

Problematic polypharmacy and deprescribing

Polypharmacy is increasingly common, particularly in the elderly population. In this *Policy Brief*, the College takes a closer look at problematic polypharmacy and how it might be tackled in general practice.

Polypharmacy and problematic polypharmacy

Polypharmacy is the concurrent use of multiple medicines by one individual.^{1,2} While polypharmacy might be appropriate and beneficial for some patients, problematic polypharmacy is of concern. Problematic polypharmacy is the prescribing of multiple medicines inappropriately or where the intended benefit is not realised.¹

Problematic polypharmacy may arise because:¹

- the risk of harm is likely to outweigh benefit
- the combination of medicines is hazardous because of their interactions
- the overall demands of taking medicine are unacceptable to the patient or make it difficult to achieve clinically useful medication adherence
- medicines are prescribed to treat the side effects of other medicines where alternative solutions are available
- treatments are not evidence-based (including the use of multiple single-disease guidelines in multimorbidity, discussed below).

In New Zealand, the Health Quality & Safety Commission (HQSC) found that, on average, 35% of people aged 65 or older received five

or more long-term medicines (2012–2014),² which is similar to those in other developed countries.³ The number of long-term medicines was also found to increase with age: 26% of those aged 65–74 were on five or more long-term medicines compared to 56.6% of those aged 85 and older.² Around one in 24 people aged 65 or older received 11 or more long-term medicines.

A New Zealand study looking at potentially inappropriate medicines in 2011 found that 40.9% of people aged 65 or older were prescribed potentially inappropriate medicines, of which diclofenac and amitriptyline were most commonly dispensed, followed by ibuprofen, zopiclone and naproxen.⁷ It is estimated that one in five medicines commonly used in older people might be inappropriate.^{3,8}

Specific numeric thresholds are often used to identify those most at risk (eg more than five regular prescribed medicines). The number of medicines being taken has been found to be the most important predictor of harm.⁴ However, defining polypharmacy by the number of medicines alone may be too simple and fails to acknowledge the wide variation in potential risk of adverse effects caused by medicines.^{5,6}

Drivers of polypharmacy

An ageing population and multimorbidity are key drivers of polypharmacy.¹ Many clinical trials and single-disease clinical guidelines do not consider polypharmacy in the context of comorbidities and patient preferences.^{1,9,10}

Key messages

- Problematic polypharmacy – the prescribing of multiple medicines inappropriately or where the intended benefit is not realised – is increasingly common in the elderly.
- Problematic polypharmacy increases the risk of adverse drug events, which contribute to ill health, disability, hospitalisation and death.
- GPs play a crucial role in ensuring patients get the best possible outcomes from medicines.
- Having clear discussions with patients is an important strategy in avoiding polypharmacy.
- Consider deprescribing for higher risk polypharmacy. A cautious approach to deprescribing includes two principles: stop one drug at a time, and wean doses slowly over weeks and months.
- There are various useful resources on optimising medicines, including how to identify and safely withdraw potentially inappropriate medicines.

Having clear discussions with patients is an important strategy in avoiding polypharmacy. The patient's needs, care goals, current level of functioning, life expectancy, and preferences should be ascertained, recognising that they might change over time. For some patients, daily living may matter more than controlling symptoms or risk factors.

Further contributors to polypharmacy:

- Visits to multiple prescribers and pharmacies, especially by patients with multimorbidity, can lead to an increased risk of medication-related problems arising from fragmented care.
- GPs may also be reluctant to stop medicines initiated by hospital specialists.
- The trend towards increased prescribing internationally^{2,9} and the increasing use of preventive interventions in asymptomatic people.¹

Why is this important?

Inappropriate polypharmacy increases the risk of adverse drug events (ADEs).^{*3} Older people (>65) are particularly affected because of the changes in their pharmacokinetic and pharmacodynamic responses to medicines.⁹ Opioids, anticoagulants, antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs) and diuretics are commonly implicated as causing ADEs.¹¹

The HQSC reports the frequency of ADEs to be 13% with two medicines, increasing to 58% with five medicines, and 82% when seven or more medicines are taken.^{2,15} ADEs are often preventable; 28% of ADEs have been judged preventable in adult hospital admissions¹² and 27.6% in older people in the ambulatory clinical setting.¹³

ADEs contribute to ill health, disability, hospitalisation and death.³ Data from three New Zealand district health boards

showed a rate of ADEs of 30 per 100 admissions, with more serious harm occurring in 5%.¹¹

In addition to ADEs, polypharmacy is also associated with reduced medication adherence, increased financial costs^{2,10,14} and geriatric syndromes such as urinary incontinence, cognitive impairment, and impaired balance with falls.¹⁵

GPs and patient-centred care

GPs play a crucial role in ensuring patients get the best possible outcomes from medicines. This includes discontinuing prescribed medication where it no longer provides a benefit, the harm outweighs the benefit, or it causes adverse effects.¹

Patient-centred care is integral to improving the quality of medicines use, and informed consent and shared decision-making are at its crux. The challenge for GPs is to prescribe medicines according to the individual's circumstances and wishes rather than purely aligned with the evidence base.

Having clear discussions with patients is an important strategy in avoiding polypharmacy.¹⁶ The patient's needs, care goals, current level of functioning, life expectancy, and preferences should be ascertained,^{17,18} recognising that they might change over time. For some patients, daily living may matter more than controlling symptoms or risk factors.¹⁹

The UK Royal Pharmaceutical Society stressed the person-centred approach in its call for a shift in thinking from

medicines management (issuing medication safely and efficiently) to medicines optimisation (supporting the best outcomes for patients).²⁰

Medicines optimisation is underpinned by four principles:

1. Aim to understand the patient's experience
2. Ensure evidence-based choices about medicines
3. Ensure medicines use is as safe as possible
4. Make medicines optimisation part of routine practice.

Consider deprescribing for problematic polypharmacy

Good practice requires regular medicine reviews, particularly for patients with multimorbidity. Medicine reviews are a good time to consider deprescribing for problematic polypharmacy.¹⁶

To identify higher risk polypharmacy during a medicine review, the King's Fund suggests focusing on patients:¹

- taking 10 or more regular medicines, or
- taking between four and nine regular medicines and also:
 - meets criteria for potentially inappropriate prescribing (using prescribing tools)
 - at risk of a potential drug–drug interaction or clinical contraindication
 - has difficulties with medicine-taking
 - no or only one major diagnosis
 - receiving end-of-life or palliative care.

* Medication errors and adverse drug reactions are the main causes of ADEs.

Deprescribing is the systematic process of tapering or stopping medicines. Deprescribing involves identifying and discontinuing medicines where the existing/potential harms outweigh existing/potential benefits in relation to an individual patient's care goals, current level of function, life expectancy, values and preferences.³

Potential benefits of deprescribing include:

- resolving adverse drug reactions
- removing the risk of future adverse reactions and interactions
- improving adherence with other medications
- reducing costs and inconvenience
- improving function and quality of life.^{3,16}

There is emerging evidence to suggest that deprescribing is feasible, safe and, in many instances, beneficial.¹⁴ Although direct evidence on the effect of deprescribing on clinical outcomes is limited,³ the strongest evidence for benefit is from cohort and observational studies of the withdrawal of specific medication classes, leading to a resolution of adverse drug reactions.²¹

Deprescribing should be undertaken as a partnership with the patient, giving information specific to them on the benefit–

harm trade-offs of continuing or discontinuing a particular medicine, why changes are suggested and what can be expected.²²

A cautious approach to deprescribing includes two principles – stop one drug at a time, and wean doses slowly over weeks and months. Patients should be warned and monitored for signs of:²³

- withdrawal reactions (26% in one study²⁴)
- rebound symptoms
- unmasked drug interactions.

These can be prevented or minimised by tapering the dose, monitoring, and restarting medicines if the condition returns.²¹ In older people, caution is needed as underprescribing (the underuse of necessary medication) has been a concern.^{5,21}

Deprescribing could be considered for patients with the highest risk of ADEs, predictors of which include:^{22,25}

- number of medicines
- past history of ADEs
- presence of major comorbidities

- marked frailty
- residential care settings
- multiple prescribers.

ADEs can mimic problems in older patients, such as falls, delirium, lethargy.²⁶

Other situations in which to consider deprescribing include where:³

- the patient presents with new symptoms suggestive of adverse medication effects
- the patient receives high-risk medicines or combinations
- treatment is ineffective
- the patient has suffered falls
- the patient's treatment goals have changed
- the patient has a terminal illness, dementia, or is fully dependent on others for care
- the patient receives preventive drugs in the absence of increased disease risk.

A deprescribing protocol

Table 1 summarises a five-step deprescribing protocol developed by Scott et al.³

Table 1. Deprescribing protocol (adapted from Scott et al., May 2015³)

Key step	Processes	Notes
1 Ascertain all current medicines and reasons for each one	<ul style="list-style-type: none"> ■ Ask patients/carers to bring in all medicines and delivery aids. ■ Ask whether any regularly prescribed medicines are not being taken and why. 	
2 Consider overall risk of medicine-induced harm to determine the required intensity of deprescribing	<p>Ascertain and assess risk according to:</p> <ul style="list-style-type: none"> ■ Medication factors: number, use of 'high-risk' medicines, past/present toxicity. ■ Patient factors: age >80, cognitive impairment, comorbidities, substance abuse, multiple prescribers, nonadherence (past/current). 	

Key step	Processes	Notes
<p>3 Assess each medicine for its eligibility to be discontinued:</p> <ul style="list-style-type: none"> ■ No valid indication ■ Part of a prescribing cascade* ■ Actual or potential harm of medicine clearly outweighs any potential benefit ■ Medicine is ineffective for disease/symptom control ■ Symptoms have completely resolved ■ Preventive medicine is unlikely to confer any important benefit over the patient's remaining lifespan ■ Medicines are imposing unacceptable treatment burden 	<ul style="list-style-type: none"> ■ Identify medicines prescribed: <ol style="list-style-type: none"> a. for a doubtful diagnosis b. for a confirmed diagnosis, but evidence of efficacy is non-existent c. that confer no additional benefit after a certain period of continuous use or certain age. ■ Identify medicines prescribed to counteract adverse effects of other medicines. ■ Reconsider indications for the initial culprit medicine or its substitution by an alternative with superior tolerability. ■ Identify medicines to avoid in older patients. ■ Identify medicines causing well-known adverse effects. ■ Ask the patient: <ol style="list-style-type: none"> a. if the medicine has made a difference to how they feel such that they prefer to stay on it. b. if they are still experiencing troublesome symptoms and if they feel the medicine is still required. ■ Consider discontinuing medicines if target condition is self-limiting, mild, intermittent, or amenable to non-drug interventions. ■ Determine patient's expectations and preferences (eg if present day quality of life is more important than prolonging life or preventing future morbid events). ■ Estimate patient's life expectancy (eg risk prediction tools or 'surprise' question†). ■ Identify medicines unlikely to confer benefit over patient's remaining lifespan. ■ Ask patient about any concerns other than side effects with the medicine. ■ Identify medicines that are particularly burdensome. 	<p>What are the current indications for each medicine?</p> <p>Collect as much information as possible to answer:</p> <ul style="list-style-type: none"> ■ Why and when was therapy initiated? ■ Was the diagnosis substantiated? ■ Was the medicine prescribed to counter adverse effects of another medicine? ■ Is the medicine continuing to confer evident patient benefit? ■ Are there alternative, equally effective non-pharmacological therapies available? <p>Some well-tolerated medicines are continued for years on the assumption that they are useful. An expiry date would prompt reappraisal and earlier review if the patient's clinical status changed substantially.</p> <p>Is the patient actually taking the drug?</p> <p>Older patients avoid using medicines that make them feel unwell or when given conflicting advice on benefit and harm. Cost and burden of monitoring are also disincentives.</p> <p>Does the medicine fit with the patient's life circumstances?</p> <p>Medicines are rarely indicated if they do not confer an important benefit within the context of the patient's life circumstances.</p> <p>Does the likely benefit of the medicine outweigh its potential for harm?</p> <p>Older patients are particularly vulnerable to adverse effects from 'high-risk' medicines such as opioids, benzodiazepines, psychotropic drugs, NSAIDs, anticoagulants, digoxin, cardiovascular drugs, hypoglycaemic agents and drugs with anticholinergic effects.</p> <p>In 'high-risk' medicine combinations, each individual medicine augments the level of toxicity.</p> <p>It can be helpful to group medicines into two categories:</p> <ol style="list-style-type: none"> 1. Disease and/or symptom control medicines. 2. Preventive medicines – consider absolute risks and benefits of treatment for individual patients, the time to benefit, patient preferences, and estimated lifespan.

* The prescribing cascade occurs when a medicine is prescribed to counter the adverse effect of another medicine. For example, hypertension is an adverse drug reaction to NSAIDs, for which antihypertensive medication is prescribed.

† The 'surprise' question in advanced cancer patients, "Knowing all that I know about this patient, would I be surprised if he or she were to die in the next 12 months?", has been found to be reasonably predictive.²⁷

Key step	Processes	Notes
4 Prioritise medicines for discontinuation	<p>Prioritisation may depend on the combination of:</p> <ol style="list-style-type: none"> medicines with the greatest harm and least benefit medicines easiest to discontinue (ie lowest likelihood of withdrawal reactions or disease rebound) medicines that the patient is most willing to discontinue first. <p>Discontinue medicines with greatest harm/benefit ratio and lowest likelihood of adverse withdrawal reactions or disease rebound syndromes.</p>	
5 Implement discontinuation regimen and closely monitor patients for improvement in outcomes or onset of adverse effect	<ul style="list-style-type: none"> ■ Explain and agree on management plan. ■ Cease one medicine at a time (so harms and benefits can be attributed to specific medicines and rectified if necessary). ■ For medicines more likely to cause adverse withdrawal effects, wean off medicine and instruct patient on what to look for and to report, and on self-initiating actions. ■ Communicate plan to all involved health professionals and carers. ■ Document reasons for deprescribing and outcomes. 	

Interprofessional care

Medicines optimisation requires health professionals to work together to individualise care, monitor outcomes more carefully, review medicines more frequently, and support patients.^{1,10,16,20}

The evidence for the effectiveness of pharmacist-led interventions for complex polypharmacy in primary care is mixed.^{10,15} However, the pharmacist-led information technology intervention (PINCER trial) has been shown to substantially reduce the frequency of a range of clinically important prescription and medication monitoring errors.²⁸ Thus, commentators recommend close collaboration between pharmacists and doctors,¹⁰ and multidisciplinary care¹⁵ as sensible approaches.

Collaborative prescriber–pharmacist medicine reviews using validated criteria to identify unnecessary or harmful medicines can help initiate and guide deprescribing.³

In New Zealand, Medicines Therapy Assessment (MTA) services may be provided by accredited pharmacists working as part of a multidisciplinary team alongside patients to optimise medication treatment for those with long-term conditions and comorbidities. Multidisciplinary review programmes have been implemented in some areas and have the potential to make a marked difference in reducing inappropriate polypharmacy²⁹ and associated costs.⁵

Electronic decision support systems may also assist with identifying potentially inappropriate prescribing.^{9,16,30} Shared care records would enable GPs, pharmacists and hospital doctors to access more complete information on prescribing for individual patients.

Tools and guidance

Deprescribing is highly individualised and time-consuming. Some of the various resources on optimising medicines,

including how to identify and safely withdraw potentially inappropriate medicines, are listed below.

Prescribing tools

- **STOPP START Toolkit Supporting Medication Review** (NHS Cumbria, 2013). The STOPP (Screening Tool of Older People's potentially inappropriate Prescriptions) START (Screening Tool to Alert doctors to Right, ie appropriate, indicated Treatments) Toolkit helps to assess medicines in the context of the patient's current clinical condition.
- **The Beers Criteria to identify potentially inappropriate medication use in older adults** (American Geriatrics Society, 2015).
- A new scale, the Drug Burden Index (DBI), is currently being investigated in New Zealand to assess whether the DBI predicts adverse effects of medicines taking into account other comorbidities.³¹
- The Medication Appropriateness Index (MAI) requires ratings on 10 explicit criteria to determine whether a given

medicine is appropriate. The MAI provides operational definitions and instructions on evaluation.^{1,32}

- The Assessment of Underutilisation (AOU) used in conjunction with the MAI comprises 11 questions and accommodates assessment of under-prescribing.³⁰

Practical guidance

- **A practical guide to stopping medicines in older people** (bpac^{nz}; 2010) provides guidance on stopping medicines, including antidepressants, benzodiazepines, antihypertensive, statins, warfarin, NSAIDs, acid suppressants, bisphosphonates, oral corticosteroids, antiparkinson agents.
- **Polypharmacy in primary care: managing a clinical conundrum** (bpac^{nz}; 2014) sets out how to perform a medicine review (recommended periodically in high-risk patients and following hospital discharge) and provides practical tips on optimising prescribing.
- **Polypharmacy and medicines optimisation** (The King's Fund; 28 November 2013) provides practical tips in medicines management of polypharmacy.
- **Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes** (NICE guideline; 4 March 2015) offers best practice advice on the care of all people using medicines and those receiving suboptimal benefit from medicines, and advice on medication review.

Clinical audit

- **HQSC's clinical audit template on polypharmacy in older people** encourages reflection and action to improve clinical practice by identifying variation between a local DHB's prescribing practice and other DHBs (Atlas of Healthcare Variation), reviewing prescribing patterns,

and considering individual patients who might benefit from medication review (by running patient management system (PMS) queries on polypharmacy). The audit has been accredited by the College for CPD requirements.

- **Atlas of Healthcare Variation: Polypharmacy in older people** (HQSC; 2015) shows regional variation between health care provided using data drawn from claim and payment information from community pharmacists for subsidised dispensing. The Atlas is based on the premise that reducing variation potentially improves undertreatment and overtreatment.
- **Instructions on how to run PMS queries on polypharmacy queries** (MedTech and MyPractice)

Medicine reconciliation

- **Medicine reconciliation guidance tools and training materials** (HQSC; 2012). Medicine reconciliation has been demonstrated to significantly reduce medication errors caused by incomplete or insufficient documentation of medicine-related information.

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