Osteoporosis in older people

Reducing risk of falls and fractures

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People over 70 years of age have an increased risk of fragility fractures and adverse outcomes and benefit most from treatment; however, they are often poorly assessed and undertreated. Management is multifactorial, and the patient's comorbidities and life expectancy should be considered before initiating therapy and the need for ongoing treatment regularly revisited. Reducing risk of falls and fractures will have a direct impact on a patient's morbidity and mortality.

The increasing prevalence of osteoporosis and its associated effects on morbidity, mortality and health care costs is a growing concern and, with our ageing population, one that is only going to continue to grow. At present 2.2 million Australians have osteoporosis, with affects one in two women and one in three men over the age of 60 years.[1] It is estimated that this will increase to 3 million Australians by 2021.[2] Unfortunately the first presentation of osteoporosis is often a fragility fracture, most commonly of the wrist, hip or spine. Hip fracture is the dominant fracture in patients over 80 years of age. About 75,000 fragility fractures occur annually in Australia, of which 21,000 are hip fractures – the most significant of fragility fractures due to the associated morbidity, mortality and healthcare costs. The average cost of hospitalisation for posthip fracture is $23,000 and the one-year mortality posthip fracture is 20%. [3,4] Of patients with a hip fracture, 50% will experience permanent disability and 25% require permanent nursing home care.[3,4]

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Key points

- **Osteoporosis is a disease associated with significant morbidity, mortality and healthcare costs and its prevalence will rise significantly with our ageing population.**
- **All patients over the age of 70 years should be viewed as high risk and investigated appropriately with validated risk assessment tools and/or bone mineral density scans.**
- **Simple lifestyle changes and falls prevention measures need to be addressed alongside osteoporosis management.**
- **Several pharmacological options have been shown to be effective in reducing future fracture risk in people aged over 70 years and to be well tolerated in this age group.**
- **Reducing fracture risk will have a direct impact on morbidity, mortality and economic costs associated with osteoporosis.**

In women, osteoporosis increases exponentially after menopause. The over 70's represent a patient cohort who have an increased risk of fragility fractures and adverse outcomes and who benefit most from treatment, yet ironically they are poorly represented in clinical trials and are often poorly assessed and undertreated.[1-3] Management options in this age group need to be multifactorial and include pharmacological and nonpharmacological strategies. Available therapies can reduce the risk of recurrent fractures by 30 to 60% within a year of starting treatment.[3] Several pharmacological therapies, including strontium ranelate, bisphosphonates, denosumab and teriparatide, have been found to be effective and well tolerated in this age group.

Postmenopausal versus age-related osteoporosis

Bone mass peaks in the third decade of life, after which there is a progressive decline of approximately 0.5% per year. In addition to this, in women there is rapid bone loss in the years immediately following menopause leading to postmenopausal osteoporosis. This occurs as a result of oestrogen deprivation, which mainly affects trabecular bone resulting in a high risk of vertebral and wrist fractures, and is a predominantly high bone turnover state, secondary to increased osteoclast activity.

In addition, in both men and women there is an age-related bone loss, which tends to affect cortical bone, as well as predisposing to hip fractures. It is associated with several hormonal changes and accumulation of bone marrow fat at the expense of osteoblastogenesis, resulting in decreased osteoblast activity and a low bone turnover state.[5] As a result, hip fracture is the predominant fracture after the seventh decade of life in both men and women. These considerations need to be taken into account when considering treatment options in the older adult because reducing bone remodelling rates without improving bone formation may be inadequate. Hence agents with anabolic effects or weaker antiresorptives (e.g. teriparatide and strontium ranelate, respectively), which do not inhibit formation, may be advantageous.

Importance of assessment and prevention in primary care

Despite its prevalence, poor outcomes, successful treatment options and evidenced-based guidelines, osteoporosis is often under-recognised and poorly managed in the primary care and emergency settings. Even after sustaining a minimal trauma fracture, the number of postmenopausal women receiving specific osteoporosis treatment has been reported to be as low as 20%.[1] Most GPs agree it is their responsibility to assess and manage patients' osteoporosis.[1] However, management remains suboptimal. A collaborative approach between specialist clinics and GPs using a multimodal approach, including use of a specialised fracture liaison nurse, has been shown to be more effective in improving investigation (including bone mineral density [BMD]) and secondary prevention through use of calcium and vitamin D supplementation, specific osteoporosis treatment and patient follow up.[1]

Investigations and risk assessment

A BMD scan is the most widely used investigation for osteoporosis screening and BMD results are often required to access PBS-funded treatments (see Figure and Table 1). In 2007, all people in Australia aged 70 years or older became eligible for a Medicare subsidised BMD scan for osteoporosis screening. Despite this, audits in primary care reveal that only 55% of eligible patients had a BMD scan performed.[2]

BMD scanning may not be a feasible option in all older adults, in which case validated tools such as the Fracture Risk Assessment Tool (FRAX) and Garvan fracture risk calculator may be useful to at least assess absolute risk. These tools provide an assessment of fracture risk, taking into consideration significant risk factors for

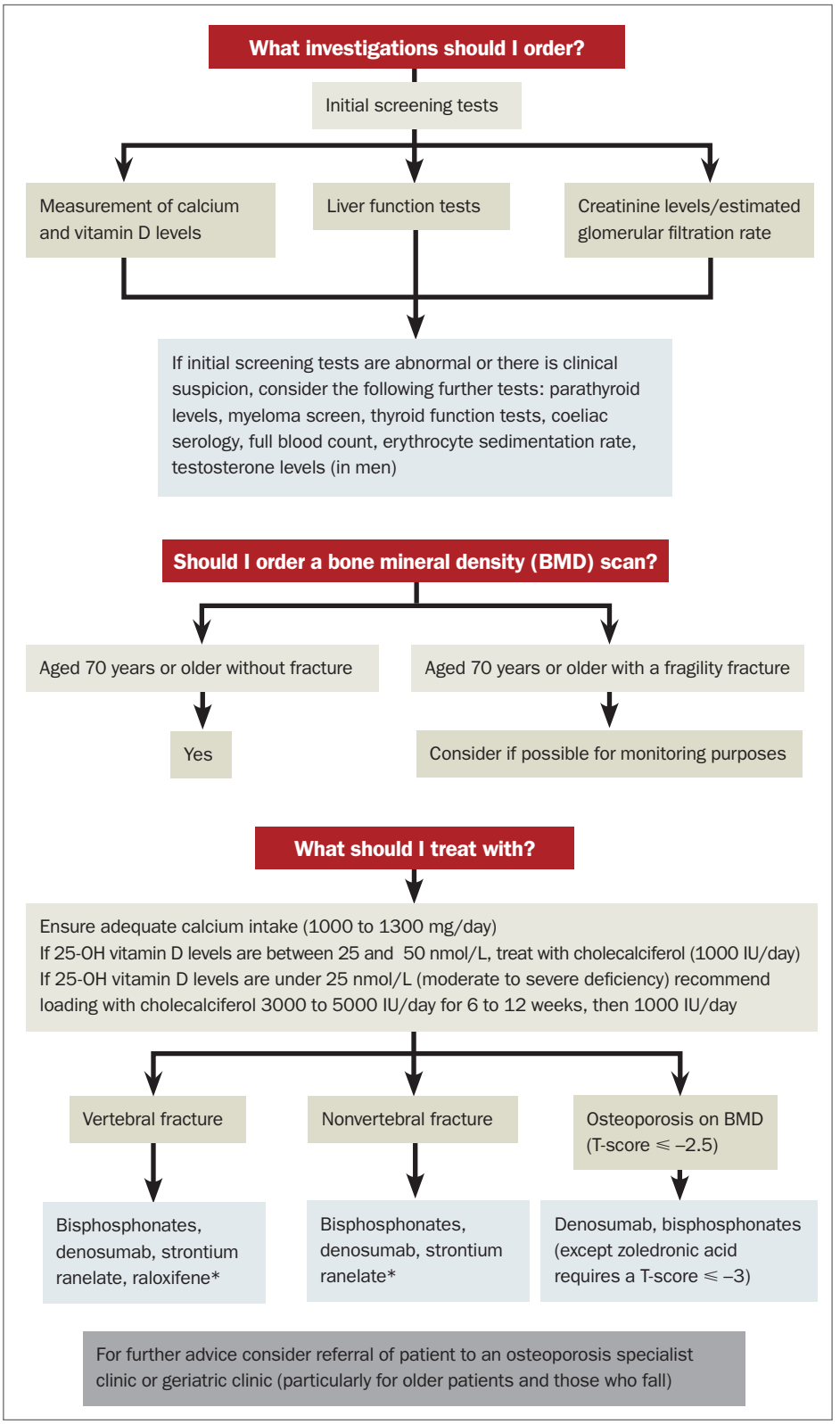

Figure. Guidelines for the management of osteoporosis risk in older people (70 years and older).[3]

* There is only evidence to date for fracture prevention with antiresorptive agents in patients with low bone density on densitometry. PBS-subsidised antiresorptive agents in patients with minimal trauma require radiological demonstration of the fracture. Raloxifene is PBS listed only for postmenopausal women. Bisphosphonates include risedronate, alendronate and zoledronic acid.

bone health, such as age, gender, falls and previous fractures. Unfortunately in Australia, PBS-subsidised osteoporosis treatments cannot be initiated with FRAX or Garvan results alone because the PBS criteria require patients to have a previous minimal trauma fracture and/or a low BMD. In addition to diagnosis, BMD can also be used to monitor response to treatment and is often performed in patients after three to five years of treatment.

All high-risk patients should at least have routine blood tests performed, including creatinine levels/estimated glomerular filtration rate, liver function tests and measurement of vitamin D and calcium levels, to identify reversible or secondary causes of bone loss. Further tests, such as measurement of parathyroid hormone levels, thyroid function tests, erythrocyte sedimentation rate, coeliac serology, myeloma screen and measurement of testosterone levels (in men), should be considered if initial tests are abnormal or there is clinical suspicion (Figure).

Management

Nonpharmacological management

Identifying and informing patients of their risk factors for osteoporosis (see Box) and risk of fracture empowers them to make lifestyle changes and encourages compliance with prevention and treatment strategies for osteoporosis. People over the age of 70 years are recognised as high risk for osteoporotic fracture and hence all patients over the age of 70 years should be encouraged to undertake appropriate lifestyle modifications to reduce their risk of falls and fractures. These include exercise, nutrition (especially intake of calcium- and protein-rich foods), maintaining weight and safely increasing sunlight exposure.

Falls prevention

Approximately 90% of fractures occur after a fall and 5% of falls result in a fracture. Hence, it is imperative that

Table 1. WHO and the International Osteoporosis Foundation DEXA assessment diagnostic categories[3]

Category	Hip bone mineral density
Normal	T-score ⩾ –1
Low bone mass (osteopenia)	T-score between < –1 and > –2.5
Osteoporosis	T-score ⩽ –2.5
Severe osteoporosis (established osteoporosis)	T-score ⩽ –2.5 and presence of at least one fragility fracture

Abbreviations: DEXA = dual energy x-ray absorptiometry; T-score = number of standard deviations below the mean value of the young healthy population.

falls assessment and prevention is coupled with osteoporosis management. In people aged over 65 years, about 30% of those living in the community and 50% living in residential care facilities fall each year. There is a large body of evidence supporting falls prevention with the use of multidisciplinary risk factor assessment, modification of environment, engagement in balance and strengthening exercise program, as well as targeting reversible risk factors, such as ceasing some medications (especially psychotropic and antihypertensive medications) and managing visual impairment. Strength and balance training for community dwelling older adults can reduce the risk of falls by 15 to 50%.[3]

Calcium and vitamin D

Calcium and vitamin D supplementation have demonstrated efficacy in reducing risk of vertebral, nonvertebral and hip fractures in older cohorts (Table 2).[3] Adequate levels of calcium and vitamin D are fundamental in bone homeostasis, for muscle strength and to reduce falls risk, and are often deficient in older populations. An increasing number of Australians are becoming vitamin D deficient as a result of reduced sunlight exposure, decreased oral intake of vitamin D and reduced ability to metabolise vitamin D in the skin.[5] Adequate vitamin D status is essential for active calcium absorption from the gut and normalisation of parathyroid hormone levels. Vitamin D deficiency is also an independent predictor of falls and fragility fractures. Recommended serum levels should be above 50 nmol/L, with an optimal level of over 75 nmol/L in older populations to reduce falls and fracture risk.[8,9] Once a patient is established on treatment and the optimal level is achieved, regular monitoring is not required.

Calcium and vitamin D supplementation in combination is more beneficial in reducing fracture rates than either treatment in isolation.[3] The recommended daily calcium intake is 1000 to 1300 mg, which is equivalent to three serves of calcium-rich foods per day, mainly dairy. If dietary intake is inadequate, supplementation is necessary.

There is ongoing controversy regarding use of calcium supplementation and the modest increased risk of cardiovascular events, including myocardial infarction and stroke as reported in the Women's Health Initiative reanalysis.[10] In the elderly population there is little conclusive evidence to support this and the combination of vitamin D and calcium supplements has even been found to reduce mortality in the elderly by 7%.[11] The priority in older adults should be to optimise intake of calcium (through increasing dairy intake) and vitamin D (through safe sunlight exposure) . However, this is not always achievable for various reasons. In these people, calcium and vitamin D supplementation is recommended and safe, and there is no evidence to suggest increased risk of cardiovascular disease with use of supplements in those who are deficient or insufficient.

Risk factors for osteoporosis fractures[3,6,7]

General population (evidence level 1)

Low bone strength (as assessed by dual x-ray absorptiometry or ultrasound)
Female*
Older age*
Maternal history of fracture
History of previous fractures*
Being tall at age 25 years
Previous hyperthyroidism
Diabetes
Psychotropic medication use
Higher caffeine intake
Postural instability*

Institutionalised older persons (in addition to list above; evidence level III-2)

Hostels

Male*
Low serum vitamin D levels*
Bowel or bladder incontinence*
Cognitive impairment*
Poor balance*
Ambulatory*

Nursing homes

Male*
Low serum vitamin D levels*
Bowel or bladder incontinence*
Cognitive impairment*
Use of anxiolytics*
High serum phosphate levels*

* High hazard ratio in institutionalised older persons versus community-dwelling individuals.

Pharmacological management

Despite the high absolute fracture risk in the older adult population, there is a paucity of evidence-based literature, randomised controlled trials and head-to-head studies with fractures as an outcome in older patients. Few studies include patients over 75 years and, if they do, the numbers are often small and infrequently analysed as subgroups. Most of the evidence is based on pooled analyses.[12]

A review of the published literature on the clinical efficacy and safety of specific osteoporosis treatments in reducing fracture risk in women 75 years of age and older confirms the benefit of treatment (Table 2).[3,13-23] Denosumab and strontium ranelate are the only agents

Table 2. Osteoporosis treatments and evidence of fracture risk reduction efficacy in women aged 75 years and over[3,13-23]

Drug	Route	Fracture risk reduction			Studies with a significant number of women aged 75 years and older
		Vertebral fracture	Nonvertebral fracture	Hip fracture	
Calcium and vitamin D	Variable*	+	+	+	
Alendronate	Oral	+	N/A	N/A	Ensrud et al[13]
Risedronate	Oral	+	=	=	Boonen et al[14], McClung et al[15], Masud et al[16]
Clodronate	Oral	N/A	N/A	–	
Strontium ranelate	Oral	+	+	+	Reginster et al[20], Seeman et al[21]
Raloxifene	Oral	=	–	N/A	
Zoledronic acid	Intravenous	+	+	–	Boonen et al[17], Black et al[18], Lyles et al[19]
Teriparatide	Subcutaneous	+	–	N/A	
Denosumab	Subcutaneous	+	N/A	+	Boonen et al[22], McClung et al[23]

* Oral/intramuscular and variable dosing.
+ Fracture risk reduction demonstrated; – Fracture risk reduction not demonstrated; = Mixed subgroup evidence; N/A = Data not available.

in which randomised controlled trials have been specifically designed and powered to demonstrate a benefit in reduction of the risk of hip fracture in the over 75's cohort.[3,20,22] Risedronate has been demonstrated to be beneficial in a mixed cohort of patients from the age of 70 to 100 years with demonstrated osteoporosis compared with those over 80 years with risk factors only.[14-16] In regards to nonvertebral fracture, there is evidence for fracture risk reduction with use of strontium ranelate[20,21] and zoledronic acid[19] in the 75 years plus cohort, and in the cohort of patients aged 70 to 79 years for risedronate.[14] Unfortunately, there is inadequate conclusive data for most agents in terms of nonvertebral fracture risk reduction.[3,22,23] All currently available agents are effective for vertebral fracture risk reduction.[3,13-23]

Adverse events

Although there is little published data on adverse outcomes in the older patient groups, the available evidence suggests that most treatments, including risedronate, strontium ranelate and denosumab, have similar rates of adverse events, withdrawal due to adverse events or serious deaths compared with younger groups.[3,12,22,23] Recent concerns raised in regard to the risks of cardiovascular disease and venous thrombosis need to be considered before commencing strontium ranelate in all patient groups. In teriparatide subgroup analysis, higher rates of diarrhoea were reported in the over 75's.[12]

Patient specific considerations

Older patients are at higher risk of recurrent fracture than younger cohorts and have a greater risk of morbidity, mortality and disability. The imperative to treat, comply and persist is greater in older adults because osteoporosis is a chronic condition and its risk increases with age, frailty, falls risk, medical comorbidities and polypharmacy.

As with any prescribing in older adults, individual patient considerations, such as risk/benefit, frequency of dosing and administration route, should be tailored appropriately to improve tolerability and adherence (compliance and persistence).[24] Patients generally prefer the convenience of less frequent dosing if it is deemed to be of equal efficacy to alternative regimens. The multitude of oral formulations, options for dosing frequency (daily, weekly and monthly) and availability of parenteral options (subcutaneous six monthly or annual intravenous) has made treatment choices easier to tailor to specific patient profiles (Table 3). Parenteral treatment may be preferable for patients who have gastrointestinal intolerance or prefer less frequent dosing and provide 'absolute' compliance for six to 12 months. New oral formulations that do not require fasting offer more options for people who are unable to fast for medical or other reasons. Patients with cognitive impairment require special consideration; agents that do not require fasting and have less frequent dosing (to reduce burden of care) or parenteral options may be preferable to ensure compliance.

As with most medications, special precautions are required in older people who have comorbidities, especially renal impairment and dental problems. It is particularly important to consider the patient's comorbidities and life expectancy before initiating therapy and to regularly revisit the need for ongoing treatment as a patient progresses. Treatment benefits versus risks needs regular and closer monitoring in older people compared with younger cohorts because older people decline more rapidly in terms of their comorbidities, medication use, and physical, functional, cognitive and life expectancy status. It is as important to decide when to stop therapy as it is to initiate therapy in older adults. This decision should be based on medical comorbidities, drug interactions,

Table 3. Dosing for the available forms of osteoporosis treatments

Drug	Oral dosing			Intravenous (annual)	Subcutaneous	Special formulations
	Daily	Weekly	Monthly			
Alendronate	5 and 10 mg*	35 and 70 mg*				
Denosumab					60 mg (six monthly)	
Raloxifene	60 mg					
Risedronate	5 mg*	35 mg*	150 mg*			35 mg weekly EC formulation (does not require fasting)
Strontium ranelate	2 g*					
Teriparatide					20 µg (daily)†	
Zoledronic acid				5 mg		

* Empty stomach and fasting required (see product information for more details); † Lifetime duration of treatment less than or equal to 18 months.

drug toxicity concerns, and the risk of atypical fractures after prolonged bisphosphonate use.

Conclusion

Osteoporosis is a major public health issue and its prevalence will continue to increase as the population ages. The older the patient is, the greater the risk of falls and osteoporosis. Both pharmacological and nonpharmacological treatments have roles to play in the management of osteoporosis and all patients, including the old-old and those in residential care facilities, should be assessed and treated according to risk. Despite the paucity of evidence, the evidence we do have show several drugs can be used effectively and safely to reduce the risk of osteoporosis in older adults. Managing falls risk simultaneously is paramount in older people. Reducing the risks of falls related to injury including fracture will have a direct impact on morbidity, mortality and economic costs associated with this disease. **ET**

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