Osteoporosis is defined as a progressive, systemic skeletal disorder characterised by low bone mass and microarchitectural deterioration of bone tissue, with consequent increase in bone fragility and susceptibility to fracture.\(^1\)

Osteoporosis is important because of the fractures it causes. Fractures result in mortality, morbidity and loss of independence, and cost around £1.8 billion per annum in the UK. Many fractures are preventable, and cost-effective drugs are available to treat osteoporosis, rapidly reducing fracture risk, even in the elderly.

Why tackle osteoporosis and fracture prevention?

In the UK, after the age of 50, 1 in 2 women and 1 in 5 men will suffer a fracture, and the majority of these are osteoporotic. Around 20% of patients die within 6 months of a hip fracture, and a further 20% previously living independently will end up in a care home. Fractures increase GP workload – there are 9 extra consultations in the year after hip fracture and nearly 13 extra after a vertebral fracture. More than 2 million bed days are consumed by fractures in the over 60s each year in England, with an average length of stay of nearly 27 days compared to 8 days for all conditions.

Current activity levels for diagnosis and management of osteoporosis are very low. Only 10–14% of postmenopausal women suffering a low trauma (fragility) fracture receive bone-sparing treatment. Acute fracture care costs are around £2.8 million annually per 100,000 population, while only around £264,000 was spent on bone-sparing drugs for the same population in 2004.

Which patients are at highest risk?

Current guidance recommends a selective-case-finding approach, identifying high-risk groups and managing them to reduce future fracture risk. The highest-risk groups are:

- those committed to at least 3 months of any dose of oral steroid
- those with a recent or previous low trauma fracture (a fracture sustained by a fall from standing height or less, after the age of 50)
- the frail, housebound elderly or those in care homes.

In addition, patients with multiple risk factors who have not yet sustained a fracture may be at high risk of future fracture. Those with a high absolute fracture risk in this group can be identified using the World Health Organization (WHO) 10-Year Fracture Risk Assessment Tool (see ‘New developments’ below). These patients can then be managed actively as well.

Tackling these high-risk, priority patients will make most impact on fracture reduction. In some areas a Fracture Liaison Service assesses all new hip fracture patients or all new fracture patients aged 65 or over, and ensures that they are appropriately investigated and counselled about fracture risk, and that bone-sparing treatment is initiated where appropriate, before discharging them back to primary care.

Diagnosing and monitoring osteoporosis

Dual energy x-ray absorptiometry

Dual energy x-ray absorptiometry (DXA) is the gold standard for identifying osteoporosis and predicting future fracture risk. For every standard deviation (SD) fall in bone mineral density (BMD) the risk of fracture doubles. DXA scans are reported as T-scores, comparing the patient’s BMD to
that of a fit, healthy young adult. Osteopenia is defined as a T-score of \(-1\) to \(-2.5\) SD and osteoporosis as a T-score \(<-2.5\) SD. Scan reports should include a clinical report incorporating the patient’s risk factors and providing advice on treatment.

Population screening cannot be justified. DXA should only be performed if the result alters management. Clinical indications for bone densitometry are shown in Table 1.

**TABLE 1. Current indications for DXA scan.**

<table>
<thead>
<tr>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Low trauma fracture or vertebral deformity, age &lt;75 years</td>
</tr>
<tr>
<td>• Oral steroid therapy, age &lt;65 years, no low trauma fracture</td>
</tr>
<tr>
<td>• Men and women with primary hypogonadism</td>
</tr>
<tr>
<td>• Premenopause (&lt;45 years) or prolonged amenorrhea</td>
</tr>
<tr>
<td>• Radiographic evidence of osteopenia</td>
</tr>
<tr>
<td>• Chronic disease associated with osteoporosis</td>
</tr>
<tr>
<td>\quad – anorexia nervosa</td>
</tr>
<tr>
<td>\quad – malabsorption</td>
</tr>
<tr>
<td>\quad – primary hyperparathyroidism</td>
</tr>
<tr>
<td>\quad – post-transplantation</td>
</tr>
<tr>
<td>\quad – chronic renal failure</td>
</tr>
<tr>
<td>\quad – hyperthyroidism</td>
</tr>
<tr>
<td>\quad – prolonged immobilisation</td>
</tr>
<tr>
<td>\quad – Cushing’s syndrome</td>
</tr>
<tr>
<td>\quad – rheumatoid arthritis</td>
</tr>
<tr>
<td>• Postmenopausal women with maternal hip fracture or body mass index (BMI) &lt;19 kg/m(^2)</td>
</tr>
<tr>
<td>• Monitoring therapy – at intervals of at least 18 months</td>
</tr>
</tbody>
</table>

The National Institute for Health and Clinical Excellence (NICE) recommends that women over 75 with a low trauma fracture should receive bone-sparing treatment without a DXA scan. Access to DXA will improve with availability of mobile axial scanners belonging to the Mobile Osteoporosis Scanning Service of the National Osteoporosis Society (NOS), covering areas of the country previously without access.

**Peripheral dual energy x-ray absorptiometry**

X-rays are useful for fracture diagnosis but not for diagnosing osteoporosis. NOS has issued guidance on the use of peripheral DXA (pDXA – measured at the calcaneus or forearm) for diagnosis of osteoporosis.\(^4\) Upper and lower device-specific thresholds should be identified for each device and those patients with a T-score below the lower threshold have osteoporosis (equivalent to T-score \(<-2.5\) on axial scanner) and can be treated, while those above the upper limit have normal bones and can be reassured. However, the remaining 30–40% will need referral for hip and spine DXA to confirm whether they need treatment.

**Practical tip:** If you are offered pDXA scanning ensure that this is being used as recommended in NOS guidance.

**Ultrasound**

In experienced hands, quantitative ultrasound of the calcaneus improves the identification of postmenopausal women at high fracture risk compared to using clinical risk factors alone. However, it cannot be used to diagnose osteoporosis or for fracture prediction in men or younger women.

**USEFUL DEFINITIONS**

- **Secondary prevention** – drug treatment after the first fracture to prevent subsequent fractures
- **Secondary osteoporosis** – osteoporosis caused by some other condition, e.g. hypogonadism or steroid therapy
- **Low trauma fracture** – fracture caused by a fall from standing height or less in those >50 years
- **Calcium and vitamin D replete** – those patients having adequate calcium intake and vitamin D production from sunlight or from diet; difficult to evaluate in primary care
- **Orthogeriatric service** – care of the elderly physicians providing medical assessment and perioperative care to elderly orthopaedic patients

**Further investigations**

Some patients with fractures or osteoporosis will need further investigation to exclude secondary osteoporosis or other bone diseases (Table 2). Patients with previous cancer, those under 65, those with vertebral fractures and men will usually need investigation.

**TABLE 2. Investigation of low trauma fractures and osteoporosis.**

<table>
<thead>
<tr>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Full blood count, erythrocyte sedimentation rate or C-reactive protein</td>
</tr>
<tr>
<td>• Renal and liver profile</td>
</tr>
<tr>
<td>• Bone profile</td>
</tr>
<tr>
<td>• Thyroid profile</td>
</tr>
<tr>
<td>• Serum immunoglobulin electrophoresis/urinary Bence-Jones protein</td>
</tr>
<tr>
<td>• Testosterone/androgen screen for men</td>
</tr>
</tbody>
</table>

**What treatments are available?**

In 2005 NICE issued guidance (Technology Appraisal 87)\(^1\) on the use of bisphosphonates, raloxifene and teriparatide for secondary prevention of osteoporotic fractures in postmenopausal women (see Table 3). Updated guidance on secondary prevention including use of strontium ranelate, guidance on primary prevention in postmenopausal women and an osteoporosis Clinical Guideline are due to be published later in 2007. The Appraisal Consultation Document for secondary prevention was published in September 2006 (a draft stage of the Technology Appraisal and not implementable) recommended use of the most cost-effective form of alendronate (generic alendronic acid) as

\(^{1}\) Technology Appraisal 87: NICE, 2005

first-line therapy, with cyclical etidronate as an alternative, at the treatment T-scores from the original 2005 Technology Appraisal 87 document. Risedronate, strontium ranelate and raloxifene were recommended at lower T-scores, as successive alternatives for those intolerant of drugs higher up the recommendation list. The draft guidance on teriparatide would allow use in postmenopausal women aged 55–64 with a T-score of ≤–4 and more than 2 previous fractures. Women aged 75 and over who were intolerant of alendronate or etidronate would still need a DXA scan to confirm a T score ≤–2.5 to qualify for alternative treatment, whereas currently these women can have treatment with bisphosphonate or raloxifene without DXA scanning.

The same hierarchy of alendronate, etidronate, risedronate and strontium ranelate features in the Appraisal Consultation Document for primary prevention in postmenopausal women, but with treatment recommended only for those aged 75 or over and raloxifene treatment not recommended. The osteoporosis community and the National Osteoporosis Society have challenged this guidance, and the final Technology Appraisal is expected in May 2007.

Six groups of drugs are currently used in fracture prevention, as summarised in Table 4.

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**TABLE 3. Secondary prevention of fractures in postmenopausal women: existing guidance (after NICE Technology Appraisal 87).**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Treatment Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥75</td>
<td>Treatment without DXA</td>
</tr>
<tr>
<td>65–74</td>
<td>Treatment if T-score ≤–2.5</td>
</tr>
<tr>
<td>&lt;65</td>
<td>Treatment if T-score ≤–3 OR Treatment if T-score ≤–2.5 AND ≥1 additional age-independent risk factors:</td>
</tr>
<tr>
<td></td>
<td>BMI &lt;19 kg/m²</td>
</tr>
<tr>
<td></td>
<td>Maternal hip fracture &lt;75 years</td>
</tr>
<tr>
<td></td>
<td>Untreated premature menopause</td>
</tr>
<tr>
<td></td>
<td>Medical disorders associated with bone loss (e.g. rheumatoid arthritis, coeliac disease) or prolonged mobility</td>
</tr>
</tbody>
</table>

**Bisphosphonates** – first-line therapy
- Bisphosphonate contraindicated or unable to comply with dosing instructions
- Unsatisfactory response (another low trauma fracture despite adhering fully to therapy for 1 year, and BMD decrease below pre-treatment baseline)
- Unable to tolerate oral bisphosphonate (oesophageal ulceration, erosion or stricture, severe lower gastrointestinal symptoms resulting in discontinuation of treatment)

**Teriparatide** – women ≥65 years, secondary prevention, secondary care treatment
- Unsatisfactory response or bisphosphonates not tolerated AND
- T-score ≤–4 OR
- T-score ≤–3.0 AND >2 fractures AND ≥1 additional age-independent risk factors:
  - BMI <19 kg/m²
  - Maternal hip fracture <75 years
  - Untreated premature menopause
  - Conditions associated with prolonged immobility

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**TABLE 4. Pharmacological therapies in fracture prevention.**

<table>
<thead>
<tr>
<th>Calcium/vitamin D (1000–1200 mg/800 IU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduces hip fractures in frail elderly in care homes with no previous fractures</td>
</tr>
<tr>
<td>Adjuvant therapy in those on bone-sparing therapy who are not replete/no contraindications</td>
</tr>
<tr>
<td>All patients on oral steroids</td>
</tr>
<tr>
<td>May increase muscle strength, decrease body sway, decrease falls</td>
</tr>
</tbody>
</table>

**Bisphosphonates**
- Alendronate and risedronate (daily or weekly) reduce vertebral, non-vertebral and hip fracture; also licensed for steroid-induced osteoporosis
- Ibandronate (monthly) reduces hip and vertebral fractures

**Strontium ranelate**
- Daily therapy, possible small increase in venous thromboembolic events (VTE)
- Dual-action bone agent, maintains bone formation
- Reduces vertebral, non-vertebral fractures; reduces hip fractures in high-risk women; reduces all fractures in those >80 years
- Increases bone mineral density (BMD) disproportionately so formula required to calculate BMD increases

**Raloxifene**
- Reduces vertebral fractures but no effect on hip fracture risk
- No effect on cardiovascular disease (CVD)
- Reduces oestrogen receptor-positive breast cancer
- Increases VTE risk and hot flushes

**Teriparatide**
- Reduces vertebral and non-vertebral fractures
- Daily subcutaneous injection for 18 months
- Secondary care use in women ≥65 years only at present
- Unsatisfactory response or bisphosphonates not tolerated AND
- T-score ≤–4 OR
- T-score ≤–3.0 AND >2 fractures AND
- ≥1 additional age-independent risk factors:
  - BMI <19 kg/m²
  - Maternal hip fracture <75 years
  - Untreated premature menopause
  - Conditions associated with prolonged immobility

**Hormone replacement therapy (HRT)**
- Reduces fracture risk at all sites
- Increases risk of breast cancer, coronary heart disease (CHD), stroke and dementia
- Not recommended for long-term use

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**Practical tip:** View the summary guidance for NICE Technology Appraisal 87 on secondary prevention and, in due course, the new Technology Appraisals and Clinical Guideline at www.nice.org.uk. (Type ‘osteoporosis’ into the search engine and then view the Quick Reference Guides as and when they appear.)
**Drug treatment**

There is variable tolerance of individual bisphosphonates and calcium/vitamin D supplements between patients so it is worth trying an alternative if one produces side-effects. Some upper gastrointestinal (GI) side-effects may be due to the calcium/vitamin D preparations so starting this first may avoid wrongly attributing side-effects to the bisphosphonate. Diarrhoea may occur in the early months of strontium ranelate therapy, so it is important to stop all laxatives before commencing therapy. Although studies suggest that average persistence with bisphosphonate therapy is around 50% at 1 year, well-motivated teams can achieve much higher rates.

**Lifestyle advice**

All patients assessed for osteoporosis risk should be encouraged to stop smoking, eat a well-balanced diet containing at least 700 mg daily calcium, and aim for 20 minutes' sun exposure to face and arms daily during summer months. Patients already diagnosed with osteoporosis should aim for 1200 mg daily calcium intake as recommended by NOS. Those with low fracture risk should be encouraged to undertake vigorous weight-bearing exercise, or resistance exercise (slow-lifting of moderate weights) to maintain or improve BMD, while t’ai chi and balance work may reduce risk of falls in the elderly. Those at risk of vertebral fractures should avoid heavy lifting or forced flexion activities.

**Management of osteoporotic fractures**

Patients should receive prompt management of the fracture by experienced orthopaedic surgeons and anaesthetists, with perioperative orthogeriatric input if needed, and adequate analgesia or non-steroidal anti-inflammatory drugs (NSAIDs) to allow early mobilisation and avoid prolonged bed-rest. Transcutaneous electrical nerve stimulation (TENS) machines, acupuncture and hydrotherapy will be helpful in many patients. Short-term treatment with nasal calcitoniin may provide acute pain relief for severe pain from vertebral fractures in some patients. Physiotherapy and rehabilitation in a specialist unit after hip or vertebral fracture can improve mobility, posture and muscle strength. There is increasing evidence for vertebroplasty or kyphoplasty in specialist centres for those with intractable pain from vertebral fractures.

**Hip protectors**

There is no evidence that hip protectors reduce hip fracture risk in community-dwelling elderly, but some evidence that they may be effective in extended care settings.

**Glucocorticoid-induced osteoporosis**

Treatment with oral glucocorticoids at any dose greatly increases the risk of osteoporosis and fracture. Bone is lost fastest in the early stages and continues throughout treatment. Bone-sparing therapy is recommended for all patients aged 65 or over and other high-risk groups (e.g. previous low trauma fracture). Patients under 65 need a DXA scan, and treatment with bone-sparing therapy if the T-score is ≤–1.5, as fractures occur at higher BMD in patients taking steroids. Alendronate, risedronate and etidronate are licensed for steroid-induced osteoporosis. All patients should receive high-dose calcium and vitamin D unless they are replete or there are contraindications.

**Practical tip:** Review the Royal College of Physicians’ glucocorticoid-induced osteoporosis algorithm and concise guidance at: http://www.rcplondon.ac.uk/ pubs/books/glucocorticoid/glucocortConcise.pdf.

**Referral to secondary care**

Metabolic bone clinics provide guidance on which patients to refer. These include those with:

- diagnostic difficulty
- intolerance of oral bone-sparing therapy
- continued fracture while on therapy
- severe osteoporosis which may require teriparatide therapy
- other metabolic bone diseases such as osteomalacia or Paget’s disease
- confirmed osteoporosis or low trauma fractures in men.

**Practical tip:** If you don’t have a metabolic bone clinic locally, find out which consultants have an interest in osteoporosis. Is there a fracture liaison service and which patients do they manage?

**Getting started**

Although osteoporosis and fracture prevention are not currently included in the Quality and Outcome Framework of the new General Medical Services (nGMS) Contract, Primary Care Teams and Primary Care Organisations (PCOs) are recognising that taking action to prevent fractures involves little workload, is important for good patient care, and is cost-effective.

An average GP list of 1700 patients would expect to have 6 new low trauma fractures in postmenopausal women each year, and around 40 postmenopausal women with previous fractures. Around 1% of adults will be taking oral steroids but only about 20% will continue therapy for >3 months. New fracture patients can be identified opportunistically from hospital letters, while those on steroids and those with previous fractures are best tackled by audits, as shown in Table 5. Audit software available from some pharmaceutical companies facilitates the process, but still depends on accurate coding.
New developments

It has long been recognised that although BMD is helpful in predicting future fracture risk, other BMD-independent risk factors contribute to absolute fracture risk. Professor John Kanis and WHO have developed a 10-year fracture risk score similar to the cardiovascular disease risk score. This uses age, sex, previous fracture history, BMI, smoking, parental history of hip fracture, steroid use and alcohol intake, with or without DXA T-scores, to estimate the absolute fracture risk for individual patients. The prediction tool will be available later in 2007.

Zoledronate, a once-yearly intravenous bisphosphonate, will simplify delivery of osteoporosis treatment and improve persistence. More cost-effective versions of recombinant parathyroid hormone may make this therapy more accessible to patients. However, the future development likely to make most impact on fracture prevention is the inclusion of osteoporosis in future versions of the Quality and Outcome Framework of the nGMS Contract.

References


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Table 5. Suggestions for practice audit.

<table>
<thead>
<tr>
<th>Baseline data collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Prescribing data on bisphosphonates, strontium ranelate, raloxifene and high-dose calcium/vitamin D</td>
</tr>
<tr>
<td>• Fractures in those ≥65 years identifiable from computer records</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Low trauma fractures</th>
</tr>
</thead>
<tbody>
<tr>
<td>• <strong>Criterion:</strong> All postmenopausal women who have had a low trauma fracture should be managed as recommended in NICE Technology Appraisal 87</td>
</tr>
<tr>
<td>• <strong>Standard:</strong> 80%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Steroid-induced osteoporosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• <strong>Criterion:</strong> Patients on oral steroids ≥3 months should be managed according to Royal College of Physicians 2002 guidelines</td>
</tr>
<tr>
<td>• <strong>Standard:</strong> 80%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hip fracture prevention in frail, elderly care-home residents</th>
</tr>
</thead>
<tbody>
<tr>
<td>• <strong>Criterion:</strong> Frail elderly in care homes with no previous low trauma fractures treated with high dose calcium/vitamin D to decrease hip fractures</td>
</tr>
<tr>
<td>• <strong>Standard:</strong> 90%</td>
</tr>
</tbody>
</table>

continued/
Osteoporosis diagnosis, prevention and treatment are challenges to GPs and hospital specialists alike. Nowhere is the opportunity, or need, greater for cooperation between primary and secondary care. Most hip and peripheral fractures present to medical services and should trigger an osteoporosis risk assessment.

Frustratingly, the majority of vertebral fractures occur in those who do not, for a variety of reasons, seek medical help. Audit tools in general practice to ensure those with low trauma fractures and those on glucocorticoids are identified is obviously vital and perhaps audit might be extended to include those with significant height loss or acute back pain, their being potential markers for vertebral fracture.

We face exciting times in tackling osteoporosis and preventing the frequently devastating consequences of fracture. We are moving away from fracture prediction based on bone density measurements relative to the mean of an aged-matched or young adult reference population and are turning towards the stratification of absolute fracture risk based on an individual’s clinical and genetic characteristics when combined with axial bone density results.

In the light of the World Health Organization’s work on 10-year fracture probability, maybe a case can now be made for screening all those aged 65 and over by means of a standardised risk-assessment questionnaire. Otherwise, how will all women who have a first-degree family history, low body mass index or are heavy smokers be identified and considered worthy of bone mineral density measurements?

While screening remains controversial, in the US matters have been taken one step further since in that managed health care system all 65-year-old women are entitled to bone density scans.

Moreover, the range of currently available treatments is increasing and particular attention is being directed towards annual intravenous zoledronate 5 mg which has impressive protection against vertebral, hip and other non-vertebral fractures. Once a product licence is available (as it is already in the same dose for Paget’s disease) it should prove superior to existing licensed bisphosphonates, particularly where compliance is concerned.

On the horizon are completely new classes of drugs and there is considerable excitement about the potential to modify the RANK ligand/osteoprotegerin pathways which have profound effects on osteoclast function. Such developments will no doubt add to the challenge facing NICE which, as indicated in Pam Brown’s article, has been experiencing some difficulty in arriving at widely accepted guidance relating to the use of existing interventions.

While the greater sophistication of available treatments means that specialists in metabolic bone disease will be kept stimulated and employed, the GP will, and should, remain a key player in identifying those with, or at risk of, osteoporosis and associated fracture and providing appropriate treatment to the majority.

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