Deprescribing in older people

Abstract

Polypharmacy and multimorbidity are both currently rising. The number of medicines taken is the single biggest predictor of adverse drug events. Deprescribing is an approach to managing polypharmacy and reducing adverse outcomes. Multiple international evidence-based guidelines are emerging to promote discontinuation of high-risk medications, and use of alternative medical and non-pharmacological management. This review outlines the evidence base behind deprescribing, and suggests some pragmatic approaches to decision making around medication review.

Key words: Polypharmacy; Polymorbidity; Deprescribing; Multimorbidity; Drug–drug interactions; Drug errors; Adverse drug event; Medication review

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Deprescribing is the process of withdrawal of an inappropriate medication, supervised by a health-care professional, with the goal of managing polypharmacy and improving outcomes (Reeve et al, 2015). It should be implemented longitudinally with regular reviews, particularly in individuals with multimorbidity and polypharmacy (Scottish Government Polypharmacy Model of Care Group, 2018). Deprescribing involves considering the individual's therapeutic goals and priorities, and any potential for common and serious adverse effects.

Polypharmacy and polymorbidity

In 2016, 18% of the UK population was aged 65 years and over, compared to 15.8% in 1991 (Office for National Statistics, 2018). By 2066, it is predicted that the number aged 65 years and over will comprise 26% of the total population (Office for National Statistics, 2018). The prevalence of chronic disease is rising in association with population ageing (Kingston et al, 2018). Managing chronic conditions either with preventative, curative or palliative intent involves increasingly complex medical strategies.

A cross-sectional study of prescribing in primary care in Scotland found that use of drugs of all classes has increased between 1995 and 2010, except for anti-infective drugs and those for musculoskeletal conditions (Guthrie et al, 2015). In this 15-year period, the proportion of adult patients dispensed five or more medications has doubled from 11.4% to 20.8%, and the proportion taking 10 or more medicines tripled to 5.8%. Much of this polypharmacy is evidence based, but problematic or potentially inappropriate polypharmacy occurs commonly (Table 1).

Of the population 65 years old and over, 95% is considered to be multimorbid, defined as being diagnosed with two or more medical or psychiatric conditions (Violan et al, 2014). One fifth of individuals aged 75–79 years were living with three or more health conditions in 2016 (Office for National Statistics, 2018). Because of alterations in pharmacodynamics

Table 1. Problematic polypharmacy

Medication may be considered problematic or potentially inappropriate when:

- It is no longer clinically indicated, or the rationale for the medication has changed
- The therapeutic goal is not being achieved
- The adverse effects of the drug, or combination of drugs, is causing more harm than good, or is putting the patient at unacceptably high risk of harm
- The medication regimen becomes impractical or too complicated to manage

Scottish Government Polypharmacy Model of Care Group (2018)

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and pharmacokinetics, older people are more likely to experience adverse effects, such as delirium and falls (Slattum et al, 2017).

Lower socioeconomic status, in addition to age, is a risk factor for polypharmacy, adverse drug events and emergency hospital admissions (Guthrie et al, 2015). Those most at risk of polypharmacy are those within the 4th and 5th deprivation quintiles, living in cities and urban areas, and those in residential or nursing homes (Guthrie et al, 2015).

A study of adverse drug reactions as a cause of hospital admissions in the UK found that 6.5% of emergency hospital admissions could be attributed to adverse drug reactions (Pirmohamed et al, 2004). With a median hospital stay of 8 bed days, hospital admissions as a result of adverse drug reactions were estimated to cost the NHS £466 million each year (Pirmohamed et al, 2004). This largely represents an avoidable expense, and more importantly avoidable harm.

A deterioration in renal function, or a multifactorial fall following changes in medication weeks before may easily be missed. Deprescribing involves thinking ahead, anticipating potential risk and managing that risk either by reducing or stopping the drug. Adverse drug events are commonly overlooked, or attributed to a deterioration in the underlying comorbidity (Pirmohamed et al, 2004).

Care home residents are particularly at risk of harm from medication errors. In the Care Home Use of Medicines study, 256 care home residents were taking a mean of eight medicines, and two thirds of this group had had one or more drug errors (Barber et al, 2009). Errors were found to occur at dispensing, prescribing, monitoring and administering stages. A total of 153 prescribing errors occurred in 100 residents, and interestingly there were more errors in residential homes than nursing homes. These errors occurred as a result of missing information, unnecessary drugs, incorrect dosing or omissions. Medicine delivery systems did not reduce the risk of error. Responsibility for and understanding of medicines are often taken away from care home residents, and there is a need to promote autonomy and empower patients to get the best use out of their medicines.

Deprescribing: an ethical perspective

Review of medication needs to be considered within an ethical framework. The General Medical Council (2019) advocates that an effective doctor–patient relationship should be based on openness, trust and good communication. Consent for treatments should be informed, including an explanation of intended benefits and potential risks (General Medical Council, 2019). Such principles are engrained in an ethical code of conduct, aiming for beneficence and non-maleficence.

Research has found patients are open to being on fewer medications – 40% of those in residential homes in an Australian study indicated willingness to stop taking one or more medication (Kalogianis et al, 2016). An American study of ambulant patients found 90% were open to stopping one or more of their medicines (Fillit et al, 1999). Those with life-limiting illnesses may wish to reduce the burden of medicines in order to focus on quality of life, but also may fear that reducing treatments may signify the end of their lives (Todd et al, 2016). Treatment decisions including deprescribing should not be based simply on chronological age. Health-care professionals and patients should be aware of limitations within the evidence base for deprescribing. There is consistent evidence that deprescribing is safe (Page et al, 2016), but there is limited evidence for beneficial effects on quality of life and in reducing harm.

Effects on mortality and health outcomes

Expected implications of stopping or reducing a treatment should be openly discussed with patients and carers. Medications may have been continued where the indication has changed or the duration of treatment has passed. New medical complications may have arisen, or altered pharmacokinetics and pharmacodynamics may now be a factor, alerting a clinician to increased potential for harm.

A systematic review and meta-analysis of 116 studies sought to assess the effect of deprescribing interventions on overall mortality (Page et al, 2016). There was no statistically significant effect on mortality in randomized studies (odds ratio 0.92, 95% confidence interval

0.61–1.11). However, when patient-specific measures were implemented in medication review, mortality was found to significantly reduce (odds ratio 0.62, 95% confidence interval 0.43–0.88). There was no change in mortality with education programmes alone. In patients with dementia, no change in mortality was seen. Overall, no increase in adverse withdrawal events was identified. The number of patients falling did not reduce, but these patients fell less frequently.

The impact of taking less medication will vary according to the patient's lifestyle, educational level and cultural background. Given medication review should be patient-centred, motivated by individual therapeutic goals, investigating quality of life is paramount for future research.

A pragmatic approach to managing polypharmacy

Several guidelines have been published in recent years to aid systematic medication review and guide the deprescribing process. They advocate a systematic approach, putting the patient and his/her views at the centre of decision making.

Prioritize those most at risk

The Scottish *Polypharmacy Guidance: Realistic Prescribing* identifies four groups most at risk of adverse outcomes (Table 2), and prioritizes patients in these groups for medication review (Scottish Government Polypharmacy Model of Care Group, 2018). Polypharmacy increases with increasing age, but it can occur in younger individuals, especially in more deprived populations (Guthrie et al, 2015). The single biggest predictor of adverse drug reactions and drug–drug interactions is the number of drugs being taken (Field et al, 2004).

The Royal Pharmaceutical Society (2019) has published guidance for England, Scotland and Wales, which outlines methods of reducing polypharmacy in frail older people, those with dementia, and those approaching the end of life.

Identify high-risk medicines and high-risk combinations

Drugs commonly associated with adverse drug reactions as a contributory factor to hospital admission are summarized in Table 3. High-risk prescribing includes high-risk combinations. Targetting patients taking 10 or more medications should help detect synergistic combinations of drugs. Steroids, when taken with non-steroidal anti-inflammatory drugs for chronic inflammatory conditions, increase the relative risk of peptic ulcer disease five-fold compared to steroids alone (Griffin et al, 1991). Anticoagulants, when taken with non-steroidal anti-inflammatory drugs, increase the relative risk of gastrointestinal bleeding approximately four-fold compared with anticoagulation without concomitant non-steroidal anti-inflammatory drugs (Shorr et al, 1993).

Anticholinergic medicines are associated with reduced physical functioning and dementia (Fox et al, 2014; Richardson et al, 2018) in the older population. Diuretics and antihypertensives commonly contribute to postural hypotension and/or acute kidney injury, particularly during acute dehydrating illness. The concept of 'sick-day rules' can be helpful, empowering patients to omit these medications temporarily during sick days (Scottish Government Polypharmacy Model of Care Group, 2018) (Figure 1).

The anticholinergic burden scale calculates the total anticholinergic burden of medications prescribed (Boustani et al, 2008). A score of 3 and above is associated with increased mortality (hazard ratio 1.83) and cardiovascular disease (hazard ratio 2.17) (Myint et al, 2015).

Table 2. Who to target

Aged 50 years and over and resident in a care home
Approaching end of life or have life-limiting illness
Prescribed 10 or more medicines
On high-risk medicines

From Scottish Government Polypharmacy Model of Care Group (2018)

Table 3. Drugs that commonly cause adverse drug events
Non-steroidal anti-inflammatory drugs
Warfarin
Diuretics
Angiotensin-converting enzyme inhibitors
Angiotensin receptor antagonists
Antidepressants
Clopidogrel
Beta-blockers
Digoxin
Prednisolone
Opiates

From Pirmohamed et al (2004)

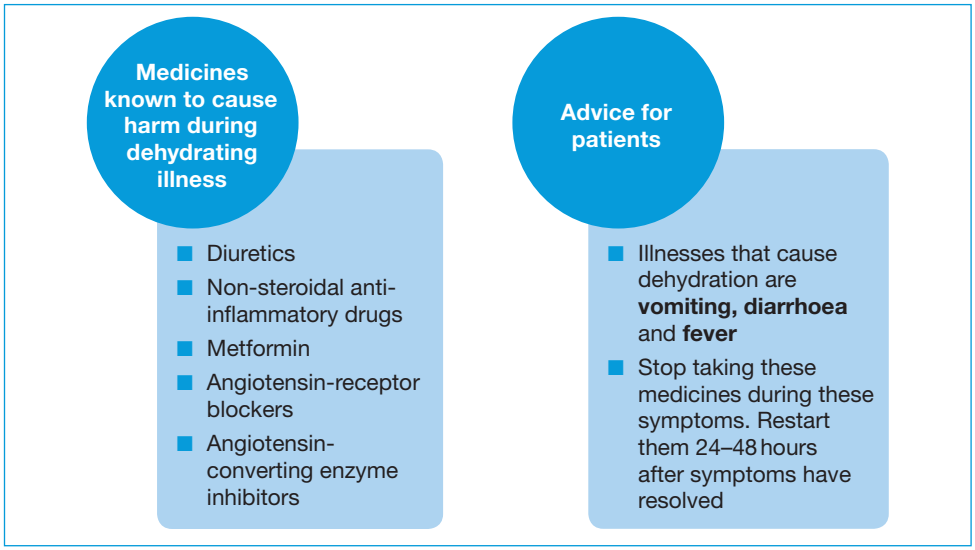

Figure 1. Medicine sick-day rules.

Opioids, benzodiazepines, calcium-channel blockers and histamine-1 receptor antagonists are known to increase the risk of delirium (Clegg and Young, 2011).

Use tools to aid systematic medication review

The STOPP/START criteria consists of a comprehensive list of medicines, with evidence-based indications (O'Mahony et al, 2015). The STOPP list identifies potentially inappropriate drugs, or combinations of drugs, in older adults because of anticipated risk. The START list includes evidenced indications for commencing a drug in older adults. Use of these criteria can reduce potentially inappropriate medications in community and long-term care settings (Hill-Taylor et al, 2016). Randomized controlled trials of STOPP/START in acute and long-term care settings have demonstrated benefits in reducing falls, delirium, hospital length of stay, and primary care and emergency care visits (Hill-Taylor et al, 2016). Beers criteria, initially developed in 2003, have been updated in 2019 by the American Geriatrics Society (By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel, 2019).

To empower patients participating in medication decisions, the National Institute for Health Research has developed a user-friendly medication passport (National Institute of Health Research and Collaboration for Leadership in Applied Health Research and Care,

2018). It contains relevant information about the patient, previous adverse events, details of compliance aids and any changes made. It can be downloaded as an app, and aims for seamless transfer of information across health-care interactions.

Take a step-wise approach to medication review with patients

Patients should be at the centre of medication review. The Scottish polypharmacy guidance is comprehensive, and advocates a seven-step medication review, seeking the patient's views, and assessing safety and risk of harm (Scottish Government Polypharmacy Model of Care Group, 2018) (Table 4).

Use evidence-based deprescribing guidelines

Researchers in Canada have developed evidence-based guidelines for discontinuing proton-pump inhibitors, benzodiazepines and Z-drugs, antipsychotics, and antihyperglycaemics. These guidelines have collated evidence on how best to withdraw medicines, examining the evidence for tapering or stopping, and how to monitor for relapse of symptoms or withdrawal effects. Patient information leaflets are available to support the patient through the process, and can be accessed at https://deprescribing.org/resources/deprescribing-information-pamphlets/.

Benzodiazepine and Z-drug deprescribing

Regular use of benzodiazepines and Z-drugs for more than 7–28 days leads to reduced efficacy, but risks of benzodiazepines remain, outweighing any likely benefit after 28 days (Vinkers and Olivier, 2012). Tapering of benzodiazepines and Z-drug doses is recommended, reducing by 25% every 2 weeks, and then tapering more slowly, with 12.5% reductions in the final weeks and/or on planned drug-free days (Figure 2). The guidance advocates vigilance in monitoring for withdrawal symptoms, ideally every 1–2 weeks during the tapering process. If insomnia persists, behavioural and psychological interventions can improve sleep outcomes (Pottie et al, 2018). Melatonin does not appear to improve benzodiazepine cessation rates. A patient information leaflet has been prepared to complement verbal advice given.

Antipsychotic deprescribing

Antipsychotics increase the risk of stroke and mortality 1.5–1.7-fold in patients with dementia (Corbett and Ballard, 2012). In a randomized controlled trial of antipsychotic withdrawal in patients with dementia, 36-month survival was reduced to 30% in patients taking antipsychotics compared with 59% in those taking placebo (Ballard et al, 2009).

Antipsychotics for behavioural and psychological symptoms of dementia should only be used as a last resort and not for long-term treatment. Treatment response should be closely monitored. Once behaviour has stabilized after approximately 3 months, doses should be tapered. Non-pharmacological measures including modifications to environment and routines can be effective in managing behavioural and psychological symptoms of dementia.

Table 4. Seven-step medication review

1. Aims – what matters to the patient?
2. Needs – identify essential drug therapy
3. Not needed – stop unnecessary medicines
4. Effectiveness – are the therapeutic goals being achieved?
5. Safety – is there potential or existing harm?
6. Efficiency – is the treatment cost-effective?
7. Patient view – is the patient willing and able to take them?

From Scottish Government Polypharmacy Model of Care Group (2018)

Antihyperglycaemic deprescribing

Therapeutic goals when treating diabetes may change with advancing age, particularly in those with increased risk of falls, developing frailty, cognitive impairment, or near the end of life.

Clinicians should be alert to hypoglycaemia in the very frail population. Neuropsychiatric symptoms like confusion and drowsiness predominate, while autonomic symptoms like sweating and shaking are often absent (Farrell et al, 2017a). Older people with hypoglycaemic episodes may present with falls or cognitive impairment. Glycaemic targets need to be reviewed in the frail, those with complex comorbidities and those near the end of life. The American Diabetes Association and the American Geriatrics Society consensus guidance suggests glycosylated haemoglobin (HbA_{1c}) level targets <69 mmol/litre in older adults with poor health (>2 activities of daily living dependencies, moderate to severe cognitive impairment, and/or end-stage chronic illness) and <58.5 mmol/litre in healthy older adults (American Diabetes Association, 2019). When withdrawing antihyperglycaemics, consideration should be given to stopping or reducing agents with a higher risk of hypoglycaemia first, such as sulphonylureas **(Figure 3).**

Proton-pump inhibitor deprescribing

Continued long-term use of proton-pump inhibitors is associated with increased risk of osteoporosis, *Clostridium difficile* infection, hyponatraemia and hypomagnesaemia (Farrell et al, 2017b). Proton-pump inhibitors should be prescribed for treatment durations in accordance with licensed indications. *Helicobacter pylori* infection should be sought as a reversible cause of symptoms. Prolonged courses of acid-lowering medications outside their indications expose patients to risk with no clear evidence of benefit. Only a minority of patients is likely to benefit from long-term use – those with Barrett's oesophagus, severe oesophagitis, previous bleeding gastrointestinal ulcer, or chronic non-steroidal anti-inflammatory drug use with bleeding risks. Short-term use for exacerbations of symptoms

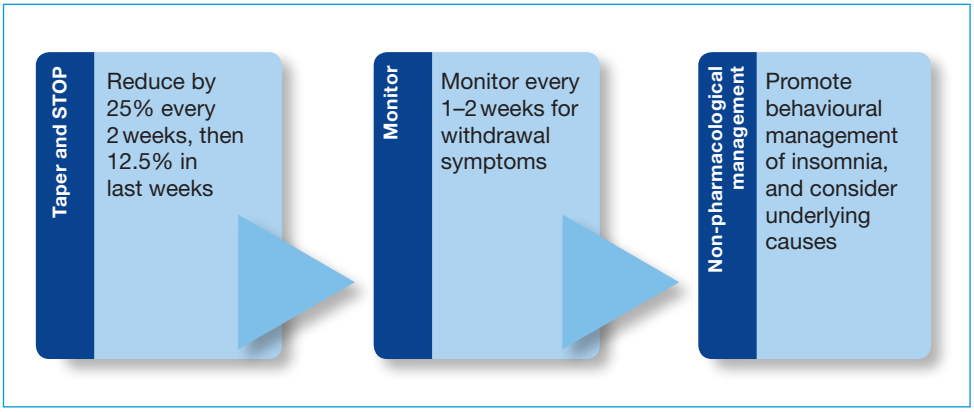

Figure 2. Deprescribing benzodiazepines and Z-drugs.

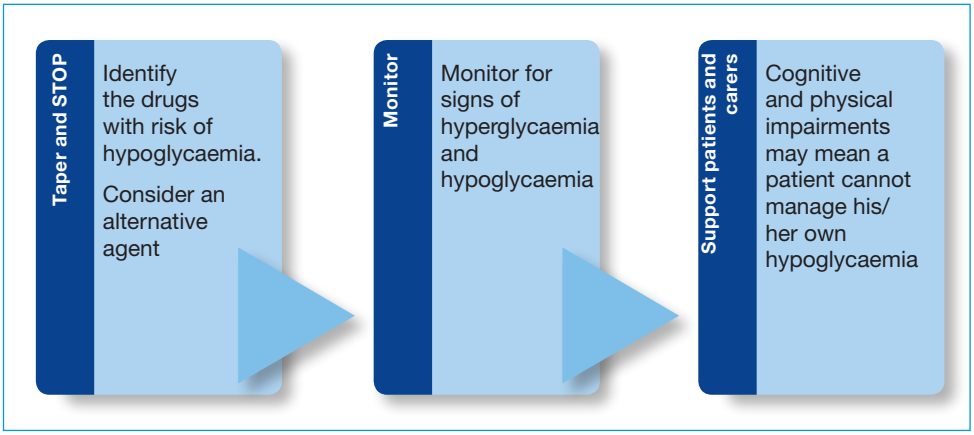

Figure 3. Deprescribing antihyperglycaemic agents.

for 4–8 weeks would be more appropriate in most cases. Patient education should include advice on non-pharmacological management, such as dietary advice and use of upright positioning in preventing reflux symptoms (Figure 4).

Deprescribing near the end of life

STOPPFRAIL is a screening tool for potentially inappropriate medicines in frail older adults with life-limiting conditions, where symptom control is the first priority (Lavan et al, 2017). It is designed for those with a prognosis of around 1 year, and severe functional or cognitive impairment. Discussions about withdrawal of futile medications should be part of a wider conversation around patient priorities and how treatment goals may have changed. Remaining life expectancy, and time to treatment benefit for each medicine should be considered. The Gold Standards Framework prognostic indicators can help identify those with poor 1-year survival prognosis (The Gold Standards Framework Centre In End of Life Care, 2011).

Challenges to deprescribing

Conversations with individuals around rationalising treatments are time consuming and complex. They often involve families or carers, and require an understanding of the conditions being managed, and expected prognosis. Current 10-minute GP appointments do not facilitate such discussions. Delays and miscommunications between secondary and primary care may cause unintended continuation of medicines. Being unable to see the same doctor consistently can be a further barrier to building trust. It can be challenging for a generalist to discontinue medicines started by a specialist. Involvement of allied health professionals, including pharmacists and nurse practitioners, can be beneficial in facilitating these complex decisions.

Conclusions

Deprescribing is an important component of delivering person-centred care, particularly in those with polypharmacy at risk of adverse events. Patients should be supported through the process with alternative treatment options, both pharmacological and non-pharmacological. Attention should be particularly directed at those with increased risk as a result of high-risk medications or combinations of medications, and frail populations.

Multiple focussed guidelines now encourage clinicians to reduce potentially inappropriate prescribing supported by robust evidence. However, the evidence base documenting patient perspectives, outcomes and effects on quality of life remains sparse. Further research is needed into the effects of deprescribing on clinically relevant and patient-related outcomes.

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Conflicts of interest

The authors declare no conflicts of interest..

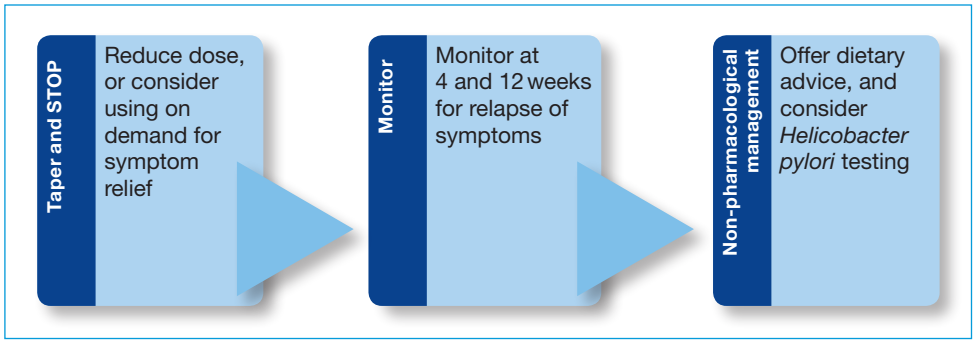

Figure 4. Deprescribing proton pump inhibitors.

Key points

- In an ageing multimorbid population, frail and vulnerable patients are often exposed to problematic polypharmacy.
- Identifying those most at risk of harm and prioritizing these patients for medication review is a pragmatic way to reduce the burden of complex medication regimens with the potential to cause harm.
- Several tools are available to aid systematic medication review, including STOPP/START, which help reduce potentially inappropriate prescribing.
- Deprescribing is complex, and should occur proactively in anticipation of harm as well as following adverse drug events.
- Deprescribing is an important component of good quality end of life care, but there is limited evidence on the impact on quality of life.

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