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# Impact of prescribed medications on patient safety in older people

**Sujo Anathhanam, Rachel A. Powis, Alison L. Cracknell and Jeremy Robson**

***Abstract:*** Appropriate prescribing for older adults presents unique challenges to the prescriber. An understanding of the scale of the problems and contributing factors is essential when designing interventions to improve patient safety. The altered pharmacology of ageing, the existence of multiple medical conditions and the exclusion of elderly patients from many trials render this subgroup of the population particularly vulnerable to underprescribing and overprescribing. Adverse drug events are common, causing significant morbidity and mortality as well as having economic implications. 'High-risk' medications such as opioids, anticoagulants and antipsychotics can have benefits in this group of patients but strategies to optimize their safety are required. Tools exist that help to identify those at risk of adverse drug reactions and to screen for inappropriate prescribing. Developments in information technology are ongoing, and it is hoped that these may enhance the process of medication reconciliation across healthcare transitions and alert the prescriber to potential adverse drug events. This review addresses commonly encountered issues when prescribing for older people, considers strategies to improve medication safety and offers a list of 'top tips' to aid the clinician.

***Keywords:*** adverse drug events, elderly, inappropriate medications, medicines, prescribing, safety

## Introduction

Appropriate prescribing for the older adult presents multiple challenges. In a primary care population, nearly 35% of 85–89 year olds were taking 10 or more medications [Hippisley-Cox *et al.* 2007]. Despite this, the elderly remain underrepresented in clinical trials [Beswick *et al.* 2008]. Findings from studies undertaken in younger patients cannot always be extrapolated to older adults [Fialová and Onder, 2009]. This renders the practice of evidence-based medicine difficult, leading to both underprescribing and overprescribing. Inappropriate prescribing in the elderly is seen throughout the healthcare system and in the transition between care providers [Spinewine, 2008]. Adverse drug events (ADEs), an umbrella term that encompasses adverse drug reactions (ADRs), medication errors, overdoses, dose reductions and cessation of therapy, are common in the elderly. These have financial implications for the entire population and consequences for clinicians, such as stress-related problems and reduction in prescribing confidence [Cresswell *et al.* 2007].

Clearly, an awareness of safe prescribing in the elderly is more important than ever for all healthcare workers because of the changing demographics of our population. In this review, we recap first the changes in pharmacokinetics and pharmacodynamics that occur in older people. Second, we discuss the scale of the problem of ADEs and the impact of underprescribing and overprescribing on patient safety. Finally, we consider the appropriate use of high-risk medications and review strategies to improve medication safety across transitions in healthcare settings.

## Pharmacokinetics and pharmacodynamics in the elderly

The pharmacokinetic changes that occur with ageing can be subdivided into changes in drug absorption, distribution, metabolism and elimination.

Correspondence to:
**Alison L. Cracknell, MBChB, MRCP**
Department of Medicine for Older People, St James' University Hospital, Beckett Street, Leeds, LS9 7TF, UK
**alison.cracknell@leedsth.nhs.uk**

**Sujo Anathhanam, BSc (Hons), MBChB, MRCP**
**Rachel A. Powis, MBChB, MRCP**
**Jeremy Robson BPharm(Hons), Msc Adv Pharm Prac, Clin Dip Pharm (Hosp)**
Department of Medicine for Older People, St James' University Hospital, Beckett Street, Leeds, UK

### Absorption

The ageing process results in several changes in gastrointestinal physiology including slowing of gastric emptying and reduced parietal cell function [Brody *et al.* 1998]. However, clinically significant effects on absorption are likely to be small because most drugs are absorbed passively via the small intestine [Holbeach and Yates, 2010].

### Distribution

Three key changes alter the distribution of drugs in elderly patients. First, a relative reduction in total body water results in a smaller volume of distribution, and therefore higher concentrations of water-soluble drugs such as ethanol and digoxin [Brody *et al.* 1998; Holbeach and Yates, 2010]. Second, an increase in the body fat percentage results in a larger volume of distribution of lipophilic drugs such as diazepam [Brody *et al.* 1998]. This may cause an increased elimination half-life [Beers *et al*. 2009]. Third, a reduction in albumin levels may result in an increase in unbound concentrations of certain drugs such as warfarin and phenytoin [Beers *et al*. 2009; Brody *et al*. 1998; Holbeach and Yates, 2010].

### Metabolism

Hepatic blood flow reduces with advancing age, partly as a result of reduced cardiac output [Brody *et al*. 1998]. This, combined with the age-related reduction in hepatic mass, has characteristic effects on drug metabolism [Beers *et al*. 2009]. Care should be taken when prescribing drugs that are metabolized by the liver and have a narrow therapeutic window (such as warfarin, theophyllines and phenytoin). Tests of liver function do not assess the effectiveness of drug metabolism in the elderly accurately [Brody *et al*. 1998].

### Elimination

Renal elimination of drugs is reduced with ageing. This can result in a prolonged half-life and higher concentrations of drugs or metabolites [Beers *et al.* 2009; Brody *et al*. 1998]. Historically, creatinine clearance, calculated using the Cockcroft–Gault equation, has been used to assess drug handling in patients with renal impairment [Cockgroft and Gault, 1976]. However, more recently, the calculated eGFR (estimated glomerular filtration rate), derived from the modification of diet in renal disease (MDRD) formula, has come into widespread use [Levey *et al.* 2006]. Prescribers need to be careful when calculating a patient's renal impairment and interpreting guidance on dose reduction. As a result of the reduced muscle mass in older people, the serum creatinine can remain within the 'normal' range despite a significant impairment in glomerular filtration rate. Most elderly patients will therefore require an adjustment in the dose of drugs that are excreted by the kidneys (such as digoxin, gentamicin and lithium) [Brody *et al*. 1998].

In terms of pharmacodynamic changes, it is generally considered that enhanced sensitivity to drugs occurs with ageing [Brody *et al.* 1998]. Reduced doses are therefore recommended. Furthermore, with increasing age, regulatory mechanisms are decreased, which may result in orthostatic hypotension when antihypertensive and antidepressant drugs are administered, and an increased risk of opiate-related respiratory depression [Brody *et al.* 1998]. However, older people show reduced sensitivity to certain medications such as beta-blockers, which is attributable to down-regulation of myocardial beta-1 adrenergic receptors [Ahmed, 2003].

## Adverse drug events and adverse drug reactions in the elderly

The occurrence of ADEs is common in the elderly as a result of physiological decline, an increased likelihood of drug–disease interactions due to multiple comorbidities, and an increased likelihood of drug–drug interactions because of polypharmacy [Cresswell *et al*. 2007]. The scale of the problem varies in the literature because of difference in the study design, types of patient studied and whether the primary end-point studied is ADE or ADR. An ADE has been defined as 'any injury resulting from the use of a drug', including harm caused by ADRs, medication errors, overdoses, dose reductions and cessation of therapy [Nebeker *et al.* 2004]. An ADR is 'a response that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physical function' [World Health Organization, 1972]. The occurrence of ADRs is underreported, compounding the problem of their recognition [Lopez-Gonzalez *et al.* 2009].

The proportion of hospitalizations in patients over the age of 75 years secondary to ADEs was 30.4% in one study [Chan *et al.* 2001]. A UK study evaluating inpatients over the age of 16

years identified that 6.5% of admissions were related to an ADR and that patients admitted with ADRs were significantly older than those without ADRs [Pirmohamed *et al.* 2004]. More recently, a German study identified ADRs in 7.6% of admissions, with elderly females being the most susceptible [Hofer-Dueckelmann *et al.* 2011]. The ADRs in the elderly can be vague and difficult to distinguish from medical diagnoses and, if unrecognized, can result in a 'prescribing cascade' where yet more drugs are added to treat the symptoms, in turn increasing drug–drug interactions and the risk of further ADRs [Rochon and Gurwitz, 1997].

The GerontoNet ADR Risk Score has been developed as a simple method to identify elderly hospital inpatients who are at increased risk of an ADR, in the hope of targeting interventions to this group of patients [Onder *et al.* 2010]. Using six variables (more than four comorbidities, renal failure, heart failure, liver disease, number of drugs, and previous ADR), a risk score is calculated, with a score of greater than 8 indicating high risk [Onder *et al.* 2010]. It remains to be seen whether this tool reduces the incidence of ADRs. Computerized physician order entry systems have been suggested to be another means of reducing the incidence of ADEs. However, there is great variability among different systems and the evidence is not clear; one study demonstrated detection rates for potentially fatal prescriptions of only 53% [Metzger *et al.* 2010].

## Identification of prescribing omissions

Much of the literature on drug safety in the elderly has focused on the problem of overprescribing and ADEs in elderly people. However, failure to provide appropriate medications to older adults can also increase harm. Using quality indicators of pharmacological care from the ACOVE (Assessing Care of the Vulnerable Elder) project, one American study reported that the prevalence of omissions of appropriate medicines was 50%, whilst the prevalence of administering inappropriate medication was only 3% [Higashi *et al.* 2004]. The START tool has been developed to help to screen for underprescribing and has good interrater reliability [Barry *et al.* 2007; Ryan *et al.* 2009]. Using this tool, prescribing omissions were detected in 57.9% of patients admitted to an Irish teaching hospital [Barry *et al.* 2007]. The most commonly omitted drugs were statins in atherosclerotic disease, warfarin in chronic atrial fibrillation, antiplatelet therapy in arterial disease, and calcium and vitamin D supplementation in symptomatic osteoporosis [Barry *et al.* 2007]. Rather counterintuitively, one study suggested that underprescribing was significantly more common in patients taking more than five medications (43%) than in patients taking four medications or fewer (13.5%) [Kuijpers *et al.* 2007]. However, these findings were not supported by Steinman and colleagues, who found that underuse was common but did not vary with the total number of medications [Steinman *et al.* 2006].

There may be valid reasons for underprescribing. These include the reluctance of patients to take medication, and situations in which the time needed to derive clinical benefit exceeds life expectancy or if the focus of care has shifted to symptom palliation [Holmes *et al.* 2006]. Other explanations may include the desire of the clinician to avoid polypharmacy, fear of ADRs, lack of convincing evidence of benefit in the elderly, low levels of therapeutic expectations or, in some cases, ageist attitudes [Barry *et al.* 2007].

## Identifying inappropriately prescribed medications

The Beers criteria outline the most widely cited list of medications to be avoided in the elderly. Initially developed in the USA to provide a list of 30 drugs to be avoided in nursing-home residents, the criteria were later modified in 1997 and 2003 and now apply to community-dwelling elderly people [Fick *et al.* 2003]. However, the clinical relevance of the Beers criteria has been questioned because the list is not comprehensive, it includes drugs such as diazepam and amitriptyline that are not absolutely contraindicated in the elderly, and it also includes medications that are unavailable or rarely used in Europe [O'Mahony and Gallagher, 2008].

The STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions) has been devised more recently by the group that created the START tool and has good interrater reliability [Gallagher and O'Mahony, 2008; Ryan *et al.* 2009]. It has been reported recently that the STOPP criteria, unlike the Beers criteria, are significantly associated with avoidable ADEs, suggesting that they are a more clinically relevant tool [Hamilton *et al.* 2011]. A randomized controlled trial that compared usual pharmaceutical care with screening using STOPP/START

criteria suggested that significantly lower rates of unnecessary polypharmacy and potential drug–drug and drug–disease interactions occurred in the intervention group, as well as reductions in underutilization of medications [Gallagher *et al.* 2011]. New educational interventions aimed at improving prescribing for the elderly incorporate START and STOPP criteria, which will hopefully raise awareness of these tools [George and Jacobs, 2011]. It remains to be seen whether widespread utilization of these tools reduces the incidence of ADEs and the associated morbidity and mortality.

## The safer use of high-risk medications

Certain classes of drugs are associated with increased harm in older people but still have a place in chronic disease management. Amongst others, these include antipsychotics, anticoagulants and opioids. Awareness of the specific risks associated with these medications is a step towards reducing harm.

### *Antipsychotic medications*

There is little evidence to support the use of antipsychotic medication to manage behavioural and psychological symptoms in dementia. However, use of these medications is widespread. It is estimated that 180,000 people with dementia in the UK are taking antipsychotics but that only 36,000 of them will derive benefit from these medications [Banerjee, 2009]. Atypical antipsychotics, such as risperidone, olanzapine, amisulpride and quetiapine, have a better side-effect profile than conventional antipsychotics, such as haloperidol, chlorpromazine and trifluoperazine, especially with regard to extrapyramidal symptoms such as parkinsonism and tardive dyskinesia. However, all classes of these medications are associated with an increased risk of falling, and it has been suggested that their use can hasten cognitive decline [Leipzig *et al.* 1999; McShane *et al.* 1997]. More recently, concerns have been raised that both atypical and conventional antipsychotics are associated with a 1.5–1.7 fold increased risk of mortality [Schneider *et al.* 2005; Wang *et al.* 2005; Gill *et al.* 2007]. In light of these concerns, the NHS Institute for Innovation and Improvement recently launched a 'Call to Action', alongside the Dementia Action Alliance, to highlight concerns about the prescription of antipsychotic drugs to people with dementia [Dementia Action Alliance, 2011].

The recommendations are that, where needed, antipsychotics should be used at the lowest possible dose for the shortest time period possible, ideally less than 12 weeks. All patients using these medications should be reviewed regularly by mental health teams. Ideally, the increased risk of stroke and cognitive impairment should be discussed with patients' next of kin when patients themselves lack capacity, although ultimately these medications are often prescribed in the best interest of the patient. Admission to hospital and attendance at outpatient clinics are opportunities for health professionals to check that review mechanisms are in place.

### *Anticoagulation for atrial fibrillation*

Among people over 80 years old, 9% have a diagnosis of atrial fibrillation (AF) [Go e*t al.* 2001]. The choice of drug strategy to reduce the associated risk of stroke lies between anticoagulants such as warfarin and antiplatelet agents such as aspirin. A Cochrane review concluded that adjusted-dose warfarin reduced the risk of stroke by one third when compared with antiplatelet agents, and that antiplatelet agents reduced stroke by approximately 20% when compared with no therapy [Aguilar *et al.* 2007]. Concerns about the applicability of these data to elderly patients have largely been laid to rest by the BAFTA (Birmingham Atrial Fibrillation Treatment of the Aged) trial, which randomized patients over 75 years to warfarin or aspirin therapy and demonstrated a statistically significant lower yearly risk of stroke, intracranial haemorrhage and arterial embolism in the warfarin group (1.8% versus 3.8%) [Mant *et al.* 2007]. Both the National Institute for Health and Clinical Excellence (NICE) and the European Society of Cardiology support these findings, stating that warfarin has a greater benefit in patients over 75 years of age because they are at higher risk of stroke [NICE, 2006; European Society of Cardiology, 2010]. Age is accounted for in the $CHA_2DS_2$-$VAS_C$ scheme for stratification of stroke risk, in which age greater than 75 years scores two points and age 65–74 years scores one point [Lip *et al.* 2010]. According to this scheme, warfarin is preferred for patients with scores of 1 or greater.

However, anticoagulants remain among the most frequently omitted medications in older people [Barry *et al.* 2007]. Factors influencing physicians' reticence to prescribe warfarin include increasing age of the patient, increased bleeding

risk, previous bleeds, risk of falls, comorbidities and inability to comply with treatment [Pugh *et al.* 2011].

In randomized controlled trials, the benefits of warfarin have not been offset by the occurrence of major haemorrhage. However, it has been argued that this may be partly due to the low proportion of elderly patients who take part in trials, because age over 80 years is a risk factor for bleeding [Hylek e*t al.* 2007]. The BAFTA investigators demonstrated low rates of bleeding in both the aspirin and warfarin groups, but this trial was not powered to detect differences in bleeding rates [Mant *et al.* 2007]. Furthermore, patients in the warfarin group had international normalized ratios (INRs) in the range 2–3 for 67% of the time, which may be better than the ratios often achieved in practice [Mant *et al.* 2007]. The HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol concomitantly) tool has been designed to support clinical decision making, with scores of greater than 3 indicating patients at high risk of bleeding complications [Pisters *et al.* 2010]. Interestingly, a risk of falls is not incorporated into the HAS-BLED tool. This risk is often cited as a contraindication to warfarin treatment, on the basis that head trauma is associated with an increased risk of bleeding.

Novel anticoagulant strategies are emerging. Dabigatran is a direct thrombin inhibitor that is available in two doses. It has a much wider therapeutic index than warfarin, does not require blood monitoring, and has few interactions. The RE-LY (Randomized Evaluation of Long-Term Anticoagulant Therapy) trial found that, at the higher dose, dabigatran was associated with lower rates of stroke than warfarin and similar rates of major haemorrhage [Connolly *et al.* 2009]. At the lower dose, it was associated with similar rates of stroke to warfarin but lower rates of major haemorrhage [Connolly *et al.* 2009]. These results appear promising but caution is needed, given that these data are new, follow-up is currently restricted to short-term outcomes, only 39% of patients in the trial were over 75 years old, and, of particular concern, there is no antidote to dabigatran to enable reversal [Jacobs and Stessman, 2011]. Elderly patients with renal failure appear to be particularly susceptible to bleeding complications related to the use of dabigatran [Legrand *et al.* 2011]. Apixaban, a novel factor Xa inhibitor, is another medication that holds promise. It was shown to be superior to aspirin in the AVERROES (Apixaban versus Acetylsalicylic Acid to Prevent Strokes) trial and therefore may be a good choice for patients unsuited to warfarin therapy [Connolly *et al.* 2011]. Whilst the roles of the new drugs in frail elderly patients are yet to be determined, it seems likely that there will be more options in the future for the treatment of elderly patients with AF who are at high risk of stroke.

### *Opioids*

Chronic pain occurs in 45–85% of older people; treatment is important to allow maintenance of a good quality of life and an active role in both family and society where possible [Gianni *et al.* 2009]. Suboptimal management of pain occurs frequently; one report suggested that up to 25% of elderly patients in nursing homes who suffered from pain received no analgesia [Won *et al.* 2004]. Opioid analgesia can be effective for the treatment of severe pain of both malignant and non-malignant origin. However opioids are often underutilized in the elderly, mainly because of concerns about polypharmacy and fear of ADEs, which include nausea and vomiting, pruritus, constipation, respiratory depression, cough suppression and rigidity [Auret and Schug, 2005; Schug *et al.* 1992]. Opioids have also been associated with an increased risk of fractures, possibly related to their sedative effect that increases the chance of falling [Solomon *et al.* 2010]. Whilst these concerns are legitimate, the use of other medications, such as nonsteroidal anti-inflammatory drugs, may also be limited by gastrointestinal and renal disease.

Steps can be taken to minimize the development of toxicity. Given the pharmacokinetic changes that occur in the elderly and the increased sensitivity of their central nervous systems to opioids, older patients may not require large doses of opioids to benefit from an effect. It is therefore recommended that prescribers 'start low and go slow' and monitor patients closely for at least the first week of treatment [Auret and Schug, 2005]. Caution should be exercised when prescribing opioids in conjunction with other sedative medications. The choice of opioid for older patients with severe renal impairment needs to be individualized and local guidance must be sought before initiating therapy. Once opiate requirements have been established, prescribing regular

opioids rather than 'as needed' doses reduces the likelihood of patients either self-administering without guidance, or failing to obtain analgesics because they have not requested them [Auret and Schug, 2005]. Laxatives and high fluid intake can reduce the risk of constipation, whilst antiemetics are recommended in the first few days of usage [Vanegas *et al.* 1998].

## Improving safety in healthcare settings and across transitions

There are several stages involved in medication provision, including prescribing, transmitting, dispensing, administering and monitoring. The National Patient Safety Agency reported that 12–20% of the 900,000 incidents reported in 2005 were related to medicines; medication errors occur most commonly in the areas of prescribing, dispensing and administration [Fertleman *et al.* 2005]. Illegible handwriting and consequent misinterpreted prescriptions also result in significant errors [Bell *et al.* 2004]. Errors in prescribing can be heightened by breakdowns in communication when patients move from one setting to another, and the Royal Pharmaceutical Society has recognized that older people are particularly vulnerable to these [Parsons *et al.* 2011; Royal Pharmaceutical Society, 2011]. The nature of modern healthcare means that elderly patients often move between their homes, multiple wards within a hospital, intermediate care establishments, and nursing and residential care facilities, encountering multiple healthcare professionals, systems and processes on the way.

On admission, challenges in obtaining an accurate account from a patient may be exacerbated by an acute condition, sensory or cognitive impairment, a lack of access to family members or carers, or language barriers. Therefore, in collaboration with the National Patient Safety Agency, NICE has produced guidance recommending that all patients undergo 'medicines reconciliation' on admission to hospital [NICE, 2007]. This process ensures that the medicines prescribed on admission correspond to those that the patient was taking before admission. Most hospitals have ward-based pharmacists to facilitate this. The presence of pharmacists on the post-take ward round has been shown to improve the accuracy of drug history documentation, reduce prescribing costs and decrease the potential risk to hospital inpatients [Fertleman *et al.* 2005]. Medication discrepancies are also recognized to occur at discharge; one study demonstrated that at least one medication discrepancy occurred in 71% of discharges from hospital to skilled nursing care facilities [Tija *et al.* 2009]. Cardiovascular medications, opiates, neuropsychiatric medications, hypoglycaemics, antibiotics and anticoagulants accounted for over 50% of discrepant medications [Tija *et al.* 2009]. The involvement of a pharmacist transition coordinator when discharging elderly people from hospital to long-term care facilities was shown to protect against worsening pain and decreased hospital usage, although no significant impact on ADEs, falls, mobility or confusion was demonstrated [Crotty *et al.* 2004]. Electronic discharge documents are now used more widely to reduce problems associated with illegible handwritten discharge notes. If other sources are unavailable, these can also act as a source of medication history when patients with recent hospital stays are readmitted.

Several American studies have looked at the use of electronic health records to improve communication between healthcare settings. However, their economic value and validity in reducing ADEs has not yet been adequately demonstrated [Boockvar *et al.* 2010; Monane *et al.* 1998]. In the UK, the National Programme for Information Technology in England was a controversial initiative of the Department of Health that was intended to move clinicians in England towards shared electronic records. An evaluation of the summary care record, which holds information on medication, allergies and adverse reactions, did not directly demonstrate evidence of improved safety [Greenhalgh *et al.* 2010]. However, there was some anecdotal evidence of reduced medication errors, and given that the shared care record was infrequently accessed in secondary care settings, the potential benefits of electronic health records may be reaped with increased usage by physicians [Greenhalgh *et al.* 2010].

## Conclusion

Prescribing medications safely for older people is complex, given their changed pharmacokinetics and altered pharmacodynamic responses, the presence of multiple comorbidities, and the high risk of falls and confusion. Consequently, there is a higher incidence of ADEs and inappropriate prescribing in this age group. Box 1 lists some 'top tips' to help the nonspecialist when prescribing in this population. Whilst it is not feasible for all older people to have a comprehensive

**Box I.** Top tips to consider when initiating medication in older people.

**What drug?**

1) Obtain an accurate drug and disease history in order to avoid drug–disease or drug–drug interactions.
2) Consider nonpharmacological treatments where possible.
3) Consider psychosocial causes of symptoms.
4) Avoid treating symptoms rather than their underlying cause.
5) Assess the risks as well as benefits. Consider START criteria [Barry *et al.* 2007].
6) Avoid discrimination when considering prophylactic treatments.

**How to prescribe?**

1) Provide information and education to the patient and their carer(s).
2) Assess the most appropriate route of administration.
3) Start with a lower dose for most drugs and titrate slowly.
4) Consider individual factors, e.g. renal function, alcohol intake, body fat, diet, cigarette smoking.
5) Consider practical factors such as packaging and dose scheduling.

**How to follow up?**

1) Monitor for clinical benefit and side effects in initial stages.
2) Ensure where appropriate that drug levels and biochemical markers are measured.
3) Undertake regular (at least annual) medication review of existing medications including 'over-the-counter' therapies, and assess adherence.
4) Medicines that are not providing benefit or that are producing unacceptable side effects should be stopped. Consider STOPP criteria [Gallagher *et al.* 2008].
5) Provide effective and accurate communication of medication regime upon transition of care.

**Where appropriate involve a pharmacist in prescribing decisions**

***Guidelines adapted from:***

Patient UK (2010). Prescribing for the older patient. Available at: http://www.patient.co.uk/doctor/Prescribing-for-the-Older-Patient.htm [Accessed on 11 December 2010].

Beers, M.H., Jones, T.V., Berkwits, M., Kaplan, J.L. and Porter, R.P. (updated 2009) *The Merck Manual of Geriatrics*, 3rd edition. Available at: www.merck.com [Accessed on 11 December 2010].

medication review by a geriatrician, tools such as STOPP and START can be used by nonspecialists, although these cannot replace individualized assessment and clinical judgement. Comprehensive geriatric assessments should be targeted at patients identified to be at high risk by general practitioners, community nurses and other health professionals, and can be offered opportunistically in inpatient and outpatient settings. More studies to assess medication effectiveness in the elderly are needed. Healthcare organizations and individual practitioners must continue to seek methods to reduce the incidence of ADEs in the elderly and to improve safety across healthcare transitions. There may be scope in the future for electronic patient records to improve prescribing across healthcare settings but further work in this area is needed.

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## References

Aguilar, M.I., Hart, R. and Pearce, L.A. (2007) Oral anticoagulants versus antiplatelet therapy for preventing stroke in patients with non-valvular atrial fibrillation and no history of stroke or transient ischaemic attacks. *Cochrane Database Syst Rev*: CD006186.

Ahmed, A. (2003) Myocardial beta-1 adrenoceptor down-regulation in aging and heart failure: implications for beta-blocker use in older adults with heart failure. *Eur J Heart Fail* 5: 709–715.

Auret, K. and Schug, S.A. (2005) Underutilisation of opioids in elderly patients with chronic pain: approaches to correcting the problem. *Drugs Aging* 22: 641–654.

Banerjee, S. (2009) The use of antipsychotic medication for people with dementia: Time for action.

*Department of Health Report*. Available at: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_108302.pdf [Accessed on 15 November 2011].

Barry, P.J., Gallagher, P., Ryan, D. and O'Mahony, D. (2007) START (screening tool to alert doctors to the right treatment): an evidence-based screening tool to detect prescribing omissions in elderly patients. *Age Ageing* 36: 632–638.

Beers, M.H., Jones, T.V., Berkwits, M., Kaplan, J.L. and Porter, R.P. (updated 2009) *The Merck Manual of Geriatrics*, 3rd edition. Available at: http://www.merck.com [Accessed on 11 December 2010].

Bell, D.S., Cretin, S., Marken, R.S. and Landman, A.B. (2004) A conceptual framework for evaluating outpatient electronic prescribing systems based on their functional capabilities. *J Am Med Inform Assoc* 11: 60–70.

Beswick, A., Burke, M. and Shlomo, Y.B. (2008) PREDICT. Increasing the participation of elderly in clinical trials. Work package 1. Literature review. London: Medical Research Council (UK). Available at: http://www.predicteu.org [Accessed on 5 November 2011].

Boockvar, K.S., Livote, E.E., Goldstein, N., Nebeker, J.R., Siu, A. and Fried, T. (2010) Electronic health records and adverse drug events after patient transfer. *Qual Saf Health Care* 19: 1–5.

Brody, T.M., Larner, J. and Minneman, K.P. (1998) *Human Pharmacology: Molecular to Clinical*, 3rd edition. St Louis MO: Mosby Inc. USA.

Chan, M., Nicklason, F. and Vial, J.H. (2001) Adverse drug events as a cause of hospital admission in the elderly. *Intern Med J* 31: 199–205.

Cockcroft, D.W. and Gault, M.H. (1976) Prediction of creatinine clearance from serum creatinine. *Nephron* 16: 31–41.

Connolly, S.J., Ezekowitz, M.D., Yusuf, S., Eikelboom, J., Oldgren, J., Parekh, A. *et al.* (2009) Dabigatran versus warfarin in patients with atrial fibrillation. *New Engl J Med* 361: 1139–1151.

Connolly, S.J., Eikelboom, J., Joyner, C., Diener, H.C., Hart, R., Golitsyn, S. *et al.* (2011) Apixaban in patients with atrial fibrillation. *New Engl J Med* 364: 806–817.

Cresswell, K.M., Fernando, B., McKinstry, B. and Shiekh, A. (2007) Adverse drug events in the elderly. *Br Med Bull* 83: 259–274.

Crotty, M., Rowett, D., Spurling, L., Giles, L.C. and Phillips, P.A. (2004) Does the addition of a pharmacist transition coordinator improve evidence-based medication management and health outcomes in older adults moving from the hospital to a long-term care facility? Results of a randomized, controlled trial. *Am J Geriatr Pharmacother* 2: 257–264.

Dementia Action Alliance and NHS Institute for Innovation and Improvement (2011) The right prescription: a call to action on the use of antipsychotic drugs for people with dementia. Available at: http://www.institute.nhs.uk/qipp/calls_to_action/Dementia_and_antipsychotic_drugs.htm [Accessed on 5 January 2012].

European Society of Cardiology (2010) Guidelines for the management of atrial fibrillation. *Eur Heart J* 31: 2369–2429.

Fertleman, M., Barnett, N. and Patel, T. (2005) Improving medication management for patients: the effect of a pharmacist on post-admission ward rounds. *Qual Saf Health Care* 14: 207–211.

Fialová, D. and Onder, G. (2009) Medication errors in elderly people: contributing factors and future perspectives. *Br J Clin Pharmacol* 67: 641–645.

Fick, D.M., Cooper, J.W., Wade, W.E., Waller, J.L., MacLean, R.J. and Beers, M.H. (2003) Updating the Beers criteria for potentially inappropriate medication use in older adults. *Arch Intern Med* 163: 2716–2725.

Gallagher, P.and O'Mahony, D. (2008) STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria. *Age Ageing* 37: 673–679.

Gallagher, P.F., O'Connor, M.N. and O'Mahony, D. (2011) Prevention of potentially inappropriate prescribing for elderly patients: a randomized controlled trial using STOPP/START criteria. *Clin Pharmacol Ther*: 89: 845–854.

George, C.J. and Jacobs, L.G. (2011) Geriatrics medication management rounds: a novel approach to teaching rational prescribing with the use of the medication screening questionnaire. *J Am Geriatr Soc* 59: 138–142.

Gianni, W., Ceci, M., Bustacchini, S., Corsonello, A., Abbatecola, A.M., Brancati, A.M. *et al.* (2009) Opioids for the treatment of chronic non-cancer pain in older people. *Drugs Aging* 26: 63–73.

Gill, S.S., Bronskill, S.E., Normand, S.L., Anderson, G.M., Sykora, K., Lam, K. *et al.* (2007) Antipsychotic drug use and mortality in older adults with dementia. *Ann Intern Med* 146: 775–786.

Go, A.S., Hylek, E.M., Phillips, K.A., Chang, Y., Henault, L.E., Selby, J.V. *et al.* (2001) Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. *JAMA* 285: 2370–2375.

Greenhalgh, T., Stramer, K., Bratan, T., Byrne, E., Russell, J. and Potts, H.W. (2010) Adoption and non-adoption of a shared electronic summary record in England: a mixed-method case study. *BMJ* 340: c3111.

Hamilton, H., Gallagher, P., Ryan, C., Byrne, S. and O'Mahony, D. (2011) Potentially inappropriate prescribing defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients. *Arch Intern Med* 171: 1013–1019.

Higashi, T., Shekelle, P.G., Solomon, D.H., Knight, E.L., Roth, C., Chang, J.T. *et al.* (2004) The quality of pharmacologic care for vulnerable older patients. *Ann Intern Med* 140: 714–720.

Hippisley-Cox, J., Pringle, M. and Ryan, R. (2007) Polypharmacy in the elderly: analysis of QRESEARCH data. Available at: http://www.qresearch.org/Public_Documents/DataValidation/Polypharmacy%20in%20the%20elderly.pdf [Accessed on 6 November 2011].

Hofer-Dueckelmann, C., Prinz, E., Beindl, W., Szymanski, J., Fellhofer, G., Pichler, M. *et al.* (2011) Adverse drug reactions (ADRs) associated with hospital admissions: elderly female patients are at highest risk. *Int J Clin Pharmacol Ther* 49: 577–586.

Holbeach, E. and Yates, P. (2010) Prescribing in the elderly. *Aust Fam Physician* 39: 728–733.

Holmes, H.M., Hayley, D.C., Alexander, G.C. and Sachs, G.A. (2006). Reconsidering medication appropriateness for patients late in life. *Arch Intern Med* 166: 605–609.

Hylek, E.M., Evans-Molina, C., Shea, C., Henault, L.E. and Regan, S. (2007) Major hemorrhage and tolerability of warfarin in the first year of therapy among elderly patients with atrial fibrillation. *Circulation* 115: 2689–2696.

Jacobs, J.M. and Stessman, J. (2011) New anticoagulant drugs among elderly patients: is caution necessary? *Arch Intern Med* 171: 1287–1288.

Kuijpers, M.A.J., van Marum, R.J., Egberts, A.C., Jansen, P.A., OLDY study group (2007) Relationship between polypharmacy and underprescribing. *Br J Clin Pharmacol* 65: 130–133.

Legrand, M., Mateo, J., Aribaud, A., Ginisty, S., Eftekhari, P., Tran Ba Huy, P. *et al.* (2011) The use of dabigatran in elderly patients. *Arch Intern Med* 171: 1285–1286.

Leipzig, R.M., Cumming, R.G. and Tinetti, M.E. (1999) Drugs and falls in older people: a systematic review and meta-analysis: I. Psychotropic drugs. *J Am Geriatr Soc* 47: 30–39.

Levey, A.S., Coresh, J.,Greene, T., Stevens, L.A., Zhang, Y.L., Hendriksen, S.K. *et al.* (2006) Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med* 145: 247–254.

Lip, G.Y., Nieuwlaat, R., Pisters, R., Lane, D.A. and Crijns, H.J. (2010) Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the EURO Heart Survey on atrial fibrillation. *Chest* 137: 263–272.

Lopez-Gonzalez, E., Herdeiro, M.T. and Figueiras, A. (2009) Determinants of under-reporting of adverse drug reactions: a systematic review. *Drug Saf* 32: 19–31.

Mant, J., Hobbs, F.D., Fletcher, K., Roalfe, A., Fitzmaurice, D., Lip, G.Y. *et al.* (2007) Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. *Lancet* 370: 493–503.

McShane, R., Keene, J., Gedling, K., Fairburn, C., Jacoby, R. and Hope, T. (1997) Do neuroleptic drugs hasten cognitive decline in dementia? Prospective study with necropsy follow up. *BMJ* 314: 266–270.

Metzger, J., Welebob, E., Bates, D.W., Lipsitz, S. and Classen, D.C. (2010) Mixed results in the safety performance of computerized physician order entry. *Health Aff (Millwood)* 29: 655–663.

Monane, M., Matthias, D.M., Nagle, B.A. and Kelly, M.A. (1998) Improving prescribing patterns for the elderly through an online drug utilization review intervention: a system linking the physician, pharmacist and computer. *JAMA* 280: 1249–1252.

Nebeker, J.R., Barach, P. and Samore, M.H. (2004) Clarifying adverse drug events: a clinician's guide to terminology, documentation, and reporting. *Ann Intern Med* 140: 795–801.

NICE; National Institute for Heath and Clinical Excellence (2006) Clinical guideline 36: the management of atrial fibrillation. Available at: http://www.nice.org.uk [Accessed on 30 December 2011].

NICE; National Institute for Health and Clinical Excellence (2007) Technical patient safety solutions for medicines reconciliation on admission of adults to hospital. Available at: http://guidance.nice.org.uk/PSG001 [Accessed on 1 January 2012].

O'Mahony, D. and Gallagher, P.F. (2008) Inappropriate prescribing in the older population: need for new criteria. *Age Ageing* 37: 138–141.

Onder, G., Petrovic, M., Tangiisuran, B., Meinardi, M.C., Markito-Notenboom, W.P. and Somers, A. (2010) Development and validation of a score to assess risk of adverse drug reactions among in-hospital patients 65 years or older: the GerontoNet ADR Risk Score. *Arch Intern Med* 170: 1142–1148.

Parsons, C., Lapane, K., Kerse, N. and Hughes, C. (2011) Prescribing for older people in nursing homes: a review of the key issues. *Int J Older People Nurs* 6: 45–54.

Pirmohamed, M., James, S., Meakin, S., Green, C., Scott, A.K., Walley, T.J. *et al.* (2004) Adverse drug reactions as cause of admission to hospital: prospective analysis of 18820 patients. *BMJ* 329: 15–19.

Pisters, R., Lane, D.A., Nieuwlaat, R., de Vos, C.B., Crijns, H.J. and Lip, G.Y. (2010) A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest* 138: 1093–1100.

Pugh, D., Pugh, J. and Mead, G.E. (2011) Attitudes of physicians regarding anticoagulation for atrial fibrillation: a systematic review. *Age Ageing* 40: 675–683.

Rochon, P.A. and Gurwitz, J.H. (1997) Optimising drug treatment for elderly people: the prescribing cascade. *BMJ* 315: 1096–1099.

Royal Pharmaceutical Society (2011) Keeping patients safe when they transfer between care providers – getting the medicines right. Good practice guidance for healthcare professions. Available at: http://www.rpharms.com/getting-the-medicines-right/professional-guidance.asp [Accessed on 4 January 2012].

Ryan, C., O'Mahony, D. and Byrne, S. (2009) Application of STOPP and START criteria: interrater reliability among pharmacists. *Ann Pharmacother* 43: 1239–1244.

Schneider, L.S., Dagerman, K.S. and Insel, P. (2005) Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. *JAMA* 294: 1934–1943.

Schug, S.A., Zech, D. and Grond, S. (1992) Adverse effects of systemic opioid analgesics. *Drug Saf* 7: 200–213.

Solomon, D.H., Rassen, J.A., Glynn, R.J., Lee, J., Levin, R. and Schneeweiss, S. (2010) The comparative safety of analgesics in older adults with arthritis. *Arch Intern Med* 170: 1968–1976.

Spinewine, A. (2008) Adverse drug reactions in elderly people: the challenge of safer prescribing. *BMJ* 336: 956–957.

Steinman, M.A., Landefeld, C.S., Rosenthal, G.E., Berthenthal, D., Sen, S. and Kaboli, P.J. (2006) Polypharmacy and prescribing quality in older people. *J Am Geriatr Soc* 54: 1516–1523.

Tija, J., Bonner, A., Briesacher, B.A., McGee, S., Terrill, E. and Miller, K. (2009) Discrepancies upon hospital to skilled nursing facility transitions. *J Gen Intern Med* 24: 630–635.

Vanegas, G., Ripamonti, C., Sbanotto, A. and De Conno, F. (1998) Side effects of morphine administration in cancer patients. *Cancer Nurs* 21: 289–297.

Wang, P.S., Schneeweiss, S., Avorn, J., Fischer, M.A., Mogun, H., Solomon, D.H. *et al.* (2005) Risk of death in elderly users of conventional vs. atypical antipsychotic medications. *N Engl J Med* 353: 2335–2341.

Won, A.B., Lapane, K.L., Vallow, S., Schein, J., Morris, J.N. and Lipsitz, L.A. (2004) Persistent nonmalignant pain and analgesic prescribing patterns in elderly nursing home residents. *J Am Geriatr Soc* 52: 867–874.

World Health Organization (1972) International drug monitoring: the role of national centres. Technical Report Series No 498. Geneva: WHO.