

THE AUSTRALASIAN SOCIETY OF CLINICAL AND EXPERIMENTAL PHARMACOLOGISTS AND TOXICOLOGISTS: TESTS, TREATMENTS AND PROCEDURES

HEALTH PROFESSIONALS AND CONSUMERS SHOULD QUESTION

ASCEPT is the professional and independent society in Australia and New Zealand with expertise in the use and toxicity of medicines and chemicals. Established in 1966, ASCEPT is affiliated with the International Union of Basic and Clinical Pharmacology (IUPHAR) and the International Union of Toxicology (IUTOX).

1. Recognise and stop the prescribing cascade.

A prescribing cascade occurs when a new medicine is prescribed to 'treat' an adverse reaction to another drug in the mistaken belief that a new medical condition requiring treatment has developed. Prescribing cascades should be avoided because they are associated with adverse outcomes due to the second or additional drugs, which places the patient at risk. One example of a prescribing cascade is when a patient is prescribed a non-steroidal drug for pain, and is then prescribed proton pump inhibitors (PPIs) to reduce the risk of stomach side effects caused by the first prescribed drug. As prescribing cascades are precipitated by adverse drug reactions, they can be prevented by avoidance and early detection of the initial adverse drug reaction. For instance, many adverse drug reactions in the elderly are dose-related. It is advised that starting treatment at low doses and titrating to effect may reduce their risk. Most adverse drug reactions occur within a few months of starting a medicine. Clinicians should consider the potential for an adverse drug reaction to be the cause of any new symptoms, particularly if a drug has been recently started or changed. Patients should be asked about new symptoms, as many patients do not report adverse drug reactions. When such reactions occur, non-drug treatment strategies should be considered as the most appropriate first-line management, rather than starting a second medicine to counteract adverse effects.

Supporting Evidence

- Caughey GE, Roughead EE, Pratt N, et al. Increased risk of hip fracture in the elderly associated with prochlorperazine: is a prescribing cascade contributing? *Pharmacoepidemiol Drug Saf* 2010;19:977-82.
- Kalisch LM, Caughey GE, Roughead EE, Gilbert AL. The prescribing cascade. *Australian Prescriber* 2011;34:162-166.
- Martin JH, Coombes I. Mortality from common drug interactions systems, knowledge and clinical reasoning to optimise prescribing. *Internal Medicine Journal* 2014;44(7):621-4.

Health Professional resources the from the Choosing Wisely NPS MedicineWise website

- [Anticipating the risks of polypharmacy](#)
- [Key points for medicines in older people](#)
- [Medicines in older people - review and rationalise](#)
- [Older, safer, wiser](#)
- [Stopping medicines](#)
- [The prescribing cascade](#)

2. Reduce the use of medicines when there is a safer or more effective non-pharmacological management strategy.

Pharmacological treatments should be avoided or minimised if safer or more effective nonpharmacological alternatives are available. Pharmacological treatments may become a panacea for chronic lifestyle-related problems, and may detract from behaviour management tools that have proven effective in managing these same problems. There is also a risk of adverse effects from particular pharmacological treatments which may be avoidable by using non-pharmacological management strategies. For instance, physiotherapy should be used instead of oxycodone for addressing non-cancer pain, because of the risk of adverse effects. Another example is the use of psychotropic medicines for behavioural and psychological symptoms of dementia when non-pharmacological management strategies are both more effective and safer.

Supporting Evidence

- Declercq T, Petrovic M, Azerman M, et al. Withdrawal versus continuation of chronic antipsychotic drugs for behavioural and psychological symptoms in older people with dementia. Cochrane Database Syst Rev 2013;3:CD007726.
- NSW Therapeutic Advisory Group Inc. Preventing and managing problems with opioid prescribing for chronic non-cancer pain. NSW TAG: Sydney, 2015.

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3. Avoid using a higher or lower dose than is necessary for the patient to optimise the 'benefit-to-risk' ratio and achieve the patient's therapeutic goals.

Therapeutic dosage should be adjusted to optimise the benefit-to-risk ratio of the treatment. Dosage should be no higher or lower than needed to achieve the patient's therapeutic goals. As patients become more frail, potential harms usually increase and potential benefits usually decrease for a given dosage of pharmacological treatment. For example, carefully assessing the risk and benefits when initiating non-steroidal inflammatory drugs in elderly patients is important, because of the increased risk of stroke associated with NSAID therapy; and use of proton pump inhibitors in the elderly should be stepped down after an initial course of therapy. Related to this, high drug doses are not necessarily more effective than low doses. An example of this is the relationship between doses of a selective serotonin re-uptake inhibitor for patients with major depressive disorder and useful clinical improvements.

Supporting Evidence

- Caughey GE, Roughead EE, Pratt N, et al. Stroke risk and NSAIDs: an Australian population-based study. Med J Aust 2011;195(9):525-9.
- Dimmitt SB, Stampfer HG. Low drug doses may improve outcomes in chronic disease. Med J Aust 2009;191(9):511-3.
- Raghunath AS, O'Morain C, McLoughlin RC. Review article: the long-term use of proton-pump inhibitors. Aliment Pharmacol Ther 2005;22:55-63.

Health Professional resources

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4. Stop medicines when no further benefit will be achieved or the potential harms outweigh the potential benefits for the individual patient.

Pharmacological treatments should cease when there are no further benefits to be achieved from the treatment, or when the potential harms from the treatment start to outweigh the potential benefits. This is particularly pertinent for elderly patients with a limited life expectancy where the treatments are unlikely to prevent disease events, and may in fact lead to adverse effects that reduce quality of life. These patients are at an increased risk of polypharmacy and increased drug events. For example, bisphosphonate treatment should not be administered to patients living in residential aged care facilities when these patients are already too frail to swallow drugs or have a life expectancy which is significantly less than 12 months.

Supporting evidence

- Maddison AR, Fisher J, Johnston G. Preventive medication use among persons with limited life expectancy. *Prog Palliat Care* 2011;19(1):15–21.
- Reeve E, Shakib S, Hendrix I, et al. The benefits and harms of deprescribing. *Med J Aust* 2014;201(7):386-9.
- Scott IA, Anderson K, Freeman CR, Stowasser DA. First do no harm: a real need to deprescribe in older patients. *Med J Aust* 2014; 201(7):390-2.

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5. Reduce use of multiple concurrent therapeutics (hyper-polypharmacy).

Polypharmacy — variously defined as more than five or up to 10 or more medications taken regularly — is common among elderly patients. However, patients who are prescribed with multiple, concurrent therapeutics may be on as many as 15 to 20 drugs at time. Research has confirmed a significant association between polypharmacy and adverse outcome among older people living in the community because the toxicities and side effects associated with prescribed drugs are accrued over many years. Polypharmacy in older people is associated with decreased physical and social functioning; increased risk of falls, delirium and other geriatric syndromes; hospital admissions; and, deaths.

Supporting evidence

- Davies EC, Green CF, Taylor S, et al. Adverse drug reactions in hospital in-patients: A prospective analysis of 3695 patient-episodes. *PLoS ONE* 4(2):e4439.
- Hubbard RE, Peel NM, Scott IA, et al. Polypharmacy among inpatients aged 70 years or older in Australia. *Med J Aust* 2015;202(7):373-7.
- Scott IA, Anderson K, Freeman CR, Stowasser DA. First do no harm: a real need to deprescribe in older patients. *Med J Aust* 2014; 201(7):390-2.

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How was this list created?

A working party of members of the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT) was established to propose an initial list of recommendations. ASCEPT's membership was then invited to participate in an online survey to comment on the appropriateness of the proposed recommendations and suggest additional items for consideration.

Based on the survey responses, six recommendations were shortlisted. Following an evidence review the top 5 list items were selected. The final list was signed off by the ASCEPT President in April 2016.