# National Osteoporosis Foundation of South Africa osteoporosis guideline

**Van Schoor J**
Amayeza Information Centre

## Abstract

The National Osteoporosis Foundation of South Africa (NOFSA) recently published a revised guideline for the diagnosis and management of osteoporosis. The 2010 revision is an update of the guideline published by NOFSA in 2000. The full guideline targets all healthcare workers. This article provides a brief summary of the revised osteoporosis guideline. The full NOFSA guideline is available online at www.jemdsa.co.za and www.osteoporosis.org.za.

 **Reprinted from S Afr Pharm J 2010;78(2):24-29**

## Introduction

The aim of the clinical guideline published by the National Osteoporosis Foundation of South Africa (NOFSA) is to improve the overall efficacy of the diagnosis and management of patients with, or at risk of, osteoporosis.[1] Major considerations in the development of the guideline include the prevention of osteoporotic fractures and reduction in morbidity and mortality.[1]

Although no accurate fracture data exist in South Africa, the incidence of osteoporosis in white, Asian and mixed-race populations appears to be similar to that in developed countries. While osteoporosis of the hip is less prevalent in the black population, vertebral bone mass and vertebral fracture prevalence appear to be similar in black and white South Africans.[1] As such, a key recommendation of the guideline is to improve awareness about osteoporosis, its prevention, treatment and complications, and to help facilitate broader access to health care for all patients with osteoporosis.[1]

To describe the quality of evidence and the strength of recommendation, the guideline made use of the Grading of Recommendation, Assessment and Development and Evaluation (GRADE) criteria. GRADE uses four categories of quality: high (ØØØØ), where further research is unlikely to change the confidence in the estimate of effect; moderate (ØØØO), where research is likely to have an important impact on the confidence in the estimate of effect and may change the estimate; low (ØØOO), where research is very likely to change the estimate; and very low (ØOOO), where any estimate of effect is unclear.

## What is osteoporosis?

The World Health Organization (WHO) has defined osteoporosis as "a systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture, which usually involves the wrist, spine, hip, ribs, pelvis or humerus".[2]

## Diagnosis of osteoporosis

Osteoporosis diagnosis is based on the measurement of bone mineral content, or bone mineral density (BMD), which is a surrogate marker of bone strength and fracture risk.[1] The diagnosis may also be made clinically on the basis of a history or evidence of a fragility fracture.[1] For example, a reduction in vertebral height of at least 20% or 4 mm is required for the diagnosis of a vertebral fracture.[1]

NOFSA recommends that a diagnosis of osteoporosis, based on a BMD measurement or the presence of a fragility fracture, should be confirmed before initiating treatment with bone-active medicines (ØØOO).[1]

## Fracture risk assessment

Studies have shown that less than 50% of women who suffer an osteoporotic fracture have a BMD within the osteoporosis range, and that most fractures occur in

women with osteopenia (i.e. low bone mass, as opposed to established osteoporosis).[3,4,5] Therefore, the sensitivity to identify fracture risk must be increased.[1]

Options to improve the sensitivity to identify fracture risk in an individual patient include combining the BMD measurement with other risk factors, such as the patient's clinical risk factors, or to combine the BMD measurement with an assessment of bone turnover.[1] However, bone turnover markers are not used routinely, but only in selected cases, e.g. to assess adherence to therapy.[1]

Several clinical risk factors have been identified and although they lack sensitivity and differ among patient populations, they impact on one other and are additive in predicting fracture.[1]

NOFSA recommends that clinical risk factors should always be included in the assessment of fracture risk (Table I).[1]

Table I. Major clinical risk factors for and causes of osteoporosis and fractures[1]

| |
|---|
| **Major clinical risk factors in postmenopausal women** |
| Advanced age |
| A prior fragility fracture |
| Low body weight or body mass index (BMI) |
| Family history of osteoporotic hip fracture |
| **Major secondary risk factors** |
| Hypogonadism |
| Glucocorticoid-induced osteoporosis |
| **Major lifestyle risk factors** |
| Alcohol consumption (three or more drinks per day) |
| Smoking |
| Diet (malnutrition, low calcium intake, vitamin and trace element deficiencies, high caffeine intake, high salt/protein intake) |
| **Other major risk factors** |
| Propensity to falls |

## Managing osteoporosis: the NOFSA integrated approach

It is important to emphasise that intervention thresholds are not always the same as diagnostic criteria. In osteoporosis, the diagnostic criteria are firmly established, while the intervention threshold as to when to start specific treatment or prophylaxis remains controversial, especially if the need to intervene is not apparent after BMD and clinical risk factor assessment.[1]

NOFSA recommends an integrated approach to managing osteoporosis in postmenopausal women and men over the age of 50 years:[1]

- Consider treatment when a prior fragility fracture is present, regardless of the results of the BMD assessment (ØØØO).
- Consider treatment in patients with established osteoporosis (decision based upon a BMD T-score of ≤ -2.5 measured at the hip or spine) (ØØØO).
- Consider treatment in patients with osteopenia (decision based upon an assessment of the BMD and clinical risk factors) (ØØOO). Age over 75 years is generally agreed upon as an intervention threshold, as is the presence of two or more major clinical risk factors in patients ≥ 65 years of age.

Note: Treatment should always be individualised and algorithmic recommendations should never replace good clinical judgment.

## Non-pharmacological management of osteoporosis

Non-pharmacological measures to improve bone strength include a healthy eating plan, physical exercise, limiting alcohol consumption, stopping smoking and avoiding the use of bone-toxic medicines.[1]

- *A healthy eating plan*, containing the correct amount of energy and all essential nutrients (including calcium 1 000-1 200 mg/day and vitamin D 800-1 000 IU/day), with adequate but not excessive protein, is recommended (ØØØO).[1] Calcium is important for the attainment of peak BMD in children.[6] Calcium deficiency has a more pronounced effect on age-related bone loss, and intervention later in life appears to be more beneficial.[1]
- *Physical exercise* is important for normal bone formation. Regular exercise (e.g. walking 5 km per day at a brisk pace, four days a week) has been shown to improve BMD in postmenopausal women.[7] Excessive exercise (e.g. marathon runners and ballet dancers), coupled with caloric restriction and a poor calcium intake, may result in functional hypogonadism (e.g. amenorrhoea) and osteoporosis.[8]
- *The effect of alcohol on bone strength* appears to be dose-related and intakes of three or more units of alcohol per day are associated with a higher risk for osteoporosis.[1] One unit of alcohol contains about 10 g of ethanol (e.g. 25 ml spirits/liqueur, 125 ml wine, 340 ml beer or 60 ml sherry).
- *Smoking* is an independent risk factor for osteoporosis.[1] It is also associated with early menopause and lower body weight. Smoking lowers the intestinal absorption of calcium and is often associated with alcohol use and a sedentary lifestyle.[1]
- A *number of medicines predispose to fracture*, either by reducing bone strength and/or by predisposing to a fall (Table II).

Table II. Medicines associated with an increased risk of osteoporosis and fracture[1,9]

| |
|---|
| **Increased risk of osteoporosis** |
| Glucocorticoids |
| Thyroid hormones |
| Anticonvulsants |
| Thiazolidinediones (e.g. pioglitazone and rosiglitazone) |
| Aromatase inhibitors (e.g. anastrozole, exemestane and letrozole) |
| GnRH[a] analogues (e.g. buserelin, goserelin, leuprorelin and triptorelin) |
| Immunosuppressive agents (e.g. ciclosporin and methotrexate) |
| Heparin and warfarin |
| Lithium |
| Aluminium |
| **Increased risk of falling** |
| Sedatives and hypnotics |
| Antidepressants |
| Antihypertensive agents |
| Hypoglycaemic agents |

[a]GnRH = Gonadotropin-releasing hormone

## Pharmacotherapy of osteoporosis

Specific medicines used in the treatment of osteoporosis are usually classified as:

- *Inhibitors of bone resorption*, i.e. bone breakdown, [e.g. hormone therapy with oestrogen alone, or in combination with a progestogen, selective oestrogen receptor modulators (e.g. raloxifene), bisphosphonates and calcitonin]. Calcium and vitamin D are only modestly effective as monotherapy, but have an additive effect when used with other antiresorptive agents and are useful adjuncts to antiresorptive therapy.
- *Stimulators of bone formation* (e.g. teriparatide).
- *Dual-acting agents* (e.g. strontium ranelate).

## NOFSA recommendations on the use of antiresorptive agents[1]

- Consider *calcium supplementation* if adequate calcium intake cannot be obtained from the diet. The elemental calcium content varies with the calcium supplement used. A calcium supplement that provides 500 mg of elemental calcium is usually sufficient to increase the calcium intake to the recommended levels (see Table III). Supplements containing calcium carbonate are best taken with meals, as the absorption is improved in the presence of gastric acid.
- The prophylactic dose of *vitamin D* is 800 to 1 000 IU/day. If serum 25-hydroxyvitamin D levels suggest vitamin D deficiency, higher doses may be required, e.g. 50 000 IU every two weeks (ØØØO).
- *Hormone therapy* with oestrogen (and progestogen in women with an intact uterus) may be considered for the treatment of menopausal women at risk of osteoporotic fracture who also present with vasomotor symptoms or urogenital atrophy, and who are in the 50-60 year age group (ØØØO). Consider a transdermal preparation in women with metabolic syndrome (i.e. obese, glucose intolerant, dyslipidaemia or hypertensive), those with hypertriglyceridaemia, and in smokers.
- *Selective oestrogen receptor modulators (SERMs)*, such as raloxifene, may be considered for women requiring predominantly vertebral fracture protection and who are also at risk of breast cancer (ØØØO).
- *Bisphosphonates,* such as alendronate, are considered to be a first-line treatment for osteoporosis in postmenopausal women, men and in glucocorticoid-induced osteoporosis. Since the anti-fracture efficacy of the bisphosphonates has largely been evaluated in patients at high fracture risk, their use should be reserved for those with established osteoporosis and/or a prior fragility fracture (ØØØØ). Oral bisphosphonates must be taken on an empty stomach with tap water only. The patient should refrain from eating and remain upright for at least 30 minutes after dosing. After five years of bisphosphonate therapy, a drug "holiday" may be considered, particularly in those patients who are not at high fracture risk. The BMD is usually maintained following discontinuation of the bisphophonate, but should be monitored after 18-24 months.

Table III. Recommended calcium intake to ensure optimal bone health[1]

| Group | Daily intake (mg) |
|---|---|
| **Infants** (birth – one year) | 500 |
| **Children** | |
| 1-5 years | 500 |
| 6-10 years | 800 |
| **Adolescents/young adults** | 1 200 |
| **Adult women and men** | |
| 25-65 years | 1 000 |
| Pregnant or breast-feeding | 1 200 |
| Over 65 years | 1 200 |

Note: The above calcium requirements are only applicable to Caucasians leading a Western lifestyle, since some evidence exists that black South Africans are more efficient at conserving calcium and probably do not need as much calcium in their diets.[1]

## NOFSA recommendations on the use of teriparatide[1]

Taking into account the costs, availability of less expensive medicines, and the need for daily injections, NOFSA recommends that the use of teriparatide/parathyroid hormone be reserved for (ØØØO):

**Table IV:** NOFSA recommendation on the choice of pharmalogical agent

| **Disease profile** | Mild osteopenia | More significant osteopenia | | | Established osteoporosis | | Glucocorticoid-induced osteoporosis | Severe osteoporosis |
|---|---|---|---|---|---|---|---|---|
| | ↓ | ↓ | ↓ | ↓ | ↓ | | ↓ | ↓ |
| **Patient profile** | No fractures<br><br>Ongoing bone loss | Women 50-60 years with menopausal symptoms | Postmenopausal woman at vertebral fracture risk and risk of breast cancer | Otherwise healthy patient<br>OR<br>Patient > 80 years | Otherwise healthy patient | | | Maintenance of BMD alone is not sufficient |
| **Bone-active therapy** | ↓ | ↓ | ↓ | ↓ | ↓ | | ↓ | ↓ |
| | | Hormone therapy if no contraindications | Raloxifene | Strontium ranelate | Strontium ranelate | Bisphosphonate | Bisphosphonate | Teriparatide |
| | ↓ | | | | | | | |
| **All patients** | Lifestyle changes<br>Calcium and vitamin D supplementation | | | | | | | |

- Patients over the age of 65 years with established osteoporosis and two or more fragility fractures, or multiple fractures and an uninterpretable dual-energy X-ray absorptiometry (DXA).
- Failed treatment (> 12 months) with bone-active agents, as evidenced by the development of a new fracture, or an unacceptable rate of bone loss on two or more consecutive follow-up BMD measurements.
- Patients on chronic glucocorticoid therapy (three months or longer using prednisone ≥ 5 mg/day or equivalent) with established osteoporosis, or one or more fragility fractures, or multiple vertebral fractures.

## NOFSA recommendation on the use of strontium ranelate[1]

Preclinical studies suggest that strontium ranelate has a dual mode of action, stimulating bone formation and inhibiting bone resorption. Strontium ranelate should be regarded as first-line therapy for postmenopausal osteoporosis. It is effective in those with osteoporosis and in those with osteopenia, including patients > 80 years of age (ØØØO). Strontium ranelate should be taken on an empty stomach. It is best avoided in patients with a history of venous thromboembolism and should be discontinued if a skin rash develops within two to three months of initiating treatment.

## NOFSA recommendation on the choice of pharmacological agent[1]

There are few studies that have compared the relative efficacy and safety of medicines used in the management of postmenopausal osteoporosis. Therefore, the choice of pharmacological therapy depends on the disease profile, the patient profile and available resources (Table IV).[1] Men, young premenopausal women and children are best referred to a specialist centre for evaluation and treatment.[1]

The full NOFSA guideline is available online at www.jemdsa.co.za and www.osteoporosis.org.za.

## References


1. Hough S, Ascott-Evans B, Brown S, et al; for the National Osteoporosis Foundation of South Africa (NOFSA). NOFSA guideline for the diagnosis and management of osteoporosis. Centurion: Medpharm Publications; 2010.
2. Consensus development conference: diagnosis, prophylaxis and treatment of osteoporosis. Am J Med. 1993;94:646-650.
3. Wainwright SA, Marshall LM, Ensrud KE, et al. Hip fracture in women without osteoporosis. J Clin Endocrinol Metab. 2005;90:2787-2793.
4. Sanders KM, Nicholson GC, Watts JJ, et al. Half the burden of fragility fractures in the community occur in women without osteoporosis. When is fracture prevention cost effective? Bone. 2006;38:694-700.
5. Siris ES, Chen YT, Abbott TA, et al. Bone mineral density thresholds for pharmacological intervention to prevent fractures. Arch Intern Med. 2004;164:1109-1112.
6. Winzenberg T, Shaw K, Fryer T, et al. Effects of calcium supplementation on bone density in healthy children: a meta-analysis of randomised controlled trials. BMJ. 2006;333:1415-1423.
7. Borer K, Fogelman K, Gross M, et al. Walking intensity for postmenopausal bone mineral preservation and accrual. Bone. 2007;41:713-721.
8. Myburgh KH, Roodt M, Noakes T, Hough FS. The effect of exercise on the development of osteoporosis in the rat. Am J Appl Physiol. 1989;66:14-19.
9. Rossiter D (Ed). South African Medicines Formulary. 9th Ed. South African Medical Association. 2010.