








FOR PERSONAL USE ONLY. NOT TO BE REPRODUCED WITHOUT PERMISSION OF THE EDITOR

PRESCRIBING IN THE ELDERLY

-  **The elderly receive the majority of prescribed medicines in practice**
-  **Ageing affects the body's ability to handle medicines, increasing the risk of adverse events**
-  **Prescribing tools and checklists are available to enhance optimal prescribing in the elderly**
-  **Regular medication review is essential for ensuring rational and effective use of medicines in the elderly**
-  **Non-pharmacological therapies should be used whenever possible**

INTRODUCTION

According to the most recent census figures, approximately 11% of persons in Ireland are aged 65 years or older.¹ However, this age group received over half (51%) of all prescriptions dispensed via the primary care reimbursement scheme (PCRS formerly GMS) in 2007.² The expected rise in the percentage of older persons in the Irish population over the coming years and their predicted increased life expectancy, will be associated with an increase in multimorbidity and health service utilisation and costs in this population.³ Therefore appropriate use of medicines in the elderly should be regarded as a major public health issue.⁴ This bulletin will review the effect of increasing age on how medicines are handled by the body and will provide guidance on ensuring the effective use of medicines in this age group in order to improve medication safety.

THE BIOLOGY OF AGEING AND ITS IMPACT ON USE OF MEDICINES

Many regulatory bodies define the elderly as those aged 65 years and older.⁵ However, ageing is a gradual process, which begins during early adulthood, and becomes more prominent and progressive in the “post-reproductive” stages of life.⁶ **There is a gradual decrease in physiological fitness and a reduction in the homeostatic capability to respond to environmental demands, which includes the handling of medicines.**⁴ In addition, the rate of the ageing process differs greatly between individuals, resulting in different subgroups within the elderly population (e.g. the healthy elderly versus the frail older group), each of which may have their own issues with respect to prescribing.⁵

Table 1 outlines the typical physiological changes that occur with ageing and shows how each may alter the pharmacokinetic parameters of a medicine and interfere with its effect within the body.

Table 1: Physiological changes related to ageing and their impact on drug usage^{4,8}

Change	Significance for drug use	Examples of drugs affected*
↑ body fat mass	↑ time to onset of action of, and prolonged $t_{1/2}$ for, fat soluble drugs	diazepam, verapamil
↓ lean body mass ↓ total body water	Higher than expected plasma levels of water soluble drugs	aspirin, lithium, alcohol
↓ renal function**	↓ creatinine clearance and potential accumulation of renally excreted drugs	lithium, digoxin
↓ liver blood flow +/- ↓ liver function**	May lead to ↓ metabolism of drugs via Phase I + II metabolic systems / ↑ bioavailability of first pass effect drugs	warfarin, amiodarone, fentanyl, nifedipine; nitrates, tricyclic antidepressants

*check individual Summaries of Product Characteristics for more detail (sections 4.2, 5.1, 5.2); **large inter-individual variability

The extent to which these changes have an impact varies greatly between individual elderly persons. For example, although the fat content in elderly females is much greater than in their male counterparts, the relative increase in fat content appears to have a greater impact in males in terms of the handling of lipophilic drugs.⁴ In addition, although renal function is known to deteriorate with age, there is large inter-individual variability and it is not possible to estimate the level of renal function by measuring serum creatinine, because of

the lower lean body mass associated with ageing.^{4,6} Formulae (e.g. the Cockcroft and Gault Equation) are available to estimate the glomerular filtration rate.^{4,6}

Although most prescribers are aware of the potential for altered pharmacokinetics of a medicine with increasing age, **the pharmacodynamic profile of many medicines may also be affected by age**, resulting in unexpected effects.^{6,9} A common example of altered pharmacodynamic effects is the increased susceptibility of elderly patients to postural hypotension in response to anti-hypertensive medication, which is due to reduced counter-regulatory effects.⁶ It has also been well documented that there is a reduction in response to β -adrenoceptor agonists and antagonists in the elderly, probably due to downregulation of the receptors with/without altered counter-regulatory mechanisms.^{5,7,9}

The central nervous system (CNS) is a particularly vulnerable drug target in the elderly. Between 20 and 80 years of age, cerebral blood flow decreases by 30%, brain weight reduces by 20%, and there is a 30% decrease in cortical neuronal density.^{6,8} Table 2 outlines some examples of potential adverse effects of CNS drugs due to the impact of ageing on their pharmacodynamic effects.

Table 2: Age-related CNS changes and their impact on pharmacodynamics of drugs^{4,6}

Age-related CNS change	CNS drugs potentially affected
↓ dopamine content	↑ frequency and severity of extrapyramidal symptoms with dopamine antagonists (neuroleptics / metoclopramide)
↓ in acetylcholine content	↑ risk of anticholinergic effects of neuroleptics and tricyclic antidepressants
Changes in GABA _A - benzodiazepine receptor complex	Possible mechanism for ↑ susceptibility to effect of, and toxicity with use of, benzodiazepines even at low dose levels

In summary, the ageing process results in changes to the body composition and function, which may alter the expected response to a medicine and predispose to adverse drug reactions (ADRs). It is important that the prescriber factors these potential alterations into the overall care plan for the individual elderly patient.

PRESCRIBING IN THE ELDERLY PATIENT

Older people tend to have a higher prevalence of chronic and multiple illnesses requiring treatment, and studies have shown that medication plays a fundamental role in their care.^{7,10} Studies undertaken in Ireland reported that 86% of those aged 70 years and over were in receipt of medicines for chronic conditions, while up to 45% were receiving ≥ 5 medicines concomitantly.^{11,12} Similar findings have been reported from Europe and North America.^{13,14}

Although the elderly population are more likely to require pharmacotherapy, they are also more likely to develop ADRs, compared with other adults. A recent UK study showed that patients admitted due to ADRs were significantly older (median aged 76 years) than patients with non ADR-related medical admissions (median age 66 years).¹⁵ This study highlighted that older medicines (diuretics, anti-thrombotic agents, NSAIDs, digoxin) continued to cause problems, and that many of the ADRs were preventable.

Prescribing in the elderly is more complex than prescribing for other adults.¹⁰ Table 3 lists some of the potential difficulties associated with prescribing in the elderly.

Table 3: Age-related issues with prescribing in the elderly^{9,10,16-18}

- **Increased susceptibility to adverse drug effects due to:**
 - **Ageing (including frailty), co-morbid conditions (drug-disease interactions, polypharmacy and risk of drug-drug interactions)**
- **Cognitive state, nutritional state and living conditions**
- **Number of additional prescribing physicians involved in care**
- **Unrecorded concomitant use of over-the-counter medicines or herbal remedies**
- **Access to health services (including costs of prescribed medicines)**
- **Lack of clinical trial data from the elderly population**

The difficulties with drug-drug interactions, including non-prescribed medicines, have been previously documented (see NMIC Bulletins on Drug Interactions 2008; 14: 4,5).^{19,20} It has been shown that patients taking 2 medicines concomitantly faced a 13% risk of adverse drug-drug interactions; this risk increased to 38% with 4 medicines and to 82% with use of 7 or more medicines concomitantly.⁷ However, concomitant diseases can also expose the patient to increased risk from medicines prescribed for a different condition: NSAIDs, can precipitate acute renal failure when used in a patient with concomitant chronic renal disease or can exacerbate high blood pressure in a hypertensive patient.⁹ Therefore **the prescriber needs to consider the possibility of a drug-drug and drug-disease interaction prior to adding any new medicine to a patient's treatment.** Several studies have shown that the risk of an adverse drug reaction increases with the number of prescribing physicians involved in a patient's care; reasons include a limited transfer of data regarding existing treatment regimens between prescribers, or unwillingness to interfere with another prescriber's activities.^{17,21}

INAPPROPRIATE PRESCRIBING IN THE ELDERLY

Inappropriate prescribing may be defined as the failure to provide the quality of care related to medicinal use that should be achieved in standard practice.²² It includes overprescribing and underprescribing and may result in increased morbidity, hospitalisation and even death. However, as outlined in Table 3, the selection of appropriate medication in older people may be a challenging and complex process, leading to increased risk of inappropriate prescribing.²³ Several validated tools have been developed to help prescribers identify potentially inappropriate prescribing (PIP) in the elderly.

Explicit criteria-based prescribing tools have been developed using expert reviews and opinions and are drug or disease-oriented. They may be applied with minimal clinical evaluation. Many of the original explicit prescribing tools came from North America (e.g. Beers Criteria; IPET).^{7,24} Recently, however, two screening tools: **S**creening **T**ool of **O**lder **P**ersons' potentially inappropriate **P**rescriptions (**STOPP**) and **S**creening **T**ool to **A**lert doctors to the **R**ight **T**reatment (**START**) have been developed by a multidisciplinary team of Irish and UK geriatricians, experts in old age psychiatry, pharmacists, pharmacologists and primary care physicians.²⁵ The criteria in each tool are arranged by physiological systems (i.e. cardiovascular system, respiratory system etc) for ease of use. **In STOPP**, each of the 65 clinically significant criteria is accompanied by a concise explanation as to why the medicine is potentially inappropriate.²⁶ **START** consists of 22 evidence-based quality prescribing indicators for commonly encountered diseases in older persons. These tools, which have shown excellent inter-rater reliability,²⁷ have the additional advantage of evaluating medicines relevant to the Irish and European marketplace. These prescribing tools are outlined in full at the following web address²⁸
<http://www.em-consulte.com/showarticlefile/245669/main.pdf>.

Table 4 gives examples of common PIP identified using the STOPP and START prescribing tools.

Table 4: Use of potentially inappropriate medicines (PIM) in the elderly identified by STOPP and START^{23,29,30}

Tool	Study Setting	Potentially inappropriate prescribing
STOPP	715 acute hospital admissions: prospective study (median age 77 years)	336 episodes in 35% patients (n=247) contributing to 11.6% of admissions (e.g. longterm use of long-acting benzodiazepines/ benzodiazepines in those prone to falls; longterm PPIs; duplicate drug classes; NSAIDs with moderate-severe hypertension; aspirin without indication)
STOPP	PCRS* prescription database (n>338,000 population >70 years)	36% prevalence of potentially inappropriate prescribing (17% longterm PPIs; 9% NSAIDs for >3months; 5% long-acting benzodiazepines for >1 month; 5% duplicate drug classes)
START	600 acute hospital admissions: prospective study (mean age 77.9 years)	Prescribing omissions (without contraindications) in 57.9% patients (e.g. no statins in CVD (26%); no warfarin in chronic atrial fibrillation (9.5%); no anti-platelet drugs in arterial disease (7.3%))

*primary care reimbursement scheme; PPIs = proton pump inhibitors; CVD = cardiovascular disease

Implicit criteria-based tools use patient-specific information in order to judge whether a specific medicine is appropriate.^{7,10,22} They review the following aspects of prescribing for the individual: **indication, effectiveness, dose, correct directions, practical directions, drug-drug / drug-disease interactions, duplication, duration of therapy** (e.g. **M**edication **A**ppropriateness **I**ndex).¹⁰ They can be used as a useful checklist for prescribers in the management of individual patients (see Table 5), although they take time to complete in clinical practice; studies have shown that implicit criteria can predict important clinical outcomes, including ADRs, with the aim of enhancing optimal prescribing.²²

PATIENT FACTORS IN SAFE USE OF MEDICINES IN THE ELDERLY

The medication-use process involves a series of steps, including prescribing, dispensing, administering, monitoring and medication review, each of which can impact on the safe use of medicines in the elderly.⁷ Therefore, even if a medicine has been prescribed appropriately, problems with subsequent steps may result in an adverse outcome. **Patients may take concomitant OTC and/or herbal remedies** in addition to their prescribed medicine, with the risk of drug-drug interactions, unless forewarned.²⁶ Although the elderly are generally more compliant than the younger population, **many factors can reduce compliance**, (see Table 3), including cognitive impairment, difficulty in understanding complex regimens, visual problems or difficulty in opening the container or blister pack.³¹ The patient may have problems with swallowing; this may result in either non-compliance or an ADR due to tablets lodging in the oesophagus.²⁶ **Therefore a multidisciplinary approach to patient education (i.e. from both the prescriber and pharmacist) is important** in ensuring that prescribed medicines will be taken properly; if there is a concern about compliance, the regimen should be simplified wherever possible or assistance should be sought in monitoring administration from a carer.^{26,31}

PRACTICAL ADVICE FOR APPROPRIATE PRESCRIBING IN THE ELDERLY

Table 5 contains a checklist that may be used to determine the appropriateness of a medicine for an individual patient

Table 5: Checklist to aid prescribing in an elderly patient^{10,22,31}

- Is there a need for pharmacotherapy in this patient?
- Is this the optimal medicine for the specific clinical diagnosis in this patient?
- Will the medicine introduce unnecessary duplication with existing medicines in this patient?
- Is the dosage correct?
- Is the formulation suitable?
- Is the duration of therapy acceptable?
- Is the medicine likely to interact with existing medication?
- Is the medicine likely to affect, or be affected by, concurrent disease?
- Are the directions for use correct and feasible for this patient?

While it is important to ensure that a necessary medicine is not omitted in the elderly patient, **consideration should be given to treating conditions associated with ageing by non-pharmacological means wherever possible.**^{10,26,31} These include physiotherapy and advice on weight loss for osteoarthritis; psychological / social support for depression due to social isolation or recent bereavement; relaxation exercises for insomnia. The patient's environmental conditions and cognitive state will also need to be taken into account in determining whether certain medications can be administered safely to an individual elderly patient. For example warfarin might not be prescribed for a patient at high risk of stroke from atrial fibrillation, because of the risk of falls at home or if there is a possibility that the patient might not be capable of adhering to the appropriate dosage regimen.³¹ Whenever a new medicine is prescribed, it is important that its effects are monitored.²⁶ **Changes in the patient's medical status over time can cause longterm medicines to become unsafe or ineffective,** therefore regular medication review is warranted to ensure continuing positive benefit/risk balance for each medicine prescribed for the elderly patient.⁴

SUMMARY

While the benefits of pharmacotherapy for the elderly are potentially substantial, the process of choosing the appropriate medicine for the individual elderly patient may be complex. Table 6 outlines some points that may be useful in promoting safe and effective use of medicines in the elderly patient.

Table 6: Summary points for safe and effective prescribing in the older patient^{15,26,31-33}

- **Prescribe cautiously: your patient's symptoms may be amenable to non-pharmacological therapy**
- **Prescribe appropriately: use a checklist (see above) to make sure that the chosen medicine is appropriate for the individual patient under your care**
- **Start low, go slow: age-related changes may have affected your patient's ability to handle the medicine**
- **Review regularly: newly prescribed medicines may not be working; longterm medicines may no longer be safe or effective**
- **Limit the range of medicines you use in the older patient: this enables you to develop expertise in their usage**
- **Remember the risky medicines: e.g. diuretics, digoxin, anti-thrombotics, NSAIDs, CNS medicines, thyroxine**

Prescribers may wish to develop a personal formulary/ preferred list of medicines for use in their older patients, which will enable them to be familiar with their profile, including optimal dosing, contraindications and potential for ADRs when used in the elderly population.²⁶

List of references available on request. Date of preparation: July 2010

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue.

Prescribers are recommended to refer to the individual Summary of Product Characteristics (SmPC) for specific information on a drug

References for NMIC Bulletin on Prescribing in the Elderly 2010; Vol 16: 3

1. Census for Ireland 2006. Available at <http://www.cso.ie/census/Census2006Results.htm>. Accessed 13th July 2010
2. Prescribing data for > 70s during 2007 from PCRS database. Personal Communication
3. Castelino R et al, targeting suboptimal prescribing in the elderly: a review of the impact of pharmacy services. *Ann Pharmacother* 2009; 43: 1096-1106
4. Turnheim K, When drug therapy gets old: pharmacokinetics and pharmacodynamics in the elderly. *Exp Gerontology* 2003; 38: 843-53
5. Hilmer S et al, Clinical pharmacology in the geriatric patient. *Fund & Clin Pharmacol* 2007; 21: 217-30
6. Turnheim K, Drug therapy in the elderly. *Exp Gerontol* 2004; 39: 1731-38
7. Page R et al, Inappropriate prescribing in the hospitalised elderly patient: defining the problem, evaluation tools and possible solutions. *Clinical Interventions in Aging* 2010; 5: 75-87
8. Sadean M and Glass P, Pharmacokinetics in the elderly. *Best Practice & Research Clinical Anaesth* 2003; 17 (2): 191-205
9. Cusack B and Branahl J, Drug Therapy in Older Persons *in Drug Benefits and Risks: International Textbook of Clinical Pharmacology*, revised 2nd Edition. Eds: CJ van Boxtel, B Santoso, IR Edwards. IOS Press and Uppsala Monitoring Centre, 2008, pp 203-224
10. Spinewine A et al, Appropriate prescribing in elderly people: how well can it be measured and optimised? *Lancet* 2007; 370:173-84
11. Naughton C et al, Prevalence of chronic disease in the elderly based on a national pharmacy claims database. *Age & Ageing* 2006; 35: 633-5
12. Odubanjo E et al, Influence of socio-economic status on the quality of prescribing in the elderly – a population based study. *BJCP* 2004; 58 (5): 496-502
13. Fialova D et al, Potentially inappropriate medication use among elderly home care patients in Europe. *JAMA* 2005; 293 (11): 1348-58
14. Sitar D et al, prescribing pattern for elderly community-dwelling heavy medicinal drug users in Manitoba, Canada and Jamtland, Sweden. *J Clin Epidemiol* 1995; 48 (6): 825-31
15. Pirmohamed M et al, Adverse drug reactions as cause of admission to hospital: prospective analysis of 18, 820 patients. *BMJ* 2004; 329: 15-19
16. Mallet L et al, The challenge of managing drug interactions in elderly people. *Lancet* 2007; 370: 185-91
17. Green J et al, Is the number of prescribing physicians an independent risk factor for adverse drug events in an elderly outpatient population? *Am J Geriatr Pharmacother* 2007; 5 (1):31-9
18. Leendertse A et al, Frequency of and risk factors for preventable medication-related hospital admissions in the Netherlands. *Arch Intern Med* 2008; 168 (17): 1890-6.
19. NMIC bulletin on Drug Interactions I: how do they occur. 2008;14: 4. Available online at www.nmic.ie. Accessed 15th July 2010
20. NMIC bulletin on Drug Interactions II: Frequently Asked Questions 2008; 14: 5. Available online at www.nmic.ie. Accessed 15th July 2010
21. Spinewine A et al, Appropriateness of use of medicines in elderly inpatients: qualitative study. *BMJ* 2005; 331: 935-9

22. Lund B et al, Inappropriate Prescribing predicts adverse drug events in older adults; *Ann Pharmacother* 2010; 44: 957-63
23. Cahir C et al, Potentially inappropriate prescribing and cost outcomes for older people: a national population study. *BJCP* 2010; 69 (5): 543-52
24. Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. *Arch Intern Med* 1997; 157: 1531-36
25. Gallagher P et al, STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation. *Int J Clin Pharmacol Ther* 2008; 46 (2): 72-83
26. Prescribing for the older patient. PatientPlus article. Available online at: www.patient.co.uk/printer.asp?doc=40000135, Accessed 26th April 2010
27. Gallagher P et al, Inter-rater reliability of STOPP (Screening Tool of Older persons' Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment) criteria amongst physicians in six European countries. *Age Ageing* 2009; 38 (5): 603-6
28. O'Mahony D et al, STOPP and START criteria: A new approach to detecting potentially inappropriate prescribing in old age. *European Geriatric Medicine* 2010; 1 (1): 45-51
29. Gallagher P and O'Mahony D. STOPP (Screening Tool of Older Persons potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. *Age and Ageing* 2008; 37: 673-9
30. Barry PJ et al, START (screening tool to alert doctors to the right treatment) - an evidence-based screening tool to detect prescribing omissions in elderly patients. *Age and Ageing* 2007; 36: 632-8
31. NMIC bulletin on prescribing in the elderly 2000; Vol 6:1. Available online at www.nmic.ie. Accessed 15th July 2010
32. Sikdar K et al, Adverse Drug Events in Adult Patients leading to Emergency Department Visits. *Ann Pharmacother* 2010; 44: 641-9
33. Howard R et al, What drugs cause preventable admissions to hospital? A systematic review. *BJCP* 2007; 63 (2): 136-147

Further useful references for background reading in this area:

Gallagher P and O'Mahony D. Inappropriate prescribing in older people. *Reviews in Clinical Gerontology* 2008; 18: 65-76

Hamilton H et al. Inappropriate prescribing and adverse drug events in older people. *BMC Geriatrics* 2009; 9:5