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Osteoporosis is a global problem that will increase in significance with the growing elderly population. The condition affects both sexes and all races, albeit to different degrees. Fractures represent the main clinical manifestation of osteoporosis, but fractures have other determinants (eg, risk factors for falling) that are external to the skeleton [1]. Osteoporosis is generally assessed in vivo by measuring bone mineral density (BMD). Although not completely representative of the bone architecture changes that are responsible for skeletal fragility (see article by Seeman in this issue), BMD is strongly correlated with bone strength in vitro and is a good predictor of future fracture risk, as reviewed by Miller in this issue. Because the relationship between bone density and fracture risk is a continuous one, like that between blood pressure and stroke, the choice of a BMD value to define osteoporosis is necessarily somewhat arbitrary. In 1994, the World Health Organization (WHO) defined osteoporosis operationally to be a femoral neck BMD value 2.5 standard deviations (SD) or more below the mean for normal young white women, or a *t* score of -2.5 [2]. Using this definition, it is possible to assess the prevalence of osteoporosis in different populations, and the increasing availability of bone densitometry has permitted such studies to be performed in various regions around the world. This article reviews the epidemiology of osteoporosis as it relates to age, gender, ethnicity, and other risk factors and makes projections for the future as populations continue to age worldwide.

Age

After the cessation of growth and a variable period of skeletal "consolidation" (see article by Gilsang in this issue), net bone loss ensues in most populations of aging women and men. Although osteoporosis is a

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systemic disease, patterns of bone loss differ by skeletal site. At the femoral neck, for example, bone loss begins before 20 years of age and is approximately linear over life in men and women of all races (Fig. 1). Among non-Hispanic white women, femoral neck BMD decreases by one third (from 0.858 g/cm^2 at age 20–29 years to 0.573 g/cm^2 in those 80 years and over) and by a comparable 25% in white men (from 0.934 g/cm^2 to 0.698 g/cm^2), with similar reductions among Mexican American and African American men and women [3]. These data from the Third National Health and Nutrition Examination Survey (NHANES), a representative sample of the United States population, are cross-sectional. However, prospective studies also confirm linear bone loss from the proximal femur [4]. By contrast, lumbar spine BMD as assessed by dual energy x-ray absorptiometry (DXA) in the customary anteroposterior (AP) projection exhibits no decline with aging in men, whereas increases can be seen in elderly women [5]; this is an artifact resulting from age-related increases in aortic calcification and vertebral osteophytosis. Bone loss is clearly evident in both sexes when vertebral bodies are isolated on lateral DXA scans [5–7], and quantitative computed tomography (QCT) data reveal greater age-related bone loss from the vertebral body than is apparent by x-ray absorptiometry [8,9]. In the appendicular skeleton, bone loss begins around the time of menopause in women and at a comparable age in men [5], but trends can be difficult to interpret because of systematic changes in bone size. Thus, age-related increases in radial diameter cause forearm BMD measurements to decline because bone area increases more than bone mineral content (BMC), although peripheral QCT studies show an

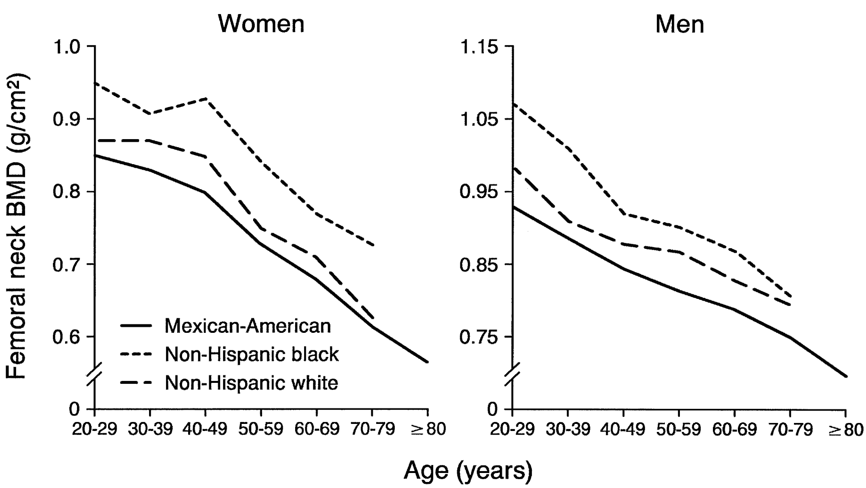

Fig. 1. Mean BMD of the femoral neck by age for US men and women of different ethnic groups. (*From* Looker AC, Wahner HW, Dunn WL, et al. Proximal femur bone mineral levels of US adults. Osteoporos Int 1995;5:389–409; with permission.)

Table 1
Prevalence of osteoporosis among an age-stratified sample of Rochester, Minnesota, residents

Age group (yr)	Total hip alone (%)	AP spine[a] alone (%)	Total wrist alone (%)	Hip or spine or wrist (%)
Postmenopausal women				
50–59 (n = 50)	4.0	2.0	6.0	8.0
60–69 (n = 50)	10.0	8.0	28.0	30.0
70–79 (n = 51)	19.6	17.6	56.9	56.9
≥80 (n = 50)	40.0	4.0	78.0	82.0
Total (n = 201)	13.6[b]	7.7	32.9	34.7[b]
Men ≥50 years				
50–59 (n = 49)	12.2	2.0	4.1	12.2
60–69 (n = 50)	16.0	0	4.0	18.0
70–79 (n = 51)	15.7	2.0	11.8	21.6
≥80 (n = 50)	26.0	2.0	30.0	40.0
Total (n = 200)	15.8[b]	1.4	8.8	19.4[b]

By World Health Organization criteria (2.5 SD or more below sex-specific young normal mean).

[a] Lumbar.

[b] Prevalence per 100 age-adjusted to 1990 U.S. white population ≥50 years old.

Modified from Melton LJ III, Atkinson EJ, O'Connor MK, et al. Bone density and fracture risk in men. J Bone Miner Res 1998;13:1915–23; with permission.

age-related decline in cancellous bone density in both sexes [10]. The redistribution of bone tissue peripherally helps maintain skeletal strength (see article by Seeman). This process is more pronounced in men than in women and may account for the lower incidence of distal forearm fractures in men [11].

Given these patterns of bone loss, changes in the prevalence of osteoporosis with age are predictable. As shown in Table 1, the age-specific prevalence of osteoporosis at the total hip among postmenopausal white women increases 10-fold, from 4% at age 50 to 59 years to 40% at 80 years of age or over, for an overall age-adjusted prevalence rate of almost 14% [12]. This compares with an age-adjusted prevalence of osteoporosis at the total hip among postmenopausal white women generally in the United States of 15% from NHANES [13]. The prevalence of osteoporosis at the femoral neck in NHANES was 17%, whereas it was 21% among postmenopausal women in Sweden [14] and 8% in Canadian women [15]. Such differences could account for the fact that hip fracture incidence is greater in Sweden and lower in Canada than in the United States [11]. NHANES did not assess bone density at the spine or wrist, but the prevalence of osteoporosis at the lumbar spine among postmenopausal Rochester, Minnesota women rose only 2-fold between ages 50 and 59 years and 80 years and over, for an overall age-adjusted prevalence 8% (Table 1). The comparable figure in Canadian women was 12% [15]. This discrepancy is due to the age-related artifacts that mask bone loss from the vertebral body. At the total wrist, the comparable age-related increase was 13-fold (from 6% to 78%), for an overall prevalence of osteoporosis of the distal forearm among postmenopausal white women of 33%. Because there is only modest correlation among bone density values measured at different skeletal sites (see article by Miller), the proportion of women with osteoporosis at any one of several sites can be greater. Thus, an estimated 35% of postmenopausal white women have osteoporosis of the total hip, spine, or distal forearm [12], and they are at greatly increased risk of future fractures [14].

Gender

By the time peak bone mass is achieved, bone mass is one fourth to one third greater in men than women [16,17]. For example, among subjects aged 18 to 20 years in Buenos Aires, total body bone mass in men was 2965 g compared with 2368 g in women [18]. The same is true for specific skeletal sites. In the NHANES study, the age-adjusted BMC of the total hip averaged 43.5 g in white men compared with 29.2 g in white women [3]. Likewise, BMC of the hip was 50% greater on average in Mexican American (41.8 versus 27.8 g) and African American (46.6 versus 31.6 g) men compared with women from their respective ethnic groups. However, male skeletons are also larger: The mean area of the total hip, for example, was 43.7 cm^2 in white men compared with 33.1 cm^2 in white women in NHANES. This is partially adjusted for in the calculation of BMD values so that, on average, areal BMD of the total hip in men compared with women was 13% higher in non-Hispanic whites, African Americans, and Mexican Americans [3]. Similar results have been seen in other Latin American populations [19,20], and detailed results from a large Spanish study are shown in Table 2. Bone density is also greater in Asian men than women [21,22]. However, two-dimensional areal BMD (g/cm^2) scans do not fully correct for the fact that wider male bones are also thicker [23]. If three-dimensional bone size is adjusted for by calculating bone mineral apparent density (g/cm^3), these sex-specific differences in bone density are reduced [24,25]. In one study [24], a 22% excess in two-dimensional areal BMD of the femoral neck in men compared with women (0.766 versus 0.627 g/cm^2) was reduced to 7% (not significant) when three-dimensional volumetric bone density of the femoral neck was assessed (0.249 versus 0.232 g/cm^3). Similarly, adjustment for body size (height and weight) reduced the male excess in femoral neck BMD from 10% to 3% in NHANES [26], but bigger male bones are still biomechanically advantageous [27].

Because aging men of all races seem to lose bone from the proximal femur at rates similar to those seen for comparable women, one would expect the prevalence of osteoporosis, at least at the hip, to increase with age in men as it does in women. Because of the limited data available, the WHO did not propose a definition of osteoporosis for men, and male prevalence estimates are affected by the specific young normal means and standard

Table 2
Comparison of lumbar spine and femoral neck bone mineral density (g/cm^2) for Spanish men and women by age group

	Femoral neck				Lumbar spine	
	Male		Female			
Age group (yr)	*n*	Mean	*n*	Mean	Male (mean)	Female (mean)
20–29	231	0.927[a]	235	0.840	1.039	1.031
30–39	222	0.869[a]	232	0.808	1.021	1.040
40–49	213	0.855[a]	230	0.806	1.010[a]	1.001
50–59	190	0.824[a]	232	0.740	0.985[a]	0.924
60–69	164	0.791[a]	210	0.694	0.992[a]	0.844
70–79	114	0.731[a]	165	0.626	0.937[a]	0.810

[a] Statistically significant for men versus women of the same age at $P < 0.0001$.

Modified from Diaz Curiel M, Carrasco de la Peña JL, Honorato Perez J, et al. Study of bone mineral density in lumbar spine and femoral neck in a Spanish population. Multicentre Research Project on Osteoporosis. Osteoporos Int 1997;7:59–64; with permission.

deviations used to calculate *t* scores. Based on the same absolute bone density cut-off level for men as for women (0.56 g/cm^2 for femoral neck BMD by DXA), the prevalence of osteoporosis among white, Hispanic, and African American men age 50 years and over was 4%, 2%, and 3%, respectively, in NHANES [13]. Similarly, data from Great Britain suggest that about 6% of men have hip BMD more than 2.5 SD below the normal mean for young women (0.545 g/cm^2 by DXA) compared with 22% of British women [2]. However, osteoporosis prevalence estimates increase substantially when male sex-specific normal values are used (Fig. 2). When NHANES prevalence rates were recalculated on the basis of femoral neck BMD levels more than 2.5 SD below the mean for young men (0.59 g/cm^2), the higher mean value caused the estimates for white, Hispanic, and African American men to increase to 7%, 3%, and 5%, respectively. The comparable figure for Canadian men was about 4% [15]. Because of their lower prevalence of osteoporosis and reduced risk of falling [28], age-specific hip fracture risk is lower in men than in women [11]. At any given level of absolute BMD, however, fracture risk in men resembles that seen in women [29,30].

Ethnicity

Although there are exceptions, bone mass is generally lower among people of Caucasian and Asian heritage than other races. Americans of African decent, particularly, have substantially greater bone density than whites of the same age and sex. In the NHANES study [3], for example, total hip BMD was 10% greater in African Americans compared with whites (1.089 versus 0.993 g/cm^2 for men and 0.966 versus 0.880 g/cm^2 for

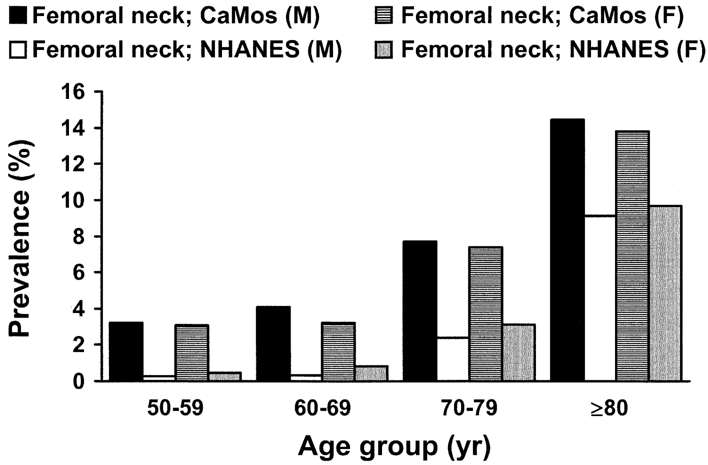

Fig. 2. Age-adjusted prevalence of osteoporosis at the femoral neck by WHO criteria in men aged ≥50 years calculated using male (M) or female (W) reference values from the present study or from NHANES. (*From* Tenenhouse A, Joseph L, Kreiger N, et al. Estimation of the prevalence of low bone density in Canadian women and men using a population-specific DXA reference standard: the Canadian Multicentre Osteoporosis Study (CaMos). Osteoporos Int 2000;11:897–907; with permission.)

women). As with the comparison of men with women, however, racial comparisons of areal BMD are confounded by residual differences in bone size that are not corrected by taking into account the projected area of the scan. Thus, femoral neck BMD was 14% higher in postmenopausal African American than white women in one study, but this was reduced to 10% by correction for three-dimensional volume [31]. However, correcting for bone size with volumetric bone mineral apparent density did not reduce the proportionate advantage in lumbar spine bone density of African American compared with white women, and similar results have been reported by others [32–34]. By contrast, differences in bone size largely account for the apparent difference in bone density between white and Asian women [21,31,35–38]. For example, BMD at various sites was similar in New Zealand women of Chinese or Indian origin but significantly less than in women of European heritage, but the latter were taller than the Chinese and Indian women [36]. When BMD was divided by the height of the subject or by the square root of the bone area, the differences in mean BMD between the Chinese, Indian, and European women were almost completely eliminated (Fig. 3).

It is unclear how osteoporosis should be defined in nonwhites but, based on the normal values for non-Hispanic white women, the age-adjusted prevalence of osteoporosis at the femoral neck among African American women is 6%, compared with 17% for postmenopausal white women in the United States [13]. Although this is consistent with the lower fracture rates

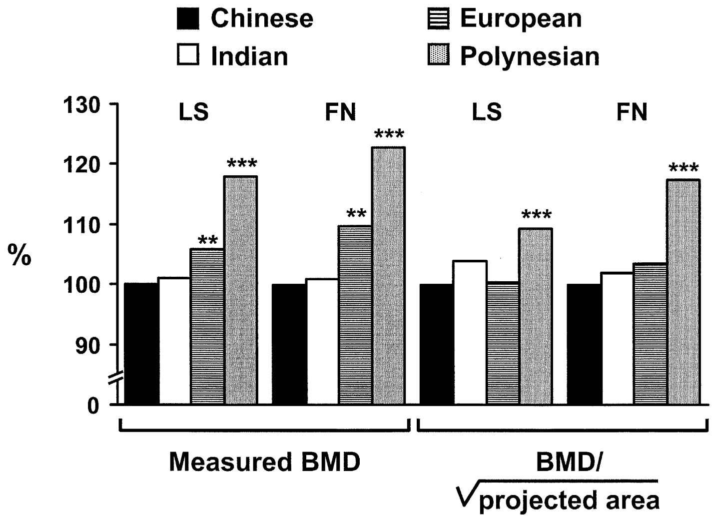

Fig. 3. Bone mineral density (BMD) of the lumbar spine (LS) and femoral neck (FN) among premenopausal New Zealand women from different ethnic groups, as originally measured and as corrected for skeletal size. (*Modified from* Cundy T, Cornish J, Evans MC, et al. Sources of interracial variation in bone mineral density. J Bone Miner Res 1995;10:368–373; with permission.)

observed in African Americans [39], native Africans have low hip fracture incidence rates yet have bone density values even lower than those of African whites, who display the usual Western pattern of hip fracture incidence [40–43]. Hispanic women in the United States have an estimated prevalence of osteoporosis of the hip of 14%, which is consistent with the somewhat lower risk of hip fractures seen in most but not all populations of Spanish origin compared with those of northern European decent [39]. In the absence of detailed data, it has been surmised that Asian Americans have a prevalence of osteoporosis similar to that in whites [44]. Data from the Japanese Population-Based Osteoporosis Study (Table 3) indicate that the prevalence of osteoporosis at the lumbar spine is as high or higher than in white women, whereas the prevalence of osteoporosis at the femoral neck (12%) is less [45]. This is consistent with the observation that vertebral fractures are almost as common among Asian women as they are in white women [46,47], whereas hip fractures are considerably less common [48]. The latter difference has been attributed to a lower risk of falling among Asian women [49,50]. More curious, perhaps, are the variations within populations of a given race and gender. Thus, hip fracture incidence [51–53] and bone density [54] differ among Asian populations. Such discrepancies, like those seen among different populations of African heritage [34] and even within European populations [55], reinforce the notion that individuals of particular races should not be viewed as members of a uniform class but

Table 3
Young adult mean and SD for bone mineral density (g/cm^2) at various sites and the cut-off values for diagnosis of osteoporosis according to WHO and Japanese Society of Bone and Mineral Research (JSBMR) criteria, together with the prevalence of osteoporosis according to each criterion in 1400 women aged 50–79 years

	Young adults' values		Cut-off values according to		Prevalence of osteoporosis according to	
Skeletal site	Mean	SD	WHO	JSBMR	WHO	JSBMR
Lumbar spine	1.031	0.109	0.759	0.722	38.0%	27.6%
Femoral neck	0.801	0.106	0.536	0.561	11.6%	17.0%
Trochanter	0.668	0.089	0.446	0.468	16.8%	22.9%
Intertrochanter	1.030	0.124	0.720	0.721	13.4%	13.5%
Ward's triangle	0.729	0.134	0.394	0.510	38.3%	71.4%
Total hip	0.886	0.105	0.624	0.620	15.3%	14.6%
Distal one third radius	0.755	0.064	0.595	0.529	56.8%	35.4%
Ultradistal forearm	0.345	0.048	0.225	0.242	36.3%	48.8%

Modified from Iki M, Kagamimori S, Kagawa Y, et al. Bone mineral density of the spine, hip and distal forearm in representative samples of the Japanese female population: Japanese Population-Based Osteoporosis (JPOS) Study. Osteoporos Int 2001;12:529–37; with permission.

rather that efforts should be made to explore differences among the component ethnic groups [56].

Other risk factors

Although a large number of putative risk factors for fracture have been linked to bone loss [57], the numerous epidemiologic studies conducted to date have found no consistent set of predictors of osteoporosis. Moreover, the relationship between many of the risk factors seen in population-based studies and the pathophysiologic basis for osteoporosis is obscure (see article by Rodan in this issue). In one of the most comprehensive investigations to date, the determinants of bone density were assessed cross-sectionally in the Study of Osteoporotic Fractures, a cohort of over 9500 elderly white and Asian women (Table 4). Later age at menopause, estrogen or thiazide use, noninsulin-dependent diabetes, and greater height, weight, strength, and dietary calcium intake were all positively associated with bone mass at the distal radius, whereas age, cigarette smoking, caffeine intake, previous gastric surgery, and maternal history of fracture were negatively associated [58]. Greater height and weight, older age at menopause, history of arthritis, greater physical activity, use of alcoholic beverages, diuretic treatment, and current estrogen replacement therapy were associated with higher lumbar spine BMD, whereas later age at menarche and a maternal history of fracture were associated with lower levels [59]. Increasing age was positively correlated with spinal BMD in

Table 4
Risk factors (–) and protective factors (+) for axial and appendicular bone density among elderly white women

Variable	Lumbar spine	Femoral neck	Distal radius
Age		– –	– –
Weight	+ + +	+ + +	+ + +
Height	+ +	+ +	+ +
Fracture in mother	– –	– –	– –
Age at menopause	+	+	+ +
Estrogen use	+ + +	+ + +	+ + +
Quadriceps strength		+ +	
Grip strength			+ + +
Thiazide use	+ + +	+ +	+ + +
Nonthiazide diuretic use	+ +		
Current smoker			– –
Number of alcoholic drinks in lifetime	+		
Dietary calcium intake		+ +	+
Lifetime caffeine intake			–
Noninsulin-dependent diabetes		+ + +	+ + +
Gastric surgery			– –
Recent or past physical activity	+	+	

The strength of correlations from multivariate analyses is indicated by the number of symbols. Three symbols indicate $\geq$3% change in bone density per unit change in the variable; two symbols, a 1%–3% change; and one symbol, a change of <1%.

From Orwoll ES, Bauer DC, Vogt TM, et al. Axial bone mass in older women. Study of Osteoporotic Fractures Research Group. Ann Intern Med 1996;124:187–96; with permission.

these elderly women, probably because of the vertebral osteophytosis noted previously because greater age was a risk factor for low radius and femoral neck BMD. Otherwise, femoral neck BMD was positively associated with most of the same protective factors, along with quadriceps strength, calcium intake, and a history of noninsulin-dependent diabetes. A maternal history of fracture and a personal history of previous wrist fracture were correlated with low femoral neck BMD. Despite the large number of potential risk factors assessed in the Study of Osteoporotic Fractures, however, models incorporating all of the independent predictors together explained only 20% to 34% of the variance in bone density at the different skeletal sites [59]. Moreover, the epidemiologic risk factors for bone loss in men [60,61] and women of other races [62,63] are only now being explored. Thus, a great deal of work remains to be done before patients at high risk for osteoporosis can be identified on the basis of clinical risk factors alone.

Future prospects

The number of individuals with osteoporosis will increase dramatically in the future as the population ages. In the United States, for example, the number of persons aged 65 years and over is expected to rise from 32 to 69 million between 1990 and 2050, and the number aged 85 years and over will increase from 3 to 15 million. Because the prevalence of low bone mass rises with age and is quite high in elderly women, these demographic changes will cause a substantial increase in the number of affected women. Considering osteoporosis of the hip alone, an estimated 7.8 million women and 2.3 million men in the United States are affected today, but these figures could rise to 10.5 million and 3.3 million, respectively, by the year 2020 [44]. These demographic changes could lead the number of hip fractures in the United States to double or triple by the year 2040 [64,65]. Worldwide, there were 323 million individuals age 65 years and over in 1990. This number will grow to an estimated 1555 million by 2050, and this demographic change alone could cause the number of hip fractures worldwide to increase from the estimated 1.7 million in 1990 to a projected 6.3 million in 2050 [66]. If, in addition, hip fracture incidence rates increase by 1% annually, the projected number of fractures in 2050 could be 8.2 million; if incidence rates stabilize in Europe and North America but increase by 3% annually in the other regions, the total number of hip fractures in the world each year could exceed 21 million by 2050 [67]. If the impact of these fractures is to be reduced, increased attention must be given to the design and implementation of effective control programs. The issue is how to accomplish this at a socially acceptable cost [68].

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