Int J Endocrinol Metab 2009;2: 56-66

ORIGINAL ARTICLE

Bone Mineral Density at Lumbar Spine and Femur. An Epidemiological Study in the Athens Metropolitan Area, Greece

Legakis I[a], Papadopoulos V[b], Tataridas V[b], Strigaris K[b]

[a]Departments of Endocrinology and [b]Radiology, Henry Dunant Hospital, Athens, Greece

We aimed at determining the prevalence of osteoporosis and osteopenia in an urban population. Materials and Methods: DXA measurements were done at the lumbar spine (4914 females, aged 50 to 93 years and 111 males, aged 50-89) and at the femur (2943 females, aged 50-95 and 105 males, aged 51-92). Bone mineral density (BMD) and corresponding T-scores were analysed using multivariate regression models.
Results: In females, the prevalence rate of osteoporosis was 19.56% (95% confidence interval (CI):18.46/20.69) at the lumbar spine and of osteopenia 41.68% (95% CI: 40.29/43.07). The corresponding numbers in males were 16.22 % (95% CI: 9.90/24.41) and 33.33% (95% CI: 24.67/42.91). In females osteoporosis rate at the femur was 18.99% (95% CI: 17.59/20.46) for the neck and 2.0% (95% CI: 1.53/2.58) for the tronchater, whereas the osteopenic rates were 54.57% (95% CI: 52.75/56.38) and 32.38% (95% CI:30.69/34.11) respectively. In males, osteoporosis rate at the femur was 38.10% (95% CI: 28.79/48.09) for the neck and 13.33% (95% CI: 7.49/21.36) for the tronchater, whereas the corresponding osteopenic rates were 46.67% (95% CI: 36.87/56.66) and 41.90% (95% CI: 32.34/51.93). A polynominal cubic model performed for age showed the steepest decline at the age of 55 years for the spine BMD (-0.973% change, 95% CI -1.031/-0.915) and at the age of 64 years for the femur BMD (-0.726% change, 95% CI -0.793/-0.658).
Conclusion: Sensitive interventions and strategies for prevention of osteoporosis in urban populations need to be designed and implementted.

Correspondence: Ioannis Legakis, MD, Alimousion 33, Thision, Athens, Greece-11851
*E-mail:*ilegak@med.uoa.gr

Keywords: Osteporosis, Osteopenia, Bone mineral density, Dual energy X-ray absorptiometry, T-score, Spine, Femur, Urban population

Received: 17.02.2009 **Accepted**: 04.04.2009

Introduction

Osteoporosis, a major health problem worldwide,[1,2] is characterized by low bone mass and microarchitectural deterioration of bone structure.[3,4] Bone mass is determined by peak bone mass and the rate of bone loss. Dual-energy X-ray absorptiometry (DXA) is a widely used technique to assess bone mineral density (BMD) at different skeletal sites and therefore suitable to stratify individuals with low bone mass who are at risk of osteoporosis and fractures. BMD is influenced by genetic, environmental, and hormonal factors.[5] Ethnic and racial variations of bone density are therefore expected.[6,7] Moreover, age and sex have such a strong impact that reference values for BMD should be age-and sex-specific, and, accordingly, for a reliable interpretation of such values, they need to be expressed in terms of established reference

values derived from an appropriate healthy population.[8]

The World Health Organization (WHO) defined diagnostic criteria for osteoporosis in terms of BMD as measured by DXA,[9] and although such criteria are based on observations in postmenopausal Caucasian females, they are widely used and applied to other at risk populations to confirm a diagnosis of osteoporosis.[10,11] The aim of the present study was to assess the incidence and the prevalence of osteoporosis in a urban population in Greece, for which DXA measurements were collected and analysed retrospectively.

Materials and Methods

Data collection was conducted through a 4 year period (2001-2005) from the Radiology Department of the Henry Dunant Hospital in Athens, Greece. Evaluation of the DXA measurements was performed in individuals with an age range of 50 to 95 years, first at the lumbar spine in 4914 females, aged 50 to 93 years and in 111 males, aged 50-89 and then at the femur in 2943 females, aged 50-95 and in 105 males, aged 51-92. All subjects in the study were considered to be in good health with no history of traumatic fractures or diseases known to affect bone, and were not on any medication known to affect bone metabolism other than oral contraception.

BMD measurements (g/cm^2) were determined for the anteroposterior lumbar spine (L2–L4) and mean of proximal right and left femur (total and subregions) by DXA using a Lunar DPX-IQ (Lunar, Madison, WI, USA), according to standard protocol.

BMD of the femur was expressed as the mean of the BMD values for the subregions: trochanter and neck. All scans were performed and analysed by the same investigator. Quality control procedures were carried out in accordance with the manufacturer's recommendations.

Instrument variation was determined regularly by a daily calibration procedure using a phantom supplied by the manufacturer. Precision error of the phantom was 0.3% and for in vivo measurements was less than 1.2% for the spine and less than 2% for femoral regions. Lunar Italian normal database supplied by the manufacturer was used to derive Z scores (matched for age and weight) and T scores (reference age 20–90 years).

Subjects were weighed on an electric scale wearing minimal clothing. Height was measured to the nearest centimeter using a stadiometer. Body mass index (BMI) was calculated as weight divided by height in meters squared (kg/m^2). For data analysis, participants were grouped on the basis of 5-year age increments.

The percentage of individuals with osteopenia or osteoporosis were calculated according to WHO) criteria.

BMD measurements and the corresponding T-scores were analysed using multivariate regression models.[12] More specifically due to nonlinear patterns observed in our data all models used here included polynomial terms for age up to the third degree (cubic model). All models' assumptions were checked using appropriate tests and graphs. All regression models were also refitted using non-parametric methods as part of a sensitivity analysis. Separate analyses for the spine and femur (neck and trochanter) were performed. The significance of somatometric characteristics such as weight, height, and BMI was also investigated. All statistical procedures were performed using Stata 8.2 (Stata corp, TX USA). The study was approved by the Ethics Committee of the Henry Dunant Hospital.

Results

Demographic data, prevalence of osteoporosis, osteopenia in both sexes and absolute levels of BMD are presented in Table 1.

Table 1: Demographic data (weight, height, and BMI), absolute levels of BMD and prevalence of osteoporosis of the study population.

		Female	Male
		n(%)	n(%)
Spine data		4,914 (97.79)	111 (2.21)
Femur data		2,943 (96.56)	105 (3.44)
		Mean (SD)	Mean (SD)
Age (years)		59.1 (7.1)	63.9 (10.0)
Weight (Kg)		69.0 (11.5)	78.9 (12.9)
Height (cm)		160.8 (5.9)	171.7 (8.0)
BMI* (Kg/m^2)		26.71 (4.32)	26.71 (3.80)
Femur Neck		Mean (SD)	
	BMD	0.787 (0.125)	0.777 (0.177)
	BMD T-score	-1.606 (1.045)	-2.229 (1.465)
		% (95% C.I.†)	% (95% C.I.†)
	Osteoporosis prevalence	18.99 (17.59, 20.46)	38.10 (28.79, 48.09)
	Osteoporosis prevalence (age adjusted‡)	19.00 (17.55, 20.46)	27.85 (19.80, 35.89)
	Osteopenia prevalence	54.57 (52.75, 56.38)	46.67 (36.87, 56.66)
	Osteopenia prevalence (age adjusted‡)	52.91 (50.99, 54.84)	39.38 (30.90, 47.87)
Trochanter			
	BMD	0.719 (0.119)	0.774 (0.162)
	BMD T-score	-0.591 (0.992)	-1.093 (1.239)
		% (95% C.I.†)	% (95% C.I.†)
	Osteoporosis prevalence	2.00 (1.53, 2.58)	13.33 (7.49, 21.36)
	Osteoporosis prevalence (age adjusted‡)	2.22 (1.59, 2.85)	9.93 (4.67, 15.18)
	Osteopenia prevalence	32.38 (30.69, 34.11)	41.90 (32.34, 51.93)
	Osteopenia prevalence (age adjusted‡)	32.24 (30.47, 34.02)	34.39 (25.72, 43.06)
Spine L2-L4			
	BMD	1.049 (0.176)	1.121 (0.210)
	BMD T-score	-1.260 (1.468)	-0.914 (1.621)
		% (95% C.I.†)	% (95% C.I.†)
	Osteoporosis prevalence	19.56 (18.46, 20.69)	16.22 (9.90, 24.41)
	Osteoporosis prevalence (age adjusted‡)	24.59 (22.74, 26.43)	16.31 (9.54, 23.08)
	Osteopenia prevalence	41.68 (40.29, 43.07)	33.33 (24.67, 42.91)
	Osteopenia prevalence (age adjusted‡)	40.22 (38.05, 42.40)	34.57 (25.51, 43.64)

*Body mass index; †Confidence interval; ‡National reference population data in Athens, Attiki-Greece, 50+ yrs, 2001.

Moreover, age adjusted prevalence rates were estimated according to National Reference data in Athens-Attiki, recorded in 2001.

According to our data, the prevalence rate of osteoporosis, based on the WHO criteria, at the lumbar spine in women was 19.56% and of osteopenia was 41.68 % (Fig 1).

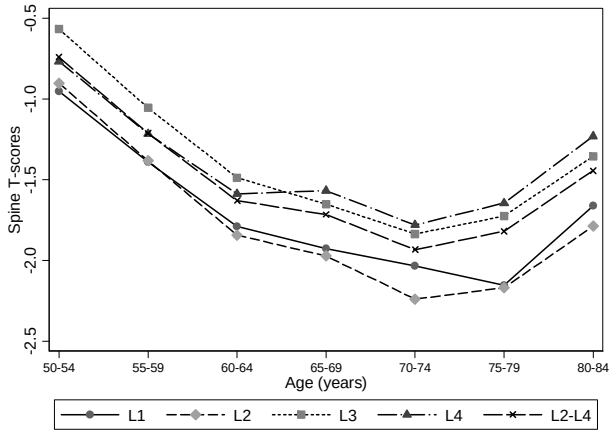

Figure 1: Mean bone mineral density of lumbar spine (L1-L4) in the female population aged 50-84 years

In males, the prevalence rate of osteoporosis at the lumbar spine was 16.22% and of osteopenia was 33.33%. In females, osteoporosis rate at the femur was 18.99% for the neck and 2.0% for the tronchater, whereas osteopenic rates at the femur were 54.57% for the neck and 32.38% for the trochanter (Fig 2).

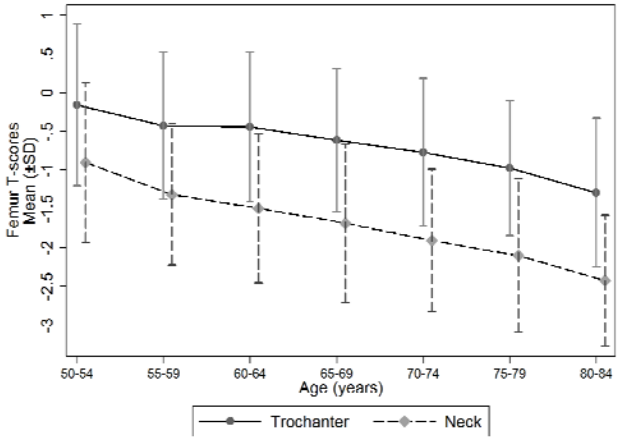

Figure 2: Mean bone mineral density of femoral neck, ward's triangle and tronchanter in the females aged 50-84 years

In males, osteoporosis rate at the femur was 38.10% for the neck and 13.3% for the tronchater and osteopenic rates at the femur in males were 46.67% for the neck and 41.90% for the tronchater (Table 2).

Initial exploratory analysis revealed that BMD and T-score age-related changes were not linear across the chronological range of our sample in the female population (50 to 84 years). Henece a polynomial cubic model was performed for age which showed good fit for the observed data, allowing the estimation of age related slopes to T-scores values. The steepest decline was observed at the age of 55 years (-0.973% change, 95% CI -1.031/-0.915) for the spine BMD (Fig.3) and at the age of 64 years for the femur BMD measurements (-0.726% change, 95% CI -0.793/-0.658) (Fig.4).

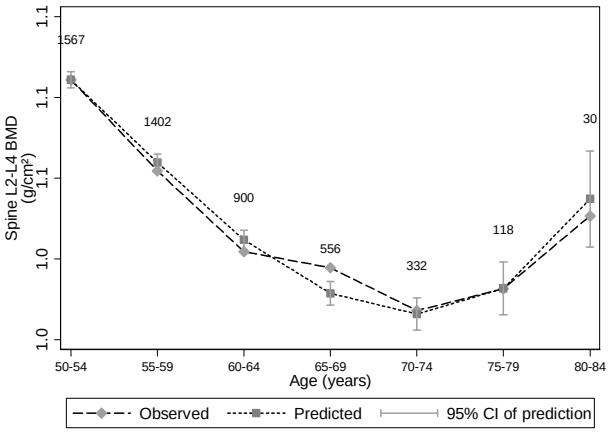

Figure 3: Mean bone mineral density of lumbar spine (L2-L4) observed and predicted by a cubic age model in the female population aged 50-84 years. (Numeric entries in the graph indicate the actual number of participants in the referred age category)

Table 2: Osteoporosis/osteopenia rates of femoral neck, ward's triangle and tronchanter based on t-scores in the males aged 50-94 years

Males — Neck

Age (years)	Normal	Osteopenia	Osteoporosis
55-59	1 (10.0)*	7 (70.0)	2 (20.0)
60-64	3 (21.4)	5 (35.7)	6 (42.8)
65-69	4 (23.5)	8 (47.0)	5 (29.4)
70-74	1 (5.8)	9 (52.9)	7 (41.1)
75-79	1 (4.3)	13 (56.5)	9 (39.1)
80-84	1 (9.0)	5 (45.4)	5 (45.4)
85-89	0(0.0)	1 (20.0)	4 (80.0)
90-94	0(0.0)	1 (33.3)	2 (66.6)
Total	16 (15.2)	49 (46.6)	40 (38.1)

Trochanter

Age (years)	Normal	Osteopenia	Osteoporosis
55-59	6 (60.0)	4 (40.0)	0(0.0)
60-64	4 (28.5)	6 (42.8)	4 (28.5)
65-69	8 (47.0)	7 (41.1)	2 (11.7)
70-74	6 (35.2)	10 (58.8)	1 (5.8)
75-79	11 (47.8)	8 (34.7)	4 (17.3)
80-84	2 (18.1)	8 (72.7)	1 (9.0)
85-89	2 (40.0)	0(0.0)	1 (20.0)
90-94	1 (33.3)	1 (33.3)	1 (33.3)
Total	45 (42.8)	44 (41.9)	14 (13.3)

L2-L4

Age (years)	Normal	Osteopenia	Osteoporosis
55-59	10 (40.0)	10 (40.0)	5 (20.0)
60-64	7 (43.7)	4 (25.0)	5 (31.2)
65-69	3 (30.0)	6 (60.0)	1 (10.0)
70-74	11 (61.1)	5 (27.7)	2 (11.1)
75-79	8 (66.6)	4 (33.3)	0(0.0)
80-84	1 (20.0)	1 (20.0)	3 (60.0)
85-89	2 (66.6)	1 (33.3)	0(0.0)
Total	56 (50.4)	37 (33.3)	18 (16.2)

* Data are presented as n (%)

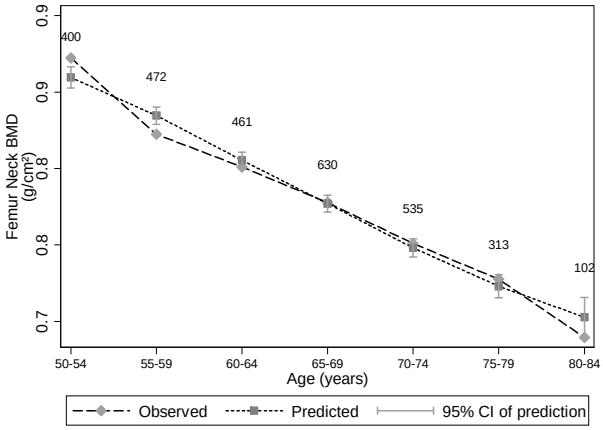

Figure 4: Mean bone mineral density of femoral neck observed and predicted by a cubic age model in the female population aged 50-84 years. (Numeric entries in the graph indicate the actual number of participants in the referred age category).

According to our data, each anatomical region displayed a different rate of bone loss. In the female population, the mean yearly percent loss of BMD in the spine was increased until the age of 65 years and thereafter a progressive decrease was observed. Moreover, the mean yearly percent loss in BMD for women was much greater at the neck as compared to trochanter at the femur site (Table 3). Although, as expected, BMI was significantly correlated with BMD and T-scores, weight and height were directly associated with BMD at all measurements sites.

No serious violations of the assumptions were found for the regression models used in this analysis. Moreover all models have been refitted, as a sensitivity analysis, using non-parametric techniques and all results remained practically unaffected.

Table 3: Mean estimated percentage of BMD change per year of the spine and femur (neck and tronchanter) in the female population

Age (years)	Region	Estimated BMD change/year %	95% CI*
50	Spine L2-L4	-0.903	(-0.958, -0.847)
	Femur Neck	-0.536	(-0.623, -0.448)
	Femur Trochanter	-0.225	(-0.319, -0.131)
55	Spine L2-L4	-0.973	(-1.031, -0.915)
	Femur Neck	-0.642	(-0.718, -0.565)
	Femur Trochanter	-0.356	(-0.437, -0.275)
60	Spine L2-L4	-0.883	(-0.942, -0.825)
	Femur Neck	-0.707	(-0.780, -0.633)
	Femur Trochanter	-0.460	(-0.536, -0.384)
65	Spine L2-L4	-0.605	(-0.673, -0.536)
	Femur Neck	-0.726	(-0.793, -0.658)
	Femur Trochanter	-0.538	(-0.608, -0.468)
70	Spine L2-L4	-0.120	(-0.238, -0.002)
	Femur Neck	-0.691	(-0.769, -0.614)
	Femur Trochanter	-0.587	(-0.666, -0.508)
75	Spine L2-L4	0.552	(0.351, 0.753)
	Femur Neck	-0.595	(-0.728, -0.462)
	Femur Trochanter	-0.604	(-0.740, -0.469)

* Confidence Interval

However, due to the diversity of the results regarding the male population BMD measurements, we did not perform similar analysis of the observed data.

Discussion

Our results showed that the prevalence rates of osteoporosis and osteopenia, according to WHO criteria, in the entire analysed population were at the higher upper limits as compared to similar studies performed in other countries,[13,14] confirming the observations that racial differences do exist in BMD reference curves.[15,16] The prevalence of osteoporosis and osteopenia increased with advancing age. Moreover, in females, the steepest decline for T-score values was observed at the age of 54 years for the spine BMD and at the age of 62 years for the femur BMD measurements. Previous studies in normal Greek population[17] in 244 women and 168 men reported that the total bone loss between ages 20 and 70 was 29.5% for the vertebrae and 32% for the femoral neck in women, whereas the values for men were 19.5% and 29% respectively. In our study, the percentage of total bone loss in women between ages 35 to 84 was 14.36% at the spine (L2-L4), 22.97% for the femoral neck, 32.7% for the ward's triangle, and 16.27% for the tronchanter, whereas the values for men were +1.49% for the spine (L2-L4),-7.01% for the femoral neck, -9.92% for the ward's triangle and +2.01% for the tronchanter. However as data for younger male individuals were sparse, these results should be interpreted with caution.

Osteoporosis in men is increasingly recognized as a problem in clinical medicine. Clinical studies performed in northern Greece[18] in 363 healthy Greek males reported a similar prevalence rate of osteoporosis, viz.11%.

The influence of body composition on the observed difference in BMD concerning population studies has long been prognostic. In particular, the NHANES III investigators have reported a marked effect of body weight on BMD values in the hip.[19] In relevance to the above data, our results showed that weight and height had a better fit to the observed data than BMI. Based on the fact that BMI had a significant correlation with BMD and T-scores, we assume that our correlations were made possible due to the large number of the population tested.

It is well known that BMD relates to the risk of fracture, with decreased BMD resulting in increased fracture risk.[4,20] In particular, bone density in elderly persons is highly relevant to the risk of osteoporotic fracture with the highest rates of osteoporosis-related fractures occuring in elderly women, although 13% of men also will experience such fractures.[21-25] Nevertheless, after adjustment for body size, race, and sex differences in regional and whole body, bone mass of adults remain at a low level.[26-27] Interestingly, our results showed that males exhibited increased osteoporosis and osteopenic rates in the femur at all measurments sites as compared to females, although that was evident at an advanced age, especially between 75-79 years.

According to literature, men and women may achieve similar peak bone density at the spine and proximal femur.[28] Bone loss in women may occur earlier and the rate may be twice that in men,[29] although this sex difference may be smaller in later life.[30] Our data suggest that bone loss in females both at the spine and the femur occurs earlier in life, from 50 years old, than in men which occurs after 70 years old. The effect of sex steroids might be taken into account to explain the above differences.

Heterogeneity of sites-related BMD was observed in our female population; bone loss was first detected at the spine at the age of 50 years. At the same age, osteopenia was detected at the femoral neck and the ward's triangle but not at the throchanter. The steepest and earlier decline of bone loss was observed in the spine, reaching T score ≤ 2.5 at the age of 70 to 74 years old. At the femur, the neck

and the ward's triangle were the primary sites of bone loss followed by the trochanter, reaching T score ≤ 2.5 at a later age, namely 80 to 90 years.

Conflicting results have been reported by several investigators concerning the difference between BMD at various skeletal sites in postmenopausal women when compared with reference means. It has been previously shown[31,32] that BMD of the spine and femoral neck in postmenopausal women aged 45–60 years tends to be similar when compared with reference means although 26% of the individuals tested had Z-scores sufficiently different to result in mischaracterization of the fracture risk at the nonmeasured site. Moreover, Davis et al[33] classified women aged 47–82y by tertiles of Z-score for BMD at any one of four skeletal sites and found heterogeneity in the BMD at different skeletal sites within an individual. On the other hand Bonnick et al,[34] showed that differences in Z-score between the BMD at the lumbar spine and proximal femoral sites are common in healthy premenopausal women and in women aged 30y and over, these differences appear to be the result of a decline in BMD at the proximal femur combined with no significant change in BMD at the lumbar spine.

In our study, the yearly mean percent loss in BMD for women was much greater in the ward's triangle and the neck as compared to trochanter at the femur site. Additionally, the yearly mean percent loss in BMD for women in the spine increased from the age of 50 years and, interestingly, a dramatic decrease occurred after the age of 65 years, presumably due to osteophytes and/or therapeutic interventions. Similar results concerning the annual reduction rate in BMD were obtained in the population of a northern part of Greece,[35] although the absolute values in our study tend to be slightly elevated. It was not possible to deduce similar information regarding the male population in our study due to discrepancy of the results obtained.

The use of an italian reference population could be considered only as a minor limitation of our study since it has been previously found[35] that this population's normal range is close to the Greek one and can be "reliably used at least as T-scores are concerned" whereas for Z-scores discrepancies are small.

It is well recognized that the BMD and soft tissue mass are mutually dependent on exercise[36-40] whereas both respond to intrinsic factors such as somatotrophic and sex hormones.[41] These common hormonal effects are not only important during the rapid growth during adolescence, in which dramatic gains in bone and muscle mass are observed,[42] but also throughout adult life.

For the people in our study, living in an urban area, physical activity and exercise are not expected to be included in an every day life routine. Also, nowadays, the elderly in Athens are exposed less to sunlight and are less active compared with previous years. In addition, abuse of sedatives or the interaction between various drugs taken commonly by the elderly are often related to changes in life-style (urbanization of population, institutionalization of elderly) that may have adverse effects on BMD. Osteoarthritis of the spine has been associated with increased BMD at the spine, femoral neck,[43,44] and total body.[45] However, increased BMD in the region affected by osteoarthritis may be an artifact due to osteophytes, intervertebral joint space narrowing and sclerosis within the region of interest, or may reflect a generalized increase in BMD on the skeleton.[45] Our results are in agreement with the above data, in that an increase in BMD was observed in the spine after the age of 74 years presumably due to osteoathritic changes.

Low bone density at the femur is a strong predictor of the increased risk for hip fracture. In one of the largest cohort studies of osteoporosis, the Study of Osteoporotic Fractures, women in the lowest quartile of BMD had an 8-fold increased risk of hip fracture compared with the women in the highest BMD quartile.[46] Earlier cross-sectional investigation study of femoral and radius BMD in the Framingham cohort showed that age was

inversely related to BMD in both men and women.[47] Both cross-sectional and longitudinal studies have also reported age-related bone loss.[48-51]

According to Hannan et al,[52] examining longitudinal changes in a population-based study of elderly men and women for BMDs at the femur, radial shaft, lumbar spine, and ultradistal radius, the mean percent loss in BMD for women was much greater than the loss for men at all sites. Even given the higher baseline BMD in men, the absolute decline in BMD was greater for women than men. Elderly men continue to lose BMD at all ages but their BMDs remain higher than those of women and their rates of loss at most sites are lower.

To our knowledge, this is the first large population based study of osteoporosis and osteopenia in the Greek people. Due to BMD and T-score age-related changes, a polynomial cubic model was originally performed for age which showed not only good fit for the observed data but also allowed the estimation of age related slopes to T-scores values.

Provided that early identification of BMD and adequate treatment when indicated[53] are needed to avoid osteoporosis-related fractures and disabilities[54] and in the light of the longer life span, the findings of this study suggest that sensitive interventions and strategies for prevention of of osteoporosis risk in such populations need to be designed and implemented.

References

1. O'Neill TW, Felsenberg D, Varlow J, Cooper C, Kanis JA, Silman AJ . The prevalence of vertebral deformity in European men and women: the European Vertebral Osteoporosis Study J Bone Miner Res 1996; 11: 1010-8.
2. Cooper C, Campion G, Melton LJ 3rd. Hip fractures in the elderly: a worldwide projection. Osteoporosis Int 1992; 2: 285-9.
3. Consensus Development Conference. Diagnosis, prophylaxis and treatment of osteoporosis. Am J Med 1993; 94: 646-50.
4. Kanis JA, Melton LJ 3rd, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis. J Bone Miner Res 1994; 9: 1137-41.
5. Riggs BL, Melton LJ 3rd. Involutional osteoporosis N Engl J Med 1986; 314: 1676-84.
6. Lunt M, Felsenberg D, Reeve J, Benevolenskaya L, Cannata J, Dequeker J, et al. Bone density variation and its effects on risk of vertebral deformity in men and women studied in thirteen European centers: the EVOS study J Bone Miner Res 1997; 12: 1883-94 .
7. Alver K, Meyer HE, Falch JA, Søgaard AJ .Bone mineral density in ethnic Norwegians and Pakistiani immigrants living in Oslo –The Oslo Health Study. Osteoporos Int 2005; 16: 623-30.
8. Lofman O, Larsson L, Ross I, Toss G, Berglund K. Bone mineral density in normal Swedish women. Bone 1997; 20: 167-74.
9. World Health Organization, editor. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Technical Support Series, No. 843. Geneva: WHO; 1994
10. Kanis JA. Diagnosis of osteoporosis and assessment of fracture risk. Lancet 2002; 359: 1929-36.
11. Cummings SR, Bates D, Black DM. Clinical use of bone densitometry. JAMA 2002; 288: 1889-97.
12. David G, Kleinbaum GD, Kupper LL, Muller EK, editors. Applied Regression Analysis and Other Multivariable Methods. 2nd ed. Publisher: Kent Pub Co; 1987.
13. Filip RS, Zagórski J. Bone mineral density and osteoporosis in rural and urban women.Epidemiological study of the Lublin region (Eastern Poland). Ann Agric Environ Med 2001; 8: 221-6.
14. Holt G, Khaw KT, Reid DM, Compston JE, Bhalla A, Woolf AD, et al. Prevalence of osteoporotic bone mineral density at the hip in Britain differs substantially from the US over 50 years of age .Implications for clinical densiometry. Br J Radiol 2002; 75:736–42.
15. Iki M, Kagamimori S, Kagawa Y, Matsuzaki T, Yoneshima H, Marumo F. Bone mineral density of the spine, hip and distal forearm in representative samples of the Japanese female population: Japanese Population-Based Osteoporosis (JPOS) Study. Osteoporosis Int 2000; 12: 529-37.

16. Díaz Curiel M, García JJ, Carrasco JL, Honorato J, Pérez Cano R, Rapado A, et al. Prevalence of osteoporosis assessed by densitometry in the Spanish female population. Med Clin 2001; 116: 86-8 (Spanish).
17. Hadjidakis D, Kokkinakis E, Giannopoulos G, Merakos G, Raptis SA. Bone mineral density of vertebrae, proximal femur and os calcis in normal Greek subjects as assessed by dual-energy X-ray absorptiometry: comparison with other populations. Eur J Clin Invest 1997; 27: 219-27.
18. Krassas GE, Papadopoulou FG, Doukidis D, Konstantinidis TH, Kalothetou K. Age-related changes in bone density among healthy Greek males. J Endocrinol Invest 2001; 24: 326-33.
19. Beck TJ, Looker AC, Ruff CB, Sievanen H, Wahner HW. Structural trends in the ageing femoral neck and proximal shaft: analysis of the third national health and nutrition examination survey dual-energy X-ray absorptiometry data. J Bone Miner Res 2000; 15: 2297-308
20. Cummings SR, Kelsey JL, Nevitt MC, O'Dowd KJ. Epidemiology of osteoporosis and osteoporotic fractures. Epidemiol Rev 1985; 7: 178-208.
21. Ross PD, Davis JW, Vogel JM, Wasnich RD. A critical review of bone mass and the risk of fractures in osteoporosis. Calcif Tissue Int 1990; 46: 149-61
22. Melton LJ III, Atkinson EJ, O'Fallon WM, Wahner HW, Riggs BL. Long-term fracture prediction by bone mineral assessed at different skeletal sites. J Bone Miner Res 1993; 8: 1227-33.
23. Kellie SE, Brody JA. Sex-specific and race-specific hip fracture rates. Am J Public Health 1990; 80: 326-8
24. Barondess DA, Nelson DA, Schlaen SE. Whole body bone, fat, and lean mass in black and white men. J Bone Miner Res 1997; 12: 967-71.
25. Visser M, Kiel DP, Langlois J, Hannan MT, Felson DT, Wilson PW, et al. Muscle mass and fat mass in relation to bone mineral density in very old men and women: The Framingham Heart Study. Appl Radiat Isot 1998; 49: 745-7.
26. Luckey MM, Meier DE, Mandeli JP, DaCosta MC, Hubbard ML, Goldsmith SJ. Radial and vertebral bone density in white and black women: Evidence for racial differences in premenopausal bone homeostasis. J Clin Endocrinol Metab 1989; 69: 762-70.
27. DeSimone DP, Stevens J, Edwards J, Shary J, Gordon L, Bell NH. Influence of body habitus and race on bone mineral density of the midradius, hip, and spine in aging women. J Bone Miner Res 1998; 4: 827-30.
28. Slosman DO, Rizzoli R, Pichard C, Donath A, Bonjour JP. Longitudinal measurement of regional and whole body bone mass in young healthy adults. Osteoporos Int 1994; 4: 185-90.
29. Burger H, van Daele PL, Algra D, van den Ouweland FA, Grobbee DE, Hofman A, et al. The association between age and bone mineral density in men and women aged 55 years and over: the Rotterdam Study. Bone Miner 1994; 25: 1-13.
30. Hannan MT, Felson DT, Anderson JJ. Bone mineral density in elderly men and women: results from the Framingham Osteoporosis Study. J Bone Miner Res 1992; 7: 547-53.
31. Pouilles JM, Tremollieres F, Ribot C. Spine and femur densitometry at the menopause: are both sites necessary in the assessment of the risk of osteporosis? Calcif Tissue Int 1993; 52: 344-7
32. Lai K, Rencken M, Drinkwater BL, Chesnut CH III. Site of bone density measurement may affect therapy decision. Calcif Tissue Int 1993; 53: 225-8.
33. Davis JW, Ross PD, Wasnich RD. Evidence for both generalized and regional low bone mass among elderly women. J Bone Miner Res 1994; 9: 305-9.
34. Bonnick SL, Nichols DL, Sanborn CF, Lloyd K, Payne SG, Lewis L, et al . Dissimilar Spine and Femoral Z-Scores in Premenopausal Women. Calcif Tissue Int 1997; 61: 263-5.
35. Molyvda-Athanasopoulou E, Sioundas A, Hathiioannou K. Dual energy X-ray absorptiometry reference data for Greek population. The impact on diagnosis of using various normal ranges for comparison. Eur J Radiol 2000; 36: 36-40.
36. Rubin CT, Lanyon LE. Regulation of bone mass by mechanical strain magnitude. Calcif Tissue Int 1985; 37: 56-61.
37. Suominen H. Bone mineral density and long term exercise: An overview of cross-sectional athlete studies. Sports Med 1993; 16: 316-30.
38. Taaffe DR, Robinson TL, Snow CM, Marcus R. High-impact exercise promotes bone gain in well-trained female athletes . J Bone Miner Res 1997; 12: 255-60.
39. Krølner B, Toft B. Vertebral bone loss: An unheeded side effect of therapeutic bed rest. Clin Sci 1983; 64: 537-40.
40. Vogel J, Whittle M. Bone mineral changes: The second manned skylab mission. Aviat Space Environ Med 1976; 47: 396-400.
41. Slemenda CW. Body composition and skeletal density mechanical loading or something more? J Clin Endocrinol Metab 1995; 80: 1761-3.
42. Schiessl H, Frost HM, Jee WSS. Estrogen and bone-muscle strength and mass relationships. Bone 1998; 22: 1-6.
43. Cooper C, Cook PL, Osmond C, Fisher L, Cawley MID. Osteoarthritis of the hip and osteoporosis of the proximal femur. Ann Rheum Dis 1991; 50: 540-2.
44. Masud T, Langley S, Wiltshire P, Doyle DV, Spector TD. Effect of spinal osteophytosis on bone

mineral density measurements in vertebral osteoporosis. BMJ 1993; 307: 172-4.
45. Peel NFA, Barrington NA, Blumsohn A, Colwell A, Hannon R, Eastell R. Bone mineral density and bone turnover in spinal osteoarthritis. Ann Rheum Dis 1995; 54: 867-71.
46. Cummings SR, Black DM, Nevitt MC, Browner W, Cauley J, Ensrud K, et al. Bone density of various sites for prediction of hip fractures. Lancet 1993; 341: 72-5.
47. Hannan MT, Felson DT, Anderson JJ. Bone mineral density in elderly men and women: Results from the Framingham osteoporosis study. J Bone Miner Res 1992; 7: 547-53.
48. Ensrud KE, Palermo L, Black DM, Cauley J, Jergas M, Orwoll ES, et al. Hip and calcaneal bone loss increase with advancing age: longitudinal results from the study of osteoporotic fractures. J Bone Miner Res 1995; 10: 1778-87.
49. Burger H, van Daele PL, Algra D, van den Ouweland FA, Grobbee DE, Hofman A, et al. The association between age and bone mineral density in men and women aged 55 years and over: The Rotterdam study. Bone Miner 1994; 25: 1-13.
50. Greenspan SL, Maitland LA, Myers ER, Krasnow MB, Kido TH. Femoral bone loss progresses with age: A longitudinal study in women over age 65 J Bone Miner Res 1994; 9: 1959-65.
51. Burger H, de Laet CE, van Daele PL, Weel AE, Witteman JC, Hofman A, et al. Risk factors of increased bone loss in an elderly population: The Rotterdam study. Am J Epidemiol 1998; 147: 871-9.
52. Hannan MT, Felson DT, Dawson-Hughes B, Tucker KL, Cupples LA, Wilson PW, et al. Risk Factors for Longitudinal Bone Loss in Elderly Men and Women: The Framingham Osteoporosis Study. J Bone Miner Res 2000; 15: 710 –20.
53. Kleerekoper M. Osteoporosis prevention and therapy: preserving and building strength through bone quality. Osteoporos Int 2006; 17: 1707-15.
54. Jonell O, Kannis A J. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos Int 2006; 17: 1726-33.