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Osteoporosis and Fracture Risk in Women of Different Ethnic Groups

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ABSTRACT: Osteoporosis and 1-year fracture risk were studied in 197,848 postmenopausal American women from five ethnic groups. Weight explained differences in BMD, except among blacks, who had the highest BMD. One SD decrease in BMD predicted a 50% increased fracture risk in each group. Despite similar relative risks, absolute fracture rates differed.

Introduction: Most information about osteoporosis comes from studies of white women. This study describes the frequency of osteoporosis and the association between BMD and fracture in women from five ethnic groups.
Materials and Methods: This study was made up of a cohort of 197,848 community-dwelling postmenopausal women (7784 blacks, 1912 Asians, 6973 Hispanics, and 1708 Native Americans) from the United States, without known osteoporosis or a recent BMD test. Heel, forearm, or finger BMD was measured, and risk factor information was obtained; 82% were followed for 1 year for new fractures. BMD and fracture rates were compared, adjusting for differences in covariates.
Results: By age 80, more than one-fifth of women in each ethnic group had peripheral BMD T scores <–2.5. Black women had the highest BMD; Asian women had the lowest. Only the BMD differences for blacks were not explained by differences in weight. After 1 year, 2414 new fractures of the spine, hip, forearm, wrist, or rib were reported. BMD at each site predicted fractures equally well within each ethnic group. After adjusting for BMD, weight, and other covariates, white and Hispanic women had the highest risk for fracture (relative risk [RR] 1.0 [referent group] and 0.95, 95% CI, 0.76, 1.20, respectively), followed by Native Americans (RR, 0.87; 95% CI, 0.57, 1.32), blacks (RR, 0.52; 95% CI, 0.38, 0.70), and Asian Americans (RR, 0.32; 95% CI, 0.15, 0.66). In age- and weight-adjusted models, each SD decrease in peripheral BMD predicted a 1.54 times increased risk of fracture in each ethnic group (95% CI, 1.48–1.61). Excluding wrist fractures, the most common fracture, did not materially change associations.
Conclusions: Ethnic differences in BMD are strongly influenced by body weight; fracture risk is strongly influenced by BMD in each group. Ethnic differences in absolute fracture risk remain, which may warrant ethnic-specific clinical recommendations.
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Key words: body weight, BMD, ethnicity, fracture risk, osteoporosis

INTRODUCTION

Osteoporosis has been considered to be a disorder of postmenopausal white women, and the predictive value of low BMD in quantifying risk of fracture in this group has been well studied. Less is known about the association of BMD with fracture risk in other postmenopausal populations. It has been shown that blacks have greater bone mass than whites,[1–4] whereas bone mass among Hispanics is more similar to whites.[1,3,5] Asians have lower bone mass than whites, although correcting for body size attenuates these differences.[4,6–8]

Differences in fracture risk do not necessarily parallel BMD differences, however. In most studies, white women have higher hip fracture rates than black, Asian, and Hispanic women.[1,9–12] A lower fracture risk for black women has been shown at other skeletal sites as well, including the distal forearm, the proximal humerus, and the ankle.[13] Differences in body size,[7,8] bone size,[14] rates of skeletal loss,[15–18] and hip geometry[19–22] have been reported to partially explain observed differences in fracture risk. Longitudinal data with baseline BMD and fracture outcomes for nonwhite North Americans are sparse, and it is un-

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known whether a T score obtained by BMD measurement in nonwhite women has the same meaning in terms of fracture prediction.[4]

The purpose of this paper is to describe the frequency of low BMD and the relation between low BMD and 1-year fracture incidence in a large cohort of postmenopausal women from five ethnic groups: black, Asian, white, Hispanic, and Native American. We evaluate the applicability of normative data derived from white women to women of other ethnicities.

MATERIALS AND METHODS

Participants

The National Osteoporosis Risk Assessment (NORA) is an observational study of postmenopausal women in the United States that began in late 1997. Details of the study design have been published.[23,24] In brief, women who were at least 6 months past their last menstrual period and at least 50 years old, who had not been diagnosed previously with osteoporosis, who had not had a bone density measurement within the preceding 12 months, and who were not taking bone-specific medications were eligible for participation. Women were recruited from 4236 primary care physician offices and included participants from 49 states and the District of Columbia. Participating physicians were identified because they had large numbers of postmenopausal women in their practices. From 100 to 300 women, randomly selected from each practice list, were invited to participate; usually no more than 100 women were invited per site, and 40–100 did participate. At baseline, participants completed a mailed set of questionnaires and had a peripheral BMD measurement (of the heel, forearm, or finger) at the physician's office. Follow-up questionnaires 6 and 12 months later inquired about fractures that had occurred since enrollment in NORA. Hip fracture reports were validated by telephone; ~80% were confirmed. All study protocols and consent documents were approved by a national Institutional Review Board, the Essex IRB.

Risk factors

Information about age, ethnicity, and risk factors was obtained using a standardized self-administered questionnaire. Ethnicity was self-reported, and groups defined for this study were white, black, Asian, Hispanic, and Native American. Risk factors investigated included weight; body mass index (BMI); years since menopause; personal and family history of fracture; maternal history of osteoporosis; use of calcium supplements; glucocorticoid, diuretic, estrogen and thyroid hormone therapy; cigarette smoking; alcohol use; and exercise habits. Each of these factors has been reported to be associated with BMD in white women. BMI (kg/m^2) was calculated from reported weight and height. A history of fracture after age 45 at each of four sites (hip, rib, spine, and wrist) was queried for the participant and her mother. Exercise was defined as engaging in any of a variety of activities for the purpose of exercise (as contrasted with physical activity undertaken for work) and was recorded as <3 or 3+ times/week. Women were asked about cigarette smoking (current, past, or never) and alcoholic drinks per week (none, 1–6, 7–13, or 14+).

BMD measurement

Each participant had BMD measured at a single site: the heel, using either single X-ray absorptiometry (SXA; Osteoanalyzer; Norland Medical Systems, Fort Atkinson, WI, USA) or ultrasound (US; Sahara; Hologic, Bedford, MA, USA); the forearm, using peripheral DXA (pDXA; Norland Medical Systems); or the finger, using peripheral DXA (AccuDXA; Schick Technologies, Long Island City, NY, USA). All BMD testing was conducted by licensed technicians, who completed manufacturer training and a certification program developed by the International Society for Clinical Densitometry. Calibration of each BMD instrument was performed daily and before use in each new location, using the manufacturer's internal standard. Instrument quality control data were reviewed throughout the project. In addition, each technician's scans were reviewed for consistency and quality.[25]

Definition of low BMD

Bone mass measurements were expressed in grams per centimeter squared and as the T score, using World Health Organization (WHO) definitions.[26] According to these criteria, BMD measurements between 1 and 2.5 SD below the average for the young normal reference population were classified as consistent with osteopenia (T score between –1 and –2.5). Measurements that were <–2.5 SD below the young adult mean were classified as osteoporosis. Because white women represent the most thoroughly studied group with regard to the relationship between BMD and fracture risk, and because one intention of the study was to determine how well these criteria predict fracture in nonwhite cohorts, T score values based on the white young adult mean were used. T scores were calculated from the normative populations used by the manufacturers of the devices. We have previously reported that T scores from peripheral devices predict fracture risk among white women in the NORA cohort.[27]

Data analysis

All analyses were conducted using SAS Version 6.12 software (SAS Institute, Cary, NC, USA). T scores were normally distributed and were used as a continuous variable in linear regression and as categories (normal, osteopenic, or osteoporotic) in analyses of bivariate associations. To select covariates for the adjustment of confounding effects in multivariate modeling, a general regression model for all ethnic groups was developed, as were separate models for each of the five ethnic groups. These models were constructed by use of backward elimination until a parsimonious model was achieved. Adequacy of model fit was assessed using log-likelihood ratio statistics.

Incident fractures of the hip, spine, forearm, wrist, and rib were identified from the first-year follow-up questionnaires. Reported new fractures were compared with fractures that had been reported at baseline. If the site was

identical, and no date between enrollment and follow-up was provided, the fracture was considered to be pre-existing and was not included in the present analysis. Participants reporting four or more new fractures, likely to reflect major trauma, were excluded from analyses. Overall fracture rates were calculated based on individuals who fractured, weighted for time of follow-up. Risk ratios, unadjusted and adjusted for important covariates, were based on Cox proportional hazards models, with analogous procedures used to develop parsimonious models. Receiver operating characteristic (ROC) curves and areas under these curves (AUC) were generated from logistic regression models adjusted for age and weight, using T score as a continuous variable. ROC models, fit by maximum likelihood, yield sensitivity and specificity throughout the T score range, assuming the logarithm of the risk per SD difference to be constant across BMD values.

RESULTS

A total of 197,848 women were included in this investigation. Table 1 shows the distribution and the baseline characteristics of the study population by ethnic group. All of the variables shown differed significantly by ethnic group ($p \leq 0.001$). Although the majority (90.7%) of the participants were white, there were 7784 blacks (3.9%), 6973 Hispanic Americans (3.5%), 1912 Asian Americans (1.0%), and 1708 Native Americans (0.9%). Asians were the youngest participants, with 3.9% ⩾80 years of age, and Native Americans were the oldest, with 13.8% ⩾80 years of age. Asians were the leanest (43% had a BMI <23 kg/m^2; mean weight, 57.4 kg), and blacks were the heaviest (45% had a BMI ⩾30 kg/m^2; mean weight, 80.2 kg). Blacks reported the lowest frequency of maternal history of osteoporosis (3.3%) and fracture (7.2%), as well as the lowest personal history of fracture (5.8%). Whites reported the highest maternal fracture history (23.3%), and Native Americans reported the highest personal fracture history (15.3%). As shown, there were also significant differences between groups for medication use and health-related behaviors.

As shown in Table 2, varying proportions of women of different ethnic groups had measurements by the four devices. BMD was measured by heel SXA in 49–68%; 26–35% had forearm pDXA measurements; 3–11% had finger pDXA measurements; and 2–5% had heel US measurements. Asian women had the lowest mean T score (–1.22 ± 1.04 [SD]); black women had the highest (–0.39 ± 1.30). The mean T score in white women was –0.89 ± 1.14, and Hispanic and Native American women had intermediate T scores (–1.13 ± 1.12 and –1.11 ± 1.24, respectively). Based on WHO criteria, 11.9% of Native American women, 10% of Asians, 9.8% of Hispanics, 7.2% of whites, and 4.2% of blacks were osteoporotic (T scores of –2.50 or lower), whereas osteopenia (T score –1.0 to –2.5) was identified in 50.1% of Asians, 46.5% of Hispanics, 44.5% of Native Americans, 39.6% of whites, and 28.1% of black women (Table 2).

Figure 1 shows mean T scores by age and ethnicity. There were no significant differences by ethnicity with respect to the pattern of the decrease in T scores with increasing age. At every age, black women had the highest BMD and Asian women had the lowest. Values for Native American and white women were quite similar, with slightly lower levels in Hispanics. After adjusting for weight and all other significant covariates except personal and family history of osteoporosis, the odds of osteoporosis relative to whites (referent odds = 1.0) were 0.55 (95% CI, 0.48, 0.62) for black women; 0.96 (95% CI, 0.81, 1.14) for Native American women; 1.20 (95% CI, 1.19, 1.32) for Hispanic women, and 1.05 (95% CI, 0.88, 1.25) for Asian women (Fig. 2). Adding height or personal or maternal history of fracture did not materially change these results.

The overall response rate to the 1-year follow-up survey was 82% (n = 162,321). Respondents were younger, better educated, and reported better self-rated health; they were less likely to have used estrogen or to exercise regularly. The response rate was highest among whites (83.3%), followed by Native Americans (76.5%), blacks (71.3%), Asians (65.7%), and Hispanics (63.3%).

During the follow-up period, 2414 clinical fractures of the hip, spine, forearm, wrist, or rib were reported (1.5% of respondents; Table 3). Wrist/forearm fractures were most common (n = 1087); spine fractures were reported least frequently (n = 239); 698 rib fractures and 430 hip fractures were reported. Fracture incidence differed significantly among ethnic groups (p = 0.001), reflecting differences in the incidence of wrist/arm fractures (p = 0.006), because incidence of fractures at other sites did not differ significantly by ethnicity.

Fracture rates per hundred person-years by age group and ethnicity are shown in Fig. 3. Some estimates of fracture rates were unstable because of small numbers of events. For each ethnic group, fracture rates increased with advancing age. In general, black and Asian women had the lowest fracture rates within each age group, whereas white and Hispanic women had the highest fracture rates. Black, white, and Hispanic women ⩾80 years of age had markedly higher fracture rates than women in younger age groups, but this age effect was less obvious among the oldest Asian and Native American women. Figure 4 shows the association between T score groups, using WHO definitions, and fracture incidence according to ethnicity. For every ethnic group, fracture rates were lowest among women with normal BMD and highest in women with osteoporosis.

In multiply adjusted proportional hazards modeling of fracture risk (Table 4), in which T score effect was constrained to be constant across ethnic groups by entering a single term for BMD in the model, a decrease of 1 SD increased fracture risk by 1.54 times (95% CI, 1.48, 1.61). In this model, black women had ~50% the risk of fracture of whites (RR, 0.52; 95% CI, 0.38, 0.70), and Asians had almost 70% lower risk (RR, 0.32; 95% CI, 0.15, 0.66). Estimates of risk for Hispanic and Native-American women were similar to those for white women. Because of the dominant effect of the wrist fracture, the most common fracture in this cohort, we repeated the analysis excluding wrist fractures to determine whether the associations would be similar. As shown in Table 4, the nonwrist fracture risks were similar (based on overlapping 95% CIs) to those observed for all fractures combined.

TABLE 1. CHARACTERISTICS OF PARTICIPANTS BY ETHNICITY

Characteristics	*Overall (*N)	*White (%)*	*Black (%)*	*Asian (%)*	*Hispanic (%)*	*Native American (%)*
N	197,848	179,470	7,784	1,912	6,973	1,708
Age						
50–59	70,356	35.5	37.9	44.0	35.2	22.7
60–69	66,591	33.7	34.4	32.0	33.5	27.6
70–79	47,947	24.3	22.0	19.8	24.2	35.8
80+	12,887	6.5	5.8	3.9	7.0	13.8
Missing/unknown	67	0.0	0.0	0.3	0.1	0.0
Education						
HS or less	115,412	57.4	63.0	41.1	75.9	81.0
Some college	31,100	42.0	35.7	57.6	21.4	17.6
Missing/unknown	1,336	0.6	1.3	1.3	2.7	1.4
Current health status						
Excellent	22,650	12.0	4.8	9.9	7.3	5.7
Very good	63,874	33.4	19.8	29.7	20.4	22.7
Good	75,901	38.2	40.9	41.8	37.2	42.6
Fair/poor	33,278	15.4	32.6	17.6	32.2	27.2
Missing/unknown	2,145	1.0	1.9	1.0	2.9	1.9
Years since menopause						
0–9	42,498	21.7	17.4	33.4	19.9	10.2
10–19	50,675	25.9	22.7	26.1	24.2	16.2
20–29	51,982	26.5	24.9	17.2	24.5	29.7
30+	29,785	15.0	16.3	7.4	15.7	26.4
Missing/unknown	22,908	11.0	18.7	16.0	15.7	17.6
Body mass index						
0–22.99	39,683	20.5	8.1	43.0	14.7	20.4
23–25.99	46,334	23.8	14.7	29.3	21.0	22.1
26–29.99	49,568	25.0	25.7	17.8	27.5	24.4
30+	55,339	27.4	44.8	6.9	30.3	28.0
Missing/unknown	6,924	3.2	6.8	3.1	6.6	5.2
History of fracture since 45						
Any fracture	21,800	11.2	5.8	7.2	11.2	15.3
Hip	2,758	1.4	1.2	0.8	1.9	2.0
Rib	7,273	3.8	1.3	1.9	3.5	5.2
Wrist	12,167	6.3	3.1	3.7	6.2	8.4
Spine	2,380	1.2	0.9	1.4	1.8	1.8
Maternal history of osteoporosis						
Yes	23,321	12.4	3.3	7.1	8.0	8.2
Maternal history of fracture						
Yes	43,969	23.3	7.2	11.6	15.3	18.6
Medication use						
Thyroid hormone	35,556	18.5	9.7	9.4	15.4	16.7
Cortisone	4,556	2.2	3.2	1.8	3.1	2.6
Diuretics	33,775	17.1	22.9	9.5	11.3	15.6
Estrogen use						
Never used HRT	67,559	33.1	47.0	43.8	43.0	41.7
Past user HRT	35,987	18.4	16.7	13.5	14.8	18.0
Current user HRT	89,429	46.4	30.3	38.9	34.7	33.2
Missing/unknown	4,873	2.0	6.0	3.9	7.5	7.1
Cigarette smoking						
Never smoked	104,582	52.5	49.0	78.6	59.8	55.7
Past smoker	69,283	35.6	35.2	15.6	27.3	29.3
Current smoker	21,206	10.8	12.5	4.3	8.5	11.8
Missing/unknown	2,777	1.2	3.3	1.5	4.4	3.2
Regular exercise (per week)						
0–2 times	98,401	49.5	54.2	46.4	53.3	45.3
3+	96,078	49.0	42.6	51.8	42.2	51.3
Missing/unknown	3,369	1.5	3.2	1.8	4.5	3.5
Alcohol use (per week)						
None	143,205	71.6	82.1	81.4	78.5	80.4
<7 drinks	33,897	17.9	9.4	8.4	10.7	9.6
7–13 drinks	10,449	5.6	1.8	1.5	1.9	3.0
14+ drinks	5,065	2.8	0.6	0.3	0.6	1.1
Missing/unknown	5,232	2.2	6.0	8.5	8.4	5.9

TABLE 2. DISTRIBUTION OF BMD, OSTEOPOROSIS, AND OSTEOPENIA BY ETHNICITY AND DEVICE

	White	*Black*	*Asian*	*Hispanic*	*Native American*
N	179,470	7,784	1,912	6,973	1,708
T score					
Mean	−0.89	−0.39	−1.22	−1.13	−1.12
SD	1.14	1.30	1.04	1.12	1.24
>−1.0	53.2	67.7	39.9	43.7	43.6
−1.0 to −2.5	39.6	28.1	50.1	46.5	44.5
≤−2.5	7.2	4.2	10.0	9.8	11.9
Device (%)					
Heel SXA	53.4	56.8	68.4	60.4	49.1
Forearm p-DXA	34.2	28.0	25.9	30.7	35.3
Sahara	5.0	3.7	2.5	3.0	5.0
AccuDXA	7.4	11.5	3.2	5.9	10.6
SXA					
N	95,849	4,422	1,308	4,210	839
T score					
% >−1.0	50.8	64.3	35.2	43.2	39.9
% −1.0 to −2.49	44.4	32.6	56.3	51.0	50.3
% ≤−2.5	4.8	3.1	8.6	5.8	9.8
p-DXA					
N	61,412	2,177	495	2,141	603
T score					
% >−1.0	54.7	70.6	48.1	42.7	44.8
% −1.0 to −2.49	35.4	24.4	38.6	41.7	40.1
% ≤−2.5	10.0	5.0	13.3	15.6	15.1
Heel US					
N	8,947	287	47	208	85
T score					
% >−1.0	62.5	67.9	76.6	56.3	60.0
% −1.0 to −2.49	34.2	27.5	21.3	35.6	37.7
% <= −2.5	3.3	4.5	2.1	8.2	2.3
AccuDXA					
N	13,263	898	62	414	181
T score					
% >−1.0	58.1	77.6	46.8	48.1	49.2
% −1.0 to −2.49	28.4	15.1	32.3	30.7	35.3
% ≤=−2.5	13.5	7.2	21.0	21.3	15.5

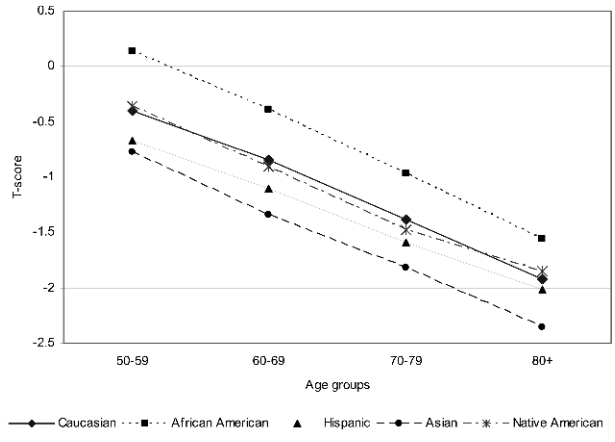

FIG. 1. Mean T score by age and ethnicity.

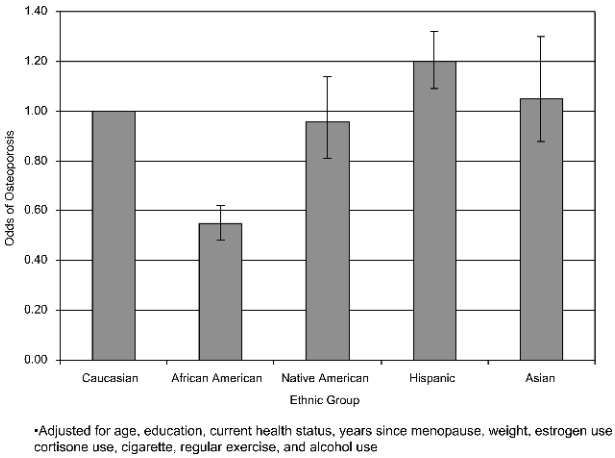

FIG. 2. Odds of osteoporosis (T score ≤−2.5 and 95% CI) by ethnicity, adjusted for *covariates.

In a separate model that allowed the magnitude of BMD effect on fracture risk to vary among ethnic groups, adjusting for age, education, self-reported health, years since menopause, weight, hormone replacement therapy (HRT), cortisone use, and measurement site/device, the effect of an ethnic-specific SD change in BMD did not differ significantly among ethnic groups except for black women, who

TABLE 3. NUMBER (PERCENT) FRACTURES REPORTED DURING FOLLOW-UP ACCORDING TO SITE OF FRACTURE AND ETHNICITY

	Overall	*White*	*Black*	*Asian*	*Hispanic*	*Native American*	p *Value*
N	162,321	149,524	5,842	1,258	4,415	1,282	
Hip	430 (0.3)	393 (0.3)	11 (0.2)	3 (0.2)	17 (0.4)	6 (0.5)	0.217
Rib	698 (0.4)	658 (0.4)	9 (0.2)	3 (0.2)	24 (0.5)	4 (0.3)	0.501
Spine	239 (0.2)	277 (0.2)	7 (0.1)	2 (0.2)	6 (0.1)	1 (0.1)	0.618
Wrist/arm	1,087 (0.7)	1,012 (0.7)	26 (0.5)	2 (0.2)	32 (0.7)	15 (1.2)	0.006
Wrist	871 (0.5)	812 (0.5)	21 (0.4)	2 (0.2)	23 (0.5)	13 (1.0)	0.015
Arm	240 (0.2)	221 (0.2)	7 (0.1)	0 (0.0)	10 (0.2)	2 (0.2)	0.402
Total	2,414 (1.5)	2,259 (1.5)	48 (0.8)	9 (0.7)	77 (1.7)	23 (1.8)	0.001

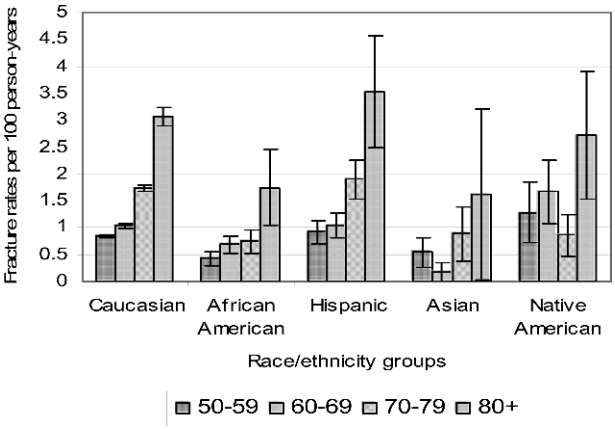

FIG. 3. Fracture rates per 100 person-years by ethnicity and age group ± SE.

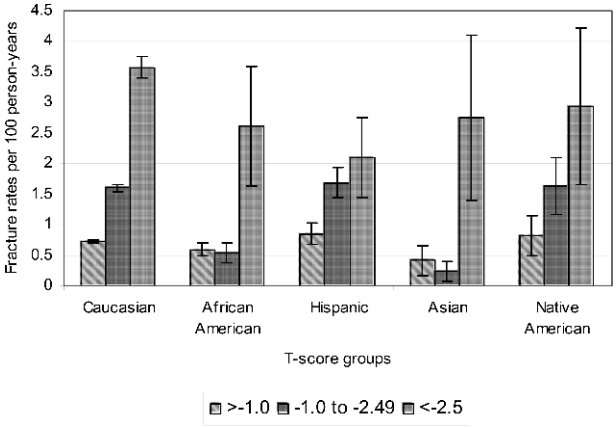

FIG. 4. Fracture rates per 100 person-years by ethnicity and T score group ± SE.

had a significantly lower fracture risk (RR, 0.63; 95% CI, 0.44, 0.90). The weakest of the positive associations was observed in Asians, which probably reflects an unstable estimate because of the small number of fractures.

The area under the age-adjusted ROC curves for BMD prediction of fracture incidence in each ethnic group was 0.67 for the white women, 0.66 for Hispanic women, 0.63 for Asian American women, 0.62 for Native American women, and 0.59 for black women. Despite the small number of fracture events in Asian and Native American women, all curves overlapped to a considerable extent. Ethnicity, BMD, and fracture relationships did not materially change when adding height or personal and maternal history of osteoporosis to these analyses. In an analysis designed to control for the different proportions using different BMD methods/sites, the analysis was repeated, restricted to women who had heel SXA. This analysis showed similar patterns (data not shown).

DISCUSSION

This study, the largest investigation of the influence of ethnicity on BMD and fractures in postmenopausal women, shows consistent ethnic differences in BMD such that blacks had the highest and Asians had the lowest BMD at every age (Fig. 1). After adjustment for body weight and other risk factor covariates, black women had the highest average BMD followed by Hispanic women, whereas Asians and Native Americans had BMD values differing little from those of whites. In models adjusted for weight and other variables, BMD predicted 1-year fracture risk equally well in whites, blacks, and Hispanics, with similar patterns but wider confidence intervals in Native Americans and Asians, reflecting smaller numbers.

Few studies have simultaneously compared BMD among women of more than two ethnic groups. BMD was measured at the hip in a multiethnic subset of 3175 women ⩾50 years in the third National Health and Nutrition Examination Survey (NHANES III).[3] In this representative sample, non-Hispanic blacks in each age group had the highest mean femoral neck and total hip BMD levels, Mexican Americans generally had intermediate levels, and whites had the lowest levels. Our results for 7784 black women are consistent with these and other smaller published studies, showing that black females, both children and pre- and postmenopausal adults, have higher BMD than whites.[2,4,18,28] Although risk factors for osteoporosis in blacks are similar to those reported for whites,[29] black women in the NORA cohort were significantly less likely to have a personal or maternal history of fracture. This information was not added to the main analyses reported here to avoid potential overadjustment for a race-related characteristic. However, adding personal and family history to the final multiply adjusted model did not materially change the observed associations.

TABLE 4. RISK OF FRACTURE BY ETHNICITY, ADJUSTED FOR COVARIATES INCLUDING BMD T SCORE

	Osteoporotic fractures [relative risk (95% CI)]	*Non-wrist fractures [relative risk (95% CI)]*
Ethnicity		
White	1.00	1.00
Black	0.52 (0.38, 0.70)	0.45 (0.30, 0.66)
Asian	0.32 (0.15, 0.66)	0.42 (0.19, 0.94)
Hispanic	0.95 (0.76, 1.20)	1.01 (0.77, 1.33)
Native American	0.87 (0.57, 1.32)	0.59 (0.32, 1.10)
BMD (per 1 SD decrease in T score)	1.54 (1.48, 1.61)	1.41 (1.34, 1.49)

Relative risk and CI based on Cox proportional hazard model adjusted for age, education, current health status, years since menopause, weight, estrogen use, cortisone use, and BMD site/device. White is referent population (RR 1.00).

NORA results for 1912 Asian participants are also consistent with the published literature showing lower BMD levels in Japanese, Chinese, and Filipino women compared with white women,[1,6,30,31] with differences in body size responsible for much of the observed difference in BMD.[4,6–8,14,32] In analyses restricted to the smallest women in the SWAN study, there were no BMD differences between white women and either Chinese or Japanese Americans.[4] Similarly, Asian women in NORA were not at increased odds of osteoporosis when weight was included in the model (OR, 1.05; 95% CI, 0.88,1.25).

Our results for 6973 Hispanic women differ from those reported in NHANES III, in which BMD in Hispanics was slightly but not significantly higher than that of whites of comparable age.[3] However, NHANES III data were not adjusted for any risk factor covariates, in contrast to this study. The 47 Hispanic women in the Postmenopausal Estrogen/Progestin Interventions (PEPI) trial had femoral neck BMD higher than that in other ethnic groups after adjustment for age and BMI, but these differences were not adjusted for weight.[33] In a San Diego study,[5] there were no differences in hip or total body BMD between Mexican Americans and whites in models adjusted for age, height, and BMI. In NORA, replacing weight with BMI in the multiply-adjusted model increased the odds of osteoporosis from 1.20 to 1.31. Peripheral BMD measurement by ultrasound of the finger has been shown to identify osteoporosis at the hip and spine in Mexican women living in San Diego.[34] The NORA Hispanic women were of diverse backgrounds (including Mexican, Puerto Rican, and Cuban), but subgroup analysis by heritage showed no important differences in BMD (data not shown).

Based on white normative databases, BMD in 1708 NORA Native Americans was similar to that of whites; the odds of osteoporosis were similar when weight or BMI was used in the multivariate analyses. Although these are the most extensive data published, numbers are insufficient to provide comparisons among tribes. One study reported much lower BMD in Alaska native women from several tribes compared with non-natives, but age-adjusted comparisons were not shown.[35] Earlier work did not provide age-specific values for BMD for postmenopausal Native American women.[15,36–38]

In NORA, black women's BMD differences were reduced but not entirely explained by adjusting for weight. Similarly, in the Health, Aging, and Body Composition (Health ABC) Study, differences in BMD between healthy elderly black and white women were not explained by differences in height, body weight, lean mass, or fat mass.[39] Black and white differences are probably not explained by differences in sex hormones, because premenopausal black women tend to have lower levels of estradiol and dehydroepiandrosterone sulfate (DHEAS) than white women.[40] Several investigators have reported black-white differences in levels of circulating biochemical bone turnover markers,[2,41,42] but this was not observed in SWAN women.[43] There is some evidence that black women may have skeletal resistance to the bone-resorbing effects of secondary hyperparathyroidism.[44]

Although the race/ethnic differences in BMD (Fig. 1) are largely explained by weight except in blacks, the clinically relevant question is whether these unadjusted differences require the use of ethnic-specific T score equivalents for fracture prediction. We have previously reported that white normative values for these four measurement devices predict fracture risk in postmenopausal white women across all age groups.[27] In this study we showed that women show a similar pattern of increasing fracture risk with decreasing BMD levels, regardless of race or ethnicity. NORA women who were found to have osteopenia or osteoporosis (by WHO criteria) had an increased risk of fracture in every ethnic group (Fig. 4). The differences between osteopenia and osteoporosis for the black and Asian women may reflect chance or the amount of time women in these ethnic groups spend in transition from normal bone to osteoporosis. For women in all ethnic groups, fracture risk increased by 54% (RR, 1.54; 95% CI, 1.48, 1.61) for each SD decline in T score. Exclusion of wrist fractures, which were the most commonly reported fracture events, and consequently, exerted a dominant effect in models of ethnic-specific associations of BMD and fracture risk, did not materially alter the findings.

Although black women had the highest BMD levels and Asian women had the lowest BMD levels, these two groups had a similarly low risk of fracture. The low fracture rate in black and Asian women has been reported previously[45,46] and may reflect musculoskeletal factors other than BMD that are important in fracture prediction. It is unlikely to be explained by postulated differences in quadriceps muscle strength, because significant wrist fracture differences were observed in NORA (Table 2), or by differences in leg length, which on average is longest in blacks and shortest in Asian women.

Strength of bone and resistance to fracture depend on structural and material properties, including the diameter of the bone, thickness and numbers of trabeculae, and cortical thickness.[47,48] Ethnic differences in hip geometry, in particular the hip axis length, have been correlated with differences in fracture risk. In one study of white women, longer hip axis length was associated with increased risk of

hip fracture.[49] Average hip axis length has been found to be shorter among Mexican-American women,[50] Asian women,[19,51] and black women[19,20] than among white women. Rates of bone loss in postmenopausal Asian women have been reported to be lower than in white women[52]; however, similar structural decrements, including cortical thinning, have been observed at the femoral neck.[53] Skeletal factors other than BMD cannot be assessed directly from the NORA study.

Other limitations of this study include possible selection bias, because participation was voluntary, and eligibility was dependent on having a personal physician and no known osteoporosis. All other major studies of osteoporosis reported from the United States have studied volunteers, convenience samples, whites only, or have had a fairly low participation rate (around 60%), each with a potential for selection bias. Having a personal physician, an eligibility criterion for NORA, should reduce bias related to socioeconomic, racial, or ethnic differences in diagnostic access and treatment. Risk factor information and fractures were self-reported and not validated by medical records; others have reported reasonable accuracy of self-report,[54–58] but we cannot exclude differences in validity of recall among ethnic groups. Only peripheral BMD was measured; results may differ at central skeletal sites. Normative ethnic-specific population databases have not been published on peripheral devices, nor indeed, for central DXA instruments. Despite large samples, the relatively low number of fractures reported in some subgroups limits the precision of estimates of association. The short follow-up may be viewed as a limitation, although it has the advantage of reducing unknown interim changes in risk factors and BMD before the incident fractures.

The prevalence of low BMD and the absolute risk of fracture at any given BMD do differ among ethnic groups (Figs. 3 and 4). Within any single ethnic group, however, fracture risk increases as peripherally measured BMD[59] decreases, and this predictive relationship holds regardless of measurement site or device or use of a white reference population. Longer follow-up of the NORA cohort, in progress, is expected to increase the number of fractures and provide more precise estimates with power to look at gradients of relative and absolute risk for different fracture types in different ethnic groups. Further follow-up is necessary to determine whether differences in absolute risks are large enough to warrant ethnic-specific screening and treatment recommendations.

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