

When is enough, enough?

Stopping medicines in older people

In New Zealand, it is estimated that 30% of people aged over 75 years are taking five or more medicines and around 10% are taking ten or more. Polypharmacy increases the risk of morbidity, hospitalisations and death and increases the likelihood of impaired mobility and placement in residential care.^{1, 2, 3}

Medicines are often prescribed to a patient by a number of different physicians, following single disease guidelines. A 70-year-old woman with three chronic diseases and two risk factors would result, on average, in being prescribed 19 different doses of 12 different medicines at five different times of the day, with ten possibilities for significant drug interactions either with other medicines or with other diseases.⁴ Using single disease measures, this regimen would rate highly in fulfilling guideline criteria for treatment, however people do not experience co-existing illnesses in isolation of each other. Symptoms are inseparable and simultaneous and wisdom and judgement are required to avoid polypharmacy. The difficulty lies in knowing which medicines to stop and when and how to stop them.

The best way to stop medicines is not to start them

In asking “when should stopping medicines be considered in older people?” the answer is invariably “all the time” but the picture would not be complete without also asking “when should they be started?” Medicines must be used appropriately.

It is much more difficult to stop medicines than it is to start them. It can be complex to review decisions, discontinue or change medicine regimens determined in secondary care, or from guidelines developed for younger populations.

Time and financial constraints mean scheduled, formal medicines review may never be performed. As much thought needs to be given to starting medicines in older people, as to stopping them.

The “golden rules” of appropriate medicine use are:

1. Prescribe the best medicine combination to treat the underlying disorder(s), not necessarily the symptoms of the disorder(s)
2. Choose medicines that are less likely to cause adverse reactions
3. Start medicines that prevent morbidity, but remember that some people will benefit from lifestyle advice alone
4. Do not use chronological age as a guide for assessing potential benefit or risk of a medicine
5. Regularly review the indications for therapy
6. Do not fix things that are not broken
7. Consider the patient’s wishes in treatment decisions

Consider stopping or reducing the dose of every medicine

Review the rationale for continuation of all medicines and consider trials of discontinuation where appropriate.

In one randomised controlled trial of simultaneous discontinuation of multiple medicines in a frail elderly rest home population, only 10% of the medicines stopped had to be re-administered because of the return of the original indication.⁵ More importantly, the annual rate of

both mortality (21% vs. 45%) and referrals to hospitals (12% vs. 30%) significantly decreased compared with the control group, while quality of life was increased.⁵ This approach has been replicated in a population of elderly people living at home, with similar effects.⁶

A systematic review of withdrawal of antihypertensives in elderly people concluded that 20 – 85% remained normotensive, or did not require reinstatement of therapy, for between six months and five years, with no increase in mortality.⁷ Similarly, studies of diuretic withdrawal found no need for reinstatement in over 50% of elderly people.

There are good reasons to reduce the dose of medicines in older people. A patient who has received antihypertensives or nitrates may not need the same regimen years later when physical activity changes and body mass is reduced. Although there is evidence of the effectiveness of treating hypertension in older people who are fit,⁸ in the frailer population over enthusiastic attempts to lower systolic and diastolic blood pressure may increase mortality and morbidity.^{9, 10} Some drugs also have a “legacy” effect, e.g. the benefit of bisphosphonates may last for five years after stopping.

Questions to ask when considering stopping medicines

1. Is the original indication for the medicine still present?
2. What is the time to effect of this medicine and is it clinically significant?
3. What is the life expectancy of the patient?*
4. What is the evidence for overall benefit on quality and quantity of life for this medicine in older people?

*Consider the “healthy survivor effect” when assessing life expectancy i.e. a person who has survived to an advanced age has an increased life expectancy compared to the average person. Life expectancy tables are available from Statistics New Zealand: www.stats.govt.nz/methods_and_services/access-data/tables/cohort-life-tables.aspx

Consider the overall benefit of medicines for prevention in older age

The aim of disease prevention is not just to extend the quantity of life but improve its quality. However there is often a lack of clarity about exactly how, or whether to, use preventive medications to those who are beyond the average lifespan.

Associate Professor Dee Mangin, University of Otago highlights the gaps in the evidence:

“Medicines are often recommended based on studies of younger populations without significant co-morbidity. Applying clinical guidelines developed from these studies to older people as standards for good care is often inappropriate. This is both because of the increased risks and because it cannot be assumed that the benefit exists in a continuum. Absolute risk is a poor guide to the relative benefits of treatment as the absolute risk of dying of any disease is greater in older people simply because the time of death is nearer. Treatment focussed only on preventing single diseases can sometimes have no beneficial effect if it simply trades one source of morbidity and mortality for another. This effect can be seen when looking at all cause mortality and morbidity with statin use in the over 70’s for example, where the reduction in cardiovascular death and disease is balanced by an equal rise in morbidity and mortality due to cancer.” – **Assoc Prof Mangin**

Associate Professor Mangin says that a different model is required for assessing medicines for prevention in old age. It should include duration of life extension, duration of treatment and take into account mortality and morbidity due to all causes, as well as the harms attributable to treatment. Using this model, some preventive interventions that have benefits across a range of conditions, will likely provide similar benefits in older populations (e.g. flu vaccination, exercise, smoking cessation). Some interventions may provide greater

benefit in older populations and some will cause more harm than benefits. In other cases the potential benefit depends on the individual to whom the evidence is applied – there is evidence of a small clinical benefit for treating hypertension to prevent stroke among fit older people, however the risk benefit balance changes as the individual becomes more frail and at greater risk of postural falls and treatment adverse effects.

Professor Ngaire Kerse, University of Auckland asserts that there is evidence of benefit of preventive medicines in older people and is opposed to the concept of denying medicines to older people because they are for prevention.

“Prevention is primary, secondary and tertiary - tertiary prevention is optimal management of chronic conditions. Management of cardiovascular disease (CVD) is a large part of practice for older people and is universally reported as being less than optimal.¹¹ Antihypertensive medicines reduce the risk of subsequent stroke, myocardial infarction and disability from cardiovascular disease (i.e. prevention). Vitamin D reduces the risk of falls in frail older people and is free of adverse effects.”¹² – **Prof Kerse**

Recognising the “brink”

Most people would probably agree that continuing any drug other than palliative is inappropriate in the time immediately before death. However extrapolating back from this is difficult. Callahan talks about the notion of technological brinkmanship: there is a point beyond which treatment has more harms than benefits, but without an effective way to approach this, treatment is continued because the “brink” is not recognisable.¹³

There is little to lose in trials of stopping nonessential medicines – they can always be restarted if the indications for the original treatment return. Good documentation and good communication with patients and families, in a shared decision making model, is essential.

Going too far – under treatment is also a problem

Inadequate treatment of illnesses can pose just as much of a problem as over treatment can.

“Pain, bone health (i.e. the use of vitamin D) and CVD are often under-treated or not managed ideally. Assessing CVD risk (for all its uncertainties) is important as this can guide the need (or not) for medicines. Outcomes from CVD are not just confined to the cardiovascular system with emerging evidence that dementia may be prevented or slowed with appropriate CVD risk management,¹⁴⁻¹⁸ however several large definitive trials are awaited. Absolute risk of new CVD events is the highest for older people. While there are risks associated with each combination of medicines, reduction in morbidity is the key and cardiovascular morbidity is the largest contributor to disability for older people”.^{19, 20}

“People in residential care are particularly vulnerable to under treatment.^{21, 22} Keeping up to date is difficult. Extra calcium should now be given in dietary form, not tablets, and aspirin only for those with established CVD of very high risk (> 20%). The aim is to prevent morbidity and maximise quality of life and appropriate use of medicines is essential. This may mean stopping them, it may mean starting them.” – **Prof Kerse**

However, Associate Professor Mangin cautions against screening for CVD risk in populations beyond the average lifespan as it is not well enough supported by evidence. A recent study in 2009, based in the Netherlands, casts doubt on the use of the Framingham risk factors in older people as the usual risk factors did not predict cardiovascular morbidity in an older population in the same way as it does in younger adults.²³ The NICE guidelines have also recently been changed to reflect the shortcomings of the Framingham approach.

“When we use treatments to relieve symptoms we apply the best science available even if it has gaps and imperfections. Introducing treatments and their risks for prevention to people who are currently well requires a much higher level of evidence.” – **Assoc Prof Mangin**

Associate Professor Mangin also points out that as yet there is no compelling evidence that dementia can be prevented through vascular manipulation by pharmacological or non-pharmacological trials.

“The evidence for dementia prevention with CVD risk management is based on assumptions without randomised controlled trial evidence which balances the harms of treatment with the magnitude of any benefit.”
– Assoc Prof Mangin

Avoiding ageism

Well considered discontinuation of medicines in older people is not ageist. Polypharmacy itself should be conceptually perceived as a “disease” threatening healthy old age, where the burden of drugs may become greater than the burden of the diseases they are used to treat.

On the other hand, age alone is not a good guide to use. Older people in their homes and in residential care, have the right to as much, or perhaps even more, thought and attention to their health issues as any other group.

Sensible application of clinical epidemiological principles, utilising the evidence base, is required. A rational approach to prescribing in older people should recognise that the gap between guideline mandated prescribing, and prescribing for real and complex individuals, might be wisdom and judgement rather than poor care. In contrast to guideline and target driven standards, such an approach will not leave patients wondering “are you doing this for me doctor or am I doing it for you?”

Practice debate When should medicines be stopped in older people? We are interested in your thoughts –  editor@bpac.org.nz

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