UPDATE
Module 1705

This module covers:

- The risk factors for osteoporosis, including lifestyle and medication
- Bone formation and diagnosis
- Management, including pharmacological and non-pharmacological approaches
- Sources of support and information

June »
Musculoskeletal month

Sprains and strains	June 7
Osteoporosis	June 14
Lower back pain	June 21
Osteoarthritis	June 28*

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Managing osteoporosis

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Osteoporosis translates from Greek as 'porous bones'. The World Health Organisation (WHO) defines the condition as a progressive systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissues with a consequent increase in bone fragility and susceptibility to fracture.

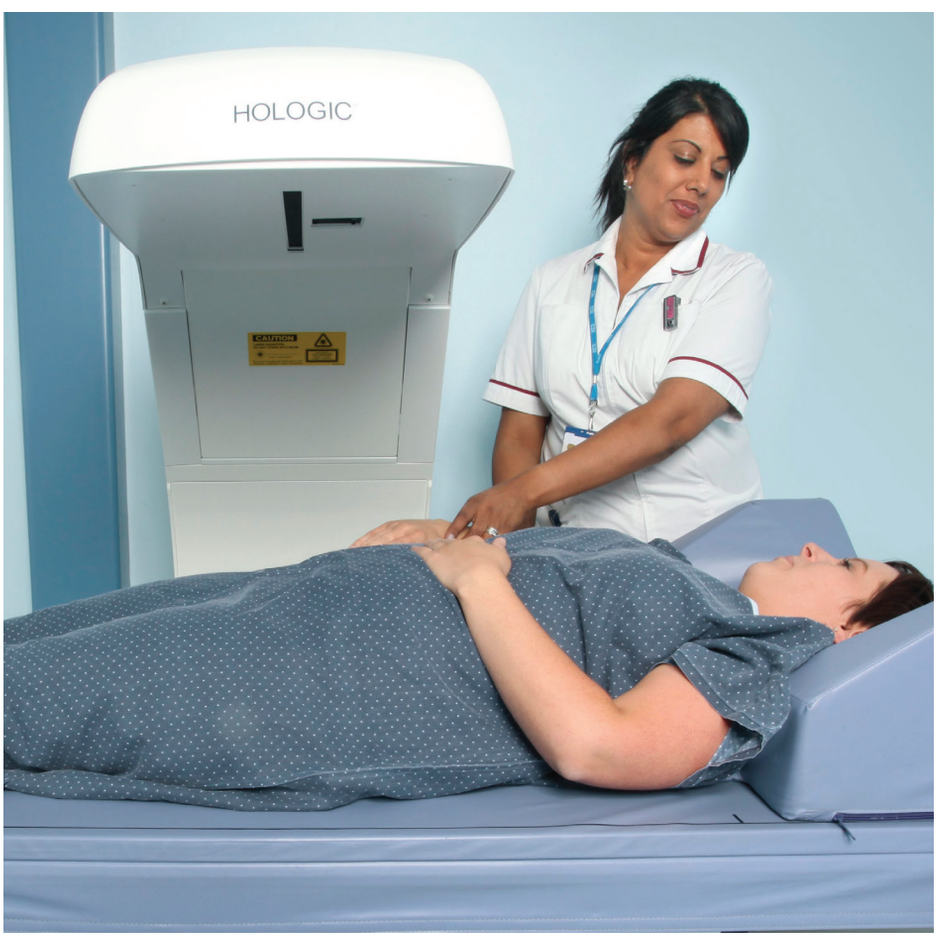
Osteoporosis is a silent disease, often not causing any problems or symptoms until a fall and subsequent fracture. However, it can have serious effects on quality of life. For example, hip fracture causes pain and reduced mobility, with 50 per cent of patients being permanently disabled and 20 per cent dying.

An estimated 3 million people in the UK have osteoporosis. Women are affected more than men (50 per cent to 20 per cent). However, women of African-Caribbean origin appear to be less susceptible than white or Asian women. The most commonly affected areas are the wrists, hips and spine. Fragility fractures (those that occur with low-level trauma) result in huge costs to the NHS, estimated at £1.8 billion in 2000.

Diagnosis

Osteoporosis is diagnosed by carrying out a dual-energy X-ray absorptiometry (DEXA) scan, which assesses bone mineral density (BMD). A measurement is usually taken from the neck of the femur. Other sites, such as the spine, can be used for patients where hip measurement is not possible. The result is expressed as a T-score, which is the number of standard deviations below the young adult mean value for BMD in young women. The same scoring is used in men, as there is no reason to assume that bone formation and destruction is any different between the sexes. A T-score of:

- 0 to 1 is normal
- between -1 to -2.5 indicates osteopenia (lower-than-average bone density, but not low enough to be classed as osteoporosis)
- below -2.5 indicates osteoporosis
- below -4 indicates severe osteoporosis.



Bone mineral density to ascertain the severity of osteoporosis can be assessed with a DEXA scan

Osteoporosis can be primary (age-related) or secondary (has an identifiable cause). It is important to investigate further to allow any underlying abnormalities to be corrected, although this may not be possible, since a number of clinical conditions pre-dispose to osteoporosis. Liver, kidney and thyroid function should be checked, as well as vitamin D and parathyroid hormone levels.

Nice guidelines state that women aged more than 75 years may not need a bone scan to diagnose osteoporosis.

Risk factors for osteoporosis

There are a number of risk factors for osteoporosis, including lifestyle, medical conditions and medication, which are shown in *Risk factors for osteoporosis* (right). Many can be modified by changes to diet and lifestyle, the underlying cause treated or the causative medication stopped. If a medication cannot be stopped, then calcium and vitamin D

supplementation may be appropriate. Some conditions have a much more significant impact on fracture risk. Rheumatoid arthritis, for example, increases fracture risk independently of BMD. Postmenopausal women are at increased risk, as they lose the protective effect of oestrogen.

Oral corticosteroids affect bones by reducing osteoblast activity, intestinal calcium absorption and circulating sex steroid levels. They significantly reduce BMD, with the greatest rate in the first six to 12 months of treatment, especially in doses of prednisolone (or equivalent) over 7.5mg daily. The condition for which the steroids are being used may in itself be a risk factor for osteoporosis, therefore increasing risk even further. High-dose inhaled corticosteroids can also contribute to osteoporosis development.

Fall risk and osteoporosis

There is an overlap between risk factors for osteoporosis and falls. By treating osteoporosis, the risk of fractures decreases even though the risk of falls remains. Furthermore, the risk of fracture increases with reducing BMD, at a rate of two-fold for each standard deviation decrease in BMD.

Nice guidelines suggest that a fracture risk tool is used before routine BMD testing. Care is required in certain circumstances, however, as risk can be underestimated in certain groups. There are two clinical assessment tools for fracture risk:

- FRAX – established by the WHO, it estimates the 10-year probability of hip fracture or major osteoporotic fracture by taking into account age, sex, BMI, BMD and clinical risk factors. It can be used for those aged 40 to 90 with or without BMD measurement
- Q-Fracture – This can be used for those aged between 30 and 99. There is no BMD measurement, but it takes into account a wider range of risk factors than FRAX.

Fracture risk should be undertaken for all women over 65 years and all men over 75 years. Younger patients with certain risk factors should be assessed, too. Routine screening is not recommended; instead, case-identification of those at risk is used to identify patients because of fragility fracture or clinical risk factors.

Pharmacological management

There are no licensed treatments for osteoporosis for women below the menopausal age; men are treated in the same way as women.

The mainstay of osteoporosis treatment are the bisphosphonates. These are inorganic pyrophosphate analogues that act by inhibiting bone resorption. Etidronate was the first of these and is taken on a cyclical basis with calcium. However, newer bisphosphonates are easier to take. Bisphosphonates have been shown to reduce vertebral, non-vertebral and hip fracture risk.

Side effects include gastro-intestinal discomfort, headache and musculoskeletal pain. Atypical femur fracture and osteonecrosis of the jaw can also occur. To avoid risk of oesophageal ulceration, they must be taken with a full glass of water and the patient should remain sitting upright or standing for at least 30 minutes (an hour for ibandronic acid). As oral bioavailability is low, they must be taken at least 30 minutes before food or medication (60 minutes for ibandronic acid). Dosage adjustments are needed in those with renal impairment.

Alendronate and risedronate can be taken daily or weekly, while ibandronic acid is taken once a month. Zoledronic acid is given annually via IV infusion.

Concerns over the safety of long-term bisphosphonate treatment have been raised, leading to use of drug holidays. These are not suitable for patients at continued high risk and, if commenced, fracture risk should be reviewed after two years (earlier if a fracture occurs). It has been shown that bisphosphonates have continued anti-resorptive effects after stopping treatment.

Denosumab is a humanised monoclonal antibody and inhibits oesteoclast formation and action. It is licensed for osteoporosis ▸

Risk factors for osteoporosis

Modifiable lifestyle	Medical conditions	Medications
• poor nutrition	• calcium or vitamin deficiency	• oral corticosteroids
• low body mass index (BMI)	• hyperthyroidism	• proton pump inhibitors (PPIs)
• physical inactivity	• rheumatoid arthritis	• phenytoin
• high alcohol intake	• Cushing's syndrome	• carbamazepine
• smoking	• diabetes mellitus	• lithium
	• haematological cancers	• selective serotonin reuptake inhibitors (SSRIs)
	• chronic liver disease	• methotrexate
	• chronic renal disease	• thiazolidinediones (pioglitazone)
	• chronic obstructive pulmonary disease (COPD)	• tamoxifen
	• malabsorption diseases (Coeliac, Crohn's)	• aromatase inhibitors

treatment in postmenopausal women at increased fracture risk and is administered as a 60mg subcutaneous injection every six months. In contrast to bisphosphonates, no adjustment is required in renal impairment. Side effects include hypocalcaemia (calcium levels must be replete prior to treatment) and atypical femoral fractures.

Teriparatide is recombinant human parathyroid hormone and is recommended by Nice as an option where other preparations are unsuitable. It is given as a subcutaneous injection of 20µg daily for a maximum of 24 months. Side effects include headache and postural hypotension. It can be used for women who have had another fracture while taking a bisphosphonate for one year and whose BMD has fallen.

Raloxefene is a selective oestrogen receptor modulator inhibiting bone resorption. It reduces vertebral fracture risk and is taken at 60mg once daily. Side effects include leg cramps and oedema. It should not be used in those of childbearing age or in hepatic or renal impairment. Caution is indicated where there is stroke history or risk factors as it increases venous thromboembolism (VTE) risk. It is not indicated for prevention of fractures in those who have not had a fracture.

There has been recent debate as to the use of strontium ranelate because of its association with increased risk of serious cardiovascular disease. At present, it remains an option where other treatments are not suitable or tolerated, but it should be stopped if heart or circulatory problems occur. It is thought to have anti-resorptive properties while maintaining bone formation.

Calcitonin is no longer recommended due to increased cancer risk. Calcitriol is taken at 0.25µg daily and acts to inhibit resorption. Serum calcium and creatinine should be monitored at one-, three- and six-month intervals and biannually thereafter.

Hormone replacement therapy (HRT) is not routinely recommended for osteoporosis treatment and prevention but has been shown to reduce hip and vertebral fractures compared to placebo; it works because of the oestrogen-replacement effects. However, the risk/benefit profile should be carefully considered due to increased risk of breast, ovarian and endometrial cancer, VTE and stroke. Use in osteoporosis prevention is therefore limited to younger postmenopausal women with high fracture risk and menopausal symptoms.

In those commencing glucocorticoid therapy, bone-protective treatment should be commenced at the same time in those at increased fracture risk, usually with alendonrate or risedronate.

It is very important to ensure adequate calcium and vitamin D intake, from the diet if possible or with supplements if not. The BNF recommends calcium at double the recommended intake to reduce the rate of bone loss. Recent concern over an increased cardiovascular risk of calcium intake has not been substantiated. Indeed, calcium and vitamin D supplementation has been shown to reduce fracture risk and improve mortality.

Pain in osteoporosis can be significant and hard to control, especially with compression fractures of the spine. Careful management is required in order to achieve adequate pain relief while avoiding too much of an increased risk of potential side effects, such as drowsiness, which would increase fall risk.

Non-pharmacalogical management

Identification and modification of external factors can help in the avoidance of falls, although studies have not shown a significant risk reduction. However, it would be prudent, for example, to ensure sufficient lighting, avoid slippery floors or rugs and use handrails. Eye tests and a review of medications that reduce alertness or increase fall-related side effects should also be undertaken.

There is evidence that hip-protectors can reduce hip-fracture risk in certain circumstances. However, they are bulky and can be uncomfortable to wear and do not work unless fitted properly.

Exercise is very important, especially weight-bearing exercises, as the bone reacts to forces placed on it to increase strength. However, this is best combined with strength-, flexibility- and balance-related exercises for full joint and bone benefits. Care should be taken in osteoporotic patients that the exercises provide benefits, but does not increase the risk of falls or fracture of already fragile bones. High-impact exercise should be avoided, as well as exercise in which the waist is bent forward or twisted (touching toes or sit-ups, for example), since this puts pressure on the spine, increasing compression fracture risk.

Bone formation

Bone formation is a balance between the activity of osteoblasts, which build bone, and osteoclasts, which destroy it.

A process of bone modelling occurs during childhood and into adulthood to cause an increase in bone length and strength. Remodelling, the replacement of old bone tissue with new, occurs mainly in adulthood in order to maintain bone mass and repair damaged bone.

Bone turnover and calcium homeostasis (regulation of the body's calcium levels) are regulated by various hormones. Parathyroid hormone (PTH), vitamin D and calcitonin are responsible for calcium homeostasis. Growth and sex hormones, glucocorticoids and thyroid hormones operate to control the function, generation and death of bone cells.

Bones continue to form to reach peak bone mass around the age of 30 years, after which BMD starts to decline. There is a marked decrease in BMD following the menopause. Therefore, it is important to ensure that the optimum BMD can be reached with good nutrition and exercise and by avoiding other modifiable risk factors.

References and further information

- *Osteoporosis, Clinical guideline for prevention and treatment, Executive Summary*, National Osteoporosis Guideline Group, March 2014, tinyurl.com/osteoporosis4
- *Osteoporosis: assessing the risk of fragility fracture*, Nice CG146, tinyurl.com/osteoporosis5
- Hip protectors and osteoporosis information leaflet, National Osteoporosis Society, tinyurl.com/osteoporosis6
- *British National Formulary (BNF)* 67, March 2014, bnf.org/bnf/index.htm
- *Falls: assessment and prevention of falls in older people*, Nice CG161, tinyurl.com/osteoporosis7
- *Osteoporosis diagnosis and risk assessment and management*, T Rokib and D Bairstow, *Clinical Pharmacist*, Vol 6, No 4, May 2014, clinicalpharmacist.com
- *SPC Electronic Medicines Compendium*, tinyurl.com/osteoporosis8
- *Vitamin D and Bone Health: A Practical Clinical Guide for Patient Management*, National Osteoporosis Society, tinyurl.com/osteoporosis9
- FRAX Osteoporosis Risk Assessment tool www.shef.ac.uk/frax
- QFracture 2013 risk calculator, qfracture.org
- Osteoporosis information leaflets, tinyurl.com/osteoporosis10

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5 minute test

■ Sign up to take the 5 Minute Test and get your answers marked online: chemistanddruggist.co.uk/update

Take the 5 Minute Test

1. The most common areas affected by osteoporosis are the wrists, hips and spine.
True or false?
2. A T-score of between -1 and -2.5 indicates severe osteoporosis.
True or false?
3. Nice guidelines state that women over 75 may not need a bone scan to diagnose osteoporosis.
True or false?
4. Medical conditions such as rheumatoid arthritis, hyperthyroidism and Cushing's syndrome increase the risk of osteoporosis.
True or false?
5. Bone turnover is regulated by thyroid hormones, glucocorticoids and growth and sex hormones.
True or false?
6. There are no licensed treatments for women below the menopausal age.
True or false?
7. Side effects of bisphosphonates include gastro-intestinal discomfort, headache and musculoskeletal pain.
True or false?
8. Denosumab is administered as a 20mg subcutaneous injection every three months.
True or false?
9. Nice recommends calcitonin as a suitable alternative for patients who are unable to take bisphosphonates.
True or false?
10. The BNF recommends calcium at double the recommended intake to reduce the rate of bone loss in patients with osteoporosis.
True or false?

Tips for your CPD entry on managing osteoporosis

Reflect **What medical conditions increase a patient's risk of osteoporosis? How are bone turnover and calcium levels in the body regulated? What are the side effects of bisphosphonates?**

Plan **This article describes osteoporosis and includes information about how it is diagnosed, risk factors and falls risk assessments. Drug treatments, doses and side effects and non-pharmacological management are also discussed.**

Act **Read the Update article and the suggested reading (below), then take the 5 Minute Test (above). Update and Update Plus subscribers can then access their answers and a pre-filled CPD logsheet at chemistanddruggist.co.uk/mycpd.**

Read about bone biology and biological causes of osteoporosis on the International Osteoporosis Foundation website
tinyurl.com/osteoporosis11
tinyurl.com/osteoporosis12

Read the MUR tips for osteoporosis on the C+D website
tinyurl.com/osteoporosis13

Revise your knowledge of the drugs used in the management of osteoporosis in the BNF Section 6.6 Drugs affecting bone metabolism

Find out how exercise can reduce the risk of osteoporosis on the International Osteoporosis Foundation website
tinyurl.com/osteoporosis14

Learn what advice you can give to prevent falls in at-risk patients on the International Osteoporosis Foundation website
tinyurl.com/osteoporosis15

Evaluate
Are you now confident in your knowledge and management of osteoporosis? Could you give advice to patients about reducing the risks of osteoporosis and falls?

ASK THE EXPERT

June is musculoskeletal month and our expert is on hand to answer your queries. Submit your questions by email to **pooja.sisodia@ubm.com**