### Diagnosis

- 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.

- ‘Osteoporosis’ denotes a value for BMD that is 2.5 standard deviations (SDs) or more below the young adult mean value for women (T-score ≤–2.5 SD).

- Severe osteoporosis (established osteoporosis) describes osteoporosis in the presence of 1 or more fragility fractures.

- Diagnostic thresholds differ from intervention thresholds for several reasons. For one, 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.

### 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
  - serum testosterone, sex-hormone binding globulin, follicle stimulating hormone, luteinising hormone (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

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

### Investigations

- 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

### 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 (see below), whereas others increase fracture risk through their association with low BMD (e.g. some of the secondary causes of osteoporosis listed below)

- Clinical risk factors used for the assessment of fracture probability:
  - age
  - sex
  - low body mass index (≤19 kg/m²)
  - previous fragility fracture, particularly of the hip, wrist, and spine including morphometric vertebral fracture
  - parental history of hip fracture
  - current oral glucocorticoid treatment (any dose 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 1 diabetes
    - hyperthyroidism
    - gastrointestinal disease
    - chronic liver disease
    - chronic obstructive pulmonary disease
  - falls (not presently accommodated in the FRAX® algorithm)

- In general, smoking and alcohol are weak risk factors; secondary causes of osteoporosis are moderate risk factors; prior fracture or a parental history of hip fracture are strong risk factors. Glucocorticoid therapy maybe a moderate or strong risk factor, depending on the dose and duration of therapy

### The FRAX® tool

- The FRAX® algorithm can integrate the number of CRFs for fracture risk with or without information on BMD

- The online FRAX® 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)

### 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 can be considered for treatment without the need for further risk assessment although BMD measurement may be appropriate, particularly in younger postmenopausal women

- In the presence of other CRFs, the 10-year probability of a major osteoporotic fracture (clinical spine, hip, forearm, or humerus) should be determined using FRAX®. This value can then be transferred on to the graphs shown in Figure 1

- Assessment and treatment threshold:
  - 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

- 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.

- The intervention threshold at each age is set at a risk equivalent to that associated with a prior fracture and, therefore, rises with age.

- In postmenopausal women and men ≥50 years of age prescribed continuous oral glucocorticoids for ≥3 months, bone protective treatment should be considered without the need for fracture risk assessment if:
  - age ≥70 years
  - previous fragility fracture or fragility fracture occurring during glucocorticoid therapy
  - high doses of glucocorticoids, depending on daily dose and presence or absence of other clinical risk factors
  - BMD T-score ≤−1.5 SD

- Probabilities of a major osteoporotic fracture (as well as hip fracture probabilities) can be plotted at the NOGG website (www.shef.ac.uk/NOGG) available through FRAX®

**Treatment of osteoporosis**

- General management includes:
  - assessment of the risk of falls and their prevention
  - maintenance of mobility
  - correction of nutritional deficiencies; in particular:
    - adequate calcium intake
    - correction of vitamin D deficiency
    - adequate protein intake

- Major pharmacological interventions:
  - bisphosphonates
  - denosumab
  - parathyroid hormone peptides
  - raloxifene
  - strontium ranelate

- 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 below)
Effect of major pharmacological interventions on fracture risk when given with calcium and vitamin D in postmenopausal women with osteoporosis

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Vertebral fracture</th>
<th>Non-vertebral fracture</th>
<th>Hip fracture</th>
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</thead>
<tbody>
<tr>
<td>Alendronate</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>Ibandronate</td>
<td>A</td>
<td>A'</td>
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<tr>
<td>Risedronate</td>
<td>A</td>
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<td>A</td>
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<tr>
<td>Zoledronic acid</td>
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<td>A</td>
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<tr>
<td>Denosumab</td>
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<td>Raloxifene</td>
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<td>Strontium ranelate</td>
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<tr>
<td>Teriparatide</td>
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<tr>
<td>PTH (1–84)</td>
<td>A</td>
<td>nae</td>
<td>nae</td>
</tr>
</tbody>
</table>

A=Recommendation based on meta-analysis of randomised controlled trials (RCT) or at least one RCT; nae=not adequately evaluated; A’ in subsets of patients (post-hoc analysis); PTH=recombinant human parathyroid hormone.


• The low cost of generic alendronate, which has a broad spectrum of anti-fracture efficacy, makes this the first-line treatment in the majority of cases

• In individuals who are intolerant of alendronate or in whom it is contraindicated, other bisphosphonates, denosumab, strontium ranelate, or raloxifene may provide appropriate treatment options. The high cost of parathyroid hormone peptides restricts their use to those at very high risk, particularly for vertebral fractures

• Other approved pharmacological interventions for postmenopausal women include calcitriol, etidronate, and hormone replacement therapy

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

• Alendronate, etidronate, risedronate, teriparatide, and zoledronic acid are approved for the prevention and treatment of glucocorticoid-induced osteoporosis

Duration and monitoring of bisphosphonate therapy

• Because of concerns over possible adverse effects of long-term bisphosphonate therapy, the need for continuation of treatment should be reviewed at regular intervals, after 5 years for alendronate, risedronate or ibandronate and after 3 years for zoledronic acid. Continuation of treatment without the need for further assessment can generally be recommended in the following groups:
  – high-risk individuals, for example:
    o those aged 75 years or more
    o those who have previously sustained a hip or vertebral fracture
    o those who are taking continuous oral glucocorticoids in a dose of ≥7.5 mg/day prednisolone or equivalent
  – individuals who sustain one or more low trauma fractures during treatment
    – if the total hip or femoral neck BMD T-score is ≤-2.5 SD

• If treatment is discontinued, fracture risk should be reassessed:
  – after a new fracture regardless of when this occurs
  – if no new fracture occurs, after 1.5–3.0 years
Assessment of fracture risk in treated individuals

- Reassessment of fracture risk in treated individuals can be performed using FRAX with femoral neck BMD. The NOGG intervention thresholds can then be used to guide the decision as to whether treatment can be stopped for a period of time (Figure 2, below).

The intervention thresholds provided in the NOGG guidance provide a starting point for making treatment decisions, but do not replace clinical judgement in the management of individual patients in clinical practice.

Figure 2. Bisphosphonates: algorithm for long-term treatment monitoring

Advise 3–5 years* treatment (Follow-up at 3 months to discuss treatment issues)

- Recurrent fracture(s)
- Prevalent vertebral fracture(s)

No fracture

FRAX + BMD after 3–5* years

Above NOGG intervention threshold or hip BMD T-score ≤-2.5
- Check adherence
- Exclude secondary causes
- Re-evaluate treatment choice
- Continue treatment

Below NOGG intervention threshold and hip BMD T-score >-2.5
- Consider drug holiday
- Repeat FRAX + BMD in 1.5–3 years

* 3 years for zoledronic acid; 5 years for other bisphosphonates
BMD=bone mineral density.

Full guidelines available from… http://www.shef.ac.uk/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 October 2008, updated May 2013

www.eGuidelines.co.uk