



# Stopping medicines in older people: the flip side of the prescribing equation

Older people are generally prescribed more medicines than younger people, which contributes to a higher risk of adverse effects. Not all medicines are intended to be used indefinitely and the balance of benefits and risks associated with each medicine and dose can change over time.

## KEY PRACTICE POINTS:

- The use of multiple medicines increases with age; Māori and Pacific peoples use multiple medicines at a younger age than Europeans, likely due to the earlier onset of chronic disease in these groups
- A higher number of medicines is associated with an increased risk of medicines interactions, adverse effects and difficulties with medicines use and adherence
- Regularly review the medicine regimen of all older patients, particularly those prescribed multiple medicines, e.g. five or more, or taking combinations of medicines with a higher risk of adverse effects
- The aim of a medicine review is to ensure that medicines and doses remain appropriate based on a current indication, that the benefits of treatment outweigh the associated harms and the regimen is as simple as possible
- If a medicine is identified that is no longer necessary, develop a plan in consultation with the patient for stopping, stop one medicine at a time and monitor for symptoms of discontinuation or recurrence of the condition being treated

*“There are many evidence-based guidelines to help clinicians start drug treatment. There is much less evidence to guide clinicians about withdrawing medicines”<sup>1</sup>*

## Medicine use increases with age

The use of multiple medicines, known as polypharmacy, is common in older people and increases the risk of adverse outcomes.<sup>2</sup> In New Zealand, 35% of people aged over 65 years were prescribed five or more medicines in 2016; approximately 4% were prescribed 11 or more.<sup>3</sup> Rates of prescribing increase sharply with age and are highest in people aged 85 years and over.<sup>3</sup>

## Polypharmacy begins earlier in people of Māori or Pacific ethnicity

People of Māori or Pacific ethnicity are more likely to receive multiple medicines at a younger age than people of European/Other ethnicity. In 2016, 32% of Māori and 45% of Pacific

peoples aged 65–74 years were prescribed five or more medicines, compared to 24% of European/Others of the same age.<sup>3</sup> This likely reflects the earlier onset of chronic disease in Māori and Pacific peoples.

 For further information on polypharmacy in older people in New Zealand, see: [www.hqsc.govt.nz/our-programmes/health-quality-evaluation/projects/atlas-of-healthcare-variation/polypharmacy/](http://www.hqsc.govt.nz/our-programmes/health-quality-evaluation/projects/atlas-of-healthcare-variation/polypharmacy/)

## More medicine does not necessarily mean better medicine

There are valid clinical reasons why older people may be prescribed large numbers of medicines, including an increasing prevalence of multiple chronic conditions in older age. For some people polypharmacy is necessary and reflects that they are receiving an appropriate evidence-based standard of care according to current guidelines, and some people receiving multiple medicines may still have unmet need in terms of pharmacological treatment. However, all medicines are associated with risks, and these risks are increased when multiple medicines are used, including:<sup>4</sup>

- Interactions between medicines
- Additive risk of adverse events, such as an increased risk of falls due to combinations of anticholinergic and sedative medicines<sup>5</sup>
- Interactions between a medicine prescribed for one condition and management of another (medicine-disease interaction), e.g. for a patient with osteoarthritis and chronic kidney disease, initiation of a non-steroidal anti-inflammatory medicine (NSAID) can worsen renal function
- Reduced adherence due to “pill burden”, i.e. confusion over the regimen, and the financial cost of multiple prescription items

## A pressure to prescribe and unclear evidence can lead to high use of medicines

Guidelines usually focus on the treatment of a single condition, which can lead to the use of multiple medicines in patients who have several co-morbidities.<sup>2</sup> An analysis of guidelines in the United States found that a patient with three chronic conditions would be recommended to take 6–13 medicines daily.<sup>6</sup> Additionally, guidelines and clinical trials often focus on when to initiate a medicine, with lesser attention paid to when to reduce the dose or stop the treatment. The evidence regarding the benefits and risks associated with a particular medicine can be uncertain for older people, especially those with frailty or co-morbidities, as these groups are often excluded from clinical trials.

Other aspects of medical practice which may contribute to the use of a large number of medicines include:<sup>2</sup>

- Time constraints leading to the renewal of prescriptions without reviewing whether continued use of the medicine is indicated. Conversations about stopping preventative medicines may bring up challenging discussions about life expectancy which require time.
- Prescribing cascades where a medicine is initiated to treat a symptom which is actually an adverse reaction to another medicine, e.g. ACE inhibitor causing dizziness, resulting in a prescription for prochlorperazine<sup>7</sup>
- Continuing to prescribe a medicine which was initiated as a prophylactic treatment after the original medicine is stopped, e.g. ongoing use of a proton pump inhibitor, prescribed for ulcer prophylaxis, in someone who has stopped taking a NSAID
- Difficulty stopping a medicine due to adverse discontinuation effects, e.g. benzodiazepines or antidepressants
- Reluctance of general practitioners to withdraw medicines initiated in secondary care
- Difficulty accessing services that provide specialist support and advice regarding appropriate prescribing in older people, e.g. geriatric medicine specialists, Long-Term Conditions pharmacy services
- Clinician and patient fears about the condition returning, worsening or an adverse event occurring if a medicine is stopped

## Stopping can be just as important as starting

Stopping medicines, often referred to as de-prescribing, is an integral part of the prescribing process, and can bring about benefits to patients and reduce harm.<sup>6</sup> In clinical trials, reductions in the numbers of medicines prescribed to older patients has been associated with fewer falls and fractures, reduced referral to acute services, improved cognitive function and better quality of life, with fewer medicines errors and improved adherence to the medicines they continue to take.<sup>8–10</sup> This information should be discussed with patients when carrying out a review to help them understand the benefits associated with reducing the number of medicines they use.

## Reviewing medicine use in older patients

General practitioners generally have a detailed knowledge of a patient’s medical history and life circumstances and are therefore well-placed to take a lead role in reviewing a patient’s prescribed medicines. Some practices may have a clinical pharmacist available to carry out a medicines review.

When reviewing the medicine regimen, consider the patient’s overall state of health, such as co-morbidities and

the presence of frailty, rather than basing treatment decisions solely on chronological age. Guidelines typically use a strict age criterion when discussing whether to prescribe or withdraw a medicine, e.g. over 70 years, however, the risks associated with medicines can vary from patient to patient. Withdrawing medicines at younger or older ages than those recommended in treatment guidelines may be appropriate.

 For further information on assessing frailty, see: "Identifying frailty in primary care" in "Frailty in older people: a discussion" available from, [www.bpac.org.nz/2018/frailty.aspx](http://www.bpac.org.nz/2018/frailty.aspx)

### Setting the scene: discussing the role of medicines for individual patients

A key aspect of reviewing medicine use is discussing with patients what their goals are for treatment, e.g. which symptoms they want to improve the most or what activities they would like to be able to do, and what benefits and harms might be associated with achieving these goals. Ensuring this information is communicated effectively enables the patient to make an informed decision. This is particularly important if the clinician and patient have different objectives or priorities; for example, a clinician may place more emphasis on a patient with atrial fibrillation taking an oral anticoagulant to prevent stroke, whereas the patient may be more interested in symptomatic relief of their osteoarthritis and feel the anticoagulant is of lesser importance. The medicine review is also an opportunity to check that the patient understands what each of their prescribed medicines are for.

If the possibility of withdrawing a preventive medicine is discussed, emphasise to patients that this does not signify that you are giving up on them, and frame the conversation around providing the best balance of benefits and risks at each stage of their life. It may be helpful to explain this in terms of

the number needed to treat or the absolute risk reduction associated with a particular medicine; consider using a visual resource to facilitate this discussion. In older adults, the possible benefits may be less than when they started taking the medicine but with the same, or increased, risk of adverse effects. Alternatively, the risk a preventive medicine was aiming to reduce may no longer be relevant for the patient's stage of life; for example, intensive blood glucose lowering to prevent the development of long-term diabetes complications may no longer be appropriate in someone nearing the end of their life as they are unlikely to live long enough for those complications to occur.

 **Best practice tip:** Provide patients with a medicines list that includes what each medicine they take is prescribed for and whether it is used for prevention or treatment of an existing condition. Alternatively, direct patients to ask their pharmacist for a medicines list. An example of a medicines list can be found here: <https://activities.nps.org.au/nps-order-form/Resources/English-Medicines-List-March-2016.pdf>

### Conduct a medicines reconciliation or "brown bag review"

A medicines reconciliation aims to ensure that the medicines a patient is actually taking are the same as what has been prescribed to them according to their medical records.<sup>2</sup> This can be done by asking patients to bring in all the medicines they are currently taking, including over-the-counter medicines and supplementary products. This process could alert the clinician to a variety of issues, such as duplicated medicines, e.g. a prescribed NSAID and a NSAID purchased over-the-counter, medicines prescribed by other clinicians in primary or secondary care, or lack of adherence, e.g. a medicine has been stopped by the patient or not taken as prescribed.

## Consider recommending Advance Care planning

Conversations about stopping medicines may involve discussion about the priorities and goals of the patient as they approach the end of their life. This may be an appropriate time to recommend resources on advance care planning which can assist people in deciding what they would want to happen to them should they be unable to make health care decisions for themselves, also known as an advance directive.

 Resources for clinicians and patients regarding advance directives can be found here: [www.hqsc.govt.nz/our-programmes/advancecareplanning/](http://www.hqsc.govt.nz/our-programmes/advancecareplanning/)

 Further reading: "End-of-life care for patients with chronic disease: have we made a difference?", bpac<sup>nz</sup>, 2015, available from: [www.bpac.org.nz/BPJ/2015/February/end-of-life.aspx](http://www.bpac.org.nz/BPJ/2015/February/end-of-life.aspx)

## Consider whether the prescribed regimen remains appropriate

Clinicians can reflect on whether any changes should be made to a patient's prescribed regimen by asking themselves or the patient/caregiver:<sup>8</sup>

- Is the original condition which the medicine was prescribed for still present?
- Are medicines initiated for symptomatic management providing adequate relief?
- Are there any medicines which do not have a clear indication for use?
- Has there been a change in the patient's health status, e.g. frailty or falls, which alters the balance between the benefits and possible harms of a particular treatment?
- Are there any duplications in the patients prescribed medicines, e.g. two medicines from the same class initiated to treat the same condition when one is sufficient?
- Are any simplifications in their prescribed regimen possible? For example, once daily medicines or combination tablets.
- Were any medicines initiated to treat an adverse reaction to another medicine, i.e. a prescribing cascade? If so, could both medicines be stopped?
- Is there a risk of medicine interactions, including with any over-the-counter medicines or supplements?
- Is the dose appropriate? For example, declining renal function may mean a lower dose is required in an older adult.
- Could a non-pharmacological treatment be used instead? For example, exercise or physiotherapy for patients with osteoarthritis, instead of non-steroidal anti-inflammatory medicines.
- Does the patient have any concerns regarding their prescription regimen?

## The balance of benefits and harms associated with a medicine may change in older people

Commonly prescribed medicines which are associated with an increased risk of adverse effects in older adults, particularly those with frailty, are shown in Table 1. Increased attention to combinations of medicines which can lead to adverse effects may be more useful than focusing on individual medicines. For example, the combination of anticholinergic medicines with medicines with sedative properties is associated with an increased risk of falls.<sup>5</sup> The "triple whammy", i.e. angiotensin converting enzyme (ACE) inhibitor/ angiotensin receptor blocker (ARB), a diuretic and an NSAID, should be avoided due to the increased risk of kidney injury.<sup>3</sup>

 For further information on the triple whammy in primary care, see: [www.bpac.org.nz/2018/triple-whammy.aspx](http://www.bpac.org.nz/2018/triple-whammy.aspx)

 Upcoming articles will discuss the use of PPIs and bisphosphonates, when and how to discontinue these medicines

## Consider whether dose reductions or de-intensifying treatment are appropriate

In older adults, increased attention to changes in hepatic or renal function may be necessary to avoid adverse effects that occur with age, frailty status or medicine use. It is recommended that the Cockcroft-Gault equation be used to assess renal function in older people as their reduced muscle mass, and consequently lower serum creatinine levels, can lead to an overestimation of renal function when using the estimated glomerular filtration rate (eGFR).<sup>15</sup> A conservative interpretation of the results is still appropriate as even the Cockcroft-Gault method may overestimate renal function.

 A tool for calculating creatinine clearance using the Cockcroft-Gault equation is available from: <https://nzf.org.nz/nzf/resource/Creatinine%20Clearance%20Calculator.htm>

De-intensifying treatment may be appropriate for some patients. For example, for people with diabetes a less stringent HbA<sub>1c</sub> target, such as < 64 mmol/mol, is recommended in a variety of situations which are more common in older people, such as limited life expectancy, increased risk of falls, multiple co-morbidities, or if lower targets are difficult to achieve in patients who have had diabetes for many years.<sup>16, 17</sup> People with frailty are more susceptible to the adverse effects associated with achieving a stringent blood pressure target, e.g. hypotension and syncope. Therefore it may be appropriate to reduce doses of antihypertensive medicines and aim for a more conservative treatment target.

## Assess whether simplifications are possible in patients with multiple conditions

For patients with multiple conditions, treatments which improve a single condition may not greatly improve their overall health or quality of life; the focus needs to be on what is most important to the patient.<sup>18</sup> Ask them about their goals for care, which aspects of their health are the most important to them to improve, to determine whether any changes can be made to help them achieve these goals while simplifying treatment.

## Review a patient's medicines before and after a stay in hospital

Medical care during an acute stay in hospital is primarily focused on the reason for admission and a patient's acute

**Table 1:** Commonly prescribed medicines associated with changes in the balance of benefits and risks in older adults.<sup>2,11</sup>

Medicine class	Potential harms, particularly in older patients
<b>Anticholinergic medicines</b>	Increased risk of falls, delirium, cognitive impairment and urinary retention
<b>Antihypertensive medicines</b>	Increased risk of hypotension and falls
<b>Antipsychotics</b>	Increased risk of mortality in patients with dementia, increased risk of falls and postural hypotension when used as sedatives or hypnotics, e.g. quetiapine
<b>Aspirin</b>	Increased risk of gastrointestinal bleeding, limited evidence of benefit for CVD prevention <sup>12</sup>
<b>Benzodiazepines or zopiclone</b>	Increased risk of falls, cognitive impairment and possible association with Alzheimer's disease
<b>Bisphosphonates</b>	Increased risk of atypical fractures with prolonged treatment.
<b>Diabetes medicines</b>	Intensive glucose lowering is unlikely to benefit older patients; risk of hypoglycaemia with some medicines
<b>Hypnotics</b>	Cognitive effects the following day, increased risk of falls, possible increased risk of Alzheimer's disease
<b>NSAIDs</b>	Greater increase in absolute risk of bleeding than in younger patients, acute kidney injury
<b>Opioids</b>	Constipation, delirium, sedation, increased risk of falls or unintentional overdose <sup>13</sup>
<b>Proton pump inhibitors (PPIs)</b>	Increased risk of fractures, <i>Clostridium difficile</i> infection and renal adverse effects such as interstitial nephritis
<b>Statins</b>	Risk of adverse effects, e.g. myalgia, new onset diabetes mellitus, limited evidence of benefit for CVD prevention <sup>14</sup>
<b>Tricyclic antidepressants</b>	Cognitive impairment, urinary retention, postural hypotension, increased risk of falls

needs during that time; reviewing their prescribed medicines following discharge can ensure that medicines initiated with the intention of short-term use are not continued long-term and any duplicated or inappropriate medicines are stopped.<sup>4</sup> A recent study conducted in the United Kingdom including over 38,000 people aged  $\geq 65$  years found that the risk of potentially inappropriate prescribing, according to the STOPP criteria\*, was higher for patients after an admission to hospital than before admission (adjusted odds ratio = 1.72; 95% confidence interval = 1.63 to 1.84).<sup>19</sup>

Reviewing medicines prior to a planned hospital admission is also useful to simplify a patient's regimen, where possible, and ensure they are aware of, and follow, instructions for withdrawing anticoagulants or other changes to their usual regimen which may apply.

\* Screening Tool of Older People's Prescriptions (STOPP) criteria identifies medicines that may be inappropriately prescribed to older people due to the risk of harms outweighing the benefits of treatment, e.g. increased risk of adverse reactions due to incorrect dose or duration of treatment.<sup>20</sup>

## Implementing changes

**Act while the patient is engaged.** Many people are open to the idea of stopping particular medicines if their general practitioner deemed it would be best. For example, a study of approximately 2000 older adults in the United States found that 92% were willing to stop one of their prescribed medicines if their doctor recommended it.<sup>21</sup> If a patient or caregiver raises questions or concerns about the number of medicines they are taking, use this as an opportunity to carry out a review.

**Withdraw one medicine at a time.** Stopping the use of one medicine at a time is a cautious approach which can help identify which medicine was causing an adverse effect, or avoid confusion if discontinuation symptoms develop after stopping.<sup>1</sup> Some medicines, e.g. benzodiazepines, antidepressants, proton pump inhibitors, should be withdrawn by tapering doses.

**Work in collaboration with the pharmacy.** Discussing a patient's medicines with their community pharmacist can help to ensure that their regimen is the most appropriate for their circumstances and co-morbidities. Pharmacies also offer services to assist patients with their medicine adherence and simplifying medicines regimens (see: "Pharmacy services can assist patients with large numbers of prescribed medicines"). Patients should be encouraged to use a single pharmacy of their choice, where possible.

 For further information on stopping medicines, including some deprescribing algorithms for specific medicines, see: [www.deprescribing.org/resources/deprescribing-guidelines-algorithms/](http://www.deprescribing.org/resources/deprescribing-guidelines-algorithms/)

### A little extra effort can go a long way

Reviewing the medicines regimen that an older patient is taking, discussing whether changes should be made and withdrawing medicines where appropriate will inevitably add

to the length of an appointment. However, evaluating whether a medicine should be continued, adjusted or stopped is part of good patient care and regular review has the potential to avoid adverse effects and improve quality of life for older patients taking multiple medicines.

 Resources from the Goodfellow Unit which provide further information on stopping medicines in older adults are:

- A podcast on "Deprescribing in the elderly" with Dr Chris Cameron, from June, 2017: [www.goodfellowunit.org/podcast/deprescribing-elderly-chris-cameron](http://www.goodfellowunit.org/podcast/deprescribing-elderly-chris-cameron)
- A podcast on "Deprescribing medications" with Leanne Te Karu, from Oct, 2018: [www.goodfellowunit.org/podcast/deprescribing-medications](http://www.goodfellowunit.org/podcast/deprescribing-medications)
- A webinar on "The impact of frailty on prescribing medication" with Dr Chris Cameron, from November, 2018: [www.goodfellowunit.org/events/impact-frailty-prescribing-medication](http://www.goodfellowunit.org/events/impact-frailty-prescribing-medication)

## Reviewing medicines for cardiovascular disease: aspirin and statins

**For patients taking aspirin,** ongoing use may be appropriate if it is prescribed for secondary prevention of cardiovascular disease, however, there is an increased risk of gastrointestinal (GI) bleeding in patients not receiving a gastroprotective medicine concurrently, e.g. a proton pump inhibitor.<sup>22, 23</sup> A study of over 3000 patients in the United Kingdom found that the combined annual risk for a life-threatening or fatal bleed was 2.5% for people aged  $\geq 85$  years taking an w medicine (>95% were prescribed aspirin) compared to <0.5% for people aged 65 to 69 years.<sup>23</sup> Prescribing aspirin for primary prevention of cardiovascular disease is not recommended for patients with a five-year cardiovascular risk <15%\*.<sup>24</sup> For patients that have a risk  $\geq 15\%$  and are aged  $\geq 70$  years, the current guidelines do not recommend using aspirin for primary prevention due to the increased risk of major bleeding associated with the treatment, without reducing the risk for cardiovascular events.<sup>24, 25</sup> Recent data from New Zealand suggest that for people aged 60–69 years, there is minimal benefit from taking aspirin if blood pressure and lipid-lowering medicines are also used, and for patients with risk factors for bleeding, such as smoking or diabetes, the number of bleeding events caused by aspirin may exceed the number of cardiovascular events prevented.<sup>26</sup> The current evidence suggests that withdrawal of aspirin initiated for primary prevention is likely to be appropriate

in older people, however, the timing of this withdrawal may vary from patient to patient depending on their overall health state, i.e. presence of frailty, life expectancy and goals of care.

\* Defined by updated New Zealand risk prediction equations, not Framingham-based risk scores. For further information, see: [www.bpac.org.nz/2018/cvd.aspx](http://www.bpac.org.nz/2018/cvd.aspx)

**For patients taking statins,** the net benefit or risk of harm for older people is less certain than for younger people. Prescribing for secondary prevention of cardiovascular events may be appropriate, however, the role of statins in primary prevention, particularly for people aged  $\geq 85$  years, is unclear and may result in exposure to unnecessary harms.<sup>14, 27</sup> In this context, patient preference plays a significant role in deciding whether statin use should be continued.<sup>6</sup> In a survey of 180 people in Australia with an average age of 78 years, 95% of participants stated they would be willing to stop a statin if advised to do so by their doctor, and the same proportion would rely on their doctor to inform them if stopping a statin was possible.<sup>28</sup> Raise the question of ongoing use or withdrawal with patients, and revisit the discussion at an appropriate interval, rather than renew prescriptions for statins indefinitely. Dose reduction may also be appropriate for some patients, particularly if they are experiencing adverse effects at a higher dose, e.g. myalgia.<sup>27</sup> For patients with limited life expectancy there is unlikely to be any benefit of ongoing statin use and clinicians can discuss withdrawal.<sup>29</sup>

## Pharmacy services can assist patients who are prescribed a large number of medicines

Some pharmacies provide services which can help older adults with their medicine use:

**A Medicines Therapy Assessment** involves assessing all medicines currently taken by a patient, including supplements and any medicines purchased over-the-counter, in order to identify, resolve or prevent medicine-related problems and optimise the effectiveness of their medicines regimen.<sup>30</sup>

**A Medicines Use Review** aims to improve adherence by identifying and addressing factors which contribute to reduced adherence, including education and improving patient or caregiver understanding of the prescribed medicines.<sup>31</sup>

**The Long-Term Conditions pharmacy service** provides support for patients with long-term conditions and difficulties with adherence, who require assistance with managing their medicines regimen.<sup>32</sup>

The availability of these services varies across the District Health Boards, therefore, general practitioners wishing to refer patients to any of these services should contact a local pharmacy to find out if they are offered or speak to their PHO or DHB. Patients can also self-refer for a Medicines Use Review or Long-Term Condition service eligibility assessment.

In addition, pharmacists can assist older patients taking multiple medicines on a more informal basis:

- Ask if they know what their medicines are for and if they have trouble remembering to take their medicines
- Ask if they have any concerns or questions about how to take their medicines, e.g. dexterity, sight, memory, swallowing. Offer blister packs and/or medicine trays if appropriate. If they would like additional assistance, consider whether a Medicines Use Review or Medicines Therapy Assessment would be beneficial.
- Encourage patients to collect their medicines from a single pharmacy of their choice, where possible
- Encourage patients to ask their general practitioner for a medicine review if they appear to have frailty, are having falls or adverse reactions to medicines. Pharmacists may also ask permission from the patient to discuss their medicines use with their general practitioner.
- Inform the prescriber if the patient is not collecting medicines and repeat prescriptions regularly, and consider a Medicines Use Review



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