

# The role of medication review in older people at risk of falls

A third of people aged over 65 years fall each year and medication review is an important part of the assessment of these patients. Both polypharmacy and specific medications increase the risk of falls and discontinuing these medications may reduce this risk. Other factors that need to be assessed include identifying and treating osteoporosis, and assessing the potential risks of anticoagulation in older people at risk of falls. This article examines the issues that need addressing during a medication review to reduce the risk of falls and related injuries in older people.

**Dr James Milton** SpR Geriatric Medicine, Kent and Sussex Hospital, Tunbridge Wells, Kent  
 email [jim\\_milton@hotmail.com](mailto:jim_milton@hotmail.com)

Falls are a common problem in older people, with about a third of older people falling each year.<sup>1</sup> Medication is a recognised cause of falls, with both polypharmacy and specific drugs being associated with an increased falls risk.<sup>2-4</sup> Both the *National Service Framework (NSF) for Older People* and the National Institute for Health and Clinical Excellence (NICE) recommend medication review and drug modification for all older people at risk of falls.<sup>5,6</sup>

The NSF for Older People states that all older people should have a regular medication review to try to reduce the complications associated with taking multiple medications.<sup>5</sup> An additional chapter to the NSF, outlines how this regular review should be undertaken.<sup>7</sup> However, additional factors need addressing when doing a medication review on an older person who is falling.

The evidence of the benefits of regular medication review in older non-fallers is limited. Studies predominantly show a reduction in the total number

of medications, an increase in concordance, reduction in adverse drug reactions and some cost benefits. However, there is little evidence that a medication review improves quality of life or has beneficial effects on a patient's health.<sup>8</sup> In older people at risk of falls, there is more convincing evidence that a medication review is beneficial, specifically by reducing future falls.

Studies that show a benefit of multifactorial interventions in reducing falls often include a medication review, along with home-hazard assessment, and strength and balance training.<sup>9</sup> Other studies that have examined the withdrawal of psychotropic medication, which is known to increase the risk of falling, have also shown benefits in reducing falls.<sup>10,11</sup>

Physicians dealing with older people who fall should be aware of what a medication review entails. One trial evaluated an education programme, conducted by pharmacists, for primary care physicians about prescribing. The

programme included the use of a medication review checklist by the doctors.<sup>12</sup> As a result, more patients in the intervention group had a medication review and there was a significant reduction in falls and fall-related injuries at 1 year. The mechanism by which falls and injuries were reduced is, however, unclear. The study examined the prescription of three target drugs (benzodiazepines, non-steroidal anti-inflammatory drugs (NSAIDs) and thiazide diuretics), none of which were significantly reduced.

With regard to tailoring a medication review to an older person at risk of falls, the general principles of a medication review remain unchanged—regardless of whether an older person is falling or not. Ideally it should occur face-to-face and review all medications the patient is taking, including over-the-counter medications, and examine the indication and dose of all medications taken. Specific issues that need addressing are: reviewing the need for medications known to increase

falls risk, modifying medications that increase or decrease the risk of injury following a fall, and identifying and treating previously undiagnosed medical problems that may increase the risk of falls.

## Medication and falls

Polypharmacy is associated with an increased falls risk.<sup>13,2</sup> However, this may be because it is acting as a surrogate marker of co-morbidity and frailty, and therefore falls risk, rather than being a causative factor. This is supported by a study that demonstrated that falls were associated with polypharmacy, but only when the regimen included at least one medication known to increase the risk of falling.<sup>13</sup> Also, a survey of older women showed an increasing number of chronic co-morbidities was a stronger predictor of falls risk than polypharmacy.<sup>14</sup> There is no evidence that reducing the total number of medications a patient takes reduces their falls risk.

Despite uncertainty about the direct influence of the quantity of medication on falls risk, there are certain individual drugs that are known to increase the risk of falls. A systemic review and meta-analysis showed that psychotropic medication seems to have the strongest association, with a pooled odds ratio of 1.73 for one or more falls.<sup>3</sup> Neuroleptic medication, antidepressants (mostly tricyclic), short- and long-acting benzodiazepines were all associated with an increased risk of falls. A further review has reinforced this message, concluding that benzodiazepines, antidepressants (including both

tricyclics and selective serotonin reuptake inhibitors), and antipsychotics are all associated with an increase in falls risk.<sup>2</sup> However, the authors said that most studies were observational, that several did not define falls, and that dose and duration of drug treatment were often not examined.

With regards to non-psychotropic medications, a review and meta-analysis concluded that certain non-psychotropic drugs were weakly associated with falls, including digoxin, type 1A antiarrhythmics, eg. procainamide and quinidine, and diuretics.<sup>4</sup>

Given the evidence, discontinuing psychotropic medication, if possible, to reduce falls risk seems logical. A small trial showed significantly fewer falls in those who had psychotropic medication withdrawn than those who remained on it, over 44 weeks, with a relative hazard ratio of 0.34.<sup>10</sup> However, this study also demonstrated one of the potential difficulties of withdrawing psychotropic medication. One month after the study was completed, nearly half of the participants in the medication withdrawal group, who had been on placebo for 30 weeks, had restarted psychotropic medication.

Another randomised, controlled study used a pharmacist to remotely review prescriptions electronically in older patients on multiple medications, including at least one psychoactive drug. An electronic message was sent to the patient's doctor with recommendations to alter the prescription. This resulted in a significant reduction in the number of psychoactive medications and falls-related

hospital encounters, but no significant difference when self-reported falls were included in the analysis.<sup>11</sup>

A 2006 prospective cohort study reported a significant reduction in falls within two months of withdrawing or reducing the dose of all drugs that increase the risk of falls, including both psychotropic and cardiovascular medication.<sup>15</sup> Medication was withdrawn in approximately half of the participants where it was felt the medication was redundant or the dose could be reduced safely, with the remaining participants continuing on their usual medication. The intervention group reported fewer falls on follow-up, with the largest benefit, surprisingly, coming in those who had cardiovascular medication withdrawn rather than psychotropic medication.

Thus, in terms of prevention, reducing or stopping medications that increase falls risk seems to be beneficial. However, decisions need to be taken on a case-by-case basis, relying on the clinical judgement of the physician, the indication for the medication, and the presence of other co-morbidities. The NICE falls guidelines only comment on psychotropic medication, stating that older people on psychotropic drugs should have their medication reviewed, and if possible stopped, to reduce the risk of falling.<sup>6</sup>

Syncope is an important cause of falls, with orthostatic hypotension (OH) being the most common cause in older people. About 18% of community dwelling older individuals have evidence of OH,<sup>16</sup> but 24%–30% of

older fallers have OH.<sup>17,18</sup> One of the commonest causative factors is medication (see Box 1). However, OH is often asymptomatic and, therefore, its presence does not warrant the immediate cessation of possible culprit medication.

If OH is not medication-related, or is due to a drug that cannot be discontinued, such as levodopa in Parkinson's disease (PD), then there are conservative methods, such as compression stockings, head-up tilt of the bed and encouraging fluid intake, that should be tried. If this fails there are pharmacological treatments, including the mineralocorticoid fludrocortisone and the  $\alpha$ -adrenoceptor agonist midodrine, although the latter is not licenced in the UK and is only available on a named-patient basis.

Rate-limiting medication, such as  $\beta$ -blockers, can also cause syncope and falls by inducing bradycardia or heart block. There are case reports of this occurring with  $\beta$ -blocking eye drops.<sup>19</sup>

If syncope is suspected, due to either bradycardia or OH,

medication may be the cause. If it is the cause, if possible, the culprit drugs should be discontinued or replaced.

## Medical conditions

Physicians should also identify new medical conditions that may increase falls risk, such as visual impairment, cardiac arrhythmias, urinary incontinence or PD. The identification and treatment of some of these conditions, such as PD, may result in the addition of more medication, while potentially reducing falls risk.

Also, a medication review may identify unrelated medical conditions, such as hypertension, that require the prescription of additional medications (if appropriate and the patient agrees). With hypertension, the treatment may actually increase the falls risk.

## Vitamin D

The possibility that vitamin D replacement may reduce falls risk has created a lot of interest.

Vitamin D deficiency is common in older populations, especially those living in residential homes: 10–15% of community-dwelling people aged over 65 have vitamin D deficiency (serum level of 25-hydroxycholecalciferol of <25nmol/L), and this rises to about a third of those in residential care.<sup>20</sup> Vitamin D is known to aid muscle strength and possibly neuromuscular junction action, as well as its role in bone metabolism. Therefore, vitamin D replacement may have a role in reducing the number of falls by increasing

muscle strength.<sup>21</sup>

However, the results of studies and reviews have been somewhat contradictory. Two meta-analyses came to different conclusions. One reported that vitamin D reduced the corrected odds ratio of falling by 22%, but the other reported no falls reduction with vitamin D supplementation.<sup>22,23</sup>

In 2004, NICE concluded that there was insufficient evidence to offer specific guidance on the use of vitamin D replacement to prevent falls. However, it did state that vitamin D replacement may be beneficial in older people in residential care.<sup>6</sup>

Since these meta-analyses, further studies have been conducted, which unfortunately still remain contradictory. A recent meta-analysis suggested a daily dose of 700–1000 IU vitamin D, to achieve a 25-hydroxy vitamin D level of >60 nmol/L, reduced falls.<sup>24</sup> A Cochrane review concluded that the benefit of vitamin D supplementation was unclear, but that it may have a role in falls reduction for those with documented vitamin D deficiency.<sup>25</sup>

The other potential role of vitamin D (and calcium) in older people is the reduction of osteoporotic fractures. A meta-analysis found that calcium, with or without vitamin D, in people aged over 50 years reduced the risk of fracture and reduced bone loss at the hip and lumbar spine.<sup>26</sup> The estimated number needed to treat for 3.5 years to prevent one fracture was 63.

Vitamin D and calcium are usually prescribed in combination formulations, and it is worth remembering that these medications are not

### Box 1: Medications associated with OH

- Angiotensin-converting enzyme (ACE) inhibitors
- Diuretics
- $\alpha$ -blockers
- $\beta$ -blockers
- Angiotensin II receptor blockers (ARBs)
- Tricyclic antidepressants
- Levodopa
- Nitrates

without potential side effects. One recent paper showed that vitamin D and calcium replacement led to an increased incidence of renal stones in postmenopausal women.<sup>27</sup> Another trial demonstrated that calcium supplementation was associated with an upward trend in cardiovascular events over a five-year period, although the results did not reach statistical significance.<sup>28</sup> This is despite calcium supplementation increasing the ratio of high density lipoprotein cholesterol to low density lipoprotein cholesterol by almost 20%, which one would expect to lower cardiovascular risk. A possible reason why calcium supplementation may increase the risk of cardiovascular disease is that the increase in serum calcium may stimulate vascular calcification, which is associated with vascular risk. In this study, the number of postmenopausal women needed to treat over five years to cause one cardiovascular event was 29, but the reported number needed to treat over the same time period to prevent one symptomatic fracture was 50.

### **The impact of a fall**

When reviewing a patient's medication, thought needs to be given to reducing the impact of a fall by either prescribing medicines that reduce injuries or discontinuing medication that may increase the chance of injury.

### **Osteoporosis**

Osteoporosis is common in older people and low-impact fractures are a common cause of morbidity and mortality, as well as having significant cost implications.

NICE has issued guidelines (Table 1) on both the primary prevention and secondary prevention of osteoporotic fractures.<sup>29,30</sup> The guidelines are not straightforward, with treatment depending on a combination of age, independent clinical risk factors (parental history of hip fracture, alcohol intake of four or more units a day and rheumatoid arthritis), indicators of a low BMI and DEXA score. For both primary and secondary treatment, first-line treatment is the generic bisphosphonate, alendronate.

NICE guidelines state that alendronate may be started in women aged over 75 years with an osteoporotic fragility fracture without the need for a dual energy X-ray absorptiometry (DEXA) scan if a scan is "clinically inappropriate or unfeasible".<sup>30</sup> However, with this approach, monitoring the effects of treatment is difficult, especially if a patient then presents with a second fragility fracture.

For younger patients and those without previous fragility fractures, physicians need to decide if patients at risk of falls need treatment or investigation for osteoporosis, as performing DEXA scans on all older people who fall is not a practical proposition.

**Table 1:** NICE guidance for osteoporosis<sup>28,29</sup>

<i>Primary prevention</i>		
Stage of treatment	Treatment	Indications for use
First line	Alendronate	Treatment dependent on T score $\leq$ -2.5 and combination of age, presence of independent clinical risk factors or indicators of low bone mineral density
Second line	Risedronate or etidronate	*Based on combination of T-score, age and presence of independent clinical risk factors, plus intolerance to previous therapies
Third line	Strontium ranelate	* Same as before
Fourth line	N/A	
<i>Secondary Prevention</i>		
Stage of treatment	Treatment	Indications for use
First line	Alendronate	T score $\leq$ -2.5 and a fragility fracture. If age 75 years or older, DEXA scan may not be required
Second line	Risedronate or etidronate	* Same as before
Third line	Strontium ranelate	* Same as before
Fourth line	Teriparatide	If previous therapies not tolerated or unsatisfactory response plus T score $\leq$ 4, or $\leq$ 3.5 with two fractures

Following a Court of Appeal judgement, NICE suspended both guidelines and has to review its original decision on strontium ranelate.<sup>30,31</sup> It is also developing guidance for the assessment of fracture risk in individuals at high risk. While NICE guidelines are awaited, assessments such as the web-based WHO Fracture Risk Assessment (FRAX) Tool can be used.<sup>31</sup> The National Osteoporosis Guideline Group (NOGG) recommend FRAX as a method of assessing the 10-year risk of a low-impact fracture in postmenopausal women without previous fragility fractures.

Physicians enter basic data (eg, age and family history) and

a 10-year risk score is given. This score can be integrated into the NOGG guidelines, putting patients in a high, intermediate or low risk group. Based on the patient's risk group, the guidelines then advise whether or not the patient requires lifestyle advice only (low risk), treatment (high risk), or further investigation with a DEXA scan (intermediate risk).

#### **Anticoagulation and falls**

Another way to avoid injury in elderly patients at risk of falls is to avoid potentially harmful medication, such as anticoagulants. Anticoagulants increase the risk of bleeding and, therefore, the idea that anticoagulating an older

person who falls is potentially dangerous seems logical. However, many patients with falls were excluded from clinical trials, meaning that there is little data to support this.

One paper suggested that physicians may overestimate the risk of subdural haemorrhage in people on warfarin for atrial fibrillation (AF) who subsequently fall. It concluded that, although the risk of bleeding is high, it is still outweighed by the decrease in ischaemic stroke risk.<sup>32</sup> It calculated that an AF patient with a 5% annual stroke risk has to fall 295 times in a year for the falls risk to outweigh the stroke reduction benefit. Only when the annual

---

stroke risk was less than 2%, was aspirin preferred to warfarin. However, this paper only calculated the risk of subdural haematomas with falls, neglecting other possible bleeds and used several estimates of prevalence. Therefore, the results need to be viewed with caution.

A recent review of this topic concluded that, although there is an increased bleeding risk, adjusted-dose warfarin should be the preferred antithrombotic in high-risk older people with AF, even if they are at risk of falls, as alternative regimens, such as aspirin and low-dose warfarin, have little, if any, benefit in this group.<sup>33</sup>

Adjusted-dose warfarin increases the risk of intracerebral bleeds and the severity and mortality afterward, but this is outweighed by the reduction in strokes. It also suggests that patient education and regular International Normalised Ratio (INR) monitoring may reduce the bleeding risk.

It is worth noting that the NICE AF guidelines suggest that patients should be assessed for bleeding risk before commencing anticoagulants, but make no mention of falls risk. The guidelines recommend treatment on an individual basis, weighing up the risk factors for stroke against the risks of anticoagulation.<sup>34</sup>

## Conclusion

---

Medication review is an important part of falls management. It provides an opportunity to identify and modify medications that increase the risk of falls and injury as well as identifying and commencing therapy for conditions, such as osteoporosis, which increase the risk of fall-induced injury.

Prescribing for older people, in general, poses many challenges due to multiple co-morbidities and the changes in pharmacodynamics and pharmacokinetics that occur with increasing age.<sup>35</sup> Falls are usually one of several co-morbidities and careful thought needs to be given to the risk–benefit ratio of adjusting treatment in that individual and any treatment changes. However, with the paucity of evidence available, we often do not know the exact magnitude of risk or benefit, from making medication adjustments.

**I have no conflicts of interest to declare**

## References

1. Blake AJ, Morgan K, Bendall MJ, et al. Falls by elderly people at home: prevalence and associated factors. *Age Ageing* 1988;**17**: 365–72

2. Hartikainen Y, Lönnroos E, Louhivuori K. Medication as a risk factor for falls: critical systematic review. *J Gerontol A Biol Sci Med Sci* 2007; **62**: 1172–81
3. Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in older people: A systematic review and meta-analysis: I. Psychotropic drugs. *J Am Geriatr Soc* 1999; **47**:30–39
4. Leipzig RM, Cumming RG, Tinetti ME. Drugs and Falls in Older People: A systematic Review and Meta-analysis: II. Cardiac and analgesic drugs. *J Am Geriatr Soc* 1999; **47**:40–50
5. Department of Health. The National Service Framework for Older People. 2001. <http://tiny.cc/yf4z7> (accessed 25 June 2010)
6. National Institute for Health and Clinical Excellence (NICE). Clinical guideline CG21. The assessment and prevention of falls in older people 2004. <http://tiny.cc/pnffz> (accessed 25 June 2010)
7. Department of Health. Medicines and older people: implementing medicines-related aspects of the NSF for older people 2001. <http://tiny.cc/2a8nk> (accessed 25 June 2010)
8. Milton JC, Jackson SH. Inappropriate polypharmacy: reducing the burden of multiple medication. *Clinical Medicine* 2007; **7**: 514–17
9. Tinetti ME, Baker DI, McAvay G, et al. A multifactorial intervention to reduce the risk of falling among elderly people living in the community. *N Engl J Med* 1994; **331**: 821–27
10. Campbell AJ, Robertson MC, Gardner MM, et al. Psychotropic medication withdrawal and a home-based exercise program to prevent falls: a randomized, controlled trial. *J Am Geriatr Soc* 1999; **47**: 850–53
11. Weber V, White A, McIlvried R. An electronic medical record (EMR)-based intervention to reduce polypharmacy and falls in an ambulatory rural elderly population. *J Gen Int Med* 2008; **23**: 399–04
12. Pit SW, Byles JE, Henry DA, et al. A quality use of medicines program for general practitioners and older people: a cluster randomised controlled trial. *Med J Aust* 2007; **187**: 23–30
13. Ziere G, Dieleman JP, Hofman A, et al. Polypharmacy and falls in the middle age and elderly population. *Br J Clin Pharmacol* 2006; **61**:218–23
14. Lawlor DA, Patel R, Ebrahim S. Associations between falls in elderly women and chronic diseases and drug use: cross sectional study. *BMJ* 2003; **327**: 712–17
15. van der Velde N, Stricker BHCh, Pols HAP, van der Cammen TJM. Risk of falls after withdrawing fall-risk-increasing drugs: a prospective cohort study. *Br J Clin Pharmacol* 2007; **63**: 232–37
16. Rutan GH, Hermanson B, Bild DE et al. Orthostatic hypotension in older adults: The Cardiovascular Health Study. CHS Collaborative Research Group. *Hypertension* 1992. **19**: 508–19
17. Milton JC, Lee TC, Jackson SH. Determinants of a positive response to carotid sinus massage and head-up tilt testing. *Eur J Intern Med* 2009; **20**: 709–11
18. McGavigan AD, Hood S. The influence of sex and age on response to head-up tilt-table testing in patients with recurrent syncope. *Age Ageing* 2001; **30**: 295–298
19. Müller ME, van der Velde N, Krulder JW, van der Cammen TJ. Syncope and falls due to timolol eye drops. *BMJ* 2006; **332**: 960–61
20. Hirani V, Primatesta P. Vitamin D concentrations among people aged 65 years and over living in private households and institutions in England: population survey. *Age Ageing* 2005; **34**: 485–91
21. Dhesi JK, Jackson SHD, Bearne LM, et al. Vitamin D supplementation improves neuromuscular function in older people who fall. *Age and Ageing* 2004; **33**:589–95
22. Bischoff-Ferrari HA, Dawson-Hughes B, Willett WC, et al. Effect of vitamin D on falls: a meta-analysis. *JAMA* 2004; **291**: 1999–06
23. Latham NK, Anderson CS, Reid IR. Effects of vitamin D supplementation on strength, physical performance and falls in older persons: a systematic review. *J Am Geriatr Soc* 2003; **51**: 1219–26
24. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, et al. Falls prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. *BMJ* 2009; **339**: 843–46
25. Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions to prevent falls in older people living in the community. 2009. The Cochrane Collaboration. J Wiley and Sons Ltd.
26. Tang BMP, Eslick GD, Nowson C, et al. Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis. *Lancet* 2007; **370**: 657–66
27. Jackson RD, LaCroix AZ, Gass M, et al. Calcium plus vitamin D supplementation and the risk of fractures. *N Engl J Med* 2006; **354**: 669–83
28. Bolland MJ, Barber PA, Doughty RN, et al. Vascular events in healthy older women receiving calcium supplementation: randomised controlled trial. *BMJ* 2008; **336**: 262–66
29. National Institute for Health and Clinical Excellence (NICE). Technology Appraisal TA160. Alendronate, Etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women 2008. <http://guidance.nice.org.uk/TA160> (accessed 25 June 2010)
30. National Institute for Health and Clinical Excellence (NICE). Technology Appraisal TA161. Alendronate, Etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women 2008. <http://guidance.nice.org.uk/TA161> (accessed 25 June 2010)
31. FRAX—WHO Fracture Risk Assessment Tool (FRAX). <http://www.sheffield.ac.uk/FRAX/> (accessed 25 June 2010)
32. Man-Son-Hing M, Nichol G, Lau A, Laupacis A. Choosing antithrombotic therapy for elderly patients with atrial fibrillation who are at risk of falls. *Arch Intern Med* 1999; **159**: 677–85
33. Garwood CL, Corbett TL. Use of Anticoagulation in Elderly Patients with Atrial Fibrillation Who Are at Risk for Falls. *Ann Pharmacother* 2008; **42**: 523–32
34. National Institute for Health and Clinical Excellence (NICE). Clinical Guideline G36. Atrial Fibrillation: the management of atrial fibrillation 2006. [www.nice.org.uk/CG36](http://www.nice.org.uk/CG36)
35. Milton JC, Hill-Smith I, Jackson SHD. Prescribing for older people. *BMJ* 2008; **336**: 606–09