Factsheet
Osteoporosis

CPPE
CENTRE FOR PHARMACY POSTGRADUATE EDUCATION

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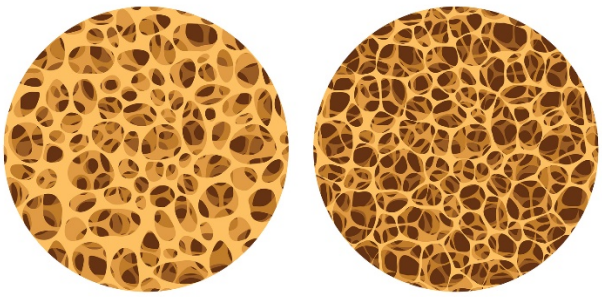
Definition

Osteoporosis is a progressive disease which is characterised by low bone mass, or bone mineral density (BMD), and structural deterioration of bone tissue, and therefore increased bone fragility and risk of fracture.[1]



Osteoporosis is defined by the World Health Organization (WHO) as a BMD of 2.5 standard deviations below the mean average BMD for a healthy 30-year-old adult. It is expressed as a T-score, ie, a T-score less than -2.5 would indicate osteoporosis.[1] A lower T-score means a lower BMD.[2] It should be noted that BMD measurement does not provide information relating to the structural deterioration, and that most osteoporotic fractures occur in women who do not have osteoporosis as defined by a T-score equal to or less than -2.5.[1]

Osteoporotic fractures, which occur as a result of osteoporosis, are classified as fragility fractures. Fragility fractures occur following a low-level trauma; WHO have quantified this as a force equivalent to a fall from standing height or less. The most commonly affected bones are wrist, spine, and hip but fragility fractures may also occur in the arm, pelvis, ribs and vertebrae.[1,3]

Vertebral fractures may occur spontaneously, or as a result of routine activities such as bending or lifting.[1]

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Prevalence and incidence

The National Institute for Health and Care Excellence (NICE) states that in England and Wales, more than 2 million women have osteoporosis,[4] with the prevalence increasing with age from approximately 2 percent at 50 years of age to almost 50 percent at 80 years of age.[3]

Osteoporosis occurs more frequently in women as not only do they suffer from age-related bone loss (which occurs in both men and women), but they experience a decrease in oestrogen production at the menopause which accelerates bone loss.[1,3] Additionally, women generally have a longer life expectancy than men, therefore, bone tissue continues to be lost over a longer period of time.[1]

In the UK, approximately 536,000 new fragility fractures occur each year,[5] and more than one in three women and one in five men will sustain one or more osteoporotic fractures in their lifetime.[1]

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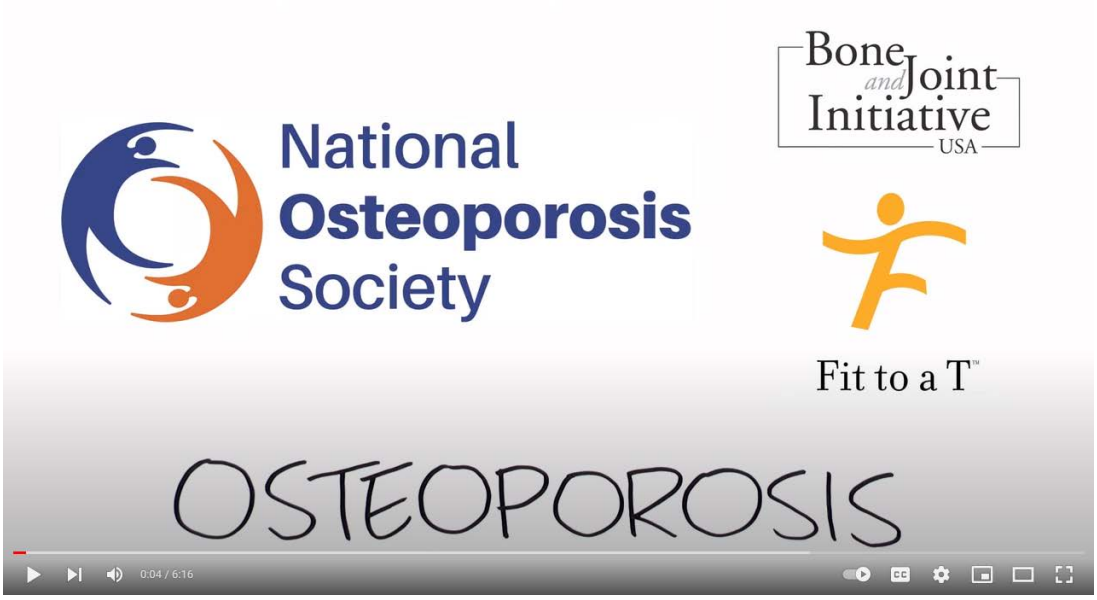
Signs and symptoms

Osteoporosis is asymptomatic and is often diagnosed as a result of a fracture[1]. Vertebral fractures, most of which are osteoporotic, may go unrecognised.[1]

To learn more about osteoporosis, watch the following video:

National Osteoporosis Society - Learn more about osteoporosis with Miriam Margolyes



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Causes/risk factors

Low BMD is one of the key risk factors for osteoporotic fractures but is poor at predicting fracture risk when used without considering other risk factors.[6]

Low body weight: a body mass index of less than 18.5 kg/m² is linked to low BMD. Additionally, older people with low body weight have less fat padding around the hips to cushion the impact of a fall, increasing fracture risk.[6,7]

Smoking: there is evidence to suggest that postmenopausal bone loss is greater in smokers[8], but the risk of osteoporotic fracture is largely independent of BMD.[5,9] Smoking is linked to earlier menopause[9,10] and a lower body weight.[7]

Alcohol: high intake of alcohol is linked to a significant risk of osteoporotic fracture which is largely independent of BMD.[11] Consumption of three or more units of alcohol daily is listed as a risk factor by NICE.[6]

Age: risk increases with age; some of this risk relates to bone loss and increasing fragility, but the effects of age are at least partially independent of BMD.[5,6] In addition, risk of osteoporotic fracture increases with age due to increased falls risk.[7] This can be due to certain medicines, poor vision, balance problems, muscle weakness or other medical conditions.[12]

Gender: risk is higher in women due to increased life expectancy, menopause, and bone size.[7]

Other factors affecting BMD include: endocrine disease, gastrointestinal conditions that cause malabsorption (for example ***inflammatory bowel disease***), ***chronic kidney disease***, chronic liver disease, ***chronic obstructive pulmonary disease*** and immobility.[6]

Other factors independent of BMD include:

- Oral corticosteroids: effect depends on the dose and duration. Corticosteroids can reduce bone formation by inhibiting the gene transcription of osteoblasts and can also reduce osteocyte viability (see pathophysiology section for more information on osteoblasts and osteoclasts). The risk of a fracture is highest during the first few months after starting treatment with a corticosteroid.[13]
  To learn more about corticosteroid-induced osteoporosis, read Sections *3.5.13 Glucocorticoids* and *7.5 Glucocorticoid-induced osteoporosis* of the Scottish Intercollegiate Guidelines Network guideline 142*,* ***Management of osteoporosis and the prevention of fragility fractures***, which also includes information on other medicines that increase fracture risk. Also access The Open Respiratory Medicine Journal article, ***Inhaled corticosteroids and bone health***.
- Previous fragility fracture: after one osteoporotic fracture, risk increases by two to three times. Risk also increases with increasing number of previous fractures.[1,6,7]
- Rheumatological conditions such as rheumatoid arthritis, and other inflammatory bone diseases.
- Parental history of hip fracture.[6]

Risk factors affecting bone strength that have unestablished mechanisms include the use of selective serotonin reuptake inhibitors, proton pump inhibitors and anticonvulsant drugs, in particular enzyme-inducing drugs, such as carbamazepine.[6]

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Pathophysiology (mechanism of disease)

A person acquires bone mass up to adolescence, where it reaches a peak, and then is maintained throughout adulthood. The combination of the process of bone acquisition and the process of bone maintenance results in a person's current BMD. If the amount of bone mass that is acquired up to adolescence is lower than normal, this can reduce BMD, additionally BMD is reduced by disruption to the process of bone remodelling. If the process of bone remodelling works well, then this maintains bone mass.

Osteoporosis is a result of abnormal bone remodelling (and can be worse if normal peak bone mass is not achieved). The diagram below shows the bone remodelling cycle. If this ordered process is functioning well, then it will keep bone tissue healthy.[14]

The bone remodelling process

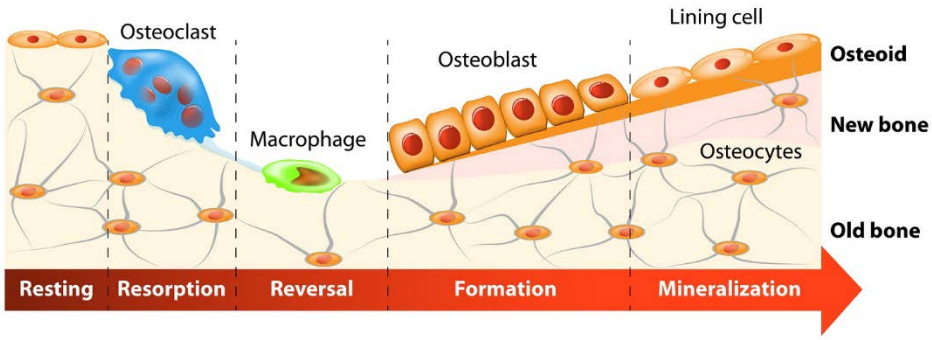

Image taken from ***Lights and shadows of NSAIDs in bone healing: the role of prostaglandins in bone metabolism.***[15]

Cells called osteoblasts are activated by endocrine signals (hormones and interleukins). They work to form new bone in a carefully ordered matrix while releasing signals that cause osteoclast cells to co-ordinate bone resorption (digestion of bone tissue). This process is complex and delicately balanced.

In osteoporosis the balance is shifted, osteoblast activity is reduced which results in loss of bone tissue.[14,16]

During mineralisation, phosphate and calcium are added to the bone matrix to strengthen it, and during the process of resorption, calcium and phosphate are released from the bone tissue into circulation. This complicated process is partly a way of ensuring that circulating calcium and phosphate levels are maintained.

There are three hormones which regulate calcium levels and play an important role in bone health:

- parathyroid hormone (PTH), which maintains the level of calcium in the blood and stimulates both resorption and formation of bone tissue
- calcitriol, a hormone derived from vitamin D, which stimulates the intestines to absorb enough calcium and phosphorus (it also acts on the bone directly)
- calcitonin, which inhibits bone breakdown and is important for maintaining bone development and normal blood calcium levels in early life.[17]

To learn more about this process and the pathophysiology of osteoporosis, access the following:

- The Annual Review of Pathology: Mechanisms of Disease article, ***Disorders of bone remodeling***.
- The Endotext [Internet] article, ***The epidemiology and pathogenesis of osteoporosis***.

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Prognosis and complications

One of the most serious complications associated with osteoporosis is hip fracture, which nearly always leads to hospitalisation. It is fatal in 20 percent of cases and permanently disables half of those affected.[3]

Treatment of hip fracture usually involves surgery and potentially a hip replacement. Visit the NHS website to learn more about ***hip fracture treatment*** and ***hip replacement***.

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Diagnosis/detection

As previously stated, osteoporosis is often undiagnosed until a fracture occurs. However, WHO and the International Osteoporosis Foundation recommend that dual-energy X-ray absorptiometry (DXA) scanning of the femoral neck to measure BMD (T-score) may be used to aid diagnosis.[5]

DXA scans may be used before a fracture occurs in those with risk factors, or after a fracture to determine if it is osteoporotic and to help determine risk of further fractures. The results are then used to aid risk assessment and diagnosis, along with assessment of other factors.[3] Women with a prior fragility fracture should be considered for treatment without the need for further assessment, although BMD measurement is sometimes appropriate, particularly in younger postmenopausal women.[5]

Fragility fracture risk is usually calculated before offering a DXA scan. NICE recommends that the predicted risk of major osteoporotic or hip fracture over ten years, expressed as a percentage, is calculated using either the **QFracture® risk calculator** or the **FRAX® tool**.

Fracture risk should be considered in women aged 65 years and over, and in men aged 75 years and over, or in patients below these ages who have risk factors for fractures. Fracture risk should not routinely be considered in patients aged below 50 unless they have a major risk factor.[3] To learn more about risk assessment with these tools, access the following NICE guidance ***Osteoporosis: assessing the risk of fragility fracture*** **[CG146]**.

To learn more about risk assessment in osteoporosis, visit the following NICE clinical knowledge summary (CKS) page, ***Osteoporosis - prevention of fragility fractures. Scenario: Assessment*****.**

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Pharmacological treatment

After clinical assessment, interpretation of the results of the risk assessment tools and BMD (if measured), a clinician may recommend pharmacological treatment to reduce the risk of fracture.

Pharmacological treatments include bisphosphonates, non-bisphosphonates, calcitriol and hormone replacement therapy (HRT). [5]

Bisphosphonates increase bone mineral density by altering the activity of osteoclasts[5] and are recommended if a person has no contraindications, as outlined in the *British National Formulary* (BNF). This class of medicines includes:

- alendronate (alendronic acid) 10 mg once daily (licenced for postmenopausal women and men, and glucocorticoid-induced osteoporosis)[5]

- alendronate (alendronic acid) 70 mg once weekly (licenced for postmenopausal women and glucocorticoid-induced osteoporosis)
- risedronate (risedronic acid) 5 mg once daily (licenced for postmenopausal women and glucocorticoid-induced osteoporosis)
- risedronate (risedronic acid) 35 mg once weekly (licenced for postmenopausal women and men).[18]

It is important to explain to people how to use bisphosphonates and the risks associated with them. Medication reviews with patients, or their clinical notes should include a review of the bisphosphonate treatment, taking into account the appropriate length of time for treatment. More information on the directions for administration of bisphosphonates can be found in the ***BNF*** under the individual monographs.[19]

One of the risks that should be communicated to people taking bisphosphonates is osteonecrosis of the jaw and external auditory canal. This risk is dependent on bisphosphonate potency, route of administration, dose, treatment duration, smoking and other medical conditions.[19] One of the ways that the risk of this can be reduced is by maintaining good oral hygiene. Additionally, it is recommended that patients visit their dentist before initiating bisphosphonates and any necessary dental treatment should be carried out before starting or at the start of treatment with bisphosphonates.[19] More information on how good oral health can be maintained for those in care homes can be found in NICE guidance ***Oral health for adults in care homes [NG48]***.

More information on the risks associated with bisphosphonates and information about dose adjustment in impaired renal function can be found in the ***BNF*** under the individual monographs, or on the following NICE CKS page, ***Osteoporosis - prevention of fragility fractures, Bisphosphonates, Advice*.**

If a person cannot tolerate oral bisphosphonates, or they are contraindicated, then a specialist may initiate treatment with zoledronic acid (a bisphosphonate administered annually by intravenous infusion),[20] or non-bisphosphonate: raloxifene (selective oestrogen receptor modulator), denosumab (monoclonal antibody), or teriparatide[18] (synthetic parathyroid hormone). Note that strontium ranelate is no longer recommended,[5] following a decision by its manufacturers to stop marketing and supply of this treatment.

Dietary **calcium** intake should be between 700 mg and 1200 mg per day. If a person is not receiving enough calcium in their diet, they should be offered a supplement containing vitamin D and at least 1000 mg of calcium daily.[5,18]

Vitamin D can be offered if a person's calcium intake is low. Calcium and 10 micrograms colecalciferol (400 international units) per day is recommended as standard, or 20 micrograms (800 international units), for postmenopausal women and men over 50 years at increased risk of fracture, and elderly people who are housebound or living in a care home.[5,19] If dietary intake of calcium is adequate but a person is not exposed to much sunlight, 10 micrograms (400 international units) of vitamin D can be offered without calcium.[18] The above should be prescribed based on local guidance. It should be appreciated that Vitamin D supplementation should also be considered for all during the winter months, as well as in people taking antiepileptic drugs.

HRT may be offered to women who experience a premature menopause before 40 years of age. This treatment has been shown to reduce the risk of frailty fractures in addition to relieving menopausal symptoms.[18]

For more detailed information access the following documents:

- Further information about the therapies discussed, monitoring requirements, and osteoporosis as a whole is available in this National Osteoporosis Guideline Group guideline, ***NOGG 2021: Clinical guideline for the prevention and treatment of osteoporosis***.
- Access the following guideline for more information about calcium and vitamin D treatment and monitoring: Royal Osteoporosis Society. ***Vitamin D and bone health: A practical clinical guideline for patient management.*** 2020.
- To learn more about the mechanism of action of synthetic parathyroid hormones (eg, teriparatide), visit the following Scandinavian Journal of Clinical and Laboratory Investigation article, ***Mechanisms for the bone anabolic effect of parathyroid hormone treatment in humans***.
- Further guidelines:
    - Scottish Intercollegiate Guidelines Network. ***Management of osteoporosis and the prevention of fragility fractures***. June 2020.
    - NICE quality standard. ***Osteoporosis*** **[QS149]**. 2017.
    - NICE technology appraisal guidance. ***Bisphosphonates for treating osteoporosis*** **[TA464]**. 2019.
    - NICE technology appraisal guidance. ***Raloxifene for the primary prevention of osteoporotic fragility fractures in postmenopausal women*** **[TA160]**. 2018.
    - NICE technology appraisal guidance. ***Raloxifene and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women*** **[TA161]**. 2018.
    - NICE technology appraisal guidance. ***Denosumab for the prevention of osteoporotic fractures in postmenopausal women*** **[TA204]**. 2010.
    - NICE CKS. ***Vitamin D deficiency in adults - treatment and prevention***. January 2022.
    - Drug Safety Update. ***Anti-epileptics: Adverse effects on bones***. April 2014.

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Non-pharmacological treatment

People should be advised to:

- eat a balanced diet to maintain a healthy weight (this advice is based on expert opinion as there is no evidence linking specific diet to fracture risk)
- stop smoking
- drink alcohol only within recommended limits
- take exercise as much as possible to improve muscle strength and reduce falls risk. Recommended exercise includes a combination of walking (preferably outdoors to increase exposure to sunlight and vitamin D production), strength training and weight-bearing exercise, and flexibility training.[18,21]

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Patient support

The **Royal Osteoporosis Society** has lots of information and support for people who are at risk of or suffer from osteoporosis, including **a local support group finder.**

The NHS also has a dedicated ***Osteoporosis*** page.

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Further resources

The Royal Osteoporosis Society offer the following free online training: ***Osteoporosis resources for primary care***. This resource is aimed at those working in primary care and gives a more detailed overview of the condition and its management.

All Wales Medicines Strategy Group have produced guidance to support the safe use of long-term oral bisphosphonate therapy.

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External websites

CPPE is not responsible for the content of any non-CPPE websites mentioned on this page or for the accuracy of any information to be found there.

All web links were accessed on 12 February 2023.

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