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Original Article

Prevalence of Low Forearm Bone Density in a Bulgarian Female Referral Population

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Abstract. Osteoporosis is one of the leading causes of morbidity and mortality in the elderly population. The prevalence of osteoporosis and osteopenia in Bulgaria is unknown except for preliminary data. We tried to determine retrospectively the prevalence of osteopenia and osteoporosis in a referral female population; 8869 consecutive Bulgarian women (age 20–87 years) were included. Information about known risk factors for low bone mass was recorded. Forearm bone mineral density was measured at the distal radius+ulna site by single X-ray absorptiometry (DTX-100 device). *T*- and *Z*-scores were calculated from Bulgarian reference data. In the total study sample 15.16% had osteoporosis and 28.8% had osteopenia. In women aged 50 years and over the corresponding prevalence was 20.45% and 32.5%. Age-adjusted prevalence of osteoporosis and osteopenia started rising after age 55 years. Corresponding mean *T*-scores also declined and the osteoporosis threshold of –2.5 SD was reached in the age group 70–74 years. *Z*-scores in all age groups were between 0 and –0.6, thus excluding major selection bias. This is the first large-scale Bulgarian study designed to look for the prevalence of osteopenia and osteoporosis in a referral population. It may become the starting point for future screening and intervention strategies in our country.

Keywords: Bulgarian female population; Forearm densitometry; Osteoporosis and osteopenia prevalence; Risk factors; *T*- and *Z*-scores

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Introduction

The world population is growing and aging. One of the leading causes of morbidity and mortality in the elderly population is osteoporosis. The incidence of osteoporosis-related fractures is estimated to be 1.5 million/year in the United States [1,2]. Osteoporotic fractures, especially hip fractures, are associated with considerable morbidity and mortality, and increasingly high human costs and costs of health care [3]. This is the reason why most epidemiologic publications in the field of osteoporosis are focused on the prevalence and incidence of fragility fractures [2,4]. The World Health Organization (WHO) has developed a consensus definition of osteoporosis based on bone mineral density (BMD) measurements and subsequent *T*-scores [5]. Regarding the skeletal site to be measured, the WHO Study Group recommended the anteroposterior spine, hip (femoral neck) and forearm. Radial BMD has been used as a surrogate determinant of fracture risk for more than 25 years [6,7]. The association between bone mass measurements at different skeletal sites and fracture risk seems to be well established [8]. However, there is a limited number of studies based on bone densitometry data looking at the prevalence of osteoporosis in large populations [9–11]. Forearm BMD is used in a few studies including a general population sample [12–14] or a specific referral population [15–17]. There are still no convincing data available on osteoporosis prevalence in Bulgaria. Preliminary data from a small population sample have recently been reported [18]. Data on larger groups at high risk for osteoporosis, such as patients referred for bone density testing, are still lacking. Statistics show that about 4500 Bulgarian patients with newly occurred hip fractures are hospitalized yearly for reconstructive surgery [19].

The objective of our study was to determine retrospectively the prevalence of osteopenia and osteoporosis in a referral female population using our own Bulgarian forearm BMD reference data as well as the derived *T*- and *Z*-scores.

Patients and Methods

Patients

This study was conducted between May 1994 and May 2000. A total of 8869 consecutive 20- to 87-year-old Bulgarian women of long-standing generations were included. About 55% of them were referrals to our Osteoporosis Center by general practitioners or other practicing medical specialists. The main reason for referral was back or lower extremity pain (60% of all referrals, while 10.1% of them were referred because of previous fractures). The remaining 45% of the study population were self-referrals and were measured because of their concern about possible osteoporosis, based mainly on a maternal history of low-trauma fractures and known risk factors. The only inclusion criteria was the patient's informed consent. Age (years), height (cm), weight (kg) and age at menopause (if menopausal) were recorded prior to BMD testing. Body mass index (BMI) was calculated from weight and height in $kg \times m^{-2}$. Data on major risk factors for osteoporosis were collected using a self-administered questionnaire. We did not establish subgroups based on risk factors but examined the group as a whole, in the belief that it would represent a true referral population.

We built our own Bulgarian BMD reference data, based on 540, 20- to 83-year-old healthy non-obese women free of major risk factors for osteoporosis, previous low-trauma fractures, medications or diseases known to affect bone mass. They came from an epidemiologic survey in nine different towns throughout the country and were recruited by advertisement. They did not differ from the whole study group in their anthropometric parameters. For the healthy controls BMI < 35 kg/m^2 was set as an inclusion criterion to exclude the possible confounding effect of excessive overweight on bone density reference data, as reported by others [20]. All healthy postmenopausal women had never received hormone replacement therapy. All premenopausal controls had a history of regular menstrual cycles.

The participants' clinical data are summarized in Table 1 (total sample) and Table 2 (healthy controls) subdivided into 5-year age strata. Table 3 shows the prevalence of reported risk factors in the total study sample.

Bone Density Measurements

BMD (in g/cm^2) was measured by single X-ray absorptiometry (SXA) at the forearm using a DTX-100 unit (Osteometer Meditech, Rodovre, Denmark). BMD was measured according to the manufacturer's procedure manual [19] at the so-called 8-mm distal site including both radius and ulna. On this specific device the distal region of interest begins at the 8 mm separation point between radius and ulna and then continues proximally for a distance of 24 mm [21]. All scans were re-reviewed and those with motion artifacts or other technical problems were excluded from further analysis.

Precision Study

Quality control was performed on a daily basis on the phantom provided by the manufacturer. For evaluating the short-term in vivo precision 20 healthy women aged 20–29 years were measured three times consecutively by two operators on the same day – twice by operator 1 and

Table 1. Age-stratified clinical data of the total study sample

Age group (years)	No. of women	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)	Age at menopause (years)
20–24	68	22.68 (2.59)	164.34 (8.5)	57.87 (18.57)	21.62 (5.31)	–
25–29	119	27.15 (1.39)	164.27 (10.44)	57.38 (14.05)	21.16 (4.61)	–
30–34	156	32.2 (1.43)	163.97 (6.94)	60.29 (12.98)	22.49 (4.58)	–[a]
35–39	308	37.33 (1.39)	163.86 (6.01)	63.42 (13.46)	23.6 (4.7)	–[a]
40–44	631	42.26 (1.39)	163.73 (5.75)	64.23 (12.59)	23.94 (4.51)	–[a]
45–49	1366	47.31 (1.38)	163.56 (6.58)	66.17 (12.72)	24.74 (4.54)	43.42[b]
50–54	2140	52.06 (1.41)	162.96 (6.98)	68.89 (14.27)	25.87 (4.54)	46.96[c]
55–59	1565	56.81 (1.41)	162.50 (8.89)	69.38 (14.07)	26.13 (4.58)	49.26[d]
60–64	988	61.95 (1.41)	162.48 (7.76)	70.35 (12.33)	26.62 (4.37)	51.26[e]
65–69	787	66.83 (1.44)	159.71 (15.49)	67.46 (15.38)	26.16 (4.3)	52.73
70–74	481	71.81 (1.38)	160.11 (9.14)	66.54 (11.24)	26.14 (4.17)	53.23
$\geqslant 75$	260	77.6 (2.47)	159.14 (11.05)	63.95 (11.07)	25.48 (4.31)	53.6

Values are mean (SD)
[a]Not calculated because only a negligible proportion of all women had a premature menopause.
[b]Only 618 women were postmenopausal.
[c]1604 women were postmenopausal.
[d]Only 86 women were still premenopausal.
[e]Only 7 women were still premenopausal.

Table 2. Age-stratified clinical data of the healthy reference group

Age group (years)	No. of women	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)	Age at menopause (years)
20–24	38	22.71 (1.27)	165.32 (5.35)	57.53 (7.19)	21.03 (2.28)	–
25–29	37	26.95 (1.39)	164.19 (6.58)	57.70 (7.67)	21.38 (2.39)	–
30–34	39	32.59 (1.39)	164.05 (6.44)	62.21 (8.64)	23.08 (2.55)	–
35–39	51	37.55 (1.27)	164.02 (5.03)	60.53 (11.15)	22.46 (3.88)	–
40–44	46	42.59 (1.22)	163.09 (5.16)	60.64 (5.75)	22.81 (2.00)	–
45–49	56	47.36 (1.26)	164.23 (4.58)	65.25 (6.10)	24.22 (2.31)	–
50–54	48	51.98 (1.28)	163.46 (6.28)	66.23 (8.77)	24.74 (2.61)	44.63[a]
55–59	49	56.94 (1.45)	136.65 (5.13)	67.65 (7.30)	25.25 (2.26)	49.41
60–64	44	62.25 (1.31)	163.11 (5.69)	65.50 (7.48)	24.61 (2.49)	51.09
65–69	51	67.14 (1.48)	160.41 (5.99)	64.04 (7.19)	24.92 (2.73)	50.96
70–74	45	71.91 (1.53)	159.84 (5.60)	66.01 (8.20)	25.83 (2.94)	50.27
$\geqslant$75	36	76.86 (2.07)	157.75 (6.89)	64.94 (9.47)	26.07 (3.23)	49.92

Values are mean (SD).
[a]5 women still premenopausal.

Table 3. Reported major risk factors and protective factors for osteoporosis as a percentage of the total study sample

	Prevalence (%)
Risk factors	
Caucasian race (whites)	100
Maternal history of low-trauma fractures after age 50 years	12.1
Previous low-trauma fractures	5.6
Body mass index $<$22 kg/m^2	22.2
Menopausal age $<$43 years	18.1[a]
Calcium intake $<$600 mg/day	85
Smoker (current or ever smoked)	35
Heavy smokers ($>$10 cigarettes/day)	11
Alcohol ($>$6 oz/weekly)	1.2
Excessive caffeine consumption (>100 mg/day)	20
Secondary causes for osteoporosis (drugs, diseases)	5
Protective factors	
Calcium and/or vitamin D supplements	8[a]
Hormone replacement therapy	1.1[a]

[a]Postmenopausal women only.

the third time by operator 2. For the calculation of the inter-operator errors the means of the first two measurements by operator 1 were obtained. Long-term precision in vivo was determined by a fourth measurement by operator 1 three months later. The precision errors were calculated as root mean square % coefficient of variation (%CV) according to Glüer et al. [22].

Statistical Analysis

A SPSS 10.0 for Windows package was used for processing anthropometric and bone density data. The Kolmogorov–Smirnov test for normal distribution was performed first, followed by tests for homogeneity of variance, ANOVA (with Tamhane's and Bonferroni's coefficients) and non-paired Student's *t*-tests. In the case of a non-parametric distribution the Kruskal–Wallis or Mann–Whitney tests were applied. Statistical significance was set at $p \leqslant 0.05$.

One-way analysis of variance (ANOVA) was used to detect differences in age and body size among the different age groups in the total sample and in the young adult premenopausal population.

T-scores and *Z*-scores were calculated according to recent guidelines [23,24]. *T*-scores were expressed in units of SDs above or below the mean of the healthy adult premenopausal population aged 20–39 years – 165 women coming from the reference population of 540 women recruited. Peak distal BMD was set at 0.463 ± 0.045 g/cm^2 (see Results). *Z*-scores were expressed in units of SDs above or below the mean BMD of the corresponding age-matched reference group. The functional relationship between *T*- and *Z*-scores was tested by correlation analysis and linear regression models.

Results

Long-term in vitro precision of the DTX-100 instrument on the manufacturer-supplied phantom expressed in %CV was 0.60%. Short-term precision in vivo for one operator was 1.65% and for two operators –1.86%. Long-term in vivo precision was 2.13%.

All anthropometric parameters and BMD values had a normal Gaussian distribution. The anthropometric differences between each consecutive two age groups were negligible and allowed comparisons of BMD data.

All BMD results are summarized in Tables 4 and 5 according to age strata. Mean BMD continued rising until age 44 years in both the total sample and the reference group. The young healthy adult premenopausal mean distal BMD derived from the 165 healthy controls was 0.463 g/cm^2 (SD 0.045 g/cm^2).

The prevalence of osteoporosis and osteopenia in age groups 45 years and over according to the WHO criteria applied to the forearm BMD is shown in Fig. 1. The mean prevalence in the total sample and separately

Table 4. Forearm distal BMD data of the healthy reference group according to age strata

Age group (years)	Reference BMD in g/cm^2 (SD) – healthy controls	95% confidence intervals for reference BMD in g/cm^2
20–24	0.462 (0.041)	0.449–0.476
25–29	0.461 (0.042)	0.447–0.475
30–34	0.465 (0.054)	0.448–0.483
35–39	0.464 (0.045)	0.452–0.477
40–44	0.468 (0.034)	0.458–0.478
45–49	0.465 (0.037)	0.455–0.474
50–54	0.457 (0.043)	0.444–0.469
55–59	0.432 (0.042)*	0.420–0.444
60–64	0.402 (0.056)*	0.384–0.419
65–69	0.370 (0.053)*	0.355–0.385
70–74	0.357 (0.059)*	0.324–0.359
$\geqslant 75$	0.343 (0.055)	0.324–0.361

Values are mean (SD) and confidence intervals.
*$p < 0.05$, when mean BMD compared with the previous age group.
**$p < 0.01$, when mean BMD compared with the previous age group.
***$p < 0.001$, when mean BMD compared with the previous age group.

Table 5. Forearm distal BMD data of the total study population acording to age strata

Age group (years)	Mean BMD in g/cm^2 in the total referral population	95% confidence intervals for mean BMD in g/cm^2
20–24	0.435 (0.053)	0.422–0.448
25–29	0.441 (0.057)	0.430–0.451
30–34	0.444 (0.063)	0.434–0.454
35–39	0.449 (0.056)	0.443–0.456
40–44	0.455 (0.047)	0.451–0.458
45–49	0.454 (0.050)	0.451–0.456
50–54	0.444 (0.056)***	0.442–0.446
55–59	0.421 (0.060)**	0.419–0.424
60–64	0.390 (0.064)**	0.386–0.394
65–69	0.364 (0.066)***	0.360–0.369
70–74	0.351 (0.063)**	0.346–0.357
$\geqslant 75$	0.321 (0.067)***	0.313–0.329

Values are mean (SD) and confidence intervals.
*$p < 0.05$, when mean BMD compared with the previous age group.
**$p < 0.01$, when mean BMD compared with the previous age group.
***$p < 0.001$, when mean BMD compared with the previous age group.

in all women aged over 50 years is summarized in Table 6. Over half of all study participants had normal BMD values. As expected, the prevalence of osteoporosis and osteopenia started rising abruptly in the early postmenopausal period (age groups 55–59 years and older).

Figure 2 shows the mean *T*-scores of the different age groups in the total sample expressed in units of SD. In the elderly mean *T*-scores are considerably lower, reaching the osteoporosis threshold of –2.5 SD around the age of 70–74 years.

Figure 3 shows the mean *Z*-scores of the different age groups in the total sample. It addresses the different selection of the total sample and the reference population. *Z*-scores of the total sample are lowest in the youngest age groups (between -0.4 and -0.6 SD until age group 30–34 years), stabilize around -0.3 until age 50–54 years and rise close to zero in the eldest age groups.

Table 6. Prevalence of normal forearm bone mineral density, osteopenia and osteoporosis in the total study sample and in women aged >50 years

	Total sample (n = 8869)	Women age >50 years (n = 6221)
Normal BMD	56.04% (n = 4970)	47.05% (n = 2927)
Osteopenia	28.80% (n = 2554)	32.50% (n = 2022)
Osteoporosis	15.16% (n = 1345)	20.45% (n = 1272)

n, number of subjects.

The correlation coefficients between *T*- and *Z*-scores in all age groups were highly significant ($p < 0.001$) and close to 1.0.

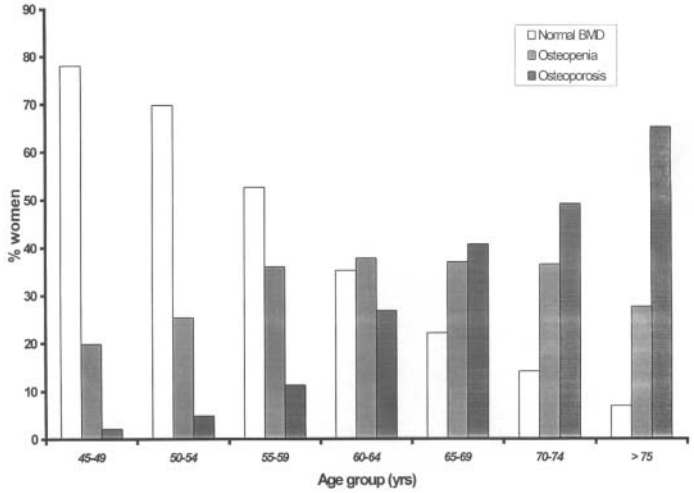

Fig. 1. Prevalence of normal bone mineral density, osteopenia and osteoporosis in the total study sample.

Fig. 2. Mean BMD *T*-scores in the total study sample according to age strata.

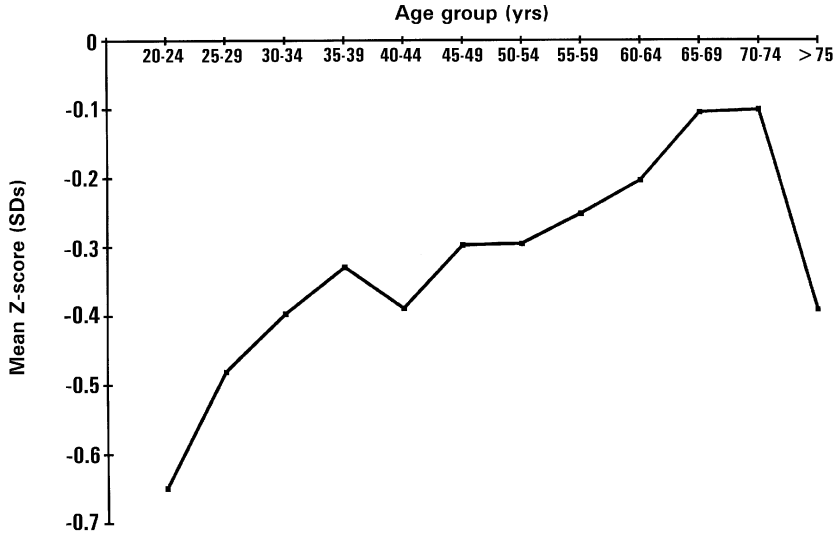

Fig. 3. Mean BMD *Z*-scores in the total study sample according to age strata.

Discussion

This study is a referral population-based cross-sectional examination of forearm distal BMD in Bulgarian women. It is the first study addressing the prevalence of osteoporosis/osteopenia and normal BMD in such a large Bulgarian sample. We built our own BMD reference ranges and tried to followthe mean *T*-score changes with advancing age. BMD data of the total sample were also expressed in *Z*-scores to test for the selection of the normal controls.

To test our normal reference population and the derived *T*- and *Z*-scores we first compared our BMD data with reference ranges published by other authors using the same device [25,26]. Their age-stratified distal BMD data are quite similar to ours.

Second, we checked the age-adjusted *Z*-scores of the total sample to test for possible selection errors in the healthy normals. As seen in Fig. 3, *Z*-scores were lowest at ages 20–24 years and close to zero at ages 70–74 years. We concluded that our selection criteria for healthy normals had been more strict in the younger age groups. Another possible explanation might be that with

advancing age the most severe cases of osteoporosis naturally dropped out from our study as they could not walk independently and visit our Osteoporosis Center. Thus we cannot exclude a possible selection bias in the elderly age groups leading to higher *Z*-scores of the total sample in advanced ages.

Third, we checked the in vivo precision error of our DTX-100 device to ensure that observed differences in BMD values and derived *T*-scores are due to real changes. Although generally considered as too small (20 duplicate measurements give only 10 degrees of freedom) [22], our precision study gave us information about the possible extent of the precision error on the DTX-100. On this specific device Kelly et al. [25] reported an in vivo CV of 1.05%, and Rey et al. [26] a CV of 1.11%. In a forearm pDXA study Xu et al. [13] reported intraoperator variations of 1.95% (interquartile range was 0.71–4.81%) and interoperator precision errors of 2.13%. Our study yielded a precision error under or around 2% and there was essentially no difference between the intra- and interoperator variations. We concluded that the observed BMD age changes, exceeding by many times the CV, were real.

In one of the few densitometric studies based on midradius bone density measurements Melton [9] found that 17.4% of all women aged over 50 years from an age-stratified random sample had osteoporosis. In our total sample the prevalence of osteoporosis is 15.16% and in the age groups 50 years and over (6221 women) it is 20.45%. We compared our results with those of studies based on patient populations referred for forearm bone density testing [11,15,16]. In a sample of 1622 consecutive female patients Mazess et al. [16] found osteoporosis defined as BMD values $>30\%$ lower than those of young healthy premenopausal females in 2–3% of all women aged 30–49 years, in 16% between 50 and 59 years, in 34% between 60 and 69 years, in 56% between 70 and 79 years, and in 62% between 80 and 89 years. These figures correlate very well to our findings shown in Fig. 1. Similar results on a DTX-100 device have been published in a Polish patient population by Czerwinski et al. [15]. In a total of 17 748 women measured at the distal site the prevalence of osteoporosis was found to be as follows: 31–50 years, 1.4%, 51–60 years, 7.9%, 61–70 years, 31.7%, 71–80 years, 53.2%. In the age group of 21–50 years osteopenia ranged from 14% to 18%. The good correlations of results from different studies suggest a similar distribution of mean *T*-scores in patient populations of different origin. Our data differ slightly from the preliminary report on the occurrence of osteoporosis in 627 screened Bulgarian women [18]. In this small general population sample osteopenia was observed in 42.8% and osteoporosis in 37.9%.

Our study has several limitations. First, it was not a truly general population-based study. There might be some bias toward lower BMD and higher prevalence of osteopenia and osteoporosis in our sample as it had generally been referred for bone density testing and was expected to have some complaints possibly due to osteoporosis. This may be the reason for the high prevalence of osteoporosis (about 30–40%) in age groups 60–69 years. Thus our results may not be applicable to the entire population.

Another important point is that radial bone density measurements may not reflect the true prevalence of osteoporotic bone loss. Peripheral bone densitometry proved better at assessing fracture risk than diagnosing osteoporosis [27]. BMD measurements at the hip and spine are the gold standard for determining the approximate prevalence of osteopenia and osteoporosis in a human population [5,10,24]. Thus additional investigations on correlations between the prevalence of osteoporosis based on the use of this specific forearm bone densitometer (the DTX-100) and axial DXA are needed.

Third, in our study we applied the *T*-score approach as advocated by the WHO (see also Fig. 2). The *T*-score decrease after age 50 years is very similar to that reported by Mazess et al. [16] and Rey et al. [26]. In the patient population of Mazess et al. [16] osteopenic levels were reached at ages 52–55 years and osteoporosis at around age 75 years. At the distal forearm Rey et al. [26] found a *T*-score reduction of –3.0 SD between 30 and 75 years of age. However, one must keep in mind the limitations of cross-sectional data in assessing bone loss compared with longitudinal evaluation [28].

The *T*-score approach is primarily designed for use in the postmenopausal population [5,23,24]. *T*-scores and the prevalence of osteoporosis can be derived also in the younger premenopausal population. However, fracture risk can not be determined. Therefore the WHO criteria can not be used for diagnosis of osteopenia and osteoporosis in the premenopausal population. An additional limitation lies in the fact that by definition 16% of a normally distributed population must have a *T*-score (*Z*-score in the young) of –1.0 or lower. Thus Fig. 1 shows the prevalence of osteopenia and osteoporosis starting at age 45 years. Mean *T*-scores are shown also in the younger age groups aged 20–44 years (see Fig. 2), reflecting the acquisition of forearm peak bone mass until age 40–44 years.

Some concerns have been raised regarding the use of *T*-scores for diagnostic classification [29,30]. Faulkner et al. [31] compared the prevalence of osteoporosis at different skeletal sites using different techniques and the manufacturer's normative data. They came to the conclusion that a single *T*-score criterion can not be universally applied to all BMD measurements. It may be necessary to provide a *T*-score criterion specific to the type of densitometric evaluation performed. The disadvantage of fixed cutoff points could be partly corrected for by estimating the gradient of risk for fracture inherent in declining BMD. In a study on the prediction of fracture from low BMD, Kanis et al. [32] found a loss of predictive value in later life and supported the view that measurements should be optimally targeted at the time interventions are contemplated. Roig-Vilaseca et al. [33] studied 148 women by applying different reference databases and

found that *T*-scores can vary according to the normal range used as reference. Similar findings of an inappropriate reference range for peak BMD and derived *T*-scores have been published by Gürlek et al. [34]. This might be even more important when applied to a general population. For example, the manufacturer of the DTX-100 provided a Danish forearm BMD reference database [35] in which peak values were 7% higher than those observed in our healthy controls.

Using *T*-scores for diagnostic use also has many advantages. Watts [36] pointed out that the WHO criteria were primarily intended for public health and not for diagnosis of osteoporosis in individual patients. The prevalence of the disease called osteoporosis might not be the same as that of low *T*-scores. However, *T*-scores of the anteroposterior spine, femoral neck, total hip, and forearm are advocated as the most reliable criterion for the diagnosis of osteoporosis and estimation of fracture risk [23,34].

This is the first large-scale Bulgarian study designed to look at the prevalence of osteopenia and osteoporosis in a referral population. Although not generally representative of the total population from an epidemiologic point of view, it may be the starting point for future screening strategies. The use of the relatively inexpensive, compact, portable and low-radiation peripheral bone densitometry is well suited for measuring bone density in large population groups.

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