

# Deciding when to stop: towards evidence-based deprescribing of drugs in older populations

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## Abstract

Minimising the harm from inappropriate prescribing in older populations is a major urgent concern for modern healthcare systems. In everyday encounters between prescribers and patients, opportunities should be taken to identify patients at high risk of harm from polypharmacy and reappraise their need for specific drugs. Attempts to reconcile life expectancy, comorbidity burden, care goals and patient preferences with the benefits and harms of medications should be made in every patient at significant risk. Drugs identified by this process of reconciliation as conferring little or no benefit and/or excessive risk of harm should be candidates for discontinuation. Evidence supporting a structured approach to drug discontinuation (or deprescribing) is emerging, and while many barriers to deprescribing exist in routine practice, various enabling strategies can help overcome them.

## Introduction

Minimising the harm of inappropriate prescribing in older populations (persons aged 65 years or more) is a major urgent concern for modern healthcare systems. Over a 5-year period, one in four older persons are hospitalised for medication-related problems,<sup>1</sup> accounting for more than 10% of all hospital admissions in this population,<sup>2</sup> with between 30% and 55% deemed preventable.<sup>3–4</sup> In the wider community, one in three subjects receiving five or more drugs suffer an adverse drug reaction (ADR) every 12 months, with more than a quarter deemed preventable.<sup>5</sup> Up to 18% of all inpatient deaths are attributable in part to ADRs<sup>6</sup> and 44% of patients at hospital discharge are prescribed at least one unnecessary drug.<sup>7</sup>

The drivers of polypharmacy are multiple: plethora of disease-specific clinical guideline recommendations (many of which may not be applicable to older patients with multiple comorbidities) coupled with guideline-derived quality indicators and performance incentives; patient and carer expectations and provider sensitivity about age discrimination; inadequate knowledge of geriatric therapeutics and toxicology; focus on treating acute disease (often with additional drugs) while neglecting reappraisal of existing drugs for chronic disease; and ADRs being misinterpreted as new diseases requiring more drugs. Clinical research, guidelines and models of care seldom support the complex and difficult decisions about when to stop existing drugs or withhold new ones in older patients with multiple comorbidities.<sup>8</sup>

## Issues to consider when discontinuing inappropriate medications

Appropriate prescribing comprises use of drugs associated with strong evidence of benefit while eliminating

medications with questionable or no evidence of efficacy, unfavourable risk–benefit trade-offs or expressed patient preference to avoid. We have formulated an evidence-based 10-step discontinuation guide based on a conceptual framework fully described elsewhere (see figure 1).<sup>9</sup> Face validity of this guide has been confirmed among an unselected group of doctors whose prescribing intentions with regard to a hypothetical case changed significantly after guide application.<sup>10</sup> Certain issues relating to this framework deserve particular emphasis.

All medications a patient is taking, including complementary and non-prescription drugs, must be accurately ascertained. Limited evidence suggests the ‘brown paper bag’ method of asking patients (or carers) to physically bring all medicines with them to the clinical encounter is the best way to reconcile medications. Asking specific questions to detect non-adherence also helps identify drugs which may be ceased.

Patients at highest risk of ADRs are those prescribed the greatest number of drugs (up to 82% risk with seven drugs or more<sup>11</sup>) or which include high-risk drugs (antithrombotic agents, insulin, oral hypoglycaemic agents, cardiovascular and central nervous system drugs). Clinicians need to look for pre-existing drug toxicity presenting as falls, confusion and lethargy, effects too often inappropriately attributed to ageing.

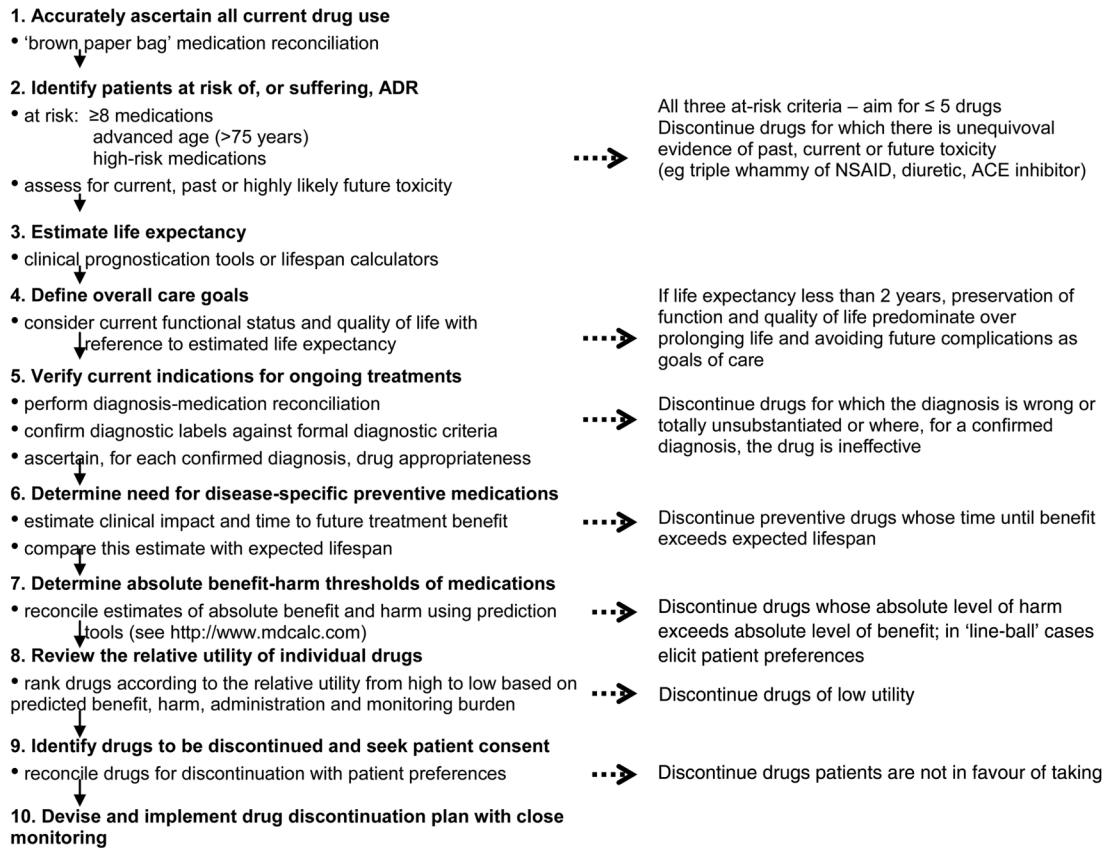
Estimating a patient’s life expectancy is important in determining the goals of care and potential long-term value of many preventive medications. Patients with a limited lifespan (12 months or less) due to marked frailty, advanced dementia, metastatic cancer and end-stage organ disease should have more conservative care goals and their preferences may call for reductions in drug burden. In particular, such patients will gain little value from medications that take more than a year for benefits to manifest, such as bisphosphonate therapy (to prevent osteoporotic fractures) or statins (to prevent cardiovascular events).

Even when medications are intended to treat current active disease, diagnoses should be verified as symptoms and signs may manifest in an unusual manner in older people. Where diseases have been misdiagnosed or are no longer active, attendant drugs should be discontinued. Cross-sectional studies suggest diagnoses of heart failure, Parkinson’s disease and depression, while prevalent in older populations, often lack substantiation in individual cases.<sup>12–13</sup>

Even when clear indications exist, recent studies have challenged the safety in older patients of aggressive ‘treat-to-target’ drug regimens for diseases such as diabetes and hypertension. Absolute disease risk must be reconciled with absolute risk of harm using tools such as the CHADS2 score for estimating thromboembolic stroke risk and HAS-BLED score for estimating



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**Figure 1** Tool for identifying and discontinuing potentially inappropriate drugs.

risk of major bleeding from anticoagulants in patients with non-valvular atrial fibrillation.

In the final evaluation, the overall utility of individual drugs spans a continuum between those of high utility (proven and sizeable benefit in virtually all eligible older patients, little administration or monitoring burden, small potential for harm) and those of low utility (questionable indications, onerous administration or monitoring burden, high risk of harm in most, if not all, patients). In between are drugs whose relative utility rests on a case-by-case consideration of the framework steps in figure 1 and the questions listed in Table 1. Validated screening tools such as the updated Beers criteria<sup>14</sup> or STOPP tool<sup>15</sup> can also identify many (although by no means all) low-utility drugs.

The final say needs to rest with the patient or, where necessary, his/her delegated advocate. Even for seemingly effective drugs with valid indications and little or no risk of serious harm, older patients place as much, if not more, emphasis on avoiding short-term toxicity affecting cognitive, physical and emotional function—even if uncommon—than on primary effects on future disease risk.<sup>16</sup> The more drugs prescribed and the greater the potential for more side-effects, the higher the rates of non-adherence—as high as 85%.<sup>17</sup> Once a discontinuation regimen has been decided, selected drugs can then be ceased or weaned, one at a time, while monitoring the patient closely for disease recrudescence or onset of withdrawal or rebound syndromes.<sup>7</sup> Table 2 lists drugs which warrant gradual weaning over extended periods of time.

**Evidence for drug discontinuation**

Evidence is emerging for more proactive approaches to drug discontinuation. In one trial involving 119 older disabled patients, 332 different drugs (average 2.8 drugs per patient) were discontinued using an algorithm, leading to reductions in 12 month mortality (21% vs 45%), referral rates to acute care facilities (12% vs 30%) and drug costs.<sup>18</sup> In another study using the same algorithm and involving 70 community-dwelling older patients prescribed a mean of 7.7 drugs, 58% of medications were discontinued with an 81% success rate with no long-term adverse consequences and almost 90% of patients reporting global improvement in health.<sup>19</sup> Another study used Medicare claims data in the USA to retrospectively identify patients prescribed inappropriate drugs, following which prescribers were mailed cautionary information which led, 6 months later, to discontinuation of 49% of these drugs.<sup>20</sup> In other cohort studies, more than 50% of drugs prescribed to older patients have been discontinued or reduced in dose without major untoward effects.<sup>21</sup> In a study of 119 nursing home residents receiving selective serotonin reuptake inhibitors for more than 12 months, withdrawal was successfully achieved in 52% following a structured drug review.<sup>22</sup>

A randomised trial showed significant decrease in numbers of drugs and trend towards fewer falls in patients whose medications were reviewed by pharmacists using STOPP criteria.<sup>23</sup> In one systematic review, between 20% and 85% of patients remained normotensive without any increase in mortality after withdrawal

**Table 1** How to determine drug utility

*What is the strength of indication (in order of decreasing utility)?*

The drug:

1. Provides immediate relief of distressing symptoms (eg, analgesics, antiemetics and antipruritics).
2. Effectively modifies an acute condition that is life threatening or will soon result in distressing symptoms if not treated (eg, antibiotics for sepsis, diuretics for acute heart failure and bronchodilators for asthma).
3. Effectively modifies a chronic condition that might progress to become life threatening or cause distressing symptoms if not treated (eg, methotrexate for rheumatoid arthritis and ACE inhibitors for chronic heart failure).
4. Has the potential to prevent serious diseases or adverse events in the future, without immediate effect (eg, antiplatelet agents to prevent cardiovascular disease, bisphosphonates to prevent osteoporotic fractures and antihypertensives to prevent stroke).
5. Is unlikely to be useful in either the short or long term (eg, vitamin supplements).
6. Is prescribed where a non-drug therapy (eg, physiotherapy instead of non-steroidal anti-inflammatory drugs for lower back pain) is more beneficial.

*What is the likelihood of misuse, toxicity or non-adherence?*

The drug:

1. Is associated with little benefit and high risk of toxicity in most older patients (on the basis of Beers' criteria or other drugs-to-avoid lists).
2. Is a duplication in drug therapy (ie, a second drug from the same class).
3. Is prescribed for an adverse drug reaction (ADR).  
If so, can the drug causing the ADR be withdrawn or substituted with another agent less likely to cause an ADR?
4. Is a potentially beneficial drug but is prescribed at a dose likely to cause toxicity.  
If so, can another effective, less toxic dose or medication be substituted?
5. Has the potential for significant drug–drug or drug–disease interactions.  
If so, can it be withdrawn or substituted with another agent less likely to cause an interaction?
6. Is taken more often than once daily.  
Can another equally effective drug be substituted that can be scheduled once daily?
7. Can be safely administered as a combination medication.
8. Is causing significant difficulties with adherence?  
If so, can it be withdrawn or substituted with another agent more likely to be taken?

of antihypertensive drugs,<sup>24</sup> while in another review, discontinuation of psychotropic medications led to fewer falls and improvement in daily function and

cognition.<sup>25</sup> Other systematic reviews of deprescribing trials<sup>26–28</sup> describe successful results arising from medication reviews by clinical pharmacists, prescriber

**Table 2** Medications commonly associated with discontinuation syndromes which require slow weaning

Medication	Type of discontinuation syndrome	Clinical manifestations
α-Blockers	W, R	Agitation, headache, hypertension and palpitations
ACE-inhibitors	D	Heart failure and hypertension
Antianginal agents	D	Angina
Anticonvulsants	W, D	Anxiety, depression and seizures
Antidepressants	W, D	Akathisia, anxiety, chills, coryza, gastrointestinal distress, headache, insomnia, irritability, malaise, myalgia and depression
Antiparkinsonian agents	W, D, R	Hypotension, psychosis, pulmonary embolism, rigidity and tremor
Antipsychotic	W	Dyskinesias, insomnia, nausea and restlessness
Anticholinergics	W	Anxiety, nausea, vomiting, headache and dizziness
Baclofen	W, R	Agitation, anxiety, confusion, depression, hallucinations, hypertonia, insomnia, mania, nightmares, paranoia and seizures
Benzodiazepines	W	Agitation, anxiety, confusion, delirium, insomnia and seizures
β-Blockers	W, D	Angina, anxiety, hypertension, acute coronary syndrome and tachycardia
Corticosteroid	W, R, D	Anorexia, hypotension, nausea, weakness, hypothalamic–pituitary–adrenal axis suppression and inflammatory states
Digoxin	D	Heart failure and palpitations
Diuretic	D	Heart failure and hypertension
Narcotic analgesia	W	Abdominal cramping, anger, anxiety, chills, diaphoresis, diarrhoea, insomnia and restlessness
NSAIDs	D	Recurrence of gout and arthritis

D, disease recrudescence; NSAID, non-steroidal anti-inflammatory drug; R, rebound; W, withdrawal.

education programmes and reminders, academic detailing, comprehensive geriatric assessments, multidisciplinary conferences and patient-centred interventions.

### Conclusion

Evidence is accumulating on the need for, and feasibility and benefits of, appropriate drug discontinuation in older patients. The systematic approach described here provides guidance in performing this increasingly important task and also serves as a checklist when considering start of additional drugs. While ceasing medications can be difficult and time consuming, prescribers have a responsibility to minimise the potential for harm and waste of resources arising from inappropriate polypharmacy in vulnerable older persons.

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