
Dilemmas in Prescribing for Elderly People

Why is it Difficult?

Prescribing decisions for elderly people are difficult because:

- **Physiological changes in elderly people often result in different and more severe drug related problems**
- **High rates of co-morbidity and polypharmacy increase the risk of interactions with other drugs and other illnesses**

The results of drug trials are often difficult to apply to elderly people

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Physiological changes in elderly people result in different and more severe drug related problems

Age related changes in pharmacokinetics and pharmacodynamics result in altered responses to many medications. These changes include decreased glomerular filtration rate, renal tubular filtration, gastric acid secretion, gastrointestinal motility, gastrointestinal surface area for absorption, splanchnic perfusion and hepatic size and perfusion.

Drug absorption, first-pass metabolism, protein binding, distribution and elimination are all affected. Overall this results in decreased clearance and greater exposure to

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the drug. Due to these physiological changes, certain drugs are associated with an increased risk of adverse drug reactions (Table 1).

Reduced renal clearance in elderly people reduces excretion of many drugs, increasing the risk of adverse effects. Acute illness, especially dehydration, may cause further reductions in renal clearance, with the potential to move some drugs (e.g. digoxin) from the therapeutic to the toxic range without alteration in dose.

Elderly people have reduced ability to maintain homeostasis, often resulting in postural hypotension and impairment of thermoregulation, cognitive function and visceral muscle function. This means that increased symptoms may occur because of the body's inability to compensate for small perturbations in function from drug effects.

Altered molecular and cellular responses to drugs occur in elderly people. For example there are decreased density and/or affinity of receptors in specific receptor sites and target organs. Therefore, increasing the dose of a drug may have little effect on the target response but substantially increase adverse effects.

High rates of co-morbidity and polypharmacy increase the risk of interactions with other drugs and other illnesses

Increasing co-morbidity results in polypharmacy and increases the risk of:

- Drug-illness interactions
- Polypharmacy and drug interactions

Drug-illness interactions are common in elderly people

The increased frequency in elderly people of co-existing illnesses, places them at particular risk of drug-illness interactions. For example, many elderly people have both heart failure and arthritis. NSAIDs used for pain relief can adversely affect the heart failure, particularly if there is a degree of impaired renal function.

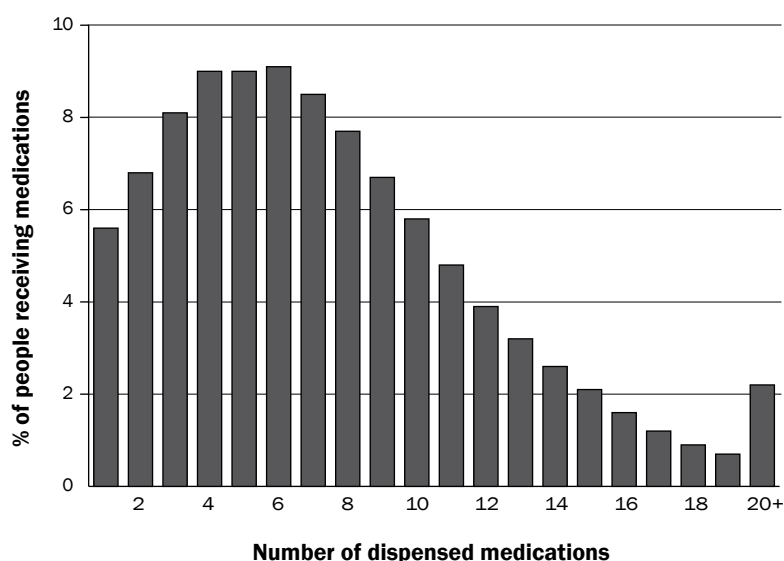
Polypharmacy increases the risk of drug interactions

The majority of elderly people take multiple medications. Latest data from the Pharmaceutical Data Warehouse (NZHIS) indicates that most people over 70 who have been dispensed any medication, are on at least four medications (Figure 1).

A steady increase in the likelihood of adverse reaction has been reported in a population of patients discharged from a hospital; from 10% of people taking two drugs to 100% of those taking twelve medications experiencing an adverse drug reaction. High prescribing rates were associated with more severe illness.¹

Figure 1: Number of unique dispensed medications in patients aged 70 or over in a six month period.

(Notes: Study period was March to August 2007, study group included people over 70 who were dispensed one or more medication in the time period)



The results of drug trials are often difficult to apply to elderly people

As the absolute risk of many adverse outcomes increases with age, the number needed to treat (NNT) for interventions for these conditions might be expected to fall. The absolute risk of a cardiovascular event is high for elderly people, and there is evidence that anti-hypertensive treatment is beneficial. For example, the Hypertension in the Very Elderly Trial (HYVET) which commenced in 2001, was halted early due to detection of a significant reduction in strokes and cardiovascular mortality in the patients receiving treatment.

While the HYVET study is highly relevant to the elderly population, there is a lack of relevant evidence in other areas. Guidelines for clinical practice are largely based upon clinical trials which are problem focused, utilise single disease models, and exclude elderly people.² When elderly people are enrolled in a trial, they are usually a highly selected group, as people with co-morbidities and polypharmacy are excluded.³ This means the results of drug trials are often difficult to apply to the elderly people seen in primary care.

Quality of life is the most relevant outcome to consider

Quality of life is the most relevant outcome to consider from treatment decisions and functional age is a much better predictor of quality of life than chronological age. In this way a functionally able person of 90 years may participate in treatment decisions and it may be appropriate to offer several drugs to manage co-morbidities.

“The good physician treats the disease; the great physician treats the patient who has the disease” —Sir William Osler 1849-1919

Table 1: Drugs commonly associated with adverse reactions in elderly people.

Drug or drug class	Comments
All drugs	Start low, go slow. Many drugs, e.g. oxybutynin, antipsychotics, TCAs and antihypertensives need much lower doses in elderly people.
Benzodiazepines	Those with a long half-life, such as diazepam and nitrazepam cause excessive and prolonged sedation. Temazepam is a better choice if necessary but all are best avoided.
Dextropropoxyphene	Can cause confusion and excessive sedation in elderly people. Avoid use.
Digoxin	Use low doses initially. Extra vigilance required for those who need to be on higher doses.
Indomethacin	This NSAID has a high incidence of CNS effects and gastrotoxicity.
Nefopam (Acupan)	CNS effects and marked anticholinergic actions. Avoid use.
NSAIDs	Use lowest effective dose for the shortest necessary duration. Avoid long-term use of full dose, longer half-life drugs such as naproxen and piroxicam.
Tricyclic antidepressants (TCAs)	Nortriptyline is the recommended first choice TCA in elderly people. Doxepin and amitriptyline are very sedating and have strong anticholinergic actions. They are not recommended as a first choice for depression in elderly people.

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3. Bene J, Liston R. The special problems of conducting clinical trials in elderly patients. *Rev Clin Gerontol* 1997; 7(1): 1-3.