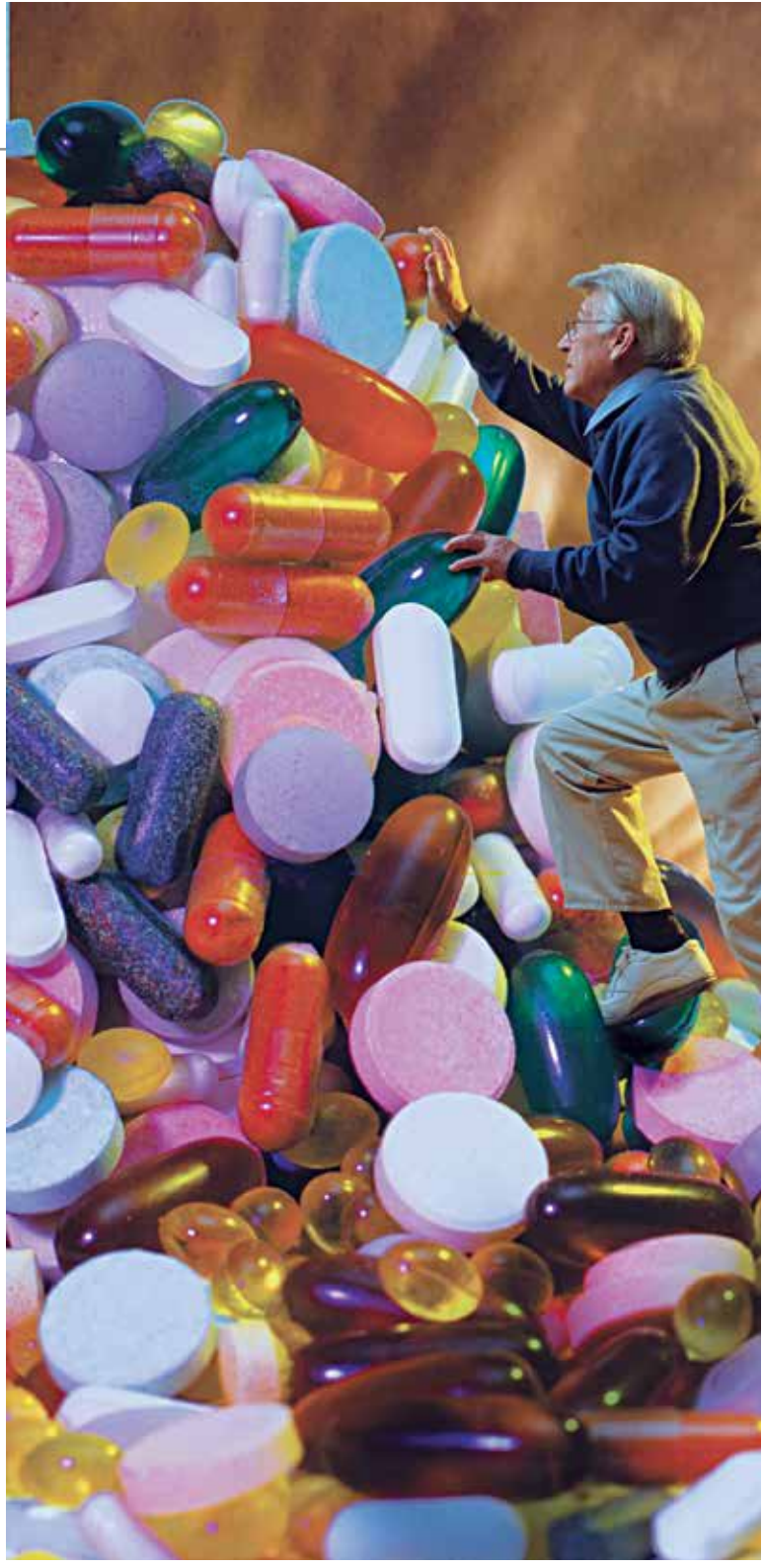
Nearly two-thirds of people aged 75 years or over take five or more medicines. Polypharmacy is associated with adverse outcomes, including geriatric syndromes (e.g. falls and confusion), institutionalisation and mortality. An individualised patient-centred approach that takes into account multimorbidity can help prioritise medicines and identify when deprescribing is indicated.

Most medicines are used by people who are old. More than half of PBS expenditure is on people aged 65 years and older (Figure 1).[1] Nearly all older Australians take prescription medicines, and two-thirds of those aged 75 years or over take five or more medicines (Figure 2).[2] Consequently, a detailed assessment of medicines (including doses, recent changes, adherence and use of over-the-counter and complementary and alternative medicines) is an essential component of any clinical assessment of older people.[3]

Polypharmacy in older people can be associated with a range of adverse outcomes. These include adverse drug reactions, hospitalisation, institutionalisation, geriatric syndromes such as frailty, falls, confusion, malnourishment and incontinence, and mortality.[4,5] A major challenge in older people is to ensure that their use of medicines improves their health and/or quality of life and minimises the adverse outcomes. In many patients this may involve deprescribing.



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KEY POINTS

- Polypharmacy and deprescribing are major challenges for clinicians caring for older people with multimorbidity.
- It is important to recognise the limitations of the evidence base in these situations and the central role of patient-centred care when prioritising medicines.
- Awareness of pharmacological principles and the concept of potentially inappropriate medicines can assist in identifying red flag medicines that should be avoided or deprescribed.
- Careful clinical monitoring after medicines have been changed is key to ensuring that patients' goals are being met and harms avoided.

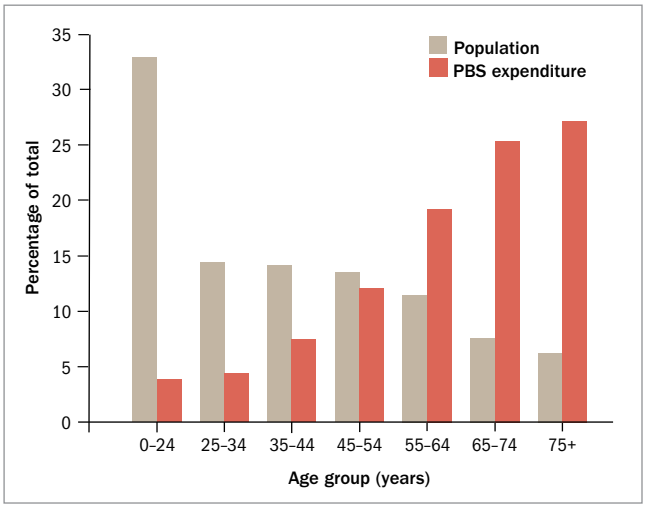

Figure 1. The relationship between age and PBS expenditure.[1] People over the age of 65 years make up fewer than 15% of the population but account for about 50% of PBS expenditure.

Characteristics of older patients

Older people may have several characteristics that make quality use of medicines a challenge (Figure 3).[6] Some of these are discussed below.

Multimorbidity. About three-quarters of people aged 75 years or older have two or more diseases. Importantly, nearly all older people with one disease have at least one other disease (typically three or four) as well.[7] Therefore, the effects of medicines prescribed for one disease have to be considered in the context of their effects on the other comorbidities, as well as the possibility of interactions with medicines prescribed for the other comorbidities. A common example is the use of an anticholinergic medicine to improve the symptoms of an overactive bladder leading to worsening of cognition in a person with mild cognitive impairment or dementia.

Limited life expectancy. The beneficial effects of some preventive treatments are accrued over years, and therefore commencing or continuing such medicines in a patient in the final months of life simply exposes them to potential adverse effects.[8] Treating or preventing a specific disease in a very elderly person may alter the cause of death without substantially impacting on life expectancy. With advances in medical care, there has been a shift in mortality from more rapid declines with malignant or cardiovascular disease to more protracted declines via frailty and dementia.[9]

Geriatric syndromes. As people move into their 80s and 90s, the geriatric syndromes become very common.[10] These syndromes include frailty, dementia, delirium, falls, incontinence, malnourishment, immobility and the complications of immobility. They occur as a result of interactions between multimorbidity, ageing biology and, in some cases, the complications of medical interventions. The goals of care may need to focus on functional outcomes associated with geriatric syndromes, and the standard disease-based approaches to prescribing may be less relevant to patients.

Age-related changes in pharmacokinetics and pharmacodynamics. Age-related changes in body composition, renal and hepatic function and drug receptors impact on many medicines, usually leading to an increased risk of adverse effects.[11] These changes usually necessitate a reduction in the doses of many medicines to avoid toxicity but might also influence their effectiveness.

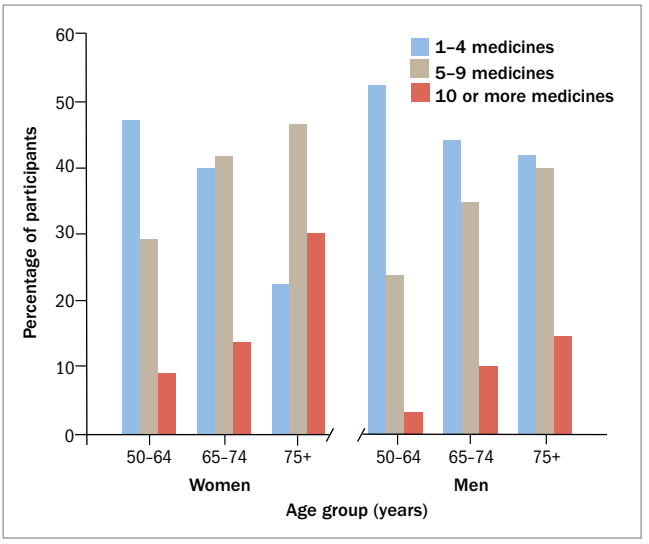

Figure 2. Number of medicines used in the previous 24 hours by age group and sex in Australia, from the National Census of Medicines Use (June 2009 to February 2010).[2] Polypharmacy is increasingly common in older age, with about two-thirds of people over the age of 75 years taking five or more medicines.

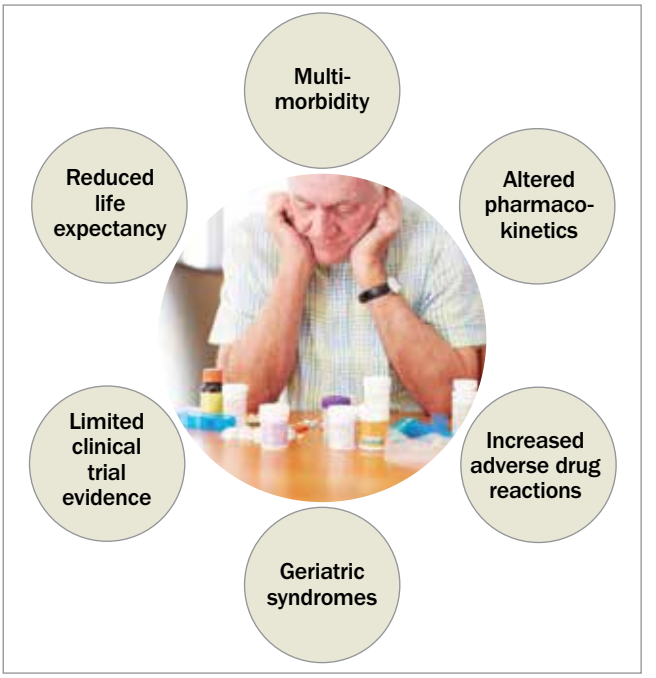

Figure 3. Major factors that need to be taken into account when prescribing for older people.

Increased susceptibility to adverse drug reactions. Older people are more likely to experience adverse drug reactions, and these are more likely to be severe and unrecognised. Although several factors contribute to this, including altered pharmacokinetics and pharmacodynamics, the main independent risk factor is obviously the number of medications that older people take. Adverse drug reactions may present atypically in older people, with exacerbation of symptoms of disease or with the geriatric syndromes, especially falls and confusion.[12] Adverse drug reactions are the 'great imitator' and should be considered as a potentially reversible cause for any new symptom in an older person.

All of these characteristics provide challenges for optimal prescribing, but perhaps one of the most challenging issues for doctors who manage older people is how to deal with the 'rising tide' of polypharmacy.[13]

Polypharmacy

Polypharmacy refers to the use of multiple medications. It is commonly defined as use of five or more medicines, and usually refers to medicines that are taken longer term. Because polypharmacy is now the norm for many older people, the terms 'hyperpolypharmacy' and 'excessive polypharmacy' have also been coined to describe use of 10 or more medicines.[14]

The prevalence of polypharmacy has increased dramatically over the past few decades. Many studies have shown a three- to fivefold increase in the prevalence of polypharmacy in older people in the community (Figure 4).[13,15,16] This shows that it is a change in medical practice and prescribing habits, rather than patient characteristics, that drive polypharmacy. However, there are patient factors that increase the likelihood of polypharmacy, including advanced age, female sex, multimorbidity and hospital admissions.

One of the causes of polypharmacy is thought to be clinical practice guidelines that focus on the optimal care for patients with only a single disease. Almost none take into account how treatments might need to be modified in the setting of multimorbidity.[17] In older people with multimorbidity, application of multiple clinical practice guidelines will inevitably lead to polypharmacy, the potential for adverse drug–drug and drug–disease interactions and a seemingly overwhelming burden of medical investigations and treatments.[18,19]

Another important contributor to polypharmacy is the prescribing cascade.[20] This occurs when one medicine is commenced to treat another medicine's side effect that has been misinterpreted as a new medical problem.[21] For example, the likelihood of being prescribed antihypertensive therapy or diuretics is increased in people who have been commenced on NSAIDs, which can increase blood pressure or cause peripheral oedema as side effects. Other common cascade dyads include metoclopramide leading to levodopa, diuretics leading to gout medicines, proton pump inhibitors leading to magnesium supplements and anticholinergics leading to cholinesterase inhibitors. For any new symptom in an older

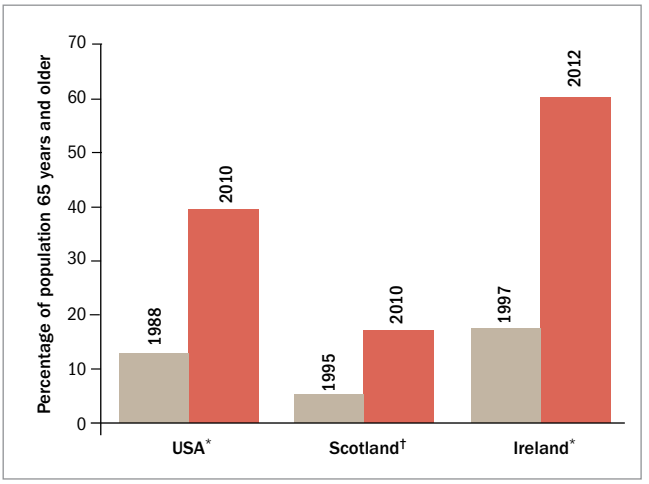

Figure 4. Prevalence of polypharmacy in people aged 65 years and older in the USA, Scotland and Ireland. There has been a three- to fivefold increase in the prevalence of polypharmacy in older people over the past few decades.[13,15,16]

* Percentage taking five or more drugs. † Percentage taking 10 or more drugs.

person, it is useful to ask which potentially causative medicine can be stopped before considering starting a new medicine.

The risks and benefits of polypharmacy

The risks of polypharmacy include adverse drug reactions and a range of other adverse outcomes, such as the geriatric syndromes (frailty, falls, confusion, malnourishment and incontinence), hospitalisation, institutionalisation and mortality.[4,5] The cut-off for the number of medications that increases the risk of falls, frailty, disability and mortality is between four and six regular medicines.[22] Polypharmacy is also associated with an increased risk of low-quality prescribing, including potentially inappropriate medicines and unnecessary medicines, underprescribing of necessary medicines and drug interactions.

On the other hand, there is only limited clinical trial evidence for any benefit from polypharmacy in the presence of multimorbidity. Most clinical trial evidence for the benefits of polypharmacy is limited to a few single disease settings, such as the use of multiple antibiotics/antivirals in infectious diseases or multiple preventive cardiometabolic therapies. Many clinical trials for single diseases specifically exclude older people or those with multimorbidity and polypharmacy. One recent observational study has shown that guideline-recommended cardiovascular prevention medicines retain their mortality benefit in patients with multimorbidity and polypharmacy.[23] In contrast, other observational studies have shown that intensive treatment of blood pressure and blood glucose in frail older or institutionalised people is associated with poorer cognitive function.[24,25]

There will be situations where clinicians feel that polypharmacy is unavoidable. In these patients – where there is little evidence for benefit and substantial evidence for harm and drug interactions – there clearly needs to be vigilant monitoring of clinical outcomes, including possible harms.

Managing polypharmacy in patients with multimorbidity

GPs report major barriers to managing patients with multimorbidity, including fragmentation of health care between primary and secondary care, inadequacy of guidelines and evidence-based medicine, and the challenges of delivering patient-centred rather than disease-focused care.[26] There are no simple algorithms for managing polypharmacy in patients with multimorbidity. Instead clinicians require a good knowledge of their patient and of pharmacology and evidence-based medicine (and its limitations). Then medication plans can be individualised to the needs and values of each patient. GPs are in the best position to do this, with long-term holistic knowledge of their patients. This can also be managed in collaboration with a pharmacist who is accredited to conduct medication reviews. The review will include a detailed medication history, reconciliation of current medicines, adherence assessment, possible medication-related problems and recommendations to the GP and patient about achieving quality use of medicines. When complex issues arise that cannot be resolved between GPs, subspecialists and patients/carers, referral to a geriatrician for a therapeutic review may be helpful.

Optimising medicine regimens

Box 1 provides a simple framework to consider when tailoring medicine regimens for the needs of older patients with multimorbidity, adapted from the American Geriatrics Society.[27]

Step 1. Determine the evidence base for single diseases

Be aware of the evidence base for managing each of the patient's diseases. This is usually straightforward and is often easily available via clinical practice guidelines, Cochrane reviews and subspecialist opinions. This may lead to a long list of medicines that are recommended for each of the diseases but not necessarily for patients with multimorbidity.

Step 2. Individualise the evidence for older subgroups

There is rarely clinical trial evidence for the efficacy for medicines in multimorbid, frail or very elderly patients, whereas there is often observational evidence for increased risks of harms. The application of multiple clinical practice guidelines to a patient with multiple diseases generates potential harms. Medicines that are useful for one disease might exacerbate another disease. The 'time to benefit' for preventive medicines may be many months or even years and may exceed the predicted life expectancy of the patient.[8] These issues usually dilute the certainty about prescribing based on single diseases and single risk factors, and reduce the number of medicines that are likely to be useful. Recommended

1. ISSUES TO CONSIDER WHEN OPTIMISING MEDICINES IN AN OLDER PERSON WITH MULTIMORBIDITY AND/OR POLYPHARMACY[27]

Step 1. Determine the evidence base for single diseases

- Gather a comprehensive and complete diagnosis and medication history
- Consider single-disease evidence-based medicine
- Consider clinical practice guidelines
- Consider subspecialist opinions

Step 2. Individualise the evidence for older subgroups, taking into account

- Multimorbidity
- Lack of clinical trial evidence
- Altered pharmacology
- Adverse drug reactions
- Shortened life expectancy

Step 3. Emphasise patient-centred care

- Identify patient's main concerns and priorities
- Share decision-making
- Consult advanced care directives
- Consider symptomatic *vs* preventive goals

Step 4. Look for red flags in the medication list

- Avoid potentially inappropriate medicines and prescribing cascades
- Avoid drug–drug and drug–disease interactions
- Consider a 'top five' medicines list

Step 5. Prescribe, deprescribe and monitor

- Obtain informed consent
- Prescribe or switch
- Deprescribe
- Reduce dosage (wean dose for medicines with known withdrawal effects)
- Consider nonpharmacological interventions
- Monitor for harms and benefits

doses will then often need to be decreased to account for age-related changes in drug disposition and the increased risks of adverse drug reactions.

Step 3. Emphasise patient-centred care and share decision-making

It is important to identify the primary concerns and values of the patient.[28] These may focus on the geriatric syndromes, quality of life or functional deficits rather than disease outcomes, mortality or management of risk factors. Advanced care directives and surrogate decision makers are sometimes required for guiding therapeutic goals if the patient has cognitive impairment. Shared decision-making will allow prioritisation of the medicine list in order of importance to the patient.

TABLE. CRITERIA AND TOOLS FOR IDENTIFYING POTENTIALLY INAPPROPRIATE MEDICINES TO BE AVOIDED OR CONSIDERED FOR DEPRESCRIBING IN OLDER PEOPLE

Criteria	Principles
Beers criteria[29]	Consensus list of medicines to be avoided in older people, including drug–drug interaction and drug–disease interactions
Drug Burden Index[30]	List of anticholinergic and sedative medicines, incorporating doses and cumulative effects
STOPP and START criteria[31]	Consensus lists of medicines that are either inappropriate or appropriate according to body system

Abbreviations: START= Screening Tool to Alert to Right Treatment; STOPP = Screening Tool of Older People's Prescriptions.

Step 4. Look for red flags in the medicine list

In most cases, GPs will be dealing with patients who are already on multiple medicines. Interpreting and identifying red flags in complicated medicine lists are important skills for clinicians managing older people. There are many different sets of tools and criteria that have been developed to identify medicines that can be avoided or stopped; the most well known are the Beers criteria, the Screening Tool of Older People's Prescriptions (STOPP) and Screening Tool to Alert to Right Treatment (START) criteria and the Drug Burden Index (Table).[29-31]

A review of these tools and criteria found similarities between them in terms of common medicines to avoid or to consider stopping.[32] This review provides a useful 'short list' of potentially inappropriate medicines:

- benzodiazepines (and z-drugs) – associated with confusion, sedation, falls and hip fractures ('z-drugs' are a group of nonbenzodiazepine drugs with similar effects to benzodiazepines, and which are used in the treatment of insomnia; most of their names start with the letter 'z')
- tricyclic antidepressants – have anticholinergic effects and are associated with impaired cognitive function, falls, constipation, urinary retention and cardiotoxicity
- medicines in people with specific conditions – anticholinergic medications in people with urinary retention or cognitive impairment; NSAIDs in people with bleeding, hypertension, heart or renal failure; alpha blockers in people with falls
- multiple medicines with the same high risk action – NSAIDs and warfarin
- multiple medicines with opposing actions – anticholinergics and cholinesterase inhibitors.

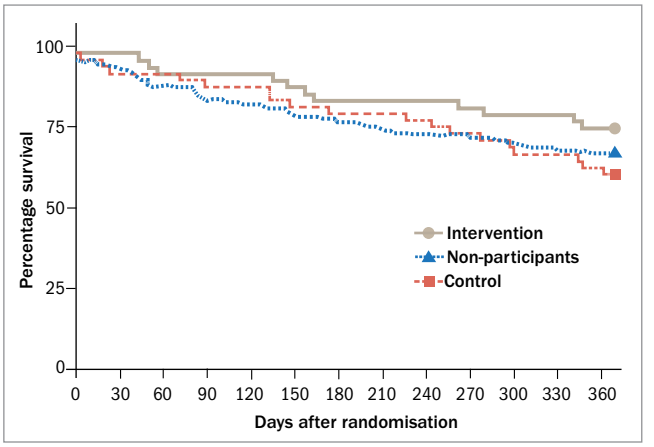

Figure 5. Mortality in frail older people in residential care facilities receiving an intervention to reduce polypharmacy (by an average of 4.4 medicines per person) compared with controls and unmatched nonparticipants.[38] There was a nonsignificant trend for mortality to be reduced with deprescribing.

The Drug Burden Index provides an important reminder that the most problematic medicines in older people are anticholinergics and sedatives. The cumulative anticholinergic and sedative loads of these medicines are associated with a range of poor outcomes including impaired cognitive and physical function.[30]

Clinicians are often more skilled and knowledgeable about the effectiveness of medications and how to start prescribing them than about how to identify the harms of medications and when to stop them.[33] To harness clinicians' skills when treating older patients with multimorbidity, it may be useful to focus on identifying which are the few medications (e.g. the 'top five') that are essential for the patient and considering reducing the rest. Pharmacists can provide assistance and advice about complex medication lists through Home Medicines Reviews and Residential Medication Management Reviews.

Step 5. Prescribe, deprescribe and monitor

It is essential to obtain genuinely informed consent prior to starting or changing medicines. Too frequently this is overlooked, particularly in older people with cognitive impairment. One of the most widely used therapeutic interventions in geriatric medicine involves carefully ceasing medicines, recently termed 'deprescribing'. If it is not possible to reduce the risk of adverse drug reactions by deprescribing then it may be possible to switch to safer medicines or to reduce the dosage. Nonpharmacological approaches can be considered when available. The patient will need to be monitored closely after any change in medicines for benefits, harms, drug interactions and withdrawal syndromes.

2. AN APPROACH TO DEPRESCRIBING*

Step 1. Ascertain all medicines the patient is currently taking and the reasons for each one

- Best possible medication history
- Brown bag review of medicines
- Dose administration aids (e.g. blister packs)

Step 2. Consider overall risk of medicine-induced harm in individual patients

- Number of regular medicines
- Potentially inappropriate medicines
- High-risk patients (age, multimorbidity, dementia)

Step 3. Assess each drug for its eligibility to be discontinued

- No valid indication
- Part of a prescribing cascade
- Actual or potential harm of drug outweighs any potential benefit
- Disease and/or symptom control drug is ineffective or symptoms have completely resolved
- Preventive drug is unlikely to confer any patient-important benefit over the patient's remaining lifespan
- Drugs are imposing unacceptable treatment burden

Step 4. Prioritise drugs for discontinuation

- Greatest risk of harm
- Easiest to deprescribe
- Patient preferences

Step 5. Implement and monitor drug discontinuation regimen

- Share decision-making and obtain consent
- Communicate with healthcare providers, carers, family
- Cease one medicine at a time
- Wean doses if withdrawal syndromes are possible
- Monitor outcomes

* Adapted from Scott et al. JAMA Intern Med 2015; 175: 827-834.[40]

Deprescribing

Deprescribing has been defined as 'the process of withdrawal of an inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes'.[34] Put simply, deprescribing is carefully ceasing medicines, but it is a positive intervention undertaken with the purpose of improving clinical outcomes. Deprescribing could be considered in the following scenarios:

- adverse drug reactions and/or lack of efficacy – in patients with multimorbidity an adverse drug reaction could include exacerbation of one disease with a medicine used to treat another disease

- geriatric syndromes – the risk of frailty, falls and cognitive impairment are increased by polypharmacy and specific classes of drugs
- end of life care – when life expectancy is limited as people become very elderly or develop terminal illnesses, preventive medicines may no longer have any significant benefits and simply expose the patient to the risk of adverse drug reactions
- inappropriate medicines and polypharmacy – there are several criteria and tools that can be useful for identifying red flag medicines (Table).[29-31] Polypharmacy and hyperpolypharmacy are associated with increased risk of adverse drug reactions and inappropriate medicines, so should prompt a medicines review and consideration of deprescribing.

There is a growing clinical trial evidence base for deprescribing. Of course, every clinical trial of a medicine has a deprescribing component embedded in it because medicines are stopped in the event of adverse drug reactions. Most deprescribing trials have focused on ceasing specific classes of drugs. For example, these have shown that deprescribing psychotropic drugs reduces the risk of falls; deprescribing antipsychotics in patients with behavioural and psychological symptoms of dementia may improve behaviour and mortality; and deprescribing statins at the end of life improves quality of life.[35-37] A number of international studies are underway on the outcomes of deprescribing in the heterogeneous settings of polypharmacy. A recent deprescribing study in residential aged care facilities in Western Australia found that reducing polypharmacy was feasible and not associated with any increase in mortality (Figure 5).[38]

Various guidelines or principles have been developed to guide deprescribing.[39] A recent Australian approach is shown in Box 2.[40] Deprescribing of some medicines might produce withdrawal syndromes, discontinuation syndromes, rebound effects and unmasking of drug interactions. These can be minimised by tapering medicines, often over weeks and months. This will be particularly important for medicines with established withdrawal syndromes, such as psychotropic medicines, beta blockers, proton pump inhibitors, levodopa and corticosteroids.[41] If the symptoms of the disease recur (these should not be confused with withdrawal reactions) then the medicine can be restarted, but this is required in only a very small number of patients.[42]

Conclusions

Multimorbidity, polypharmacy and deprescribing are major challenges for clinicians caring for older people. It is important to recognise the limitations of the evidence base in these situations and the central role of patient-centred care when prioritising medicines. Awareness of pharmacological principles and the concept of potentially inappropriate medicines can assist in identifying red flag medicines that should be avoided or deprescribed. Careful clinical monitoring after medicines have been changed is key to ensuring that patients' goals are being met and harms avoided. MT

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Further reading

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