

Osteoporosis in older people

Managing the risks

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Osteoporosis increases with age and people aged over 70 years are at high risk of nonvertebral and hip fractures. Management should be multifactorial and needs to consider the triad of osteoporosis, falls risk and the impact of a fall in older people. Pharmacological treatment can aid with increasing bone density, but adherence is key.

The skeletal system is metabolically active. Over a person's lifetime, the skeleton is continually being repaired and remodelled in response to multifaceted stresses. Osseous tissue is replaced annually at a rate of about 10 to 20%, varying by site and type. Bone remodelling is an active and highly regulated process that includes resorption (osteoclasts) and formation (osteoblasts).¹

Osteoporosis occurs when bone resorption overwhelms the bone formation capacity of the skeleton. This imbalance in bone turnover results in reduced bone density and microarchitectural deterioration of bone tissue, which leads to increased fragility and greater risk of fracture.^{2,3} The incidence of osteoporotic fracture increases with age, and one in three women and one in five men over the age of 50 years are affected.

Epidemiology of postmenopausal and age-related osteoporosis

Osteoporosis is not a homogeneous disease (Figure). Postmenopausal (type I) osteoporosis tends to present differently from age-related or 'senile' (type II) osteoporosis.⁴ Postmenopausal osteoporosis is driven mainly by increased remodelling, with predominant bone resorption resulting in trabecular bone loss. In contrast, there is reduced remodelling in age-related osteoporosis, with bone formation disproportionately suppressed, resulting in predominantly cortical bone loss in both men and women.⁴ Based on this difference in pathogenesis, younger (50 to 75 years) postmenopausal women (with an increased rate of bone resorption) mainly experience vertebral fractures, whereas older patients (with a reduction in bone formation) have significantly higher rates

of nonvertebral and hip fractures.⁵

The prevalence of type II osteoporosis, which tends to occur in people aged over 75 years, is increasing because of longer life expectancy and an ageing population.⁶ In 2010, the number of people over 50 years of age who were considered to be at high risk of fragility fractures worldwide was 158 million, and this figure is set to double by 2040.⁷ Of the 75,000 fragility fractures that occur each year in Australia, about one-third are hip fractures. The annual incidence of fragility fractures increases with age.⁸ One-third of women and one-sixth of men will sustain a hip fracture by their ninth decade, and the rate of hip fracture doubles every five years after the age of 65 years.^{5,6,9,10} Osteoporosis is undertreated after all types of fragility fractures.

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Risk factors for osteoporotic fracture

The main risk factors for fracture in older people are the triad of osteoporosis, falls risk and the impact from a fall. About 30% of older people living in the community and 50% of those in residential aged care fall each year, with an associated high risk of injury, including osteoporotic fracture.^{11,12} Hip fracture is the most common fracture in the very old. Residents of aged-care facilities and older hospitalised people are the frailest population and at highest risk of falls and fractures. They are also the most challenging to manage, as falls and fracture risks in this group are usually multifactorial, and the potential to reverse these risks is often limited. The risk factors for falls and fractures are summarised in Box 1.

Diagnosis and assessment of fracture risk

The gold standard for diagnosis of osteoporosis remains areal bone mineral density (BMD), measured by dual-energy x-ray absorptiometry (DXA).¹³ The WHO international reference standard for osteoporosis diagnosis is a T-score of -2.5 or lower at the femoral neck (Table 1). However, more than half of all minimal trauma fractures or subsequent fractures occur in people with a BMD T-score in the normal to osteopenic range. Hence, in the absence of a BMD measurement, the diagnosis of osteoporosis can be made on the basis of a fragility fracture. As most vertebral fractures are asymptomatic and diagnosed incidentally on spinal x-rays, a spinal x-ray may be a useful additional tool to identify fragility fractures.³

KEY POINTS

- Older people are at highest risk of minimal trauma fracture, requiring a multifactorial and multidisciplinary approach to fracture reduction.
- Bone mineral density testing is essential to screen for osteoporosis in this population.
- It is essential to address the triad of osteoporosis, falls risk and the impact of falls in older people.
- Safe mobility and exercise with appropriate supervision should be encouraged, and nutrition, calcium intake and vitamin D levels optimised.
- Osteoporosis medications can be chosen based on patient preferences to optimise adherence.
- Use of hip protectors should be encouraged, as the risk of falls-associated hip fracture cannot be abolished in most older people.

For patients with ready access to bone densitometry, a DXA BMD measurement is recommended before starting therapy to enable monitoring of treatment, adherence and efficacy, even in cases of typical minimal trauma fracture (Flowchart). For patients in whom DXA BMD measurement is unreliable because of osteoarthritis, quantitative CT BMD measurement could provide more reliable information on the presence of hip or spine osteoporosis.

Absolute fracture risk is the most important determinant of an individual's risk of fracture and is based on multiple factors.³ If there is uncertainty about patients with a prior fracture or osteopenia on BMD measurement, absolute fracture risk assessment may be useful for risk stratification and treatment decisions. The two calculators often used in Australia are the Garvan Fracture Risk Calculator (www.garvan.org.au/bone-fracture-risk) and the Fracture Risk Assessment Tool (FRAX; www.shef.ac.uk/FRAX).¹³⁻¹⁷

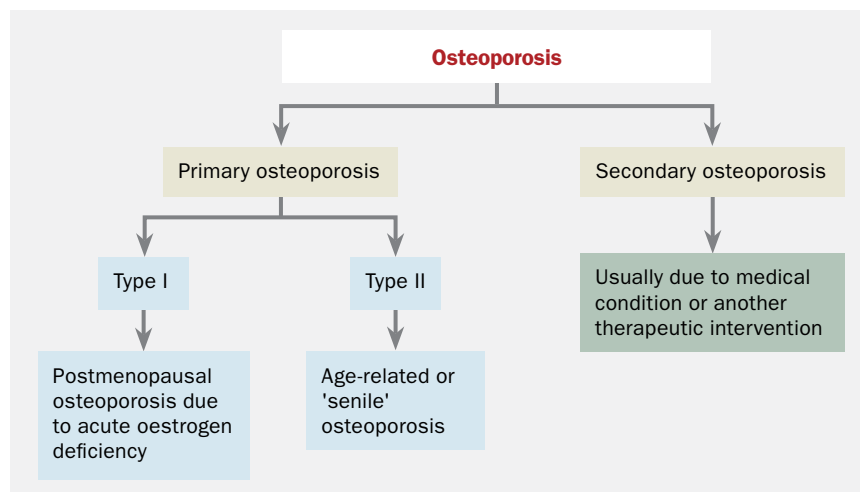


Figure. Simple classification of osteoporosis.

The Garvan calculator has an advantage over the FRAX in older populations as it includes people aged up to 96 years and stratifies risk based on the number of fractures and the number of falls. According to the US National Osteoporosis Foundation guidelines, an absolute risk of hip fracture greater than 3% and of any major fracture greater than 20% over 10 years is the threshold for intervention.^{3,18}

Increased biochemical markers of bone turnover in the blood or urine have been shown in trials to be an independent risk factor for fractures in women and men. Although their use is controversial, bone turnover markers may have a role in assessing adherence and response to treatment and in helping guide choice of treatment.^{3,19}

Nonpharmacological management of osteoporosis

Falls risk assessment and management

Community-dwelling older people

For community-dwelling older people, it is not sufficient to initiate pharmacological treatment of osteoporosis. Falls assessment and prevention are integral parts of the management of osteoporosis in older patients.²⁰ There is evidence that group and home-based exercise programs and home safety interventions reduce both the rate of falls and the risk of falling in this group.¹¹ Multifactorial assessment and intervention programs appear to be effective in reducing the rate of falls, but not the risk of falling. Tai chi reduces the risk of falling. Overall, vitamin D supplementation does not appear to reduce falls in older people living in the

1. RISK FACTORS FOR FALLS AND FRACTURES

- History of minimal trauma fracture
- Height loss of 3 cm or more and/or back pain suggestive of vertebral fracture
- Female
- Older than 70 years
- History of falls
- Parental history of hip fracture
- Premature menopause or hypogonadism
- Prolonged use of glucocorticoids (at least three months' cumulative prednisone or equivalent 7.5 mg or more daily)
- Use of other medications that cause bone loss or increase falls risk
- Medical conditions or diseases that lead to bone loss or falls risk
- Low body weight
- Low muscle mass and strength (sarcopenia)
- Low physical activity or prolonged immobility
- Poor balance
- Smoking
- High alcohol intake
- Energy, protein or calcium undernutrition
- Vitamin D insufficiency

community, but it may reduce them in those who have low vitamin D levels before treatment is initiated.¹¹ A recent Cochrane review concluded that exercise programs primarily involving balance and functional exercises, or multiple exercise programs including these two categories, reduce the rate of falls in older people living in the community (high-certainty evidence).²¹

Older people in aged care or hospital

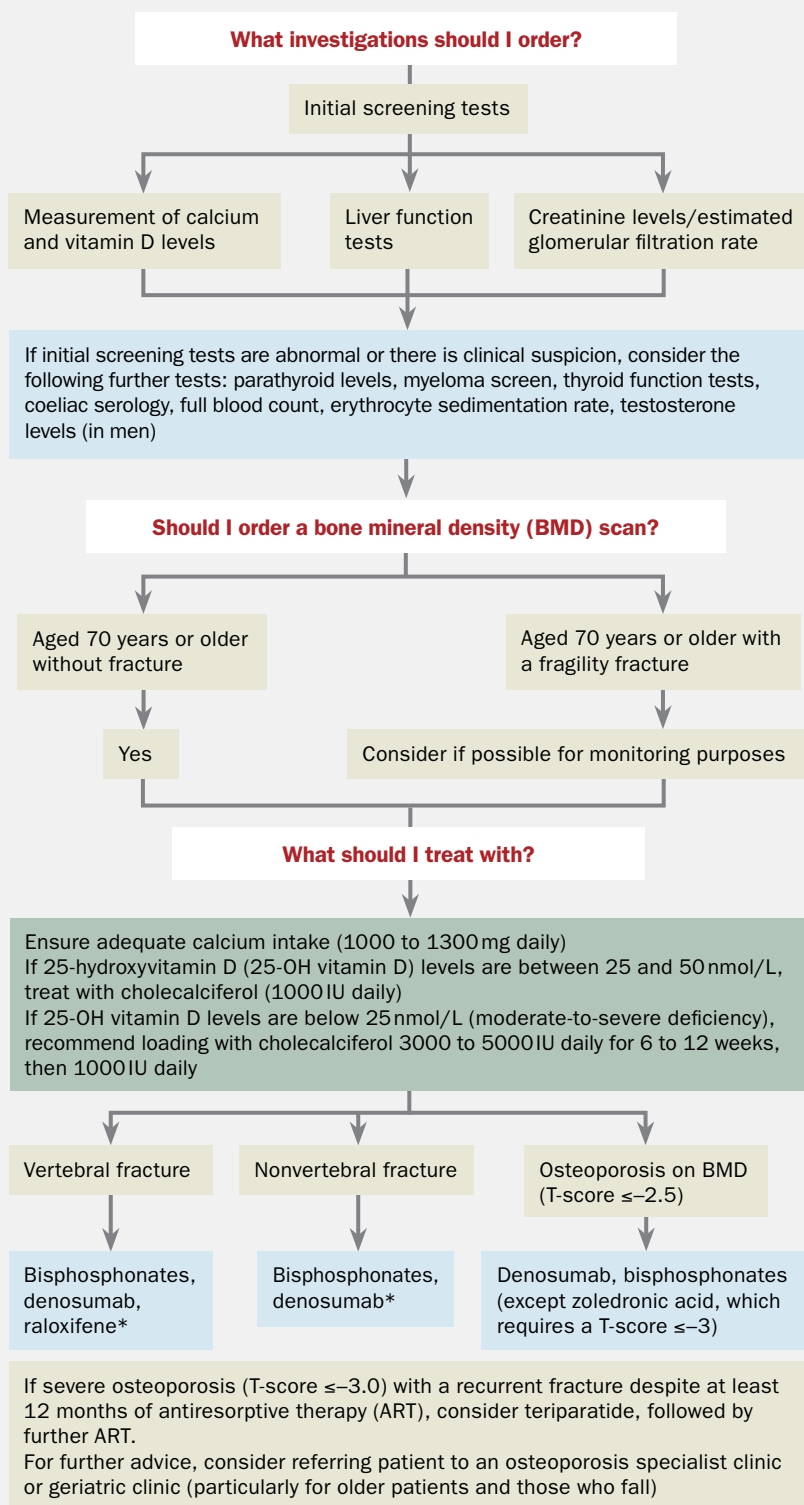
A Cochrane review of studies of older people in aged-care facilities or hospitals found that vitamin D supplementation is probably effective in reducing the rate of falls.¹² Evidence for multifactorial interventions in aged-care facilities suggests possible benefits but is inconclusive.

TABLE 1. BONE MINERAL DENSITY ASSESSMENT*

Category	Hip bone mineral density
Normal	T-score of -1 or higher
Low bone mass (osteopenia)	T-score between -1 and -2.5
Osteoporosis	T-score of -2.5 or lower
Severe osteoporosis (established osteoporosis)	T-score of -2.5 or lower and presence of at least one fragility fracture

* Based on the WHO and International Osteoporosis Foundation dual-energy x-ray absorptiometry assessment diagnostic categories. T-score is the number of standard deviations below the mean value of the young healthy population.

MANAGEMENT ALGORITHM FOR OSTEOPOROSIS RISK IN OLDER PEOPLE



* 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.

Exercise

The types of exercise that are best for bone strength are:

- weight-bearing exercise (e.g. brisk walking, jogging, skipping, basketball/netball, tennis, dancing, impact aerobics or stairs walking)
- progressive resistance training (e.g. lifting weights, ankle weights or gym equipment).²²

Regular (two to three days per week) resistance training and balance training exercises that are moderate to vigorous, progressive (incremental over time) and varied have been shown to improve BMD and reduce falls and fracture risk. The strongest evidence for benefit is for people with mild to moderately impaired mobility. The frailest populations (e.g. highly dependent people in care institutions) have limited potential for benefit and may be at higher risk of falls and fractures from exercise programs if left unsupervised. This increase in risk may be caused by an overestimation of their ability after exercise or a lag in improvement in balance despite an improvement in strength.^{23,24}

Hip protectors

Hip protectors, which protect against hip fractures by directing the force from a fall away from the hip, have been proven to be of benefit in a select group of older people in nursing or residential aged care but not in those living in the community.²⁵⁻²⁷ They are only effective with good adherence, which is difficult to achieve, but their use should nevertheless be encouraged if appropriate.

Pharmacological management of osteoporosis

Calcium and vitamin D supplementation

Lifestyle factors and frailty mean older people are at higher risk of calcium and vitamin D deficiency, in addition to being at higher risk of osteoporosis and fracture. There is a high prevalence of vitamin D insufficiency and deficiency in institutionalised and housebound older people, and

vitamin D supplementation is considered standard care in these groups.²⁸ Calcium levels are often suboptimal because of limitations in dietary intake, along with low vitamin D levels from limited sunlight exposure resulting in reduced calcium absorption.

It is especially important to resolve calcium and vitamin D deficiencies in patients with chronic kidney disease and those receiving antiresorptive therapy (ART), as they are at higher risk of hypocalcaemia and secondary hyperparathyroidism. Dietary calcium intake and serum 25-hydroxyvitamin D level should be checked before initiating osteoporosis therapy, with appropriate supplementation to be recommended if either is inadequate (Flowchart).²⁹ However, caution is warranted when considering supplementation and dosage because of the reported increased risk of complications, including gastrointestinal and cardiovascular events, renal (stones) and falls.³⁰⁻³⁵

Bone-specific treatments

In Australia, a range of medicines to treat osteoporosis are subsidised by the government on the PBS.^{6,20,36-38} It is important that these medications are taken as directed to ensure the greatest benefit.^{6,39,40} Osteoporosis medicines can increase bone density and, although the increase may appear small, it can have a positive effect on reducing fracture rate. Medication can increase bone density in the hip by about 1 to 3% and in the spine by 4 to 8% over the first three to four years, but reduce spinal fractures by 50 to 70% and hip fractures by 30 to 50% (a positive effect can be seen as early as six to 12 months after starting treatment).⁴⁰

Osteoporosis medicines are grouped into different classes depending on their active ingredient. The ARTs – bisphosphonates, monoclonal antibodies such as denosumab, selective oestrogen receptor modulators and oestrogens – reduce bone breakdown (loss).

Bisphosphonates (alendronate, risedronate and zoledronic acid) are

TABLE 2. DOSING FOR THE AVAILABLE FORMS OF OSTEOPOROSIS TREATMENT

Drug	Oral			Intravenous	Subcutaneous
	Daily	Weekly	Monthly		
Alendronate	5 and 10 mg*	35 and 70 mg*	–	–	–
Risedronate	5 mg*	35 mg* or 35 mg enteric-coated tablets†	150 mg*	–	–
Zoledronic acid	–	–	–	5 mg annually†	–
Denosumab	–	–	–	–	60 mg six monthly†
Raloxifene	60 mg†	–	–	–	–
Teriparatide	–	–	–	–	20 mcg daily†

* Empty stomach and fasting required (see product information for more details).

† Fasting not required. ‡ Use for more than 24 months' lifetime duration is not recommended.

administered orally on a daily, weekly or monthly basis or as an annual infusion (Table 2). Adherence to fasting or other requirements of some of these oral agents is essential to maximise benefit, as they are otherwise poorly absorbed. Enteric-coated risedronate tablets (oral weekly) and intravenous zoledronic acid do not require fasting.

Denosumab (six-monthly subcutaneous injection; Table 2) works differently from bisphosphonates but has the same effect of slowing the rate at which bone is broken down, with similar reductions in the risk of fractures.^{6,36-38,41} Adherence to timing and frequency of denosumab is essential. It is risky to miss doses or stop treatment abruptly as the benefit is quickly lost and may increase the risk of spinal fracture in some patients.

Raloxifene, a selective oestrogen receptor modulator, is only available on the PBS for postmenopausal women with a minimal trauma fracture. It acts on bone in a similar way to that of the hormone oestrogen, slowing bone loss and reducing the risk of spinal fractures in women who have been through menopause. It has been shown to be effective in reducing vertebral fractures but not nonvertebral

fractures in osteoporotic postmenopausal women.⁴²

Menopausal hormone therapy (MHT) helps to slow bone loss and reduce the risk of osteoporosis and fractures in women who have gone through menopause. The active ingredient is oestrogen. For women with an intact uterus, combinations also contain progesterone (combined MHT). MHT is safe and effective for most women under the age of 60 years who have osteoporosis and also need relief of menopause symptoms. It is not usually recommended to commence MHT in older women (those older than 60 years or more than 10 years after menopause), in whom caution is needed regarding the risk of heart disease, stroke and breast cancer and for whom other treatments may be considered.

Teriparatide is a self-administered daily injection for up to 24 months. In contrast to the ARTs, it is the only medicine available in Australia that stimulates bone formation, resulting in improved bone strength and structure. It is only available for people with severe osteoporosis (recurrent minimal trauma fracture despite at least 12 months of ART, and a BMD T-score of –3.0 or lower) when other

TABLE 3. OSTEOPOROSIS TREATMENTS AND EVIDENCE OF FRACTURE RISK REDUCTION EFFICACY IN WOMEN AGED 75 YEARS OR OLDER^{6,20,36,37}

Drug	Route, frequency	Fracture risk reduction			Studies*
		Vertebral fracture	Nonvertebral fracture	Hip fracture	
Calcium and vitamin D	Oral/intramuscular, variable dosing	+	+	+	
Alendronate	Oral, weekly	+	N/A	N/A	+
Risedronate	Oral, weekly	+	=	=	+
Zoledronic acid	Intravenous, yearly	+	+	–	+
Denosumab	Subcutaneous, six monthly	+	N/A	+	+
Teriparatide	Subcutaneous, daily	+	–	N/A	
Strontium ranelate [†]	Oral, daily	+	+	+	+

* Studies with a significant number of women aged 75 years or older.

[†] No longer available on the PBS due to concerns about side effects.

+ Fracture risk reduction demonstrated; – Fracture risk reduction not demonstrated; = Mixed subgroup evidence; N/A = Data not available.

osteoporosis medicines have not worked and the risk of further fractures is still very high. It can be taken for a maximum of 24 months in Australia but is only subsidised for 18 months on the PBS. Once the treatment is completed, another osteoporosis medication must be started to ensure that the new bone gained is maintained and improved. Otherwise, the benefit is lost within 12 to 24 months.

Despite the high absolute fracture risk in older adults, there is a paucity of evidence-based literature, randomised controlled trials and head-to-head studies of osteoporosis treatments that examine fractures in older patients as an outcome. Few studies include patients aged over 70 years; in those that do, the numbers are often small and infrequently analysed as a subgroup. Most of the evidence is based on pooled analyses. However, a review of the published literature on the clinical efficacy and safety of specific osteoporosis treatments in reducing fracture risk in women aged 75 years or older confirms the benefit of treatment (Table 3).^{6,20,36,37}

Denosumab and strontium ranelate (which is no longer available on the PBS due to concerns about side effects) are

the only agents for which randomised controlled trials have been specifically designed and powered to show a reduction in the risk of hip fracture in people aged over 75 years. Risedronate has been shown in a post hoc analysis to be beneficial in a mixed cohort of patients aged between 70 and 100 years (mean age, 77 ± 5 years) with severe osteoporosis, compared with those aged over 80 years with risk factors only.⁴³

For nonvertebral fracture, there is evidence of fracture risk reduction in people aged 75 years or older with the use of strontium ranelate and zoledronic acid, and in patients aged 70 to 79 years for risedronate.^{6,20,36,44-48} There are inadequate conclusive data for most agents in terms of nonvertebral fracture risk reduction, but all available agents are effective for reducing vertebral fracture risk.

Notwithstanding the limitations of these data, all agents have shown benefit in unselected populations and (other than strontium ranelate) are approved on the PBS for use in older patients. The choice of treatment is based on patient factors, including preference and adherence. Furthermore, as noted above, patients with

TABLE 4. EFFICACY OF LONG-TERM OSTEOPOROSIS THERAPY*

Study	Medication	Treatment duration (years)	Number of participants	% change in lumbar spine BMD	% change in total hip BMD	Fracture rates
FLEX ⁴⁹	Alendronate	10	86	13.7%	6.7%	Remained low
HORIZON ⁵⁰	Zoledronic acid	9	95	Not reported	4.3%	Remained low
FREEDOM ⁵¹	Denosumab	10	2626	21.7%	9.2%	Remained low
VERT-MN ⁵²	Risedronate	7	83	11.5%	3.9%	Remained low

Abbreviations: BMD = bone mineral density; FLEX = Fracture Intervention Trial Long-term Extension; FREEDOM = Fracture Reduction Evaluation of Denosumab in Osteoporosis Every Six Months; HORIZON = Health Outcomes and Reduced Incidence with Zoledronic Acid Once Yearly; VERT-MN = Vertebral Efficacy with Risedronate Therapy – Multinational.

* These data are from original publications and are not head-to-head comparisons.

severe osteoporosis and recurrent fracture despite ART can access anabolic treatment with teriparatide on the PBS.

Monitoring and long-term therapy

There is relatively little evidence on monitoring and long-term therapy, and decisions may need to be based on clinical judgement and expert advice. Similar to diabetes and hypertension, osteoporosis is a chronic condition without an imminent cure and requires long-term therapy. The RACGP and Osteoporosis Australia guidelines provide useful advice in this regard.³ As a general rule, patients should continue treatment for as long as they remain at risk or cessation would result in a loss of benefit. There is evidence of benefit up to 10 years, with the rate and severity of treatment side effects remaining low, and there is no suggestion of significant adverse effects (Table 4).^{49–52} Direct treatment comparisons are not possible, as studies have used different patient selection criteria and different study designs and there are no head-to-head comparison studies.

Bisphosphonate treatment is generally reviewed after three to five years, and the decision to interrupt or continue treatment is based on risk. It is recommended that BMD measurement is repeated after three to five years, to monitor treatment, response and need. Treatment is reviewed if fracture risk reduces to low-risk thresholds (e.g. total hip BMD T-score of -2.5 or higher). In this situation, bisphosphonates may be interrupted, with close monitoring

and review every 12 to 24 months (time for the effect of treatment to wear off), and treatment should be reinitiated if required.

With reversible agents, especially denosumab, cessation results in a rapid reduction in BMD and an increase in risk to pretreatment levels. Hence, greater caution is recommended, and treatment should be either continued (if safe to do so) or transitioned to a less readily reversible agent (e.g. bisphosphonates for a period before cessation to blunt the rapid loss of bone).

There is relatively little evidence on monitoring and long-term therapy, and decisions may need to be based on clinical judgement and expert advice

Long-term and serious complications of treatment

The main concern with potent ART is the risk of hypocalcaemia. This risk can be minimised by optimising calcium and vitamin D status. Extra caution is required in those with renal impairment (estimated glomerular filtration rate less than 30 mL/min), and treatment with ART should be used with caution or avoided in these people, depending on the severity of renal impairment (specialist advice is recommended).

Potential serious long-term complications of bisphosphonate and denosumab treatment are atypical femoral fracture (AFF) and osteonecrosis of the jaw (ONJ).³⁷ Both are extremely uncommon in people receiving osteoporosis treatment, and the benefit of treatment in terms of fracture morbidity and mortality outweighs the risk. However, the risk increases with duration of ART, and patients should be monitored and managed on an individual risk-benefit basis. To put this risk into perspective, the rate of major osteoporotic fracture in women at high risk is 3100 per 100,000 person-years, and bisphosphonates reduce fractures by 20 to 70%.³⁷ The rate of AFF attributed to long-term bisphosphonate therapy at eight years is 78 per 100,000 person-years. Many more osteoporotic fractures would be prevented for each AFF caused by ART.³⁷

The overall risk of ONJ in patients receiving bisphosphonates remains low (between one in 10,000 and less than one in 100,000 patient treatment-years).⁵³ The incidence is higher in patients with cancer, who are often treated with high-dose bisphosphonates.⁵³ Although there have been reports of an increase in incidence of oesophageal cancer in patients taking bisphosphonates, further studies are required.⁵⁴ However, it is recommended that clinicians should avoid prescribing oral bisphosphonates to people with existing oesophageal disease (e.g. achalasia, Barrett's oesophagus).⁵⁴

2. USEFUL RESOURCES FOR GPs AND PATIENTS

- **Osteoporosis Australia**
toll-free consumer helpline on 1800 242 141 and www.osteoporosis.org.au
(provides a range of publications for GPs and other healthcare professionals, as well as consumer-friendly information for patients)
- **'Know your bones'**
www.knowyourbones.org.au
(a consumer-friendly bone health assessment tool based on the Garvan Fracture Risk Calculator)
- **National Osteoporosis Foundation (US)**
www.nof.org
- **Royal Osteoporosis Society (UK)**
www.theros.org.uk
- **International Osteoporosis Foundation**
www.iofbonehealth.org
- **Royal Australian College of General Practitioners**
www.racgp.org.au
- **Australian Rheumatology Association**
www.rheumatology.org.au
- **Therapeutic guidelines**
www.tg.org.au
- **NPS MedicineWise**
www.nps.org.au
- **Carers Australia**
www.carersaustralia.com.au
- **Australian Medicines Handbook**
<https://shop.amh.net.au>

The American Dental Association recommends that a patient with active dental or periodontal disease should be treated despite the risk of ART-induced ONJ, because the risks and consequences of no treatment likely outweigh the risk of developing ONJ.⁵⁵ It is important to inform patients taking ART that there is a risk (albeit low, at less than 0.1%) of ONJ before they undergo dental care. Risk can be minimised with good hygiene practices and regular dental care. Discontinuing therapy may not eliminate ONJ risk but may increase fracture risk.

Long-term (more than five years) bisphosphonate use may be associated with higher risk of AFF (100 per 100,000 person-years), but there are few data in this area. Although the relative risk of AFF with bisphosphonate therapy appears, on this evidence, to be high, the absolute risk remains very low, ranging from 3.2 to 50 cases per 100,000 person-years.⁵⁶ The risk of AFF has been shown to significantly decrease after cessation of bisphosphonates, irrespective of the duration of treatment.⁵⁷ It is not known if the same is true of ONJ. The European Menopause and Andropause Society suggests that all bisphosphonates should be discontinued after five years. If there is no evidence of high risk (BMD T-score less than -2.5 or fragility fracture on treatment), a drug holiday is recommended for one to two years.⁵⁸ Fracture risk increases after two years off therapy, so patients should be closely monitored during this time. If fractures occur or BMD decreases (T-score of -2.5 or less), ART should be recommenced.

Case reports and an observational trial have suggested that BMD declines rapidly and vertebral fracture risk increases after discontinuation of long-term denosumab.⁵⁹⁻⁶¹ Oral alendronate for 12 months after denosumab prevents bone loss in the majority of patients.⁶² However, the protective effect of prolonged exposure to bisphosphonates before denosumab initiation against vertebral fractures after denosumab discontinuation has not been confirmed. Data from small studies have suggested this, but further studies are required.⁶³

Conclusion

Osteoporosis is undertreated after all fragility fractures, including hip fracture. Hip fractures are a common osteoporotic fracture in older people; they usually require surgical intervention and can have serious consequences. Osteoporosis is a chronic condition that requires timely and ongoing treatment. ART is the current mainstay, and choice of

medication depends on patient factors and adherence. Adherence to oral bisphosphonates is often poor because of specific oral dosing requirements, and enteric-coated risedronate, which does not have these requirements, may be the preferred option if oral therapy is chosen. Parenteral treatment can reduce adherence concerns, as long as patients are followed up regularly for dosing, and it can also reduce polypharmacy. Anabolic therapies, such as teriparatide, add value to treatment but must be followed by ART to consolidate and maintain their benefit. Adherence is important to maintain benefit, and cessation or interruption of therapy eventually results in loss of benefit and increased fracture risk. Long-term therapy appears to be safe, with a very low risk of serious adverse effects. Useful resources for GPs and patients are listed in Box 2. MT

References

A list of references is included in the online version of this article (www.medicinetoday.com.au).

COMPETING INTERESTS: None.

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References

- Vega D, Maalouf N, Sakhaee K. The role of receptor activator of nuclear factor-kappaB (RANK)/RANK ligand/osteoprotegerin: clinical implications. *J Clin Endocrinol Metab* 2007; 92: 4514-4521.
- Wheater G, Elshahaly M, Tuck SP, Datta HK, van Laar JM. The clinical utility of bone marker measurements in osteoporosis. *J Transl Med* 2013; 11: 201.
- Royal Australian College of General Practitioners (RACGP) and Osteoporosis Australia. Osteoporosis prevention, diagnosis and management in postmenopausal women and men over 50 years of age. 2nd ed. Melbourne: RACGP; 2017. Available online at: www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines/osteoporosis (accessed July 2019).
- Riggs BL, Melton LJ 3rd. Evidence for two distinct syndromes of involutional osteoporosis. *Am J Med* 1983; 75: 899-901.
- Inderjeeth C, Nair P, Chan K, Raymond W, Lim EEM. Bone turnover markers in old vs early postmenopausal women. *MOJ Gerontol Ger* 2019; 4: 22-26.
- Inderjeeth CA, Foo AC, Lai MM, Glendenning P. Efficacy and safety of pharmacological agents in managing osteoporosis in the old old: review of the evidence. *Bone* 2009; 44: 744-751.
- Odén A, McCloskey EV, Kanis JA, Harvey NC, Johansson H. Burden of high fracture probability worldwide: secular increases 2010–2040. *Osteoporos Int* 2015; 26: 2243-2248.
- European Prospective Osteoporosis Study Group. Incidence of vertebral fracture in Europe: results from the European Prospective Osteoporosis Study (EPOS). *J Bone Miner Res* 2002; 17: 716-724.
- Gullberg B, Johnell O, Kanis JA. World-wide projections for hip fracture. *Osteoporos Int* 1997; 7: 407-413.
- Access Economics. A future less fragile. Sydney: Access Economics; 2010.
- Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2012; (12): CD007146.
- Cameron ID, Gillespie LD, Robertson M, et al. Interventions for preventing falls in older people in care facilities and hospitals. *Cochrane Database Syst Rev* 2018; (9): CD005465.
- Nguyen TV, Center JR, Eisman JA. Osteoporosis: underrated, underdiagnosed and undertreated. *Med J Aust* 2004; 180 (5 Suppl): S18-S22.
- Nguyen ND, Frost SA, Center JR, Eisman JA, Nguyen TV. Development of prognostic nomograms for individualizing 5-year and 10-year fracture risks. *Osteoporos Int* 2008; 19: 1431-1444.
- Nguyen ND, Frost SA, Center JR, Eisman JA, Nguyen TV. Development of a nomogram for individualizing hip fracture risk in men and women. *Osteoporos Int* 2007; 18: 1109-1117.
- Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E. FRAX and the assessment of fracture probability in men and women from the UK. *Osteoporos Int* 2008; 19: 385-397.
- Kanis JA, Oden A, Johnell O, et al. The use of clinical risk factors enhances the performance of BMD in the prediction of hip and osteoporotic fractures in men and women. *Osteoporos Int* 2007; 18: 1033-1046.
- Inderjeeth CA, Raymond WD. Case finding for the primary prevention of fragility fractures with FRAX (without BMD) in those over 70 years: reducing the reliance on BMD as the primary tool. *Int J Clin Rheumatol* 2018; 13: 20-27.
- Vasikaran S, Cooper C, Eastell R, et al. International Osteoporosis Foundation and International Federation of Clinical Chemistry and Laboratory Medicine position on bone marker standards in osteoporosis. *Clin Chem Lab Med* 2011; 49: 1271-1274.
- Connelly F, Inderjeeth C. Osteoporosis in older people: reducing risk of falls and fractures. *Endocrinology Today* 2014; 3(4): 10-16.
- Sherrington C, Fairhall NJ, Wallbank GK, et al. Exercise for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2019; (1): CD012424.
- Osteoporosis Australia (OA). Exercise: medical guide. 2nd ed. Sydney: OA; 2014. Available online at: www.osteoporosis.org.au/sites/default/files/files/oa_medical_exercise_2nd_ed.pdf (accessed July 2019).
- Kemmler W, Haberle L, von Stengel S. Effects of exercise on fracture reduction in older adults: a systematic review and meta-analysis. *Osteoporos Int* 2013; 24: 1937-1950.
- Howe TE, Shea B, Dawson LJ, et al. Exercise for preventing and treating osteoporosis in postmenopausal women. *Cochrane Database Syst Rev* 2011; (7): CD000333.
- Sawka AM, Boulos P, Beattie K, et al. Do hip protectors decrease the risk of hip fracture in institutional and community-dwelling elderly? A systematic review and meta-analysis of randomized controlled trials. *Osteoporos Int* 2005; 16: 1461-1474.
- Duque G, Close JJ, de Jager JP, et al. Treatment for osteoporosis in Australian residential aged care facilities: consensus recommendations for fracture prevention. *Med J Aust* 2010; 193: 173-179.
- Santesso N, Carrasco-Labra A, Brignardello-Petersen R. Hip protectors for preventing hip fractures in older people. *Cochrane Database Syst Rev* 2014; (3): CD001255.
- Geddes JA, Inderjeeth CA. Evidence for the treatment of osteoporosis with vitamin D in residential care and in the community dwelling elderly. *Biomed Res Int* 2013; 2013: 463589.
- Adami S, Giannini S, Bianchi G, et al. Vitamin D status and response to treatment in post-menopausal osteoporosis. *Osteoporos Int* 2009; 20: 239-244.
- Bolland M, Barber PA, Doughty R, et al. Vascular events in healthy older women receiving calcium supplementation: randomised controlled trial. *BMJ* 2008; 336: 262-266.
- Cummings SR. ACP Journal Club: a single, annual, high dose of oral vitamin D increased falls and fractures in older women. *Ann Intern Med* 2010; 153: JC3.
- Avenell A, Mak Jenson CS, O'Connell D. Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men. *Cochrane Database Syst Rev* 2014; (4): CD000227.
- Lewis JR, Radavelli-Bagatini S, Rejnmark L, et al. The effects of calcium supplementation on verified coronary heart disease hospitalization and death in postmenopausal women: a collaborative meta-analysis of randomized controlled trials. *J Bone Miner Res* 2015; 30: 165-175.
- Bolland MJ, Grey A, Avenell A, Gamble GD, Reid IR. Calcium supplements

- with or without vitamin D and risk of cardiovascular events: reanalysis of the Women's Health Initiative limited access dataset and meta-analysis. *BMJ* 2011; 342: d2040.
35. Galior K, Grebe S, Singh R. Development of vitamin D toxicity from overcorrection of vitamin D deficiency: a review of case reports. *Nutrients* 2018; 10: pii: E953.
36. Inderjeeth CA, Poland KE. Management of osteoporosis in older people. *J Pharm Pract Res* 2010; 40: 229-234.
37. Inderjeeth CA, Inderjeeth AJ, Raymond WD. Medication selection and patient compliance in the clinical management of osteoporosis. *Aust Fam Physician* 2016; 45: 814-817.
38. Duque G, Lord SR, Mak J, et al. Treatment of osteoporosis in Australian residential aged care facilities: update on consensus recommendations for fracture prevention. *J Am Med Dir Assoc* 2016; 17: 852-859.
39. Lee S, Glendenning P, Inderjeeth CA. Efficacy, side effects and route of administration are more important than frequency of dosing of anti-osteoporosis treatments in determining patient adherence: a critical review of published articles from 1970 to 2009. *Osteoporos Int* 2011; 22: 741-753.
40. Inderjeeth C, Chan K, Kwan K, Lai M. Time to onset of efficacy in fracture reduction with current anti-osteoporosis treatments. *J Bone Miner Metab* 2012; 30: 493-503.
41. Papapoulos S, Lippuner K, Roux C, et al. The effect of 8 or 5 years of denosumab treatment in postmenopausal women with osteoporosis: results from the FREEDOM extension study. *Osteoporos Int* 2015; 26: 2773-2783.
42. Ettinger B, Black DM, Mitlak BH, et al. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. *JAMA* 1999; 282: 637-645.
43. Masud T, McClung M, Geusens P. Reducing hip fracture risk with risedronate in elderly women with established osteoporosis. *Clin Interv Aging* 2009; 4: 445-449.
44. Seeman E, Vellas B, Benhamou C, et al. Strontium ranelate reduces the risk of vertebral and nonvertebral fractures in women eighty years of age and older. *J Bone Miner Res* 2006; 21: 1113-1120.
45. Meunier PJ, Roux C, Seeman E, et al. The effects of strontium ranelate on the risk of vertebral fracture in women with postmenopausal osteoporosis. *N Engl J Med* 2004; 350: 459-468.
46. Reginster JY, Seeman E, De Vernejoul MC, et al. Strontium ranelate reduces the risk of nonvertebral fractures in postmenopausal women with osteoporosis: Treatment of Peripheral Osteoporosis (TROPOS) study. *J Clin Endocrinol Metab* 2005; 90: 2816-2822.
47. Boonen S, Black DM, Colon-Emeric CS, et al. Efficacy and safety of a once-yearly intravenous zoledronic acid 5 mg for fracture prevention in elderly postmenopausal women with osteoporosis aged 75 and older. *J Am Geriatr Soc* 2010; 58: 292-299.
48. Boonen S, McClung MR, Eastell R, El-Hajj Fuleihan G, Barton IP, Delmas P. Safety and efficacy of risedronate in reducing fracture risk in osteoporotic women aged 80 and older: implications for the use of antiresorptive agents in the old and oldest old. *J Am Geriatr Soc* 2004; 52: 1832-1839.
49. Bone HG, Hosking D, Devogelaer JP, et al. Ten years' experience with alendronate for osteoporosis in postmenopausal women. *N Engl J Med* 2004; 350: 1189-1199.
50. Black DM, Reid IR, Cauley JA, et al. The effect of 6 versus 9 years of zoledronic acid treatment in osteoporosis: a randomized second extension to the HORIZON-Pivotal Fracture Trial (PFT). *J Bone Miner Res* 2015; 30: 934-944.
51. Bone HG, Wagman RB, Brandi ML, et al. 10 years of denosumab treatment in postmenopausal women with osteoporosis: results from the phase 3 randomised FREEDOM trial and open-label extension. *Lancet Diabetes Endocrinol* 2017; 5: 513-523.
52. Mellstrom DD, Sorensen OH, Goemaere S, Roux C, Johnson TD, Chines AA. Seven years of treatment with risedronate in women with postmenopausal osteoporosis. *Calcif Tissue Int* 2004; 75: 462-468.
53. Khosla S, Burr D, Cauley J, et al. Bisphosphonate-associated osteonecrosis of the jaw: report of a task force of the American Society for Bone and Mineral Research. *J Bone Miner Res* 2007; 22: 1479-1491.
54. Wysowski DK. Reports of esophageal cancer with oral bisphosphonate use. *N Engl J Med* 2009; 360: 89-90.
55. Hellstein JW, Adler RA, Edwards B, et al. Managing the care of patients receiving antiresorptive therapy for prevention and treatment of osteoporosis: recommendations from the American Dental Association Council of Scientific Affairs. Chicago: American Dental Association; 2011. Available online at: www.aae.org/specialty/wp-content/uploads/sites/2/2017/07/bonj_ada_report.pdf (accessed July 2019).
56. Shane E, Burr D, Abrahamsen B, et al. Atypical subtrochanteric and diaphyseal femoral fractures: second report of a task force of the American Society for Bone and Mineral Research. *J Bone Miner Res* 2014; 29: 1-23.
57. Schilcher J, Michaëlsson K, Aspenberg P. Bisphosphonate use and atypical fractures of the femoral shaft. *N Engl J Med* 2011; 364: 1728-1737.
58. Anagnostis P, Paschou SA, Mintziori G, et al. Drug holidays from bisphosphonates and denosumab in postmenopausal osteoporosis: EMAS position statement. *Maturitas* 2017; 101: 23-30.
59. Trovas G. Letter to the editor: severe rebound-associated vertebral fractures after denosumab discontinuation: nine clinical cases report. *J Clin Endocrinol Metab* 2017; 102: 1086.
60. McClung MR, Wagman RB, Miller PD, Wang A, Lewiecki EM. Observations following discontinuation of long-term denosumab therapy. *Osteoporos Int* 2017; 28: 1723-1732.
61. Reid IR, Horne AM, Mihov B, Gamble GD. Bone loss after denosumab: only partial protection with zoledronate. *Calcif Tissue Int* 2017; 101: 371-374.
62. Freemantle N, Satram-Hoang S, Tang ET, et al; DAPS Investigators. Final results of the DAPS (Denosumab Adherence Preference Satisfaction) study: a 24-month, randomized, crossover comparison with alendronate in postmenopausal women. *Osteoporos Int* 2012; 23: 317-326.
63. Tripto-Shkolnik L, Rouach V, Marcus Y, Rotman-Pikielny P, Benbassat C, Vered I. Vertebral fractures following denosumab discontinuation in patients with prolonged exposure to bisphosphonates. *Calcif Tissue Int* 2018; 103: 44-49.