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Classification of Osteoporosis in the Elderly is Dependent on Site-Specific Analysis

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Abstract. Vertebral osteoporosis accounts for over 500,000 spinal fractures annually, the majority of which occur in older women. Despite these statistics, data regarding the rate of spinal bone loss in this population are conflicting. Moreover, the site of skeletal evaluation may significantly alter classification of osteoporosis in this age group. To examine trabecular-rich spinal bone loss with a measurement less affected by age-related artifacts than the AP spine, we measured lateral lumbar spine bone density (BMD) using dual-energy X-ray absorptiometry in 120 healthy, ambulatory, community-dwelling women 65 years of age and older (mean 70 ± 5 years, range 65–88). We also examined cortical-rich sites in the forearm and total body along with AP spine and femoral BMD to assess the impact of site specificity using the World Health Organization (WHO) classification of osteoporosis. Significant losses in BMD were observed at the lateral spine (−1.1%/year, $P < 0.01$), forearm (−0.77%/year, $P \leq 0.01$), total hip (−0.75%/year, $P \leq 0.01$), femoral neck (−0.70%/year, $P \leq 0.05$), and trochanter (−0.78%/year, $P \leq 0.01$), but not the AP spine. Using the WHO criteria, lateral spine BMD determinations classified 66% of women with osteoporosis in contrast to 29% using the AP projection. Osteoporosis was diagnosed in 55% of women using measurements of the femoral neck, 43% using the total radius, and 19% using the total body. We conclude that elderly women lose bone at trabecular- and cortical-rich sites (lateral spine and total radius, respectively) in addition to sustaining significant age-related bone loss at mixed cortical/trabecular sites such as the hip. Classification of osteoporosis in this age group more than doubles using lateral versus AP spinal projections, supporting the necessity of developing more uniform agreement on site-specific analyses.

Key words: Osteoporosis — Elderly women — Lateral BMD — Classification.

Vertebral osteoporosis is associated with over 500,000 fractures annually [1], the majority of which occur in women over age 65 [1, 2]. Data regarding the rate and degree of spinal bone loss in this population are conflicting. Recent cross-sectional studies using anterior-posterior (AP) spinal bone mineral density (BMD) measurements in women over age 50 have demonstrated decreasing BMD with age [3, 4], whereas longitudinal studies focusing on AP measurements suggest that bone loss actually ceases in women over age 65 [5]. By contrast, cross-sectional and longitudinal analysis of the rate of bone loss at the hip show no such discrepancies [6].

In addition to conflicting reports regarding the rate of age-related bone loss at the AP spine [5–7], such measurements may not accurately reflect skeletal integrity, since aortic, sclerotic, and osteophytic calcifications can produce falsely elevated BMD values [3, 8–11]. Previous studies in women ranging from age 20 to 84 years have demonstrated that lateral dual energy X-ray absorptiometry (DXA) detects osteopenia more often than AP DXA [12, 13]. However, the number of elderly women in these studies has been limited. Obtaining a single AP BMD measurement in such women can have significant clinical ramifications. Using the new World Health Organization (WHO) classification for osteoporosis (BMD more than 2.5 SDs below peak BMD [14]), AP assessments of vertebral bone could misclassify women as "nonosteoporotic," whereas lateral measurements that omit these artifacts would suggest a classification of "osteoporosis," thereby carrying a greater risk of fracture. Furthermore, in addition to establishing a potentially misleading fracture risk of the spine, the single measurement may not represent BMD and fracture risk at other skeletal sites. Discrepancies between appendicular and axial sites are not uncommon. Feyerabend et al. [15] reported that 50% of women have clinically significant differences between the hip and spine measurements. Other investigators have demonstrated age-related differences in classification when radial versus spinal BMD measurements were obtained [16, 17]. Finally, site-specific classification could impact decisions regarding estrogen replacement therapy or other therapeutic interventions [18, 19].

To determine if healthy, elderly women lose bone at clinically relevant, trabecular-rich sites, we examined lateral spine BMD, which is less affected by artifact than the AP assessment. BMD of the lateral and AP spine were then compared along with BMD of the forearm (cortical-rich bone) and hip (mixed cortical/trabecular-rich bone) in order to assess the impact of site on the rate of bone loss and classification of osteoporosis.

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Materials and Methods

Subjects

Healthy, ambulatory, community-dwelling women of age 65 or greater were recruited from the greater Boston area by advertisement. Subjects with concomitant diseases or medications known to affect bone mineral metabolism were excluded. The study was approved by the Committee on Clinical Investigations at the Beth Israel Hospital. Subjects were advised on the nature of the study and informed consent was obtained.

Measurement Variables

BMD of the hip, spine, forearm, and total body was obtained by DXA using a Hologic QDR-2000 densitometer (Waltham, MA) located in the Clinical Research Center of the Beth Israel Hospital. Spinal measurements included lateral (L2–L4) and AP (L1–L4) using standard protocols. The patients were supine for both the AP and lateral measurements, and the arm of the densitometer was rotated over the patient for the lateral measurement. Fractured vertebrae were eliminated from analysis as in our previous studies of elderly subjects [6, 20, 21]. BMD of the total body and forearm was assessed using standard protocols provided by the manufacturer (Hologic Inc.). Measurements of the radius included total, ultra-distal, mid- and one-third distal radius. Measurements of the femur included total hip, femoral neck, trochanter, intertrochanteric region, and Ward's triangle. The coefficient of variation of BMD in elderly women (mean age 71 ± 7 years) using our densitometer was 1.7% for the lateral spine and 1.5% for the AP spine. We have previously reported a coefficient of variation of 1.2% for the total hip and 1.9% for the femoral neck in elderly women [6]. Measures of body habitus included height (m), weight (kg), and body mass index (BMI) ($w \div h^2$ in kg/m^2). Height was obtained with a Harpenden stadiometer and weight was measured by an ACME Digital In-Bed Scale.

Data Analysis

The cross-sectional association between age and BMD at each site was examined by linear correlation. The annual change in BMD (g/cm^2/year) was determined from the slope of the linear regression of BMD versus age. Multiple linear regression was used to determine the annual change in BMD while adjusting for weight and height. Percent change was expressed as the percent of the mean intercept at age 65. Annual percent change was then determined as the slope of the regression of percent change versus age [3], as in previous studies [3, 6]. Standard deviations (SD) from adult peak BMD (T-score) were obtained from the Hologic QDR-2000 normative databases [22]. Osteoporosis was defined as BMD more than 2.5 SDs below peak BMD, as suggested by WHO criterion [14]. Associations among BMD sites, height, weight, and BMI were analyzed linearly using Pearson or Spearman correlations.

Results

Clinical Characteristics

One-hundred twenty women were recruited ranging in age from 65 to 88 [mean = 70 ± 5 years (±SD)]. Mean subject profile was as follows: height 1.59 ± 0.60 m (±SD), weight 65 ± 10 kg, and BMI 26 ± 4 kg/m^2. Mean BMD measurements and SD from adult peak BMD values are shown in Table 1. SD from adult peak BMD for the lateral view of the spine were significantly lower than those of the AP view (−3.1 ± 1.4 versus −1.7 ± 1.4, $P < 0.01$), SDs from adult peak femoral BMD ranged from −3.1 at Ward's triangle to −1.7 at the trochanteric and intertrochanteric regions. At radial sites, these SD scores did not differ significantly from each other. As predicted, lateral measurements of the spine detected osteoporosis (BMD more than 2.5 SDs below young adult peak BMD) more often than AP measurements (66.4% and 29.2% respectively, Fig. 1). Using femoral neck values, osteoporosis was diagnosed in 55.0% of women; when other hip sites were examined, this figure ranged from 17.5 to 74.2% (Fig. 1). Using the one-third distal radius or total body measurement as the criterion, 45.4% and 19.3% of women, respectively, were identified as osteoporotic.

Table 1. BMD measurements and SD scores

Site	BMD (g/cm^2)	SD below adult peak BMD[a]
Spine		
Lateral (L2–L4)	0.568 ± 0.113	−3.1 ± 1.4
AP (L1–L4)	0.864 ± 0.155	−1.7 ± 1.4
Hip		
Total hip	0.758 ± 0.110	−1.8 ± 0.9
Femoral neck	0.638 ± 0.092	−2.6 ± 0.9
Trochanter	0.570 ± 0.087	−1.7 ± 1.0
Intertrochanter	0.908 ± 0.140	−1.7 ± 1.0
Ward's triangle	0.454 ± 0.103	−3.1 ± 0.9
Radius		
Total radius	0.455 ± 0.061	−2.3 ± 1.1
Ultra-distal	0.342 ± 0.060	−1.7 ± 1.0
Mid-radius	0.479 ± 0.064	−2.3 ± 1.2
One-third distal radius	0.543 ± 0.068	−2.5 ± 1.1
Total body	0.991 ± 0.105	−1.5 ± 1.1

Results are mean ± SD
[a] Peak BMD based on T-score of Hologic normative database [22]

BMD was negatively associated with age at nearly all sites, except for the AP spine and total body (Figs. 2 and 3). Weight was positively correlated with BMD at all sites (correlation coefficients ranged from 0.19 to 0.45, all $P < 0.05$, data not shown), and BMI was positively associated with BMD at all sites (correlation coefficient ranged from 0.22 to 0.42, all $P < 0.05$, data not shown) except the lateral spine. Height was only positively correlated with total hip BMD ($r = 0.18$, $P < 0.05$) and trochanteric BMD ($r = 0.25$, $P < 0.01$). Vertebral BMD measurements decreased by 1%/year as assessed by lateral measurements, but did not significantly change when assessed by the AP view (Fig. 4, Table 2). Similarly, bone loss at the hip ranged from 0.7 to 1.4%/year, and radial BMD decreased by approximately 0.7%/year ($P < 0.05$). Bone loss for the total body was insignificant. When adjusted for weight and height, correlations between BMD and age were only significant at Ward's triangle, total radius, mid-radius, one-third distal radius, and lateral spine.

The lateral and AP spinal measurements were highly correlated with one another ($r = 0.59$, $P < 0.01$, Fig. 2). In addition, lateral spine measurements were significantly correlated with those at all femoral sites (correlation coefficient 0.34–0.41, $P < 0.01$), the total radius (correlation coefficient 0.34, $P < 0.01$), and the total body (correlation coefficient 0.40, $P < 0.01$). AP spine values were correlated with all hip sites (correlation coefficient 0.60–0.67, $P < 0.01$), radial sites (correlation coefficient 0.62–0.63, $P < 0.01$), and total body (correlation coefficient 0.78, $P < 0.01$).

Discussion

We found that BMD decreases at a rate of approximately

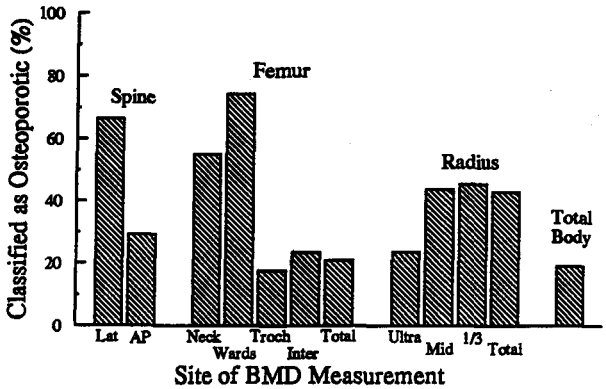

Fig. 1. Mean percent of elderly women classified as osteoporotic based on BMD measurement site using WHO criterion [14] (BMD more than 2.5 SDs below young adult peak BMD). Sites include the spine (lateral and AP), femur (neck, Ward's triangle, trochanter, intertrochanter, total), radius (ultra-distal, mid-distal, one-third distal, total), and total body.

1%/year at trabecular-rich sites, as demonstrated by lateral spine BMD measurements; the AP spine projection revealed no statistically significant bone loss. Furthermore, more than double the number of women were classified as osteoporotic using lateral versus AP spine measurements. Consistent with our previous cross-sectional and longitudinal study [6], femoral bone loss in this group of elderly women was 0.7–1%/year. Approximately double to triple the number of women were classified as osteoporotic when values for Ward's triangle and femoral neck were examined and compared with other hip sites. Osteoporosis was diagnosed in 23–45% of the patients using radial sites; BMD at these sties decreased by 0.7–0.8%/year. As with other studies [3, 12, 23], we observed a modest correlation (0.6–0.7) between AP spinal BMD and other sites.

The bone loss we observed in the AP spine and radius of elderly women was representative of other studies in this age group [3, 24]. In a large, cross-sectional, multicenter trial, Steiger et al. [3] reported that bone loss at the AP spine was approximately 0.3%/year. The authors qualified their findings by suggesting that the data may have been affected by artifacts in the spine, such as osteophytes, sclerosis, and aortic calcifications which interfere with AP assessments. They also reported losses of 0.88–0.93%/year at the proximal and distal radius, similar to our findings and those of other investigators [4] of 0.7–0.8% at radial sites. Uebelhart et al. [11] examined AP and lateral spinal measurements in women with and without osteoporosis. There were no statistically significant differences in SD scores at these sites, although lateral assessments demonstrated greater bone loss than AP measurements. However, the authors reported significant differences in SD scores between these 2 assessments in patients with osteoarthritis. Because osteoarthritis is common in the elderly, our data support the contention that the lateral spine projection—which is less influenced by calcifications of osteoarthritis—may be a superior assessment of vertebral skeletal integrity in this age group. The unadjusted annual changes computed by linear regression analysis ranged from a minimum of 0.39%/year for the total body to a maximum of 1.39%/year at Ward's triangle. After adjusting for weight and height, the dependence of BMD on age was only significant at the lateral spine, radial sites, and Ward's triangle, with similar trends noted at other hip sites.

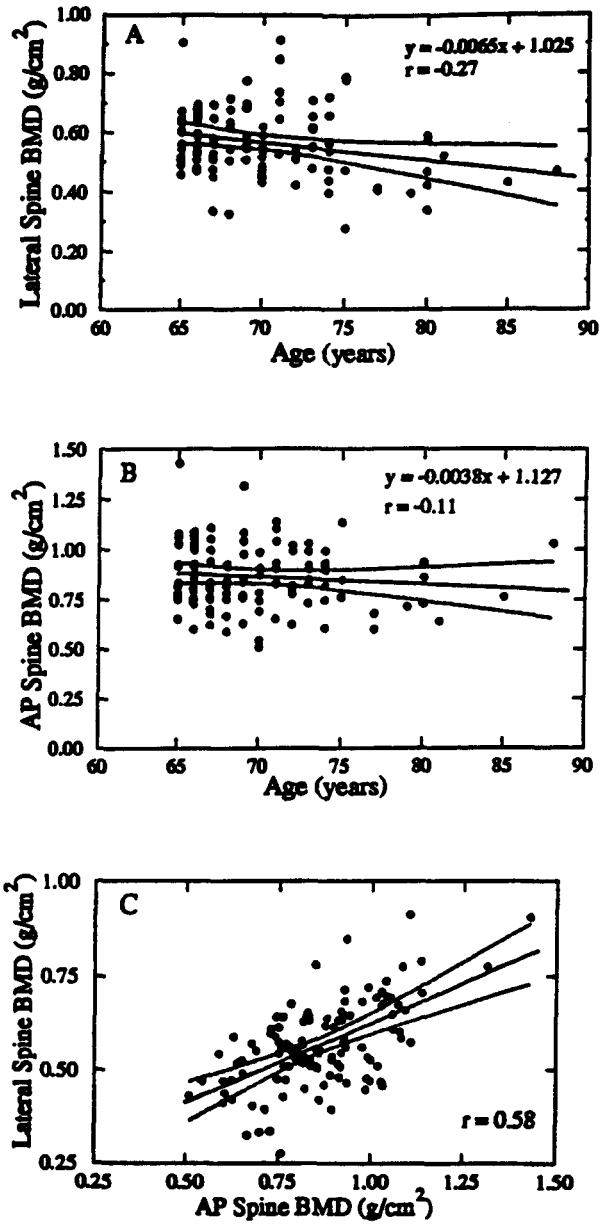

Fig. 2. **(A)**Lateral spine (L2–L4) BMD versus age in elderly women ($P = 0.003$). **(B)** AP spine (L1–L4) BMD versus age in elderly women ($P = 0.23$). **(C)** Lateral spine (L2–L4) versus AP spine (L1–L4) BMD in elderly women ($P \leq 0.001$). Dotted line represents 95% confidence limits.

There are several limitations to consider with this study. First, changes in the lateral spine may have been over- or underestimated since this is a cross-sectional analysis of BMD in aging women [18, 25]. However, our previous study of femoral BMD changes in a similar age group showed that results by cross-sectional or longitudinal analysis were relatively similar for areas of the hip not affected by artifacts. Secondly, we realize that the classification of osteoporosis using a cutpoint is limited. The gradient of fracture risk is continuous if a variable such as BMD is used, and the diagnosis of osteoporosis with a cutpoint such as more than 2.5 SD below peak BMD will in all likelihood result in both false positives and false negatives even at a single site.

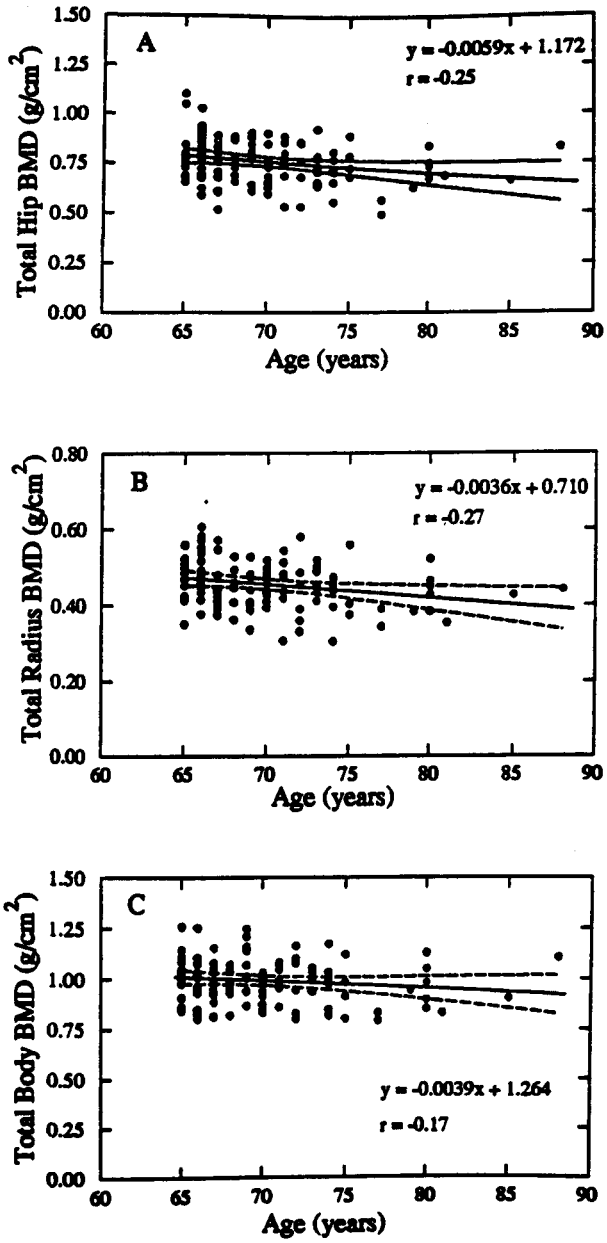

Fig. 3. (**A**) Total hip BMD versus age in elderly women (P = 0.006). (**B**) Total radius BMD versus age in elderly women (P = 0.003). (**C**) Total body BMD versus age in elderly women (P = 0.063). Dotted line represents 95% confidence limits.

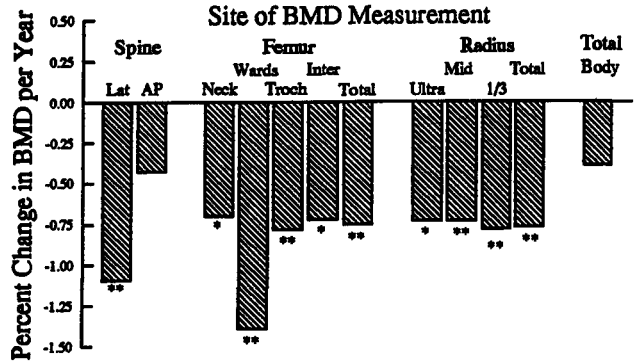

Fig. 4. Mean percent change in BMD per year in elderly women at the spine (lateral and AP), femur (neck, Ward's triangle, trochanter, intertrochanter, total), radius (ultra-distal, mid-distal, one-third distal, total), and total body. *P < 0.05, **P < 0.01.

Moreover, classification of osteoporosis in the elderly may vary depending upon the site used (spine, hip, or radius) [15, 17]. In addition, BMD values should always be considered in the context of the loads that will be applied to the skeleton if the individual falls or participates in other high risk activities. Finally, it could be argued that SD scores based on the manufacturer's young adult normative database may not be representative of normative data in our geographic area. We recognize that peak adult BMD based on differing reference populations would likely result in differences in classification [26, 27]. Faulkner et al. [28] have identified discrepancies between the normative databases of various DXA manufacturers. However, it was not our intention to characterize older women based on our reference database. Rather, our primary objective was to determine how classification of an "osteoporotic" individual within our patient population might vary by site of analysis according to the manufacturer's normative database since clinicians ultimately compare their patients to the manufacturer's norms.

Despite these issues, there are several advantages to our study. Although other investigators have previously demonstrated that lateral DXA measurements identify patients with osteoporosis more often than AP DXA [12, 13], we focused exclusively on women over age 65, the segment of the population that will experience the majority of vertebral fractures. Secondly, we have used state-of-the-art lateral DXA measurements, a method with low radiation, good reproducibility, low cost, and short scan time—all important factors for patient acceptability [7]. Though QCT has been shown to provide a sensitive assessment of vertebral trabecular BMD measurements compared with earlier techniques, the radiation exposure is significantly higher, scan time longer, cost greater, and reproducibility inferior to that of DXA [29, 30]. Finally, we simultaneously assessed sites rich in trabecular and cortical bone to allow comparison between and within sites to demonstrate how classification of osteoporosis can vary significantly depending upon the site chosen.

The present study has important clinical ramifications. Elderly women are now the fastest-growing segment of the United States population [31]. It is important to determine if they continue to lose spinal BMD with age since decreased BMD has been associated with increases in vertebral and femoral fractures [32, 33]. Our data support the hypothesis that older women are losing both cortical and trabecular bone and continue to lose bone at all clinically relevant sites including the lumbar spine, femur, and radius. Furthermore, these data suggest that classifications for osteoporosis vary significantly by site and subregional analysis, emphasizing the need for more uniform agreement for site-specific analysis and utilization of a lateral BMD measurement of the spine as a more realistic assessment of vertebral skeletal integrity in this age group. We observed that approximately 60% of these elderly women were classified as osteoporotic with femoral neck and lateral spine assessments, emphasizing the enormity of this problem even in a healthy, ambulatory cohort. Most importantly, these findings provide further impetus for continued development and testing of

Table 2. Associations of age with BMD: multiple linear regression coefficients

Site		Age (g/cm^2/year)	Height (g/cm^2/cm)	Weight (g/cm^2/kg)	r^2 or multiple r^2
Lateral spine	Unadj	−0.0065[b]			0.07
	Adj†	−0.0055[a]	0.0007	0.0014	0.09
AP spine	Unadj	−0.0038			0.01
	Adj	0.0001	0.0020	0.0062[b]	0.18
Total hip	Unadj	−0.0059[b]			0.06
	Adj	−0.0034	0.0006	0.0044[b]	0.23
Femoral neck	Unadj	−0.0046[a]			0.05
	Adj	−0.0029	0	0.0034[b]	0.18
Trochanter	Unadj	−0.0046[b]			0.06
	Adj	−0.0025	0.0019	0.0028[b]	0.19
Intertrochanter	Unadj	−0.0068[a]			0.05
	Adj	−0.0040	−0.0005	0.0058[b]	0.21
Ward's triangle	Unadj	−0.0068[b]			0.09
	Adj	−0.0060[b]	−0.0008	0.0022[a]	0.13
Total radius	Unadj	−0.0036[b]			0.07
	Adj	−0.0028[a]	−0.0009	0.0023[b]	0.20
Ultra-distal radius	Unadj	−0.0026[a]			0.04
	Adj	−0.0018	−0.0014	0.0026[b]	0.21
Mid-radius	Unadj	−0.0037[b]			0.07
	Adj	−0.0030[a]	−0.0011	0.0022[b]	0.18
One-third radius	Unadj	−0.0044[b]			0.09
	Adj	−0.0032[a]	0.0001	0.0022[b]	0.19
Total body	Unadj	−0.0039			0.03
	Adj	−0.0019	0.0015	0.0029[b]	0.11

[a] $P < 0.05$, [b]<0.01, †adjusted for height and weight

therapeutic strategies to prevent vertebral bone loss in this age group.

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