

# Clinical Use of Bone Densitometry

## Scientific Review

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**O**STEOPOROSIS IS IMPORTANT because it is common and often occult, yet it causes substantial morbidity and costs \$13.8 billion a year (1995 dollars) in the United States alone.<sup>1</sup> Hip fractures account for most of the costs and deaths due to osteoporosis, but vertebral fractures also cause substantial pain and disability, and only about a third of these fractures are recognized clinically.<sup>2,3</sup> Osteoporosis is defined by low bone mass and increased fragility of bone that increases the risk of fracture.<sup>4</sup> Measurement of bone mass by densitometry has become central to the diagnosis of osteoporosis and decisions about treatment to prevent fracture.

### METHODS

There are no randomized trials of densitometry. We emphasize results from prospective cohort studies, meta-analyses, and systematic reviews when these were available. Specifically, we updated 2 meta-analyses<sup>5,6</sup> of the relationship between bone mineral density (BMD) and fractures by searching MEDLINE for and including in the meta-analyses subsequent prospective cohort studies of the relationship between various measurements of bone density and risk of vertebral and hip fracture. Additionally, we used data from the Study of Osteoporotic Fractures,<sup>7</sup> a prospective community-

**Context** Osteoporosis causes substantial morbidity and costs \$13.8 billion annually in the United States. Measurement of bone mass by densitometry is a primary part of diagnosing osteoporosis and deciding a preventive treatment course. Bone mineral densitometry has become more widely available and commonly used in practice.

**Objective** To review evidence about the value of various clinical applications of bone densitometry.

**Data Sources** A MEDLINE search was performed to update previous meta-analyses of the relationship between various measurements of bone density and risk of vertebral and hip fracture. We used data from the prospective Study of Osteoporotic Fractures to estimate risk of fracture from bone density and age in postmenopausal women.

**Study Selection and Data Extraction** When available, meta-analyses and systematic reviews are emphasized in the review.

**Data Synthesis** Bone mineral density (BMD) predicts fracture and can be used in combination with age to estimate absolute risk of fractures in postmenopausal white women. Hip BMD predicts hip fracture more strongly than other measurements of BMD. There are insufficient data to translate BMD results into risk of fracture for men and nonwhite women. The benefits of treatments to prevent fractures depend on BMD: women with osteoporosis have a greater risk of fractures and greater benefit from treatments than women without osteoporosis.

**Conclusions** Guidelines based on systematic reviews and a cost-effectiveness analysis have suggested that it is worthwhile to measure BMD in white women older than 65 years and perhaps to use risk factors to select younger postmenopausal women for densitometry. Other potential clinical applications of BMD that have not yet been adequately studied include screening men or nonwhite women, monitoring BMD in patients receiving treatment, and using BMD to identify patients who should be evaluated for secondary causes of osteoporosis.

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based study of a cohort of 9704 white women aged 65 years or older, to generate estimates of the risk of fracture from bone density and age in postmenopausal women. Regarding other clinical applications, we emphasize results

from randomized trials of pharmacologic treatments, prospective cohort studies, and the systematic reviews and analyses by the National Osteoporosis Foundation<sup>8</sup> and the US Preventive Services Task Force.<sup>9</sup> Many clinical appli-

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**Box 1. Common Terms Used in Bone Densitometry**

**Areal Bone Density** The bone mineral content divided by the area of the image of a bone projected in 2 dimensions, which is the type of bone density that is produced by dual- and single-energy x-ray absorptiometry.

**Bone Density or Bone Mineral Density** The average concentration of mineral in a 2- or 3-dimensional image or defined section of bone. This term is also used to refer to the results of all types of bone densitometry.

**Bone Mass** A nonspecific term that refers to the amount of bone tissue as the total of protein and mineral or the amount of mineral in the whole skeleton or in a particular segment of bone.

**Bone Mineral Content** The amount of mineral measured in a defined section of bone. Total body bone mineral content refers to the mineral content of the whole skeleton.

**Broadband Ultrasound Attenuation** The slope of the line of attenuation of sound energy across a spectrum of sound frequencies.

**Osteopenia** A term coined by the Working Group of the World Health Organization to refer to T scores between  $-1.0$  and  $-2.5$ .

**Osteoporosis** Defined by the Working Group of the World Health Organization as a bone density T score at or below  $2.5$  ( $2.5$  SDs below normal peak values for young adults). A diagnosis of osteoporosis is also made on the basis of a vertebral fracture confirmed by radiograph.

**Speed of Sound** The fastest rate of transmission of a specific frequency of sound through a defined section of bone.

**Trabecular Bone Density** The mineral density of a section of bone that contains only trabecular bone.

**T Score** The difference in number of SDs between the value for an individual and the mean value of a group of young (usually 25- to 45-year-old) adults of the same sex. The mean value and size of an SD of the measurement vary between techniques and among sites of measurement.

**Volumetric Bone Density** The bone mineral content of a section of bone divided by the volume of that section, which can be measured by quantitative computed tomography.

**Z Score** The difference in number of SDs between the mean bone mineral density value of the individual and a group of people of the same sex and age.

cations of densitometry have not been rigorously studied, and we note these limitations.

**RESULTS****Bone Densitometry**

Bone is composed of mineral, principally calcium hydroxyapatite, embedded in type I collagen and specialized proteins that make up the bone matrix. Calcium absorbs much more radiation than protein or soft tissue. The amount of x-ray energy that is absorbed by calcium in a section reflects the bone mineral content (BMC) (Box 1). Bone mineral content divided by the area or volume of the bone estimates BMD. In laboratory studies, there is a high correlation ( $R^2=0.4-0.9$ ) between BMD and the force needed

to break a bone.<sup>10-12</sup> Other determinants of bone strength include size (larger bones are stronger), macroscopic structure (long bones with greater cross-sectional areas are more resistant to bending), microscopic structure (microscopic cracks and loss of normal trabecular architecture weaken a bone), and the composition of bone proteins (abnormal collagen weakens bones).

**Terminology: Bone Mass, Bone Density, and BMD.** Many terms are used to describe the amount and density of a bone (Box 1). *Bone mass* refers to the amount of bone in the skeleton or in one location. However, no technology produces a measurement called bone mass. Bone mineral density is defined as the average concentration of min-

eral per unit area (for single-energy x-ray absorptiometry [SXA] and dual-energy x-ray absorptiometry [DXA]), which is also referred to as areal BMD to emphasize that it is based on the area of the projected image of the bone. Bone mineral density assessed in 2 dimensions is affected by the section size of the bone: if a large and a small bone have the same mineral density, the larger will appear to have a higher BMD. The term *volumetric bone density* refers to bone mineral per defined volume of bone; volumetric BMD does not depend on the size of a bone.

**T Scores and Z Scores.** Densitometry results are reported as T scores and Z scores. Both of these rely on an SD for the measurement. An SD represents the normal variability in a measurement in a young normal population—the distance between the 5th and 95th percentile of a group covers about 4 SDs. Standard deviations vary from technique to technique and among various reference populations that are used to define normal values. For hip and spine BMD, 1 SD corresponds to about 10% to 15% of the mean value for young adults.

A Z score is the number of SDs below or above the mean BMD value for people of the same age. A Z score of 0 means that the patient has a value that is exactly at the mean for her age. A Z score of  $-2.0$  means that the patient has a BMD at that site, by that method, that is 2 SDs below the mean BMD value of others the same age.

In contrast, a T score is the number of SDs below the mean BMD for young (25- to 45-year-old) adults. A T score of 0 means that the patient has a BMD value that is exactly at the mean for young adults. A T score of  $-2.5$  means that the patient has a BMD value at that site and by that method that is 2.5 SDs below the mean.

Because BMD declines with age, T scores are consistently lower than Z scores after about age 40 years, and the difference increases with age. For example, a 70-year-old patient who has a Z score of  $+1.0$  at the hip (above average for women of the same age) will

have a T score of about  $-0.8$  (below average compared with young women).

### BMD in Men and Nonwhite Patients

In general, men have higher BMD than women, and African Americans and Latinos have higher BMD than whites.<sup>13</sup> Asians tend to have slightly lower BMD than whites mainly because of their smaller size.<sup>14,15</sup> Densitometers report T and Z scores that are specific to the patient's sex, and some manufacturers report values compared with those of patients of the same race. When BMD results are interpreted in nonwhite patients, it is important to know whether the T and Z scores are based on comparison to whites or the patient's racial group. Prospective studies of BMD and fracture in white women provide data that permit BMD results for white women to be translated into risks of fracture (FIGURE). However, analogous studies have not been done for men or nonwhite women.

### Techniques for Assessing Bone Mass

A number of technologies can be used to assess mineral density (TABLE 1), including DXA and SXA, quantitative computed tomography (QCT), and radiographic absorptiometry. The radiation doses for all techniques except QCT are low (less than a patient gets from a mammogram). Quantitative ultrasound uses sound waves rather than radiation to assess properties of bone that are related to density and bone strength.

The relationship between BMD and fracture risk is conventionally quantified by the relative risk per SD (RR/SD), which is the increase in risk associated with a 1-SD decrease in the BMD measurement. For example, an RR/SD of 1.6 means that fracture risk increases by 60% for each 1-SD decrease in BMD. A larger RR/SD implies a stronger predictive value of BMD for fracture risk. TABLE 2 presents a summary of meta-analyses of RR/SD for various types of BMD and fractures.

**Dual-Energy X-ray Absorptiometry.** Table model DXA machines can

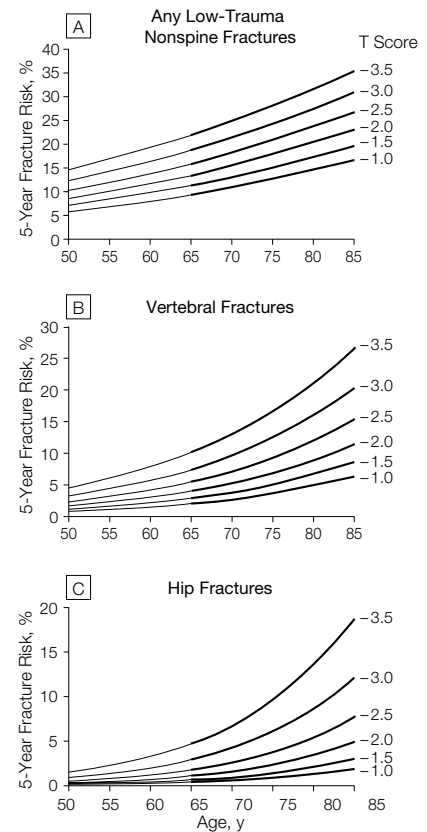
measure BMD at the hip or spine but can also be used to measure the total amount of mineral in the whole skeleton or forearm. Hip BMD generally refers to BMD of the femoral neck or total hip. Bone mineral density measured at either site is a strong predictor of hip fracture and predicts hip fracture better than BMD of other sites. Hip BMD also predicts risk of all fractures, as do measurements at other sites (Table 2),<sup>5,6</sup> and is unaffected by degenerative arthritis.

Spine BMD measures vertebrae L1 through L3 or L4. Vertebral bodies are largely made of trabecular bone that, because of its high ratio of remodeling surface to bone volume, is more sensitive to the effects of hormones and drugs than is cortical bone. Therefore, spine BMD tends to change more in response to some medical conditions, such as corticosteroid excess, and to treatments than does BMD of other sites. On the other hand, standard spine BMD, measured in the anteroposterior direction, includes mineral in the posterior elements and facet joints as well as the abdominal aorta, none of which contribute to the strength of the vertebral body. Consequently, spine BMD is increased by degenerative arthritis and, for this reason, tends to increase after about age 65 years rather than decrease, as seen in other BMD measurements.<sup>19</sup>

**Peripheral Densitometry.** Smaller devices use DXA or SXA to measure bone density in the forearm or heel. The distal radius is often used because it contains trabecular and cortical bone. A peripheral test generally costs much less than DXA of the hip and spine (Table 1). These tests are predictive of fractures<sup>20</sup> but less predictive than BMD at the hip for hip fractures and somewhat less accurate at predicting vertebral fractures than hip or spine BMD (Table 2). The proportion of patients with T scores less than  $-2.5$  varies considerably from one type of device to another.<sup>20,21</sup>

**Quantitative Computed Tomography.** Quantitative computed tomography of the spine is available on stan-

**Figure.** Five-Year Risk of Fractures in White Women at Various Ages and Femoral Neck T Scores



Risk is based on the following relationships observed during 5 years of follow-up in the Study of Osteoporotic Fractures (SOF)<sup>16,17</sup>: A, between femoral neck bone mineral density (BMD) and radiograph-confirmed nonspine fractures; B, between femoral neck BMD and the risk radiograph-defined vertebral fractures; and C, between femoral neck BMD and hip fractures. Estimates for women 65 years or older are based on a logistic model of the association between femoral neck BMD and fracture risk. Bone mineral density was measured on a QDR 1000 densitometer (Hologic Inc, Waltham, Mass). T scores are based on normal values from the National Health and Nutrition Examination Survey.<sup>18</sup> The SOF included women 65 years or older, so the estimates below age 65 years are based on extrapolation from the logistic regression model of the relationship between age, BMD, and risk of fracture in older women.

dard computed tomography devices, and a smaller device, known as peripheral QCT, performs QCT at the distal forearm. Quantitative computed tomography is unique because it assesses 3-dimensional bone density and permits isolated measurement of trabecular bone density.<sup>22</sup> The value of QCT measurements for prediction of

**Table 1.** Summary of Common Techniques for Assessment of Bone Mass\*

	Site	Scan Time, min	Precision Error, %	Approximate Radiation Exposure, mrem	Medicare Allowable Charge, \$†
Peripheral DXA and SXA‡	Radius, calcaneus	5-15	1-3	1	39-41
DXA, or DEXA	Spine, hip, whole body	5-10	1-2	1-5	128
Quantitative computed tomography	Spine	10-30	2-4	50	185
Radiographic absorptiometry	Hands	5-10	1-2	5	38
Ultrasound	Calcaneus, tibia	5-10	3-4	0	53

\*Adapted from *Osteoporosis* with the permission of the American College of Physicians–American Society of Internal Medicine.<sup>8,18</sup>

†Information on charges was provided by Mike Lewiecki, MD, International Society of Clinical Densitometry. Medicare allowable charge indicates that Medicare covers 80% of the cost. Actual charges are often substantially higher than those listed in this table.

‡DXA and DEXA indicate dual-energy x-ray absorptiometry; SXA indicates single-energy x-ray absorptiometry.

**Table 2.** Relationships Between Bone Mass Measurements and Risk of Fractures\*

Measurement Site for Bone Mineral Density	Type of Fracture, Relative Risk per SD (95% Confidence Interval)			
	Hip	Vertebral	Forearm	All
Hip	2.4 (2.2-2.6)	1.9 (1.8-2.1)	1.4 (1.4-1.6)	1.6 (1.4-1.8)
Lumbar spine	1.5 (1.3-1.7)	1.9 (1.8-2.0)	1.5 (1.3-1.8)	1.5 (1.4-1.7)
Distal radius	1.5 (1.3-1.8)	1.7 (1.5-1.9)	1.7 (1.4-2.0)	1.4 (1.3-1.6)
Calcaneus	1.8 (1.5-2.1)	1.7 (1.5-1.9)	1.6 (1.4-1.8)	1.5 (1.4-1.6)
Ultrasound Calcaneus	1.6 (1.4-1.8)			1.5 (1.4-1.7)

\*Numbers are the relative risk for fracture per SD decrease in the measurement. Forearm and all fractures are from a 1996 meta-analysis,<sup>11</sup> hip fracture is from a 1999 meta-analysis,<sup>12</sup> and vertebral fractures are from an unpublished analysis prepared for this article. We performed a meta-analysis of bone mineral density and vertebral fractures by using data derived from publications and presentations (available as of January 2002) and by using original unpublished analyses from the Study of Osteoporotic Fractures and from the placebo group of the Fracture Intervention Trial. A fixed-effects model was used to combine data from the studies.

**Table 3.** Lifetime Risk (Percentage) of Hip Fracture for White Women\*

Age, y	Femoral Neck Bone Mineral Density T Score							
	-3.5	-3.0	-2.5	-2.0	-1.5	-1.0	-0.5	0
50	49	41	33	27	21	16	13	10
60	47	40	33	27	21	17	13	10
70	46	39	33	27	21	17	13	10
80	41	35	30	24	20	16	12	10

\*These estimates are based on a stochastic model using a logistic model of the relationship between bone mineral density and risk of hip fracture derived from the Study of Osteoporotic Fractures (relative risk = 2.6/SD decrease). T scores were based on bone mineral density results from Hologic QDR 1000 densitometers, with T scores derived from the National Health and Nutrition Examination Survey III 1995 database. Overall mortality rates are based on US Vital Statistics. Statistical methods are published in part in Black et al.<sup>34</sup>

fractures, and therefore for making clinical decisions, has not been well studied.

**Measurements Based on Radiographs.** Radiographic absorptiometry compares the density of proximal phalanges to that of a wedge of aluminum that has known densities and is placed on the film alongside the hand.<sup>23</sup> Other hand radiograph-based techniques allow estimation of bone density from cortical thickness.<sup>24</sup> Characteristics and costs of methods based on hand films are similar to those of peripheral densitometry.

The integrity of bundles of trabeculae that run through the proximal femur can be qualitatively rated by the Singh index.<sup>25</sup> The cortical width of the femoral neck is another index of osteoporosis. Prospective studies have shown that these measurements also predict hip fracture risk.<sup>26,27</sup>

**Quantitative Ultrasound.** The transmission of sound through bone reflects its density and structure and can be assessed quantitatively by the speed of sound, the pattern of absorption of different wavelengths of sound, called broadband ultrasound attenuation, or

calculations derived from these parameters.<sup>28-30</sup> Quantitative ultrasound of the heel resembles other peripheral measurements in terms of ability to predict fractures (Table 2), and the combination of calcaneal broadband ultrasound attenuation and femoral neck BMD predicts hip fracture risk somewhat better than either measurement alone.<sup>16,31</sup>

**Clinical Uses of Densitometry**

**Prediction of Fracture Risk.** Prospective studies have established that fracture risk increases as BMD decreases, and there is no fracture threshold below which fracture risk abruptly increases (Figure).<sup>7,32,33</sup> Therefore, BMD is best thought of as a continuous risk factor: the lower the BMD, the higher the risk of fracture.

A woman's risk of fracture can be estimated from her age and BMD. TABLE 3 provides estimates of lifetime risk of hip fracture for white women at various ages and levels of femoral neck bone density. The Figure also provides estimates of risk of nonspine, vertebral, and hip fracture at various ages and levels of hip BMD. These estimates would be somewhat different for hip BMD measured with another device (other than a Hologic brand) and very different for BMD at other sites, such as the spine or forearm.

One might expect that a BMD measurement at a specific site would be most predictive of fractures at that site, as is true for hip BMD predicting hip fracture (Table 2). However, hip and spine BMD have similar accuracy for predicting vertebral fractures, and all

sites and types of measurement seem to have similar accuracy in predicting the general risk of all fractures.<sup>5,35</sup>

**Value of Risk Factors for Assessing Risk.** Several risk factors, especially age, sex, weight, and race, are correlated with BMD. However, it is impossible to predict BMD from combinations of risk factors with clinically useful accuracy.<sup>36-38</sup> Guidelines have used the presence of risk factors to recommend measurement of BMD (BOX 2). Several short instruments have been developed to identify women who have a low probability of having osteoporosis on measurement of BMD. These instruments and scoring systems have high sensitivity (identifying 95%-99% of women who have osteoporosis defined as a T score  $\leq -2.5$  at the hip) but poor specificity (only 10%-25% of postmenopausal women without osteoporosis would avoid testing).

Some risk factors for fracture are independent of BMD, that is, they improve the prediction of fracture even when BMD is known. For example, a woman who has a vertebral fracture has a 4-fold increase in risk of another vertebral fracture regardless (or independent) of her BMD.<sup>39,40</sup> Risk factors that predict hip fracture independently of BMD include age, history of fracture,<sup>41,42</sup> maternal history of hip fracture, conditions that increase the risk of falling,<sup>43,44</sup> increased levels of markers of bone resorption,<sup>45</sup> and very low serum levels of estradiol.<sup>46</sup> In prospective studies, Black et al<sup>47</sup> found that risk factors obtainable by history can also be used to estimate risk of hip fracture, and measurement of BMD improves the prediction somewhat. Assessing risk factors might help in making decisions about treatment when densitometry is unavailable or when the best course is unclear from a patient's bone density.

**Diagnosing Osteoporosis and "Osteopenia."** Since the relationship between decreasing bone density and increasing risk of fractures is a continuous one, there is no threshold or cutoff value to distinguish low- and high-risk people. However, medical

## **Box 2. Guidelines for Measuring Bone Mineral Density in Women for Assessing Risk of Fracture**

### **National Osteoporosis Foundation**

The decision to test for bone mineral density (BMD) should be based on an individual's risk profile, and testing is never indicated unless the results are likely to influence a treatment decision.

### **BMD Testing Recommendations**

1. Postmenopausal women 65 years or older, regardless of additional risk factors. This recommendation includes women 65 years or older who have been taking osteoporosis therapy and have not had a BMD test.
2. Postmenopausal women younger than 65 years and with 1 or more additional risk factors for osteoporosis.\*
3. Postmenopausal women who have had a fracture of any type as an adult after age 45 years.

### **US Preventive Services Task Force (USPSTF)**

**Summary of Recommendations.** The USPSTF "recommends that women 65 years of age and older be screened routinely for osteoporosis. The USPSTF recommends that routine screening begin at 60 years of age for women at increased risk for osteoporotic fractures."<sup>9</sup>

"The USPSTF makes no recommendation for or against routine osteoporosis screening in postmenopausal women who are younger than 60 years of age or in women 60 to 64 years of age who are not at increased risk for osteoporotic fractures."<sup>9</sup>

\*Risk factors include parental history of hip fracture, current cigarette smoking, a body weight less than 57.2 kg, use of (or plans to use) oral corticosteroids longer than 3 months, or serious long-term conditions thought to increase fracture risk, such as hyperthyroidism or malabsorption.

practice and reimbursement sometimes require a diagnosis of osteoporosis. The World Health Organization defined osteoporosis as a T score of  $-2.5$ .<sup>48</sup> This cutoff has no inherent biological meaning; it was created to allow comparisons of the prevalence of osteoporosis in different countries and was not intended to be used to make treatment decisions.

The diagnosis of osteoporosis according to BMD can be confusing because, if 2 or more sites are measured, patients will sometimes have a T score of  $-2.5$  or less and so-called osteoporosis at one site and above that level at other sites.<sup>21</sup> Some experts and guidelines consider a T score at or below  $-2.5$  at the femoral neck or total hip to be the gold standard for the diagnosis of osteoporosis. Others prefer to diagnose osteoporosis if the T score at either the hip or spine is at or below  $-2.5$ ; the latter approach designates more women as osteoporotic who will, on av-

erage, have a somewhat lower risk of fracture.<sup>49</sup>

Osteopenia was defined by the WHO conference as a bone density T score between  $-1.0$  and  $-2.5$ .<sup>48</sup> The upper cutoff, a T score of  $-1.0$ , was also chosen arbitrarily to indicate women whose bone density was below normal for young adults. More than half of postmenopausal women could be called osteopenic at at least 1 site of measurement.<sup>13,50</sup> The term has limited value because it encompasses a broad range of women, including some with a relatively high risk for their age and others whose risk is lower than average for their age (Figure). It is more useful and less alarming to patients to avoid this term and instead to focus on their risk of fractures.

### **Deciding to Evaluate a Patient for Causes of Low BMD**

Most of a person's BMD, even after age 65 years, is genetically determined.

Some uncommon conditions, including Cushing disease, malabsorption, hyperparathyroidism, and hyperthyroidism, can decrease bone density. Finding and treating these conditions might decrease a patient's risk of fractures. Unfortunately, the chance of finding a secondary cause in patients with low BMD, especially in primary care settings, is unknown, and the value of testing for secondary causes in women with low BMD has not been adequately studied. It is believed that the chance of finding a secondary cause increases as BMD decreases at a specific age.<sup>51</sup> If so, then a low Z score ( $<-2.0$  or  $-3.0$ ) might be a more useful guide than the T score in deciding whether to look for secondary causes of osteoporosis. Some physicians also screen for secondary causes in women with osteoporosis defined by a low T score, although the best approach is uncertain.

Bone mineral density can help determine whether a fracture is due to osteoporosis. For example, BMD may be valuable if a patient has a vertebral fracture in a location that would be unusual for osteoporosis, such as T4.<sup>52</sup> Although there is no evidence about this point, it is reasonable to believe that the higher the BMD, the greater the chance that another process, such as cancer or trauma, caused the fracture.

### **Making Decisions About Starting Drug Treatment**

Women with vertebral fractures have a high risk of fractures, and several approved treatments decrease their risk of future vertebral fracture. Among women without a vertebral fracture, the potential benefit of treatment depends on the patient's bone density: the lower the BMD, the greater the likelihood that she will benefit from treatment to prevent fractures.

A systematic review and cost-effectiveness analysis used data available up to 1996 and estimated that it was worthwhile to recommend drug treatments that reduce risk of hip fracture to women with low femoral neck BMD (T scores below  $-3.0$  to  $-1.5$ , depending on age, risk factors, and

type of treatment).<sup>8</sup> Several drugs have been approved by the Food and Drug Administration for treatment of osteoporosis (alendronate, risedronate, raloxifene, and calcitonin) because they reduce the risk of fractures among women who have vertebral fractures or osteoporosis defined as a T score of  $-2.5$  or less at the femoral neck or spine.<sup>53-58</sup> The value of treating women without vertebral fractures who have higher levels of BMD is less certain. In the Fracture Intervention Trial,<sup>54</sup> 4 years of alendronate treatment significantly reduced the risk of hip and other nonspine fractures, including hip fractures among women whose hip BMD T score was less than  $-2.5$ , but not in women with a higher starting BMD. Women with T scores above  $-2.5$  had a reduction in risk of vertebral fractures, although the absolute reduction in risk was much greater in women with osteoporosis than in those with T scores above  $-2.5$ . Risedronate reduced the risk of hip fracture among women who were younger than 80 years and whose femoral neck BMD T score was at least below  $-3.0$ , but it did not significantly reduce the risk of hip fractures among women who were older than 80 years and were included because they had risk factors for hip fracture regardless of BMD. These studies suggest that hip BMD may be a valuable indicator of who will benefit most from reduction in risk of nonspine and hip fractures after several years of treatment with bisphosphonates. In contrast, no published study has evaluated the ability of spine and peripheral measurements of BMD to identify women who benefit most from treatments to reduce the risk of fractures.

### **Which Patients Should Have a Measurement of BMD?**

Using a systematic review and cost-effectiveness analysis,<sup>8</sup> the National Osteoporosis Foundation recommended measuring BMD, preferably of the hip, for all white women 65 years or older who are not receiving drugs that are approved for treating osteoporosis.<sup>59</sup> Additionally, these guidelines suggested measuring BMD for younger postmenopausal women who were aged 50 to 65 years and had another strong and well-established risk factor for osteoporosis.

The United States Preventive Services Task Force recommended routine screening for osteoporosis beginning at age 65 years in all women and at age 60 years in women with risk factors indicating an increased risk of osteoporotic fractures. It made no recommendation about screening for women younger than 60 years (Box 2).

Men and nonwhite women have a lower overall fracture rate than white women, but there are insufficient data on which to base recommendations about BMD in men and nonwhite women. Alendronate reduces fracture risk in men,<sup>60</sup> and it is reasonable to believe that treatment would be worthwhile for men and nonwhite women who have a decreased BMD and risk of fracture that is similar to that of white women with osteoporosis. However, there is controversy about what levels of BMD should be considered osteoporotic and what values should trigger a recommendation for drug treatment in men and nonwhite women.

**Women Who Are Considering Stopping Estrogen Therapy.** Estrogen therapy improves bone density<sup>61</sup> and reduces the risk of fracture<sup>62</sup> but does not fully prevent women from developing osteoporosis. One large study found that 4% of women who were older than 65 years and had taken estrogen continuously since menopause and 11% who started after menopause had hip BMD T scores below  $-2.5$ .<sup>63</sup> Women who stop taking estrogen generally lose bone and appear to lose any protection against fractures within a few years.<sup>64,65</sup> Therefore, it is reasonable to recommend densitometry to women 65 years or older and younger women who have risk factors for fracture and wish to stop long-term estrogen therapy. If they have osteoporosis, it is reasonable to recommend treatment with an agent that has been shown by randomized trials to reduce fracture risk.

## Monitoring

Bone mineral density is often measured every 1 or 2 years during treatment to determine whether a patient is responding to treatment. However, interpreting these results is tricky; the meaning of changes in BMD during treatment is uncertain because responding is not the same as gaining BMD. A patient who loses BMD, eg, 3%, during treatment may be responding because she could have lost more (eg, 5% to 6%) without treatment. Furthermore, most patients who seem to lose BMD during the first period of treatment regain much of that BMD during the next period, even if treatment is unaltered.<sup>66</sup> In addition, women who seem to lose BMD while taking alendronate may have a reduction in risk of vertebral fracture similar to that of women who gain BMD.<sup>67</sup> Thus, treatments should not be changed because the patient appears to lose BMD during the first period of monitoring. The value of changing or adding treatments in women who persistently lose BMD has not been studied.

It is also important to recognize that small changes in BMD may be due to the random variability in the test. The least significant change in BMD is the percentage of change that is unlikely (usually <5% chance) to be due to the precision error of the test.<sup>68</sup> Least significant change is calculated as 2.8 times the precision error of the test on a specific machine and site of measurement. Femoral neck BMD has about a 2% precision error in expert centers; therefore, changes of less than about 5.6% can often be due to precision error.

The best approach to monitoring BMD in patients who are not receiving pharmacological treatment is uncertain. Many patients have BMD levels too high to warrant treatment at screening, but their BMD may later decline to a level at which pharmacological treatment is indicated. It would be reasonable to repeat BMD when the result probably would change treatment. After about 60 years of age, women generally lose less than 1% of hip BMD an-

nually, and their rate of change at the spine is on average even slower,<sup>69</sup> so that it would usually take more than 10 years to decline a full point in T score (for example, from -1.5 to -2.5). Bone mineral density may decline somewhat more rapidly in women who are within 5 years of menopause. The timing of the repeat measurement depends on the current BMD: the closer the current value is to a threshold where treatment would be started, the sooner the BMD measurement should be repeated.

## Common Issues in Measuring Bone Density in Clinical Practice

**Which BMD Site Should Be Measured?** Because BMD at the hip is the best predictor of hip fracture, hip BMD may be particularly useful in women older than 65 years, since risk of hip fracture rises rapidly after age 65. Reports of hip DXA include several subregions of the hip, but these results are highly correlated and have similar predictive value for fractures.<sup>7,70</sup> If only 1 site is measured, then BMD of the hip (femoral neck, total hip, or both) may be preferable because of its predictive value for hip fractures, and it has been better standardized for diagnosis of osteoporosis.<sup>13</sup> Spine and hip BMD have similar value for predicting spine fractures (Table 2). As noted earlier, spine BMD tends to be artificially increased in women 65 years or older, which may limit its predictive and diagnostic value in that age group. Spine BMD is more sensitive to the effects of corticosteroids and may be the best choice for assessing and monitoring corticosteroid-treated patients.<sup>71</sup>

**Peripheral vs Central Measurements.** As noted earlier, peripheral measurements (such as the forearm) are less expensive, more widely available in some areas, and predictive of overall fracture risk, but peripheral measurements do not predict hip fractures as well as hip BMD. Treatments tend to produce smaller changes in peripheral measurements than in spine or hip BMD.<sup>53,72</sup> Peripheral measurements might be used as initial

screening tests for referring patients who have low BMD for DXA of the hip or spine.

**How Many Measurements Should Be Made?** Dual-energy x-ray absorptiometry examinations usually include hip and spine BMD for the same price as 1 measurement. The T and Z scores from these sites often differ, which can confuse physicians and patients. Because of the stronger relationship of hip BMD to hip fracture and weaker influence of degenerative arthritis after age 65 years, it is reasonable to give more weight to the results of hip BMD. However, some practitioners base decision making on the lowest value. There are insufficient data to determine which approach is best. If hip or spine BMD has been measured, there is generally no reason to measure a peripheral site.

## Future Developments in Densitometry

Prospective studies are under way to better describe the relationship between BMD and risk of fractures in men, and groups are developing models that will allow physicians to combine BMD results and risk factors into estimates of a patient's absolute risk of fractures.<sup>73</sup>

There is a growing appreciation that current methods of measuring average BMD in a 2-dimensional projection of bone may miss important information about bone structure; connectivity of trabecular bone, the width of cortical bone, or the degree of aggressive remodeling along the endocortical surface might all play an important role in determining bone strength. Research is under way to develop and test the clinical value of new methods such as magnetic resonance imaging or high-resolution QCT for assessing risk of fractures and response to treatment.

## CONCLUSION

Current methods of bone densitometry are powerful tools for assessing the risk of fracture and identifying patients who will benefit most from the treatments that have been shown to reduce fracture risk in patients with os-

teoporosis. Selective use of densitometry is a valuable part of primary care of postmenopausal women.

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It is the man of science, eager to have his every opinion regenerated, his every idea rationalized, by drinking at the fountain of fact, and devoting all the energies of his life to the cult of truth, not as he understands it, but as he does not yet understand it, that ought properly to be called a philosopher.

—Charles S. Peirce (1839-1914)