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Section 1 **Ambulatory office practice**

Chapter 1

Osteoporosis

Tamara J. Vokes

Key points

- Osteoporosis is asymptomatic until a fracture occurs; making the diagnosis and initiating treatment in the presymptomatic stage may prevent fractures.
- Measurement of bone mineral density (BMD) is a good but not perfect predictor of fractures. Introduction of the FRAX tool, which combines clinical risk factors and BMD, has improved assessment of fracture risk and therapeutic decision making.
- Secondary causes of osteoporosis (e.g. osteomalacia or hyperparathyroidism) should be considered in the evaluation of a patient with low BMD and fractures.
- Several effective therapies that improve BMD and reduce fracture risks are available; the choice of the drug should be individualized.
- Pregnancy and lactation are associated with demineralization of the mother's skeleton, which is fully restored after weaning; consequently, multiparity is not a risk factor for osteoporosis.

Introduction

Osteoporosis is a systemic skeletal disorder characterized by compromised bone strength (Fig. 1.1) and an increased risk of fracture.[1] This susceptibility to fractures occurs at considerably lower levels of trauma in osteoporotic subjects than in those with normal bone. The osteoporotic fracture is, therefore, defined as a fracture that occurs from a fall from standing height during normal physical activity. Although the typical osteoporotic fractures are those of the wrist, vertebrae, and hip, almost any fracture is dependent on the quantity and quality of bone. The problem with the fracture-based definition of osteoporosis is that fractures occur relatively late in the course of the disease and have long-term consequences that are largely irreversible. This suggests a need for using surrogate markers for osteoporosis such as the finding of low bone mass, which usually is present during the long asymptomatic phase of the disease. Introducing this concept into the understanding of osteoporosis allows recognition of the disease before fracture occurs and the use of diagnostic criteria based on bone mineral density (BMD) for osteoporosis (Table 1.1).[2,3] More recently, realization that the fracture risk is determined not just by BMD but also by other clinical characteristics has led to the development of FRAX model, a clinical tool for predicting fracture probability based on BMD and clinical risk factors.[2]

The evolution of the human skeleton has resulted in bones that are light enough to allow adequate mobility and strong enough to avoid disabling fractures during the reproductive years. However, with advancing age in both sexes, and particularly after the menopause in women, bone becomes weaker and neuromuscular function declines. These changes produce a dramatic increase in the risk of fracture, which is the only symptom of osteoporosis. Osteoporotic fractures are a major public health problem as they are a significant cause

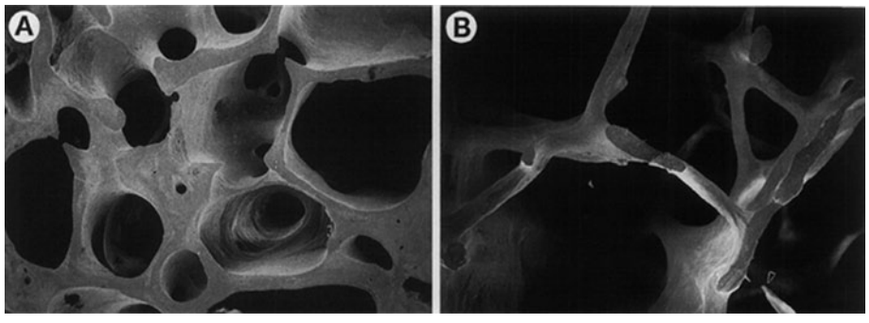

Fig. 1.1 Scanning electron micrographs of normal (A) and osteoporotic (B) cancellous bone from human iliac crest. Note that the osteoporotic bone has both lower mass and altered bone microarchitecture. (From Dempster DW. The contribution of trabecular architecture to cancellous bone quality. *J Bone Miner Res* 2000;15:20–23. Reproduced with permission from the American Society for Bone and Mineral Research.)

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Table 1.1 World Health Organization definition of osteoporosis based on bone mineral density

Category	Bone mineral density	T-Score
Normal	No more than 1SD below the young adult mean	>–1
Osteopenia	1–2.5SD below the young adult mean	–1 to –2.5
Osteoporosis	More than 2.5SD below the young adult mean	<–2.5
Severe (established) osteoporosis	More than 2.5 SD below the young adult mean and at least one fragility fracture	<–2.5

From National Osteoporosis Foundation, 1993.[3]

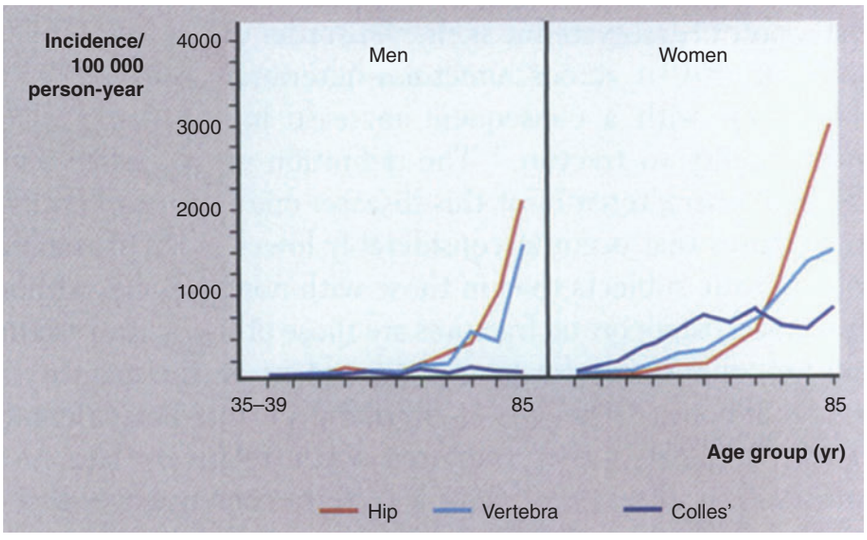

Fig. 1.2 Age-specific incident rates for hip, vertebral, and distal forearm fractures in men and women. (From Melton LJ. Epidemiology of fractures. In Riggs BL, Melton LJ [eds.] *Osteoporosis: Etiology, Diagnosis and Management*. New York: Raven Press, 1988, pp. 133–154.)

of disability in the aging population and a major contributor to the cost of healthcare in many countries.

Epidemiology and clinical presentation

Osteoporosis is a common disease. Currently, an estimated 10 million Americans ≥50 years of age have osteoporosis according to World Health Organization (WHO) criteria, while over 33 million more have "osteopenia." The total number with low bone mass could reach 61 million by 2020. Consequently, the estimated 2 million osteoporosis-related fractures in 2005 could exceed 3 million by 2025, with an associated increase in cost from US$16.9 billion to $25.3 billion annually.[4] In 2000, there were an estimated 9 million osteoporotic fractures worldwide, including 1.6 million at the hip, 1.7 million at the forearm, and 1.4 million clinical (symptomatic) vertebral fractures.[5] The annual cost of osteoporotic fractures has been estimated at $20 billion in the USA and €30 billion in the European Union. A Caucasian woman aged 50 years has a 40% chance of having at least one of the typical osteoporotic fractures during her lifetime and a 70% chance if fractures other than spine, hip, and wrist are considered (e.g. pelvic, humeral, tibial, and other fractures). The probability of fracture in men is about one-third that of women. Because women have a higher fracture risk and because they live longer, they account for 80% of all hip fractures. Although the fracture probability is overall lower in African-Americans, they too will suffer fractures if they have low bone mass.

Hip fractures are the most devastating and costly consequence of osteoporosis. Most require hospitalization and surgical intervention, which are often associated with thromboembolic, cardiovascular, and infectious complications. The high rate of these complications is at least in part linked to the advanced age of the subjects who sustain hip fractures. As a result, during the first year following hip fractures, there is an excess mortality of approximately 36% in men and 21% in women, greater in older men and in those with higher level of comorbidities or declining cognitive function. In those who survive, there is often residual disability or decline in functional status, resulting in a loss of independence that necessitates nursing home admission in almost 50% of patients. The degree of functional recovery is inversely proportionate to age and prefracture functional status.

The incidence of hip fractures increases exponentially with age (Fig. 1.2). There is significant geographic variation in the rates of hip fractures (Fig. 1.3). In addition, the rates are higher in urban than in rural areas, probably because urbanization

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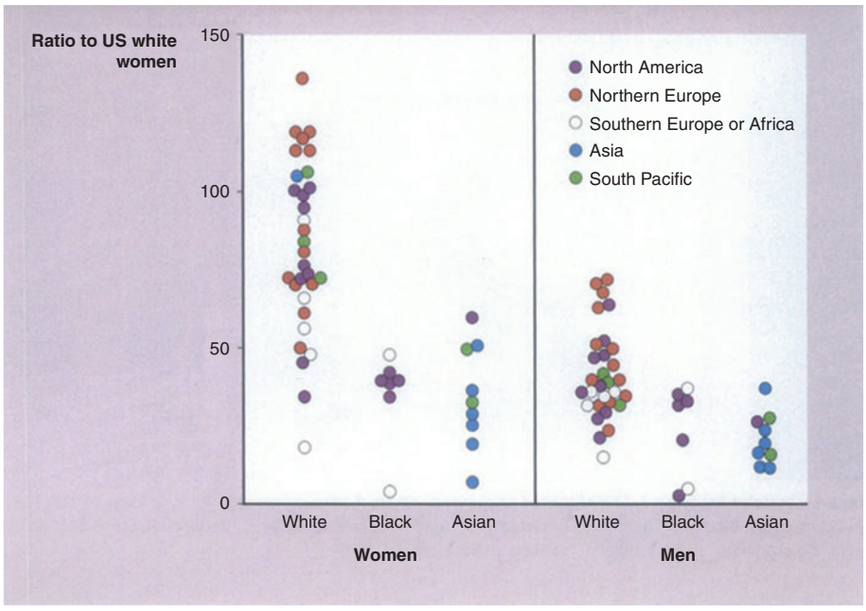

Fig. 1.3 Geographic variation in hip fracture incidence. (From Melton LJ III. Differing patterns of osteoporosis across the world. In Chesnut CH III [ed.] Proceedings of the Second Asian Symposium on Osteoporosis: New Dimensions in Osteoporosis in the 1990s, 1990. Hong Kong, Asia Pacific Congress Series No. 125, *Excerpta Medica*, 1991, pp. 13–18.)

results in decline in physical activity and because change from softer ground to hardwood, tile, concrete, and asphalt surfaces increases the impact of falling. The rates of hip fracture are increasing worldwide, because of the aging population and because of an absolute increase in age-adjusted hip fracture rates. The most likely explanation for this is a decline in physical activity and possibly increased frailty of the aging population. More recently however, there has been a decline in the hip fracture rates in Western countries,[6–8] but a continued increase in Asian countries. The reasons for the decline in hip fracture rates in the industrialized countries are not clear but may include better nutrition and overall health status, higher body weight of the population, or improved recognition and management of osteoporosis.

Vertebral fractures usually occur in the course of routine daily activities, with only one-quarter resulting from a fall. Although approximately 500 000 vertebral fractures occur each year in the USA, most are not clinically apparent; only about one-third of fractures that are found on radiographs come to medical attention and less than 10% require hospital admission. Interestingly, even when a vertebral fracture is present on the radiograph it often is not mentioned by the radiologist, is not noted in the chart, and does not lead to diagnosis or treatment of osteoporosis.[9] Although vertebral fractures are often undiagnosed, they are commonly associated with significant morbidity and increased mortality. Multiple fractures lead to height loss and kyphosis, chronic pain resulting from altered biomechanics of the kyphotic back, restrictive lung disease resulting from decreased thoracic cavity, and digestive complaints of early satiety, gastroesophageal reflux, and constipation resulting from decreased volume of the abdominal cavity (Fig. 1.4). Vertebral fractures should be suspected in older people with kyphosis or height loss of

Fig. 1.4 Vertebal fractures. MRI of the thoracic and lumbar spine showing multiple vertebral fractures (T7, T11, T12, L1, and L2).

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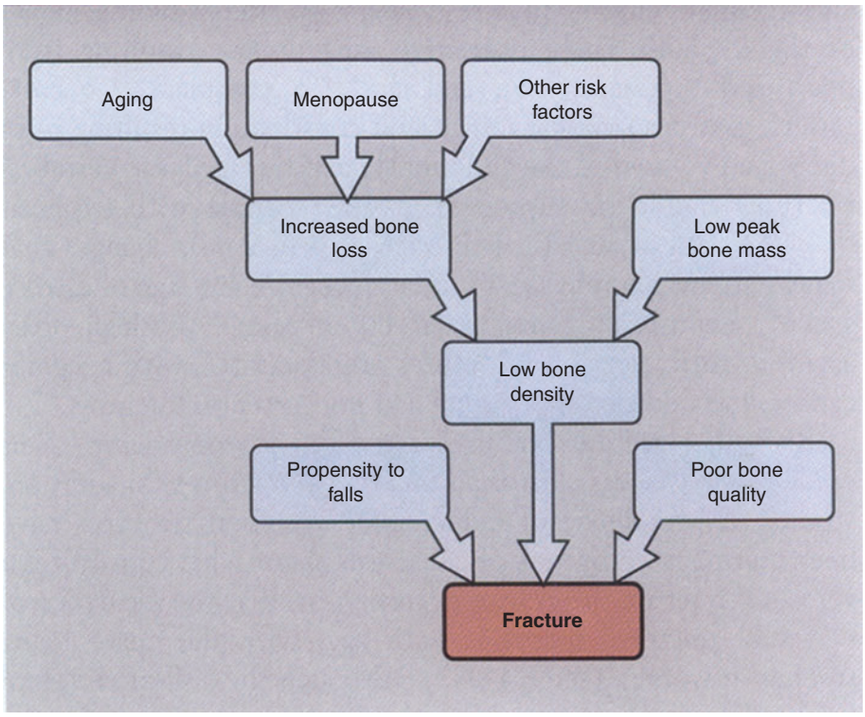

Fig. 1.5 Pathogenesis of osteoporotic fractures.

at least 4–5 cm (1.5–2 in), changes that many patients and physicians fail to recognize as a sign of disease and erroneously attribute to effects of aging. Other clinical consequences are breathing difficulties, reflux and other gastrointestinal symptoms, and depression. Although often asymptomatic, vertebral fractures are associated with a significant risk of additional vertebral and non-vertebral fractures (reviewed by Cummings and Melton[10]).

Because vertebral fractures are often asymptomatic, their epidemiology is less clear than that of hip fractures. In addition, studies of prevalence of radiographic vertebral fractures have been complicated by lack of consensus about what constitutes a vertebral fracture. It is clear, nevertheless, that the incidence of vertebral fractures increases with age, with the curve being steeper in women (Fig. 1.2). Although the risk of vertebral fractures is about three times higher in women over 65 years of age, the prevalence is similar in men and women aged 50 to 60 years, possibly reflecting a higher risk of traumatic vertebral fractures in younger men as a result of greater occupational and recreational physical activity. There is less geographic variability in the risk of vertebral fractures compared with hip fractures.[11]

Distal forearm fractures almost always follow a fall on the outstretched arm. Because this pattern of falling is seen in younger people (in comparison with the elderly, who tend to fall to the side or backward and sustain a hip fracture), the peak incidence of these fractures in Caucasian women is between ages 40 and 65 (Fig. 1.2). The main importance of wrist fracture is that it often is a first manifestation of osteoporosis, which should prompt appropriate evaluation and therapy.

Pathogenesis

Osteoporosis or low bone mass can result from inadequate accumulation of bone in young adulthood (low peak bone mass) or excessive bone loss later in life (Fig. 1.5). The increase in bone mass that occurs during childhood and puberty results from a combination of bone growth at the endplates (endochondral bone formation) and change in bone shape (modeling). The rapid increase in bone mass during puberty associated with an increase in sex hormone levels continues for 3 to 4 years and then slows down with the closure of growth plates. Further increase in BMD in the next several years is relatively modest and the consequence of periosteal apposition (modeling). The peak bone mass is achieved by age 20 to 30 and is greater in men than in women and greater in African-American than in Caucasian, Asian, or Hispanic populations. Genetic factors are the main determinants of peak bone mass and account for 50–85% of the variance in bone density and size. It is likely that several genes regulate bone mass, each with modest effect.[12] Non-genetic factors associated with low peak bone mass include low calcium intake during childhood, low body weight, sedentary lifestyle, chronic disease, and delayed puberty. Anorexia

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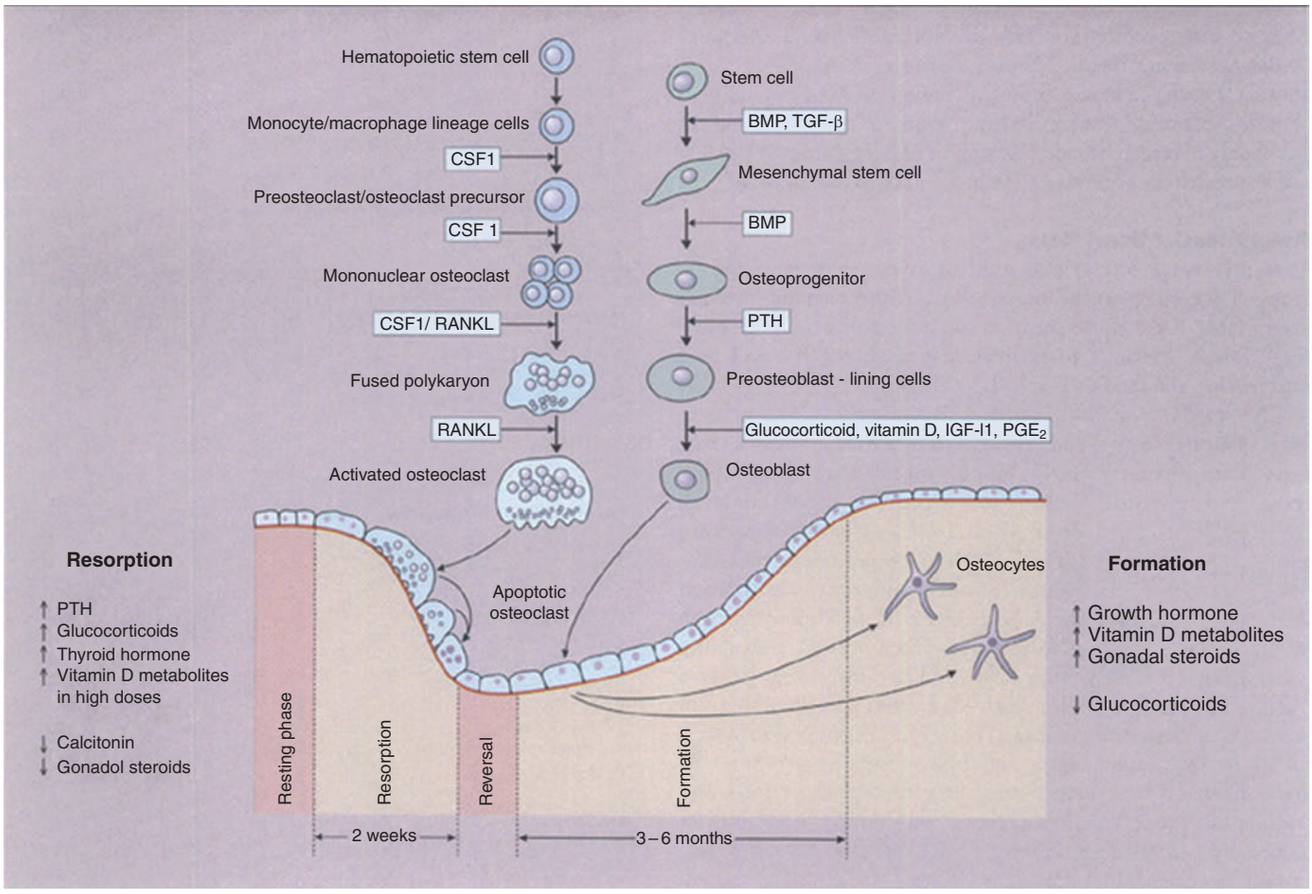

Fig. 1.6 Bone remodeling. Note that the resorption phase lasts approximately 2 weeks, whereas the formation phase requires 3 to 6 months for completion. As a result, conditions associated with increased bone turnover often result in a net loss of bone. Osteoclast is a tissue-specific macrophage polykaryon created by the differentiation of the monocyte/macrophage precursor cells at or near bone surface. One of the main physiological regulators of osteoclast differentiation and function is RANKL, which binds to RANK on the surface of the osteoclast and its precursors. RANKL is transmembrane protein expressed on osteoblasts, as well as secreted into the surrounding extracellular fluid. Osteoblasts also produce a soluble factor osteoprotegerin (OPG), which acts as a decoy receptor for RANKL and decreases osteoclast-mediated bone resorption. BMP bone morphogenic protein; CSF, colony-stimulating factor; IGF-I, insulin-like growth factor-1; PGE_2, prostaglandin E_2, PTH, parathyroid hormone; RANKL, receptor activator of nuclear factor-κB ligand; TGF-β, transforming growth factor-β.

nervosa may be the most common acquired cause of low peak bone mass, which has its effects through loss of sex steroids, excess cortisol, poor nutrition, and low body weight. Although many of affected girls eventually recover and resume menses, they never achieve their genetically determined peak bone mass because they miss the fixed window of opportunity during which the adolescent bone growth occurs. Consequently, they often develop osteoporosis and have a lifelong increase in fracture risk.

After the peak bone mass is attained, further changes in bone, including bone loss associated with aging and menopause, are determined by bone remodeling (Fig. 1.6). Bone remodeling is responsible for repair of microdamage of bone, maintenance of skeletal strength, and supply of calcium from the skeleton when needed to maintain normal serum calcium. Bone remodeling involves osteoclast-mediated bone resorption followed by osteoblastic bone formation. The initial stimulus is often a microcrack, which leads to *activation* – recruitment and fusion of osteoclast precursors into mature osteoclast. The mature osteoclast then attaches to the bone surface by binding with the ruffled border. *Resorption* of bone trapped by the osteoclast produces a cutting cone (cortical bone) or a trench (trabecular bone). Bone resorption is followed by *bone formation*, the process during which osteoblasts synthesize bone matrix, which subsequently mineralizes. After the matrix fills a resorption cavity, osteoblasts remain trapped in the bone and become osteocytes. The latter are believed to be responsible for mechanotransduction and bone response to mechanical loading. While the process of osteoclastic bone resorption of a single cavity usually takes approximately 2 weeks, osteoblastic bone formation requires 3 to 6 months to fill in a resorption pit. Consequently, any physiological or pathological process (e.g. decrease in estrogen level during menopause) that increases activation frequency (rate of initiation of new bone remodeling cycle) results in a net loss of bone. Numerous

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circulating or locally produced factors influence bone remodeling (Fig. 1.6). Imbalance in bone remodeling (i.e. greater resorption than formation) results in bone loss. This manifests as increased cortical porosity in cortical bone and perforation of trabecular plates in trabecular bone. These processes greatly diminish the biomechanical competence of the aging skeleton. Multiple diseases and medications are associated with these processes (Table 1.2). Therapeutic agents used to treat osteoporosis act primarily by either decreasing bone resorption ("antiresorptive agents") or increasing bone formation ("anabolic agents").

Diagnosis

Because osteoporosis is largely asymptomatic, it is necessary to diagnose bone fragility before fractures occur. Since bone mass is the major determinant of fracture risk, its measurement is the mainstay of diagnosing osteoporosis.

Assessment of bone mass

In the USA, the standard method used for assessment of bone mass in both clinical practice and the research setting is dual energy X-ray absorptiometry (DXA) of the central sites (i.e. lumbar spine and proximal femur).[13] The reason that central DXA is the method of choice is its high precision and a large body of data relating its measurements, particularly for the femoral neck, to fracture risk. Measurement of bone mass at peripheral sites such as distal radius, calcaneus, and phalanges is widely available and less costly.[13] Although peripheral measurements can be used for assessment of fracture risks in population studies, their use in making a diagnosis of osteoporosis in an individual is problematic because their fracture prediction ability is lower than that of central BMD and because the proportion of patients with T-score less than –2.5 varies considerably from one type of device to another (Fig. 1.7).[14] Because of lower precision and lack of adequate prospective data, peripheral measurements should not be used for monitoring therapy.[13]

Quantitative computed tomography (CT) scans of the spine can also be used for assessing bone mass.[13] The advantage of CT scans is that they are three dimensional, permitting a separate assessment of trabecular and cortical bone. In addition, arthritic changes of the spine, which falsely elevate DXA, do not affect CT measurement. The disadvantages of CT include high cost and high radiation exposure, competing needs for clinical scanners and, most importantly, lack of standardized data regarding the ability of the CT measurements to predict fractures. Applying WHO BMD criteria for osteopenia and osteoporosis to CT measurements leads to a tendency to overdiagnose osteoporosis in younger women. The difficulties associated with CT measurements largely limit its application to that of a research tool. When CT measurements are used in clinical practice, care should be taken that WHO criteria are not strictly applied.

Numerous studies have documented a strong inverse relationship between fracture risk and central, particularly hip, BMD,[15,16] making DXA measurement the gold standard for assessing bone mass and predicting fracture risk. Several organizations have produced recommendations for selecting individuals for bone density testing (Table 1.3).[2,13,17] Most agree that testing is recommended for women over 65 and men over 70 years and in younger people if they have a fragility fracture or risk factors for fractures.

Bone mineral density is measured at the lumbar spine and proximal femur. Spine DXA measures BMD of the L1–L4 vertebrae. Since vertebrae are composed primarily of metabolically active trabecular bone, this site is more likely to show the earliest changes in menopause, during exposure to glucocorticoids, and in response to therapy. A potentially limiting factor of spine DXA is that spine BMD is measured in the anteroposterior projection, which includes the mineral in the posterior elements and facet joints and calcifications in the abdominal aorta, none of which contribute to the mechanical strength of the vertebrae. For this reason, the spine BMD is often artifactually elevated in elderly subjects, which is only partly remedied by exclusion of artifact-laden vertebrae when interpreting it (Table 1.4).[13]

The proximal femur (hip) has more cortical bone than the spine and is less likely to show large changes with therapy. Since hip BMD is not affected by the artifacts that may affect spine BMD, it may be a more reliable site for measuring BMD in patients over 65 years of age. Bone density of the hip is the best predictor of the risk of hip fractures and indeed of overall fracture risk.[15] Several regions of interest of the proximal femur can be used for diagnosis (Table 1.4).[13]

For each patient, BMD is compared with two sets of normative data. First, it is compared with BMD obtained in the healthy young adult Caucasian population, which yields a T-score (the number of standard deviations above or below the young adult mean). The T-score is used for diagnosing osteopenia and osteoporosis because it is the best predictor of fracture risk. The second comparison is to an age-, race-, and sex-matched population and is the basis for calculating the Z-score (the number of standard deviations above or below the mean of the age-, race-, and sex-matched population). While a low Z-score (below –1.5 or –2) is thought to suggest the presence of secondary causes of osteoporosis, no studies support that belief.

The WHO criteria for diagnosing osteoporosis and osteopenia based on BMD measurements (Table 1.1) are applicable only to postmenopausal women and men over 50 but not in younger subjects (Table 1.5).[13] T-scores can also be applied to women in menopausal transition (perimenopause).[13] In premenopausal women and men with low bone mass, particularly if associated with fracture, a thorough search for secondary causes should be undertaken.

Role of clinical risk factors

Bone mineral density accounts for approximately 80% of fracture risk in population studies, and in vitro biomechanical testing confirms the importance of bone mass in determining

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Table 1.2 Diseases and medications associated with osteoporosis/low bone mass

Types	Conditions
Hypogonadal states (primary or secondary)	Amenorrhea Hyperprolactinemia Anorexia nervosa Turner syndrome Kleinfelter syndrome
Endocrine disorders	Cushing syndrome Hyperparathyroidism, primary Thyrotoxicosis Idiopathic hypercalciuria Insulin-dependent diabetes mellitus Acromegaly Hypopituitarism
Nutritional and gastrointestinal disorders	Malnutrition Parenteral nutrition Malabsorption syndromes Crohn disease Gastrectomy Liver diseases (biliary cirrhosis)
Rheumatological disorders	Rheumatoid arthritis Ankylosing spondylitis
Malignant and hematological disorders	Multiple myeloma Lymphoma and leukemia Tumors with ectopic parathyroid hormone-related protein production Mastocytosis Thalassemia Hemophilia
Inherited and miscellaneous conditions	Pregnancy and lactation (transient) Osteogenesis imperfecta Scoliosis Marfan syndrome Hemochromatosis Hypophosphatasia Glycogen storage diseases Immobilization Multiple sclerosis Weight loss Porphyria
Medications	Glucocorticoids Anticonvulsants Alcohol Chemotherapy/immunosuppression Cyclosporine Excess thyroid hormone Gonadotropin-releasing hormone agonists Progestin contraception (depo-medroxyprogesterone acetate) Heparin Lithium Aluminum Excess vitamin A Tobacco Tamoxifen (premenopausal women) Bile acid–binding resins (?)

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Table 1.3 Indications for bone mineral density testing according to different societies

National Osteoporosis Foundation[2]	International Society for Clinical Densitometry[13]	US Preventive Task Force[17]
• Women aged ≥65 and men aged ≥70, regardless of clinical risk factors • Younger postmenopausal women and men aged 50–69 about whom there is concern based on their clinical risk factor profile • Women in the menopausal transition if there is a specific risk factor associated with increased fracture risk such as low body weight, prior low-trauma fracture, or high-risk medication • Adults who have a fracture after age 50 • Adults with a condition (e.g. rheumatoid arthritis) or taking a medication (e.g. glucocorticoids in a daily dose ≥ 5 mg prednisone or equivalent for ≥3 months) associated with low bone mass or bone loss • Anyone being considered for pharmacological therapy for osteoporosis • Anyone being treated for osteoporosis, to monitor treatment effect • Anyone not receiving therapy in whom evidence of bone loss would lead to treatment • Postmenopausal women discontinuing estrogen	• Women aged ≥65 • Postmenopausal women aged <65 with risk factors for fracture • Women during the menopausal transition with clinical risk factors for fracture, such as low body weight, prior fracture, or high-risk medication use • Men aged ≥70 • Men aged <70 with clinical risk factors for fracture • Adults with a fragility fracture • Adults with a disease or condition associated with low bone mass or bone loss. • Adults taking medications associated with low bone mass or bone loss • Anyone being considered for pharmacological therapy • Anyone being treated for bone loss, to monitor treatment effect • Anyone not receiving therapy in whom evidence of bone loss would lead to treatment	Women aged ≥65 years and younger women whose fracture risk is equal to or greater than that of a 65-year-old white woman who has no additional risk factors

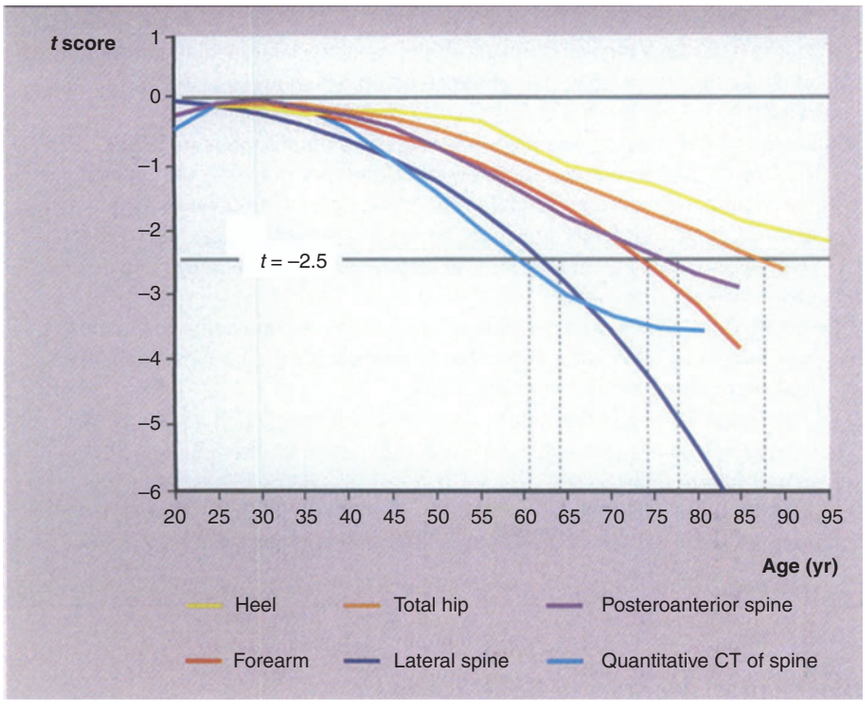

Fig. 1.7 Prevalence of osteoporosis, defined as T-score of –2.5 and below, depends on the site and technique used to assess bone mass. (From Faulkner *et al.*, 1999.[14])

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Table 1.4 Use of central dual-energy X-ray absorptiometry for diagnosis of osteoporosis[a]

Sites	Measurements
Skeletal sites to assess	Measure BMD at both posteroanterior spine and hip in all patients Forearm BMD should be measured under the following circumstances: • hip or spine cannot be measured or interpreted • patient has hyperparathyroidism • very obese patient (over weight limit for scanning table)
Spine region of interest	Use posteroanterior L1–L4 for spine BMD measurement BMD-based diagnostic classification should not be made using a single vertebra If only one evaluable vertebra remains after excluding other vertebrae, diagnosis should be based on a different valid skeletal site Anatomically abnormal vertebrae may be excluded from analysis if: • they are clearly abnormal and non-assessable within the resolution of the system, or • there is more than a 1.0 T-score difference between the vertebra in question and adjacent vertebrae When vertebrae are excluded, the BMD of the remaining vertebrae is used to derive the T-score Lateral spine should not be used for diagnosis, but may have a role in monitoring
Hip region of interest	Use femoral neck, or total proximal femur whichever is lowest BMD may be measured at either hip There are insufficient data to determine whether mean T-scores for bilateral hip BMD can be used for diagnosis The mean hip BMD can be used for monitoring, with total hip being preferred
Forearm region of interest	Use 33% radius (sometimes called one-third radius) of the non-dominant forearm for diagnosis Other forearm ROI are not recommended Use total proximal femur, femoral neck, or trochanter, whichever is lowest

BMD, bone mineral density.
[a] Recommended by the International Society for Clinical Densitometry.[13]

bone strength. However, it is not the sole predictor of fragility, as evidenced by a large overlap in BMD values between subjects with and without fractures (Fig. 1.8). Among the non-BMD factors that predict fragility, the paramount variable is age (Fig. 1.9): at any level of BMD, fracture risk is considerably higher in older subjects.[15]

Recognition of the importance of age and other clinical risk factors in influencing fracture risk has led to the development of several models for predicting fracture risk by combining BMD measurement with other patient characteristics. Among these, FRAX has been most widely applied and has been endorsed by various societies that set guidelines for management of osteoporosis. FRAX is a publically available electronic web-based clinical tool (www.shef.ac.uk/FRAX) that uses clinical risk factors to estimate the 10-year probability of major osteoporotic fractures and hip fractures. The FRAX model is based on primary data from 12 prospective population studies of osteoporotic fractures, which include almost 60 000 men and women with 250 000 person-years of observation. The model was then validated in an additional 11 cohort studies with 230 000 men and women and 1.2 million person-years of observation. The model includes the risk factors for fractures and their interactions to calculate the probability of fracture taking into account the competing risk of dying for the respective populations. The risk factors included in FRAX are geographic region, race, age, sex, height and weight, prior fracture, parent with hip fracture, current smoking, use of glucocorticoids ($\geq$5 mg prednisone or equivalent for at least 3 months), rheumatoid arthritis, secondary osteoporosis (type 1 diabetes, osteogenesis imperfecta, hyperthyroidism, hypogonadism, inflammatory bowel disease, immobility), alcohol ($\geq$3 drinks/day), and BMD (femoral neck BMD and the make of DXA). The main improvement in clinical care of osteoporosis resulting from the introduction of FRAX is that it encourages assessment of the whole patient, rather than the BMD measurement alone, and it provides an estimate of absolute fracture risk, which is more informative than the T-score-derived relative risk. However, there are some disadvantages: it does not capture the dose–response effect for variables such as glucocorticoid use or cigarette exposure; it ignores the family history of osteoporosis other than hip fracture; and the increase in fracture risk associated with vertebral fractures is likely to be underestimated. In addition, at least some authors believe that a much simpler tool which uses only age, prior fracture, glucocorticoid use, and BMD can provide fracture estimates that are as good as those derived from FRAX and require less time in the clinic.[6,18]

As mentioned above, vertebral fractures also strongly predict future fractures,[19,20] but they are often not clinically recognized and require imaging for detection. This can be accomplished using conventional radiographs, or more recently, using vertebral fracture assessment (VFA), a spine

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Table 1.5 Definition of T-scores and diagnosis of osteoporosis in various populations[a]

Population	Diagnosis
Reference database for T-scores	Use a uniform Caucasian (non-race-adjusted) female normative database for women of all ethnic groups[b] Use a uniform Caucasian (non-race-adjusted) male normative database for men of all ethnic groups[b] The NHANES III database should be used for T-score derivation at the hip regions
Reference database for Z-scores	Z-scores should be population specific where adequate reference data exist; for the purpose of Z-score calculation, the patient's self-reported ethnicity should be used
Fracture risk assessment	A distinction is made between diagnostic classification and the use of BMD for fracture risk assessment For fracture risk assessment, any well-validated technique can be used, including measurements of more than one site where this has been shown to improve the assessment of risk
Use of the term osteopenia	The term osteopenia is retained, but low bone mass or low bone density is preferred; people with low bone mass or density are not necessarily at high fracture risk
BMD reporting in postmenopausal women and in men aged ≥50	T-scores are preferred; the WHO densitometric classification is applicable
BMD reporting in females prior to menopause and in males aged <50	Z-scores, not T-scores, are preferred; this is particularly important in children: • Z-score of −2.0 or lower is defined as "below the expected range for age," • Z-score above −2.0 is "within the expected range for age"
Osteoporosis in men aged <50	Cannot be diagnosed on the basis of BMD alone
Women in the menopausal transition	WHO diagnostic criteria may be applied

BMD, bone mineral density; NHANES III, Third National Health and Nutrition Examination Survey.
[a] Recommended by International Society for Clinical Densitometry.[13]
[b] Application of recommendations may vary according to local requirements.

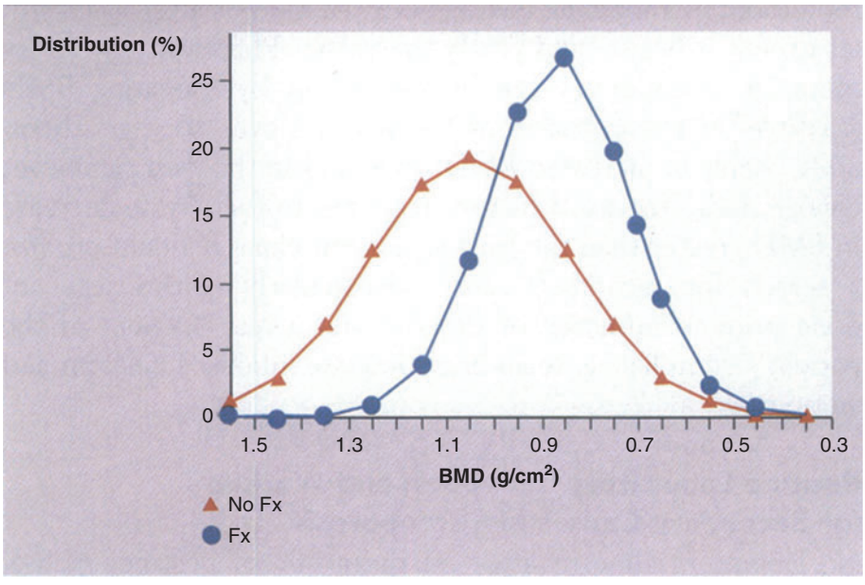

Fig. 1.8 Distribution of bone mineral density (BMD) of the lumbar spine in women with and without vertebral fractures (fx). (From Melton LJ III, Kan SH, Frye MA, *et al.* Epidemiology of vertebral fractures in women. *Am J Epidemiol* 1989;129:1000–1011.)

image obtained on the densitometer (Figs. 1.10 and 1.11).[21] This new method has the advantage of low radiation exposure and greater patient convenience since it can be performed during the visit for BMD measurement. Presence of atraumatic vertebral fractures, even in a patient who does not have BMD criteria for osteoporosis, is considered diagnostic of osteoporosis and should prompt more aggressive evaluation and treatment.[2]

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