



THE EUROPEAN SOCIETY
FOR CLINICAL AND
ECONOMIC ASPECTS
OF OSTEOPOROSIS
AND OSTEOARTHRITIS

**European guidance
for the diagnosis and
management of
osteoporosis in
postmenopausal women**

Produced by JA Kanis, C Cooper,
N Burlet, PD Delmas, J-Y Reginster,
F Borgstrom and R Rizzoli,
on behalf of the European Society for Clinical
and Economic Aspects of Osteoporosis and
Osteoarthritis (ESCEO)

EUROPEAN GUIDANCE FOR THE DIAGNOSIS AND MANAGEMENT OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN

Ten years ago the European Foundation for Osteoporosis and Bone Disease (subsequently the International Osteoporosis Foundation) published guidelines for the diagnosis and management of osteoporosis.¹ Since then, significant advances in the field of osteoporosis include the development of many new techniques for measuring bone mineral, improved methods of assessing fracture risk and new treatments that have been shown to significantly reduce the risk of fractures at vulnerable sites. Against this background, the European Society for Clinical and Economic Evaluation of Osteoporosis and Osteoarthritis (ESCEO), in collaboration with the International Osteoporosis Foundation, revised the original guidelines,² a practical summary of which is detailed below. The management algorithms are based on a health economic analysis applied to the epidemiology of fracture in the UK and may require adaptation for other European countries.

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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.³

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

INVESTIGATION OF PATIENTS WITH OSTEOPOROSIS

The same approach should be undertaken in all patients with osteoporosis. However, the range of clinical and biological tests will depend on the severity of the disease, age at presentation and the presence or absence of vertebral fractures. The aims of the clinical history, physical examination and clinical tests are to:

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

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

TABLE 1 ROUTINE PROCEDURES PROPOSED IN THE INVESTIGATION OF OSTEOPOROSIS

ROUTINE

- History and physical examination
- Blood cell count, sedimentation rate, serum calcium, albumin, creatinine, phosphate, alkaline phosphatase and liver transaminases
- Lateral radiograph of lumbar and thoracic spine
- Bone densitometry (dual energy X-ray absorptiometry)

OTHER PROCEDURES

- X-Ray – vertebral fracture assessment
- Markers of bone turnover, when available

Many other investigations are reserved for specialist centres to exclude secondary causes of osteoporosis.

CLINICAL RISK FACTORS

At present there is no universally accepted policy for population screening in Europe to identify patients 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 risk factors. The risk factors that are used for clinical assessment are summarised in Table 2.

TABLE 2 CLINICAL RISK FACTORS USED FOR THE ASSESSMENT OF FRACTURE PROBABILITY

Age

Sex

Low body mass index

Previous fragility fracture, particularly of the hip, wrist and spine including morphometric vertebral fracture

Parental history of hip fracture

Glucocorticoid treatment (by mouth for 3 months or more)

Current smoking

Alcohol intake of 3 or more units daily

Secondary causes of osteoporosis include

- Rheumatoid arthritis
- Untreated hypogonadism in men and women
- Inflammatory bowel disease
- Prolonged immobility
- Organ transplantation
- Type I diabetes
- Thyroid disorders
- Chronic obstructive pulmonary disease

Algorithms that integrate the weight of clinical risk factors for fracture risk with or without information on BMD have been developed - FRAX™. The FRAX™ tool (www.shef.ac.uk/FRAX) computes the 10-year probability of hip fracture or a major osteoporotic fracture (clinical spine, hip, forearm and humerus fracture)^{3,4} Probabilities can be computed for several European countries, categorized for different levels of risk. The fracture risks in the UK are chosen in this guide.

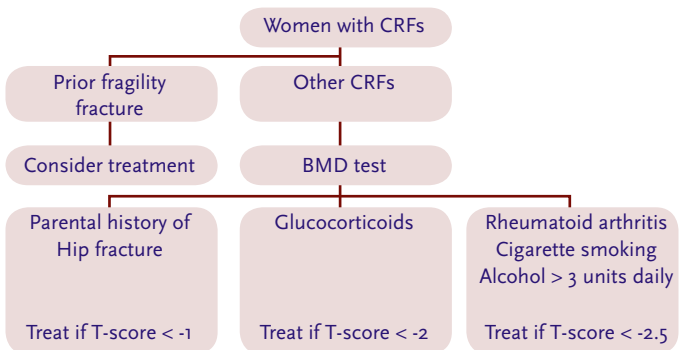
CASE FINDING

Fracture risk should be assessed in postmenopausal women with the risk factors outlined *where assessment would influence management*.

There are two approaches for decision making on the basis of clinical risk factors. The first is an extension of previous guidelines and the second, based on fracture probabilities derived from FRAX™.

The first approach uses BMD as the intervention threshold. Postmenopausal women with a previous fracture can be considered for treatment without the need for a BMD test (to decide on treatment). Women with other (weaker) clinical risk factors should be considered for BMD testing and treatment should be considered where the T-score for BMD at the femoral neck is -1 SD or lower for postmenopausal women with a parental history of hip fracture, -2.0 SD in women committed to long-term oral glucocorticoids, and -2.5 SD or lower for women with rheumatoid, who smoke or women that drink 3 units of alcohol or more daily. A possible management algorithm is shown below.

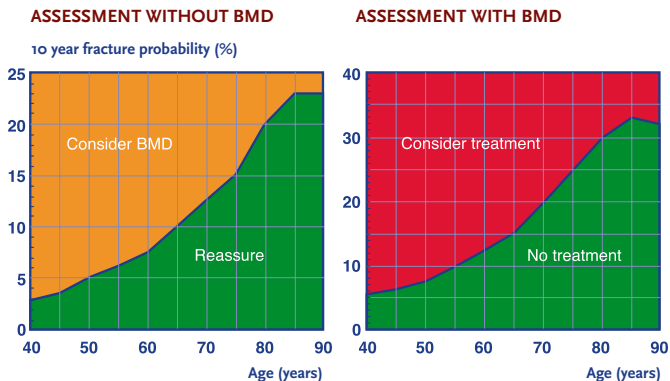
FIGURE 1 Management algorithm in postmenopausal women based on an health economic analysis for the UK



Probability based assessment (the second approach)

Women with a prior fragility fracture should be considered for treatment. 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). Women with probabilities below the lower assessment threshold can be reassured. Women with probabilities above the upper assessment threshold can be considered for testing with BMD and their fracture probability reassessed. Women with probabilities above the intervention threshold should be considered for treatment. The intervention threshold at each age is set at a risk equivalent to that associated with a prior fracture and, therefore rises with age. But the proportion of women in the UK potentially eligible for treatment rises from 20 to 40% with age.

FIGURE 2 Assessment threshold for BMD testing (left) and treatment threshold (right)

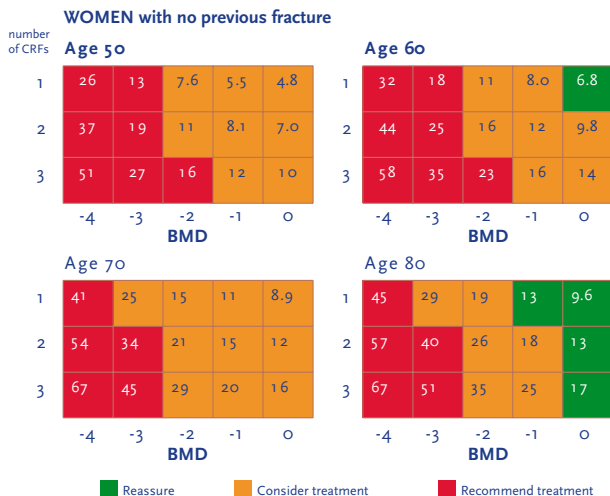


Without computer access, the following management algorithm can be used. Women with a prior fragility fracture should be considered for treatment. In the presence of other CRFs, BMD should be measured at the femoral neck.

The chart below gives average fracture probabilities according to BMD T-score 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 ordinarily be strongly recommended. The intermediate category (orange) denotes that probabilities lie between these limits and that treatment can be recommended in those with the stronger risk factors. 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 women with no previous fracture according to femoral neck T-score (NHANES) for BMD and clinical risk factors (CRFs)



An example is given in Figure 3 for a woman (from the UK) with rheumatoid arthritis aged 60 years on oral glucocorticoids with a BMD T-score of -1 SD (i.e. two clinical risk factors). The chart gives an average 10-year fracture probability of 12 % for any combination of 2 CRFs and is coded orange. With the 2 moderate risk factors in this woman, the probability is close to the average (11%) and exceeds the treatment threshold. With weak risk factors (e.g. smoking and alcohol), the probability would be lower (6.8 %) and fall below the treatment threshold. The range (6.7-12%) is not a confidence interval but, because the weight of different risk factors varies, is a true range.

TREATMENT OF OSTEOPOROSIS

General management includes the maintenance of mobility, avoidance of falls and correction of nutritional deficiencies, particularly of calcium, vitamin D and protein. Intakes of at least 1000 mg/day of calcium, 800 IU of vitamin D and of 1 g/kg body weight of protein can be recommended.

Major pharmacological interventions in Europe are raloxifene, the bisphosphonates, agents derived from parathyroid hormone and strontium ranelate. Until recently hormone replacement treatment was also widely used. 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 non-vertebral fractures, in some cases specifically at the hip (see Table 3).

TABLE 3 Effect of major pharmacological interventions on fracture risk

	Vertebral fracture	Non-vertebral fractures
Alendronate	+	+(including hip)
Risedronate	+	+(including hip)
Ibandronate	+	+a
Zoledronic acid	+	+(including hip)
HRT	+	+
Raloxifene	+	NA
Teriparatide and PTH	+	+
Strontium ranelate	+	+(including hip)

NA, No evidence available; +, effective drug; *in subsets of patients only (post-hoc analysis)

Other pharmacological interventions include calcitonin, hormone replacement treatment, clodronate, etidronate and derivatives of vitamin D.

Monitoring of treatment commonly uses repeated estimations of BMD and markers of bone formation and/or bone resorption.

GLOSSARY

BMD	Bone mineral density
BMI	Body mass index; weight (kg)/height (m) ²
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

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4, quai Godefroid Kurth
4020 LIÈGE
BELGIUM

e-mail : esceasbl@skynet.be

Tel. : + 32 4 270 32 57

Fax : + 32 4 270 32 53

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