

# nogg

NATIONAL  
OSTEOPOROSIS  
GUIDELINE GROUP

## Guideline for the diagnosis and management of osteoporosis

in postmenopausal women  
and men from the age of  
50 years in the UK

Updated March 2014



Osteoporosis<sup>+</sup>  
2000



National  
Osteoporosis  
Society



Society for  
Endocrinology



Royal College  
of Physicians  
Setting higher medical standards

Produced by J Compston, A Cooper,  
C Cooper, R Francis, JA Kanis, D Marsh,  
EV McCloskey, DM Reid, P Selby, C Davies  
and C Bowring, on behalf of the National  
Osteoporosis Guideline Group (NOGG).

# Guideline for the diagnosis and management of osteoporosis in postmenopausal women and men from the age of 50 years in the UK

In 1999 and 2000 the Royal College of Physicians published guidelines for the prevention and treatment of osteoporosis.<sup>1-3</sup> Since then, there have been significant advances in the field of osteoporosis including the development of new techniques for measuring bone mineral density, improved methods of assessing fracture risk and new treatments that have been shown to significantly reduce the risk of fractures. Against this background, the National Osteoporosis Guideline Group (NOGG), in collaboration with many Societies in the UK, have updated the original guidelines,<sup>4</sup> a practical summary of which is detailed below. The management algorithms are underpinned by a health economic analysis applied to the epidemiology of fracture in the UK.

*The recommendations in the guideline should be used to aid management decisions but do not replace the need for clinical judgement in the care of individual patients in clinical practice.*

Supported by the

'Invest in your Bones Campaign' of the International Osteoporosis Foundation

## Diagnosis of osteoporosis

The diagnosis of osteoporosis relies on the quantitative assessment of bone mineral density (BMD), usually by central dual energy X-ray absorptiometry (DXA). BMD at the femoral neck provides the reference site. It is defined as a value for BMD 2.5 SD or more below the young female adult mean (T-score less than or equal to  $-2.5$  SD). Severe osteoporosis (established osteoporosis) describes osteoporosis in the presence of 1 or more fragility fractures.<sup>5</sup>

Diagnostic thresholds differ from intervention thresholds for several reasons. Firstly, the fracture risk varies at different ages, even with the same T-score. Other factors that determine intervention thresholds include the presence of clinical risk factors and the cost and benefits of treatment.

## Investigation of osteoporosis

The range of tests will depend on the severity of the disease, age at presentation and the presence or absence of fractures. The aims of the clinical history, physical examination and clinical tests are to:

- exclude diseases that mimic osteoporosis (e.g. osteomalacia, myeloma);
- identify the cause of osteoporosis and contributory factors;
- assess the risk of subsequent fractures;
- select the most appropriate form of treatment;

The procedures that may be relevant to the investigation of osteoporosis are shown in Table 1.

**Table 1 Procedures proposed in the investigation of osteoporosis**

### **Routine**

- History and physical examination
- Blood cell count, sedimentation rate or C-reactive protein, serum calcium, albumin, creatinine, phosphate, alkaline phosphatase and liver transaminases
- Thyroid function tests
- Bone densitometry ( DXA)

### **Other procedures, if indicated**

- Lateral radiographs of lumbar and thoracic spine/DXA-based vertebral imaging
- Protein immunoelectrophoresis and urinary Bence-Jones proteins
- 25OHD
- PTH
- Serum testosterone, SHBG, FSH, LH (in men),
- Serum prolactin
- 24 hour urinary cortisol/dexamethasone suppression test
- Endomysial and/or tissue transglutaminase antibodies (coeliac disease)
- Isotope bone scan
- Markers of bone turnover, when available
- Urinary calcium excretion

SHBG – sex-hormone binding globulin; FSH – follicle stimulating hormone; LH – luteinising hormone

Other investigations, for example bone biopsy and genetic testing for osteogenesis imperfecta, are restricted to specialist centres.

### Clinical risk factors

At present there is no universally accepted policy for population screening in the UK to identify individuals with osteoporosis or those at high risk of fracture. Patients are identified opportunistically using a case-finding strategy on the finding of a previous fragility fracture or the presence of significant clinical risk factors (CRFs). Some of these risk factors act independently of BMD to increase fracture risk (Table 2) whereas others increase fracture risk through their association with low BMD (e.g. some of the secondary causes of osteoporosis in Table 2).

**Table 2 Clinical risk factors used for the assessment of fracture probability**

Age
Sex
Low body mass index ( $\leq 19\text{kg/m}^2$ )
Previous fragility fracture, particularly of the hip, wrist and spine including morphometric vertebral fracture
Parental history of hip fracture
Current glucocorticoid treatment (any dose, by mouth for 3 months or more)
Current smoking
Alcohol intake of 3 or more units daily
Secondary causes of osteoporosis including:
• Rheumatoid arthritis
• Untreated hypogonadism in men and women
• Prolonged immobility
• Organ transplantation
• Type I diabetes
• Hyperthyroidism
• Gastrointestinal disease
• Chronic liver disease
• Chronic obstructive pulmonary disease
Falls*

\* Not presently accommodated in the FRAX<sup>®</sup> algorithm

Algorithms that integrate the weight of CRFs for fracture risk with or without information on BMD have been developed - FRAX<sup>®</sup>. The FRAX<sup>®</sup> tool ([www.shef.ac.uk/FRAX](http://www.shef.ac.uk/FRAX)) computes the 10-year probability of hip fracture or a major osteoporotic fracture (clinical spine, hip, forearm or humerus).<sup>5,6</sup> Probabilities can be computed for several European countries, including the UK.

## Case finding

Fracture risk should be assessed in postmenopausal women and in men aged 50 years or more with the risk factors outlined where assessment would influence management.

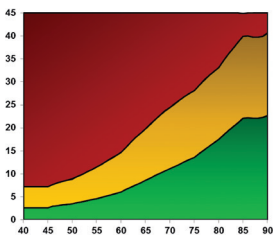
- Women with a prior fragility fracture should be considered for treatment without the need for further risk assessment although BMD measurement may sometimes be appropriate, particularly in younger postmenopausal women.
- In the presence of other CRFs, the ten year probability of a major osteoporotic fracture (clinical spine, hip, forearm or humerus) should be determined using FRAX® ([www.shef.ac.uk/FRAX](http://www.shef.ac.uk/FRAX)). Men and women with probabilities below the lower assessment threshold can be reassured. Those with probabilities above the lower assessment threshold but below the upper assessment threshold can be considered for testing with BMD using DXA and their fracture probability reassessed. Men and women with probabilities above the intervention threshold should be considered for treatment.
- Fracture probability of glucocorticoids is dose dependent. When the UK model glucocorticoid box is filled, 2 points now appear on the NOGG graphs, one for medium dose and one for high dose.
- In men and women who require a BMD test, fracture probabilities should be recomputed with FRAX®. Treatment can be considered in those in whom fracture probabilities lie above the intervention threshold.
- There are a number of other indications for bone densitometry including monitoring of treatment, determination of the extent of bone loss and assessment of suitability for certain treatments

The intervention threshold at each age is set at a risk equivalent to that associated with a prior fracture and, therefore rises with age. The proportion of women in the UK potentially eligible for treatment rises from 20 to 40% with age.<sup>7</sup>

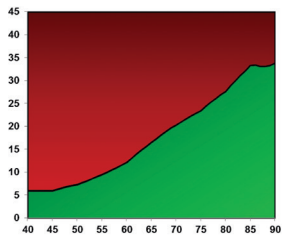
**Figure 1** Assessment and treatment thresholds in the absence of a BMD test (left) and with a BMD test to compute fracture probability (right) for men and women

### ASSESSMENT WITHOUT BMD

10 year probability of major osteoporotic fracture (%)



### ASSESSMENT WITH BMD



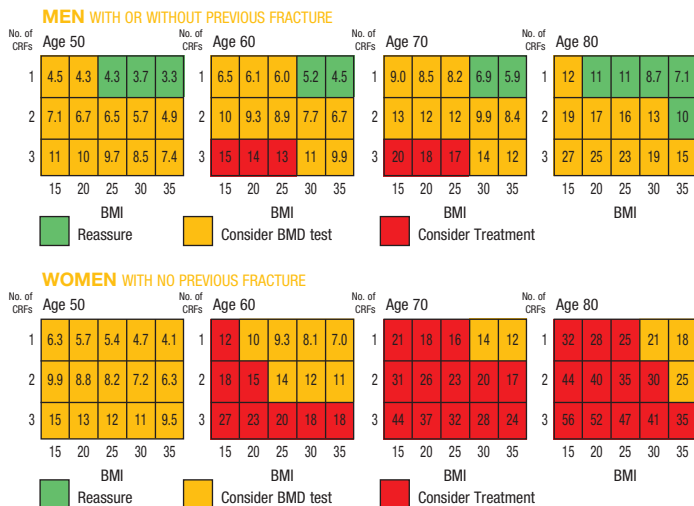
Age (years)

Probabilities of a major osteoporotic fracture (as well as hip fracture probabilities) can be plotted at the NOGG web site ([www.shef.ac.uk/NOGG](http://www.shef.ac.uk/NOGG)) available through FRAX®. Without computer access, the following management algorithm can be used:

- Women with a prior fragility fracture should be considered for treatment without the need for further risk assessment, although BMD measurement may sometimes be appropriate, particularly in younger postmenopausal women.
- In women with other CRFs, and in men with any CRF, FRAX® probabilities should be approximated according to body mass index ( $\text{weight}/[\text{height}]^2$  where weight is in kg and height is in metres).

The chart below (Fig. 2) gives average fracture probabilities according to BMI and the number of CRFs. The chart is colour coded. Green denotes that an individual's risk lies below the intervention threshold i.e. treatment is not indicated. Red denotes that the fracture probability is consistently above the upper assessment threshold, irrespective of the mix of CRFs, so that treatment can generally be strongly recommended. The intermediate category (orange) denotes that probabilities lie between these limits and that a BMD test should be considered to improve the estimate of fracture risk

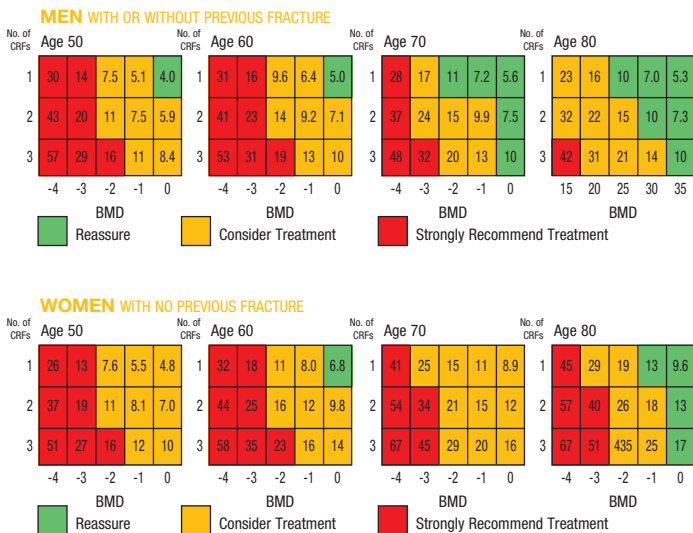
**Figure 2 Assessment of men and assessment of women with no previous fracture according to body mass index (BMI) and the number of clinical risk factors (CRFs)**



In men and women in whom BMD is available at the femoral neck, fracture probability can be approximated according to BMD T-score and the number of CRFs. The chart (Fig. 3) is colour coded. Green denotes that an individual's risk lies below the intervention threshold i.e. treatment is not indicated. Red denotes that the fracture probability is consistently above the upper assessment threshold, irrespective of the mix of CRFs, so that treatment can be strongly recommended in most cases. The intermediate category (orange) denotes that probabilities lie between these limits and that treatment can be recommended in those with the stronger risk factors. In general, smoking and alcohol are weak risk factors, glucocorticoids and secondary causes of osteoporosis are moderate risk factors, and a parental history of hip fracture is a strong risk factor.

Note that the only secondary cause of osteoporosis that should be used with BMD is rheumatoid arthritis.

**Figure 3 Assessment of men and assessment of women with no previous fracture according to femoral neck T-score for BMD and clinical risk factors (CRFs)**



## Treatment of Osteoporosis

**General management** includes assessment of the risk of falls and their prevention. Maintenance of mobility and correction of nutritional deficiencies, particularly of calcium, vitamin D and protein, should be advised.

**Major pharmacological interventions** are the bisphosphonates, denosumab, strontium ranelate, raloxifene and parathyroid hormone peptides. All these interventions have been shown to reduce the risk of vertebral fracture when given with calcium and vitamin D supplements. Some have been shown to also reduce the risk of nonvertebral fractures, in some cases specifically at the hip (see Table 3).

The low cost of generic bisphosphonates, which have a broad spectrum of anti-fracture efficacy, makes these the first line treatment in the majority of cases. In individuals who are intolerant of generic bisphosphonates or in whom they are contraindicated, other bisphosphonates, denosumab, or raloxifene may provide appropriate treatment options.

**Strontium ranelate should be restricted to individuals with severe osteoporosis for whom treatment with other approved drugs is not possible.** The high cost of parathyroid hormone peptides restricts their use to those at very high risk, particularly for vertebral fractures.

**Table 3 Effect of major pharmacological interventions on fracture risk when given with calcium and vitamin D in postmenopausal women with osteoporosis**

	Vertebral fracture	Non-vertebral fracture	Hip fracture
Alendronate	A	A	A
Ibandronate	A	A <sup>1</sup>	nae
Risedronate	A	A	A
Zoledronic acid	A	A	A
Denosumab	A	A	A
Raloxifene	A	nae	nae
Strontium ranelate	A	A	A <sup>1</sup>
Teriparatide	A	A	nae
PTH (1-84)	A	nae	nae

nae: not adequately evaluated

<sup>1</sup>in subsets of patients (post-hoc analysis)

PTH: recombinant human parathyroid hormone

Alendronate, risedronate, zoledronic acid, strontium ranelate and teriparatide are also approved for treatment of men at increased risk of fracture.

Alendronate is approved for the prevention and treatment of glucocorticoid-induced osteoporosis. Risedronate and etidronate are approved for the prevention and treatment of glucocorticoid-induced osteoporosis in postmenopausal women. Teriparatide and zoledronic acid are approved for treatment of glucocorticoid-induced osteoporosis in both men and women at increased risk of fracture. Other approved pharmacological interventions for postmenopausal women include calcitriol, etidronate and hormone replacement therapy.



## Monitoring of treatment

Please refer to the algorithm in the Executive Summary.

## Glossary

BMD	Bone mineral density
BMI	Body mass index; weight (kg)/height <sup>2</sup> (m)
CRF	Clinical risk factor for fractures due to osteoporosis
DXA	Dual energy x-ray absorptiometry
FRAX®	The WHO fracture risk assessment tool
SD	Standard deviation (of BMD measurements)
T-score	The number of standard deviations that a BMD measurement lies above or below the average value for young healthy women

## References

1. Royal College of Physicians (1999) Osteoporosis: clinical guidelines for the prevention and treatment. 1999. Royal College of Physicians, London
2. Royal College of Physicians and Bone and Tooth Society of Great Britain (2000) Update on pharmacological interventions and an algorithm for management 2000. Royal College of Physicians, London UK.
3. Royal College of Physicians (2002) Glucocorticoid-induced osteoporosis. Guidelines on prevention and treatment. Bone and Tooth Society of Great Britain, National Osteoporosis Society and Royal College of Physicians. Royal College of Physicians, London UK
4. National Osteoporosis Guideline Group on behalf of the Bone Research Society, British Geriatrics Society, British Orthopaedic Association, British Society of Rheumatology, National Osteoporosis Society, Osteoporosis 2000, Osteoporosis Dorset, Primary Care Rheumatology Society, Society for Endocrinology (2008) Osteoporosis. Clinical guideline for prevention and treatment, Executive Summary. Supporting Societies to be finalized. University of Sheffield Press
5. Kanis JA on behalf of the World Health Organization Scientific Group (2008) Assessment of osteoporosis at the primary health-care level. Technical Report. WHO Collaborating Centre, University of Sheffield, UK.
6. Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E (2008) FRAX® and the assessment of fracture probability in men and women from the UK Osteoporosis Int 19: 385-397
7. Kanis JA, McCloskey EV, Johansson H, Strom O, Borgstrom F, Oden A and the National Osteoporosis Guideline Group (2008) Case finding for the management of osteoporosis with FRAX® - Assessment and intervention thresholds for the UK. Osteoporosis Int (19:1395-408).



NATIONAL  
OSTEOPOROSIS  
GUIDELINE GROUP

The guideline development process was conducted without financial support from any commercial organization and members of the National Osteoporosis Guideline Group have maintained complete editorial independence. All members of NOGG have provided details of potential competing interests to the International Osteoporosis Foundation.

Contributions to funding for the implementation of these guidelines have been received from Amgen, the International Osteoporosis Foundation, Novartis, Procter & Gamble, Roche, Servier, and the WHO Collaborating Centre, Sheffield UK.

The National Osteoporosis Guideline Group gratefully acknowledges the collaboration of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and the support of the Bone Research Society, British Geriatrics Society, British Orthopaedic Association, British Orthopaedics Research Society, Bone Research Society, British Society of Rheumatology, National Osteoporosis Society, Osteoporosis 2000, Osteoporosis Dorset, Primary Care Rheumatology Society, Royal College of Physicians and Society for Endocrinology.