accrued by the underlying disease from that attributable to the medication. For example, both depression and diabetes are risk factors for fracture by themselves.

CIGARETTE CONSUMPTION

The use of cigarettes over a long period has detrimental effects on bone mass. These effects may be mediated directly by toxic effects on osteoblasts or indirectly by modifying estrogen metabolism. On average, cigarette smokers reach menopause 1–2 years earlier than the general population. Cigarette smoking also produces secondary effects that can modulate skeletal status, including intercurrent respiratory and other illnesses, frailty, decreased exercise, poor nutrition, and the need for additional medications (e.g., glucocorticoids for lung disease).

MEASUREMENT OF BONE MASS

Several noninvasive techniques are available for estimating skeletal mass or density. They include dual-energy x-ray absorptiometry (DXA), single-energy x-ray absorptiometry (SXA), quantitative CT, and ultrasound (US). DXA is a highly accurate x-ray technique that has become the standard for measuring bone density. Although it can be used for measurement in any skeletal site, clinical determinations usually are made of the lumbar spine and hip. DXA also can be used to measure body composition. In the DXA technique, two x-ray energies are used to estimate the area of mineralized tissue, and the mineral content is divided by the area, which partially corrects for body size. However, this correction is only partial because DXA is a two-dimensional scanning technique and cannot estimate the depth or posteroanterior length of the bone. Thus, small slim people tend to have lower than average bone mineral density (BMD), a feature that is important in interpreting BMD measurements when performed in young adults, and something that must be taken into account at any age. Bone spurs, which are common in osteoarthritis, tend to falsely increase bone density of the spine and are a particular problem in measuring the spine in older individuals. Because DXA instrumentation is provided by several different manufacturers, the output varies in absolute terms. Consequently, it has become standard practice to relate the results to "normal" values by using T-scores (a T-score of 1 equals 1 SD), which compare individual results to those in a young population that is matched for race and sex. Z-scores (also measured in SD) compare individual results to those of an age-matched population that also is matched for race and sex. Thus, a 60-year-old woman with a Z-score of –1 (1 SD below mean for age) has a T-score of –2.5 (2.5 SD below mean for a young control group) (Fig. 425-6). A T-score below –2.5 in the lumbar spine, femoral neck, or total hip has been defined as a diagnosis of osteoporosis. As noted above, because more than 50% of fractures occur in individuals with low bone mass rather than BMD osteoporosis, attempts are ongoing to redefine the disease as a fracture risk rather than a specific BMD. Consistent with this concept, fractures of the spine and hip that occur in the absence of major trauma would be considered to be sufficient to diagnose osteoporosis, regardless of BMD. Fractures of other sites, such as pelvis, proximal humerus, and wrist, would be tantamount to an osteoporosis diagnosis in the presence of low BMD. CT can also be used to measure the spine and the hip, but is rarely used clinically, in part because of higher radiation exposure and cost, in addition to a lesser body of data confirming its ability to predict fracture risk, compared with BMD by DXA. High-resolution peripheral CT is used to measure bone in the forearm or tibia as a research tool to noninvasively provide some measure of skeletal architecture. Magnetic resonance imaging (MRI) can also be used in research settings to obtain some architectural information on the forearm and perhaps the hip.

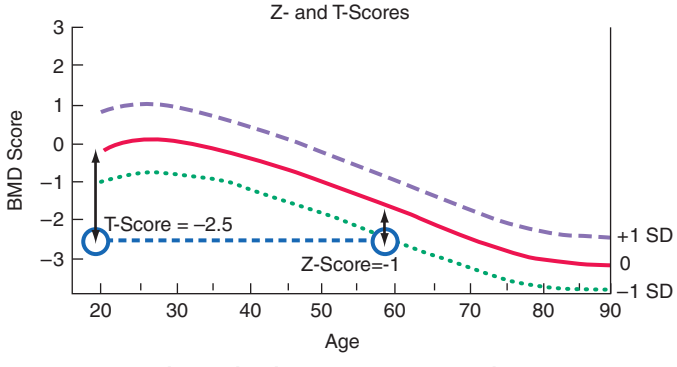

FIGURE 425-6 Relationship between Z-scores and T-scores in a 60-year-old woman. BMD, bone mineral density; SD, standard deviation.

DXA equipment can also be used to obtain lateral images of the spine, from T4 through L4, a technique called vertebral fracture assessment (VFA). Although not as definitive as radiography, it is a useful screening tool when height loss, back pain, or postural change suggests the presence of an undiagnosed vertebral fracture. Furthermore, because vertebral fractures are so prevalent with advancing age, screening vertebral imaging is recommended in women and men with low bone mass (T-score <1) by age 70 and 80, respectively.

US is used to measure bone mass by calculating the attenuation of the signal as it passes through bone or the speed with which it traverses the bone. It is unclear whether US assesses properties of bone other than mass (e.g., quality), but this is a potential advantage of the technique. Because of its relatively low cost and mobility, US is amenable for use as a screening procedure in stores or at health fairs.

All of these techniques for measuring BMD have been approved by the U.S. Food and Drug Administration (FDA) on the basis of their capacity to predict fracture risk. The hip is the preferred site of measurement in most individuals, because it predicts the risk of hip fracture, the most important consequence of osteoporosis, better than any other bone density measurement site. When hip measurements are performed by DXA, the spine can be measured at the same time. In younger individuals such as perimenopausal or early postmenopausal women, spine measurements may be the most sensitive indicator of bone loss. A risk assessment tool (FRAX) incorporates femoral neck BMD to assess 10-year fracture risk (see below).

WHEN TO MEASURE BONE MASS

Clinical guidelines have been developed for the use of bone densitometry in clinical practice. The original National Osteoporosis Foundation guidelines recommend bone mass measurements in postmenopausal women, assuming they have one or more risk factors for osteoporosis in addition to age, sex, and estrogen deficiency. The guidelines further recommend that bone mass measurement be considered in *all* women by age 65, a position ratified by the U.S. Preventive Health Services Task Force. Criteria approved for Medicare reimbursement of BMD are summarized in Table 425-2.

WHEN TO TREAT BASED ON BONE MASS RESULTS

Most guidelines suggest that patients be considered for treatment when BMD is >2.5 SD below the mean value for young adults (T-score ≤–2.5), in either spine, total hip, or femoral neck. Treatment also should also be considered in postmenopausal women with fracture risk factors even if BMD is not in the osteoporosis range. Risk factors (age, prior fracture, family history of hip fracture, low body weight, cigarette consumption, excessive alcohol use, steroid use, and rheumatoid arthritis) can be combined with BMD to assess the likelihood of a

TABLE 425-2 INDICATIONS FOR BONE DENSITY TESTING

Consider BMD testing in the following individuals:

- Women age 65 and older and men age 70 and older, regardless of clinical risk factors
- Younger postmenopausal women, women in the menopausal transition and men age 50–69 with clinical risk factors for fracture
- 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

Source: From the 2014 National Osteoporosis Foundation Clinician's Guide to the Prevention and Treatment of Osteoporosis. © National Osteoporosis Foundation.