Original Article

First Update of the Lebanese Guidelines for Osteoporosis Assessment and Treatment

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Abstract

With the demographic explosion, the human, social, and economic costs of osteoporosis in developing countries, including the Middle East, will continue to rise. In 2002, the Lebanese Guidelines for Osteoporosis Assessment and Treatment were developed to optimize quality of osteoporosis care in Lebanon and the region. They were endorsed by 5 Lebanese medical scientific societies, and by the Eastern Mediterranean Regional Office branch of the World Health Organization (WHO). In April 2006, the Lebanese Society for Osteoporosis and Metabolic Bone Disorders (OSTEOS) led an initiative to update several recommendations detailed in the original document, based on relevant new local and international data. Data from a population-based sample of elderly Lebanese validated the following recommendations: fracture risk assessment, expressed as relative risk per standard deviation (RR/SD) decrease, was comparable in Lebanese subjects to similarly derived estimates from Western studies; the use of the NHANES database (hip), and the densitometer American database (spine) was as good, if not superior to the use of a Lebanese database for identifying subjects with prevalent vertebral fractures. The original recommendation regarding the use of a gender-specific western database, densitometer for spine and NHANES for T-score derivation for men, remains unchanged. For skeletal site selection, the update recommends measuring the spine and hip for women ≤65 yr, hip only for subjects >65 yr, and adding the forearm in conditions associated with cortical bone loss or in the case of inability to measure axial sites. The original recommendations for conservative management in premenopausal women were reiterated.

This First Update of the Lebanese Osteoporosis Guidelines validates previous recommendations using evidence from a population-based sample of elderly Lebanese, and lays the ground for transitioning the Lebanese Osteoporosis Guidelines to the WHO global fracture risk assessment model.

Key Words: Database; guidelines; Lebanese; osteoporosis; update.

Introduction

Osteoporosis is a major public health problem incurring increasingly heavier social and economic tolls in view of the aging population worldwide in general, and in developing

countries, including the Middle East, in particular. In the Eastern Mediterranean region, the high prevalence of osteoporosis risk factors (high smoking rates and low vitamin D levels), and the expected further increase in life expectancy underscore the pressing need to provide guidance to address a foreseeable epidemic of this disease in the next 15−20 yr.

In an effort to optimize the quality of care of osteoporosis in Lebanon, an initiative was launched in Beirut in the spring of 2002, which led to the development of Lebanese Guidelines for Osteoporosis Assessment and Treatment using dual-energy X-ray absorptiometry (DXA) *(1)*. These

guidelines provided a structural framework—based on the evidence then available—on which to build sound clinical decision making in the management of the patient at risk or with osteoporosis *(2)*. They were meant to reinforce uniformly high standards of care for patients with osteoporosis *(3)*, but were not to be considered rigid yardsticks for management. They were drafted with the intention of periodic reviews and updates as our knowledge based on this challenging silent disease continues evolving globally, regionally and, last but not least, nationally.

The purpose of the current initiative was to revisit several of the original recommendations based on new data and assess their relevance to the applicability of the World Health Organization (WHO) global fracture risk assessment model.

Methods

Guidelines Development and Update

In 2002, an expert panel developed the original guidelines that addressed 3 essential questions for the management of the patient at risk or with osteoporosis using DXA. These were "Who to test, what measures to use, and when to treat?" A Medline Internet search, current to 2002, and then updated to July 2003 (the time at which the final document was revised, endorsed and finalized) was undertaken entering the 2 key words "guidelines" and "osteoporosis" *(2)*. The guidelines for "who to test" and "when to treat" were stratified into 3 categories, based on the strength of the evidence available at the time the guidelines were drafted. The guidelines were reviewed and endorsed by the Lebanese scientific societies of Endocrinology, Orthopedics, Obstetrics and Gynecology, Radiology, Rheumatology, and subsequently by the Eastern Mediterranean Region Organization of the WHO. They were submitted to the AGREE appraisal instrument (www.agreecollaboration.org), and have been posted on the web site of the International Osteoporosis Foundation (IOF) since then http://www.iofbonehealth.org/health-professionals/national-regional-guidelines/references. The expert panel was since extended to involve other members from the multidisciplinary Lebanese Scientific Society for Osteoporosis and Metabolic Bone Disorders "OSTEOS." The specific guidelines to be revisited were prespecified by the core panel of national experts in 2006. These were as follows:

A. Which database should be used: local or western universal database?
B. Should a gender-specific database be used in men?
C. How many skeletal site(s) should be measured?
D. What is the relevance of universally used risk factors in the Lebanese?
E. Recommendations in premenopausal women.

An update on the previous Medline search was conducted through a similarly targeted search for years 2003 till February 2006. Also considered were any articles relevant to the topic up to the time of submission of this document for publication, provided by the national and guest international experts who contributed to this initiative.

The panel of local experts composed a report outlining the rationale and/or evidence for the specific recommendations; these were circulated to an international expert panel (Juliet Compston, John Kanis, and Michael McClung) for input. The update was first discussed in a closed meeting between founding members of OSTEOS and the international panel, and presented and discussed in an open meeting to members of the 5 founding societies the following day April 30, 2006. Members of the international expert panel gave presentations on the process of guidelines development (Juliet Compston), on the clinical relevance of osteoporosis guidelines (Michael McClung), and on the WHO global fracture risk assessment model (John Kanis). Members of OSTEOS presented the suggested update and recommendations for "which database to use and how many skeletal sites to measure" (Ghada El-Hajj Fuleihan), for "should a gender-specific database be used in men and relevant national risk factors" (Rafic Baddoura) and for "recommendations in premenopausal women" (Hassane Awada). The guidelines were revised again based on the open meeting discussions, submitted for endorsement by the 5 Lebanese scientific societies and for rereview by the international expert panel in parallel. The current document summarizes the update/recommendations endorsed in 2007 by the 5 Lebanese scientific societies, OSTEOS, WHO Lebanon and the Ministry of Health. This initiative is currently followed by a national dissemination effort of the updated guidelines scheduled over 1 yr 2007−2008.

Study Subjects

A total of 449 apparently healthy Lebanese subjects, 292 women and 157 men of Lebanese descent, aged 65−85 yr, mean age 73.6 ± 5 yr, were randomly selected from the Greater Beirut area using geographic maps and a multilevel cluster technique. There are no discernible ethnic differences within the Lebanese population. Greater Beirut constitutes 33% of the Lebanese population at large (Ministry of Social Affairs and WHO, 1996). Inhabitants of that area represent the various communities in the country, in view of migrations from the countryside to the city, due to seasons, urbanization, and the war. Exclusion criteria include any medical condition or medications likely to affect bone metabolism *(4)*.

Bone Density Measurements and Identification of Vertebral Fractures

Bone density was measured at the lumbar spine (L1−L4), nondominant femur (total hip, femoral neck) and nondominant forearm (1/3 radius) using Hologic 4500A DXA (Hologic Waltham, MA) at the American University of Beirut Medical Center and Hologic 4500W DXA at Hotel-Dieu de France. Details regarding cross-calibration, T-score calculation using local, NHANES database for the hip, and densitometer-derived western database for the spine, and quality assurance measures are provided elsewhere *(4)*. Presence of vertebral fractures was assessed using the semiquantitative

method of Genant, as described previously *(4)*. Mild fractures, less than 20% height loss, were excluded.

Statistical Analyses

Subjects were classified as osteoporotic or nonosteoporotic according to the WHO T-score based criteria. Sensitivity, specificity, positive and negative predictive values, and receiver operator curve (ROC) for identifying subjects with vertebral fractures using the local or the western database were calculated. The risk of having a vertebral fracture per 1 standard deviation (SD) decrease in bone mineral density (BMD) before and after adjustment for age were calculated by building logistic regression models; the dependent variable was the presence of vertebral fractures and the independent predictors were T-score or T-score and age. These risk estimates were derived using the local Lebanese database (spine and hip) and the western densitometer database for the spine and NHANES database for the hip, for T-score calculation. Risk estimates were provided with their 95% confidence interval (CI) between brackets. The derived estimates from local and western database were considered significant if their CI did not overlap one, and comparable to one another if their CI did overlap. The statistical analyses were performed using STATA software version 7 and SPSS software version 10. Significance was set at a $p < 0.05$; p values were unadjusted for multiple testing.

A. Which Database Should Be Used: Local or Universal Western Database?

It is generally agreed that the relationship between BMD and fracture risk is an inversely exponential one. For each SD decrease in BMD, fracture risk almost doubles as described in large epidemiologic studies conducted mostly on Caucasian populations from the United States *(5)*, the Netherlands *(6)*, France *(7)*, and Hawaii *(8)*, although scarcer data from other races are available *(9)*.

At present, fracture risk can be expressed in 1 of 2 ways:

1. As an absolute risk, either a lifetime, a 10-yr, or a 5-yr risk for a specific BMD at a certain age (because age is another independent predictor of fractures), such as provided in the Rotterdam and the Swedish studies *(6,10)*. The expression of risk in absolute terms, that is, as probability of fracture in a discrete time frame is more relevant clinically, and has the added advantage of giving a unified output regardless of the technique or site of assessment used for risk estimates *(10)*.

2. More commonly, at least for now, but in less practical terms, as a RR expressed as relative risk per standard deviation (RR/SD) decrease in BMD. Therefore, an individual with a T-score (or Z-score) of −3 has a fracture risk that is twice that of an individual with a T-score (or Z-score) of −2. Such assessment is less useful in the clinical setting, as it expresses risk in relative rather than in absolute terms *(5,7,11−13)*, and the absolute risk in the comparative arm in relation to which the RR is expressed often is not readily available.

Very few studies have expressed absolute fracture risk as a function of BMD, as in the Rotterdam and the Swedish studies *(6,10)*. However, because the value of BMD measured in gm/cm^2 may vary depending on the central DXA manufacturer, appropriate conversions have to be implemented before such data can be used *(14)*. In view of the paucity of absolute fracture risk data published in the past, the practice has been to try to use the more abundant data using RR/SD decrease in BMD, and hence the practice to use T-scores to assess fracture risk and to establish T-score-based thresholds for intervention.

Two important points are to be made at this juncture. The WHO T-score cut-points for the diagnosis of osteoporosis were originally derived to be applied to bone density data derived mainly from DXA devices, and to be used as diagnostic but not therapeutic thresholds in postmenopausal Caucasian female subjects only *(15)*.

The second issue of relevance to non-Western countries, such as Lebanon, is whether the BMD-fracture relationship derived from European and American Caucasian subjects applies to populations from the Middle East in general, and Lebanon in particular. This raises the question of how absolute BMD/fracture curves compare across populations within the same racial category, because for the purposes of this debate Lebanese are considered White Caucasians *(16)*. A comparison of absolute BMD vs fracture risk across various Caucasian populations would be needed to address that question and such data are not available to date for populations from the Middle East. Therefore, resorting to T-scores was the next available strategy to assess fracture risk expressed as RR/SD decrease in individuals in the Middle East. This would be a sound approach if the following 2 assumptions were met:

1. The absolute BMD/fracture relationship is the same in all Caucasians regardless of the specific population. We had previously suggested that there was no a priori reason to think differently *(1)*. Indeed, analyses of recently available national data, presented herein (see below), demonstrate that the BMD/fracture relationship is similar in the Lebanese to that of Western populations, confirming the above presumption.

2. The appropriate device and database in which the BMD-fracture relationship and therefore T-score cut-off was derived are used. These would be a central DXA device, and the Caucasian postmenopausal female normative database (at least in women, see section ''Should a Gender-Specific Database be Used in Men?'') on which the WHO operational definition for osteoporosis was based. We had previously detailed the rationale for such a recommendation *(1)*. This document now presents recent national data that shows that the use of a standard universal Western database in elderly Lebanese subjects is as good, if not superior, in identifying elderly patients with prevalent vertebral fractures, to the use of a local Lebanese database (see below).

Peak BMD in subjects from the Middle East has been studied mostly in nonpopulation-based *(17−21)* and in few

population-based samples (22−24). The above studies reveal that peak BMD may be slightly lower than or equal to that of European and American Caucasians. This might be explained by differences in body size, chronic vitamin D deficiency, lower calcium intake, and physical activity and genetic factors (22,23,25−28). However, the prevalence of vertebral fractures in postmenopausal women and hip fracture rates are comparable to those for Western counterparts (29−32). Finally, as importantly, mean BMD in Lebanese subjects with hip fracture is comparable to that in hip fracture subjects from the West (31,33). The latter information suggests that the absolute BMD-fracture relationship may be the same in the Middle East as it is in the West.

There is a wide variation in practice patterns regarding the selection of databases to analyze BMD between densitometry centers across Lebanon. Some centers use a Lebanese nonpopulation-based database, some use a western Spanish or French database as provided by the densitometer manufacturer, whereas others use a western universal densitometer database for spine and forearm, and the NHANES total hip database for the hip, in accordance with the recommendations of the Lebanese Guidelines (1,2) and the IOF (34,35).

Do Lebanese subjects have the same BMD/fracture risk relation (RR/SD) as Western Caucasian subjects? To investigate the applicability of estimates of fracture risk expressed as RR/SD decrease in BMD derived from Western populations on the identification of elderly Lebanese patients with osteoporosis, we took advantage of the study evaluating BMD and vertebral fracture prevalence in a population-based sample of 460 elderly Lebanese, briefly described under Methods and detailed elsewhere (4). Fifty-six women (19%) and 18 men (12%) had at least 1 vertebral morphometric compression fracture (36). Analyses were performed to assess the ability of BMD to predict the patients with prevalent fractures using a logistic regression model adjusting for age. BMD was expressed as T-score, Z-score, or absolute BMD in gm/cm^2. T-scores derived from a gender-specific Lebanese population-based peak database (22) and T-scores derived from the densitometer using a gender-specific Western database (Hologic for spine and NHANES for hip) were used.

As detailed in Table 1, the ability of BMD to identify patients with prevalent vertebral fractures, expressed as RR/SD decrease, was comparable in Lebanese subjects to other similarly derived estimates from Western studies, for the hip and forearm in women, demonstrating that the RR/SD decrease does not vary widely within large racial groups (13,37). In men, the data did not achieve significance because of small sample size and the number of fractures. These new analyses based on local data validate the recommendation in the original set of guidelines to apply fracture risk assessment estimates, that is, RR/SD, derived from western Caucasian populations to the Lebanese (1,2).

Table 1

Age-Adjusted OR (95% CI) for Vertebral Fracture per SD Decrease in BMD[a] in Lebanese Elderly Subjects, According to Site, and Comparison to Similarly Derived Estimates in Caucasians From Western Countries

Site	OR/SD decrease in Lebanese elderly using Western database n = 292 women (56 fractures) and n = 157 men (18 fractures)	Western meta-analyses, women only, based on 90.000 person year[b]	Western women (n = 2067) and 317 men (n = 317)[c]
Women			
Spine	1.22 (0.91; 1.6)	2.3 (1.9; 2.3)	1.36 (1.26; 1.47)
Hip	1.61 (1.16; 2.2)	1.8 (1.1; 2.7)	1.66 (1.5; 1.8)
Forearm	1.58 (1.23; 2.05)	1.7 (1.4; 2.1)	
Men			
Spine	0.99 (0.89; 2.1)		1.20 (0.99; 1.45)
Hip	1.59 (0.93; 2.71)		1.37 (1.08; 1.7)
Forearm	0.99 (0.73; 1.33)		
Overall			
Spine	1.32 (1.04; 1.68)		
Hip	1.67 (1.27; 2.19)		
Forearm	1.31 (1.09; 1.56)		

Abbr: OR, odds ratio; SD, standard deviation; CI, confidence interval; BMD, bone mineral density.
[a]T-score was derived using NHANES database for the hip and the manufacturer database for spine and forearm.
[b]Marshall et al. BMJ 1996;18:1254−1259.
[c]Cauley et al. Osteoporos Int 2004;15:32−37.

Is the selection of a universal western database, densitometer derived for spine and NHANES for hip, for the BMD-based diagnosis of osteoporosis, preferable to the selection of a Lebanese database in the identification of Lebanese subjects with vertebral fractures? Taking advantage of the same data set in the Lebanese elderly, aged 65−85 yr, the ability of BMD to predict prevalent vertebral fractures, expressed as RR/SD decrease, was investigated with the use of peak BMD in the Lebanese BMD *(22)* or the peak BMD in the Western database (NHANES for hip, 4). As shown in Table 2, RR/SD decrease in BMD was similar or a bit higher when using the western peak BMD database, as compared to the Lebanese peak BMD database, in women using hip or forearm BMD. Conclusive statements could not be made in men due to the smaller sample size, low number of vertebral fractures, and therefore wide CIs. A related methodology to RR/SD decrease parameter is deriving estimates for sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the ROC of BMD measurements to identify subjects with prevalent vertebral morphometric fracture, using the western and local databases. As shown in Table 3, the area under the ROC for detecting patients with prevalent vertebral fractures was the same or even a bit higher using the NHANES database compared to

Table 2
Age-Adjusted OR (95% CI) for Vertebral Fracture per SD Decrease in BMD in Lebanese Elderly Subjects, Using Western or Local Database[a]

Site	RR/SD decrease in BMD using Western database	RR/SD decrease in BMD using Lebanese database
Women		
Spine	1.22 (0.91; 1.6)	1.16 (0.90; 1.50)
Hip	1.61 (1.16; 2.2)	1.49 (1.14; 1.95)
Forearm	1.58 (1.23; 2.05)	1.47 (1.19; 1.82)
Men		
Spine	0.99 (0.89; 2.1)	1.37 (0.86; 2.19)
Hip	1.59 (0.93; 2.71)	1.66 (0.93; 2.94)
Forearm	0.99 (0.73; 1.33)	0.99 (0.70; 1.39)
Overall		
Spine	1.32 (1.04; 1.68)	1.26 (1.03; 1.56)
Hip	1.67 (1.27; 2.19)	1.52 (1.25; 1.96)
Forearm	1.31 (1.09; 1.56)	1.35 (1.16; 1.58)

Note: The elderly Lebanese group consisted of n = 292 women (56 with vertebral fractures) and n = 157 men (18 with vertebral fractures).

Abbr: OR, odds ratio; CI, confidence interval; RR/SD, relative risk/standard deviation; BMD, bone mineral density.

[a]Western database NHANES for hip, and densitometer for spine and forearm. Local database from El-Hajj Fuleihan G et al. Bone 2002;31:520−528.

Table 3
Sensitivity, Specificity, PPV, NPV, and Area Under the ROC, for BMD Measurements of the Hip, Using NHANES or the Lebanese Database,[a] to Identify Patients With Vertebral Fractures

	Women (N = 292)		Men (N = 157)	
	Western database	Local database	Western database	Local database
Sensitivity	51	26	38	11
Specificity	71	89	79	99
PPV	30	35	20	66
NPV	86	83	90	89
ROC (area)	0.65	0.57	0.64	0.57

Note: The study group consisted of 292 women, 56 with vertebral prevalent fractures and 157 men 18 with vertebral fractures.

Abbr: BMD, bone mineral density; PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operator curve.

[a]El-Hajj Fuleihan G et al. Bone 2002;31:520−528.

local database, for both genders. These differences may be partially explained by differing SD in the 2 data sets, and perhaps argues for an international reference standard, possibly NHANES, in view of its sampling technique, sample size, and stable SD. Similarly, the sensitivity for detecting vertebral fractures was slightly higher using the western as opposed to the local database in both genders; as anticipated the specificity was lower (Table 3). Moreover, with NHANES database and a total hip T-score ≤−2.5 for osteoporosis diagnosis, osteoporosis was present in 51.8% of women and 38.9% of men with prevalent vertebral fracture compared to 24.6% in women and 11.1% in men had we used the population-based database. These new data demonstrate that the use of a universal NHANES database is as good, if not better, than the use of a Lebanese database for identifying subjects with prevalent vertebral fractures *(4)*, thus trading increased sensitivity for a slightly lower specificity. Furthermore, the application of a validated universal standard database, such as NHANES, would provide a unified basis for osteoporosis evaluation, and forego contradicting BMD-based diagnoses that are due to the differing practices of the densitometry centers in Lebanon. Although the data in men are somewhat limited due to the small sample size, they nevertheless show the same trend.

In summary, data from the Lebanese elderly population-based survey validate the application of Western standards, that is, NHANES for hip database and densitometer database for the spine, for the BMD-based diagnosis of osteoporosis, and also validate the use of western fracture risk estimates (RR/SD), for the assessment of fracture risk in Lebanese subjects *(4)*. Finally, such data will provide the basis to apply the upcoming unified paradigm for fracture risk assessment worldwide *(38,39)*. The above evidence-based recommendations are consistent with the recommendations from the International

Osteoporosis Foundation *(34,35)*, the International Society of Densitometry *(40)*, and the WHO global fracture risk assessment model *(38,39)*. We anticipate that similar recommendations would apply to subjects from other countries in the Middle East.

B. Should a Gender-Specific Database Be Used in Men?

The gender difference in the incidence of fractures varies with age and site of fracture. In young adults, the incidence of fractures is higher in men than women, and after the age of 50 yr the trend is inverted at all sites, and incidence rates increase with age but increments vary by the site of fracture *(41,42)*.

It remains a matter of debate whether to use gender-specific databases *(43)*. We screened the available literature as it pertains to 3 questions:

1. Is the BMD-fracture relationship similar in men and women?
2. Do men and women fracture at the same BMD?
3. How does the database selection (men vs women database) affect the diagnosis of osteoporosis and approximate fracture risk?

1. *Is the BMD-fracture relationship similar in men and women?*

There is disagreement whether the BMD-fracture relationship in women and men is the same.

The association between total hip BMD and risk of nonvertebral fractures, namely hip fracture was stronger in men in Mr. Os study than in women in the Study of Osteoporotic Fractures, a 3.2- vs 2.1-fold increase risk per sex-specific SD decrease in BMD, $p < 0.001$ for interaction *(44)*. The use of 0.1 g/cm^2 instead of sex-specific SD did not alter the results *(44)*. The approximate 3-yr risk of nonvertebral fractures based on sex, age, and total hip T-score was higher in women than in men, a finding that was consistent whether sex-specific or female database was used *(44)*. These results were however based on post hoc analyses of 2 different studies.

Conversely, similarities in the relationship between hip fracture and BMD among men and women were reported in the Rotterdam study *(6,45)*. This was further confirmed by Johnell et al *(9)*, who studied over 9000 men and 29,000 women from 12 different cohorts from Europe, Canada, the United States, and Asia, and found that at the age of 65 yr, risk ratio of hip fracture increased by 2.94 (95% CI = 2.02−4.27) in men and by 2.88 (95% CI = 2.31−3.59) in women for each SD decrease in BMD. Moreover, at the age of 65 yr, the risk of any osteoporotic fractures increased by 1.41 per SD decrease in BMD in men (95% CI = 1.33−1.51) and by 1.38 per SD in women (95% CI = 1.28−1.48) (8). The authors concluded that the age-specific gradient of risk of hip fracture in men seems to be similar in women of the same age.

2. *Do men and women fracture at the same BMD?*

Studies have demonstrated that men fracture at higher BMD than women. This was evident in epidemiological studies *(46−48)* and in interventional studies *(49)*. In the Dubbo study, men with fragility fractures had higher average BMD at the spine and at the hip by approximately 20% than those of women with fragility fractures *(46)*. Similarly, in the Rotterdam study, men with hip fracture had a BMD that was on the average 0.07 gm cm^2 higher than that in women with hip fractures; but fracture risk was the same in men and women for the same absolute BMD *(50)*. Orwoll compared data in placebo arms of several interventional trials, where all BMD were measured using densitometers from the same manufacturer *(49)*. The mean ages in the 3 trials were 71, 69, and 62 yr, respectively. Although men were younger and had higher average lumbar spine and femoral neck BMD than women, their fracture rates were higher *(49)*.

3. *How does the database selection affect the diagnosis of osteoporosis and approximate fracture risk?*

In Rochester study, the overall prevalence of osteoporosis in men when a women database was used was only 3%. This prevalence increased to 13% when 20−24-yr old male reference range was used and to 19% when the 20−29-yr old male reference range was used *(51)*. The lifetime risk of any fracture of the hip, spine, or distal forearm in white men is about 13% over the age of 50 yr *(12)* and about 25% over the age of 60 yr *(49)*. Thus, using a gender-specific database better approximates the lifetime fracture risk estimates in men. However, the lifetime risk may not be the appropriate fracture risk tool in clinical management of osteoporosis following the paradigm of the high-risk case-finding strategy. Conversely, for any given BMD the probability of hip fracture is comparable between men and women *(49)*.

De Laet et al demonstrated that a larger proportion of fractures occur at a T-score below −2.5 in women compared to men using the same absolute BMD, but using a male-specific T-score largely solves that diagnostic problem *(50)*. Similarly, based on data from Mr. Os study using a female database instead of gender-specific database would underestimate the prevalence of osteoporosis and result in a large number of men at risk for fragility fracture diagnosed as nonosteoporotic *(49)*.

How do these findings translate in terms of recommendations for osteoporosis assessment and management from the perspective of the high-risk case-finding strategy?

International guidelines recommend searching for clinical risk factors for osteoporosis and suggest DXA measurements based on age and a number of clinical risk factors regardless of gender. Concerning reference database selection, the IOF recommends the female reference base for men *(35)* and so will WHO *(38)*. Conversely, in its most recent Position Development statement, the ISCD still recommends the use of a gender-specific database *(52)*.

What does the Lebanese elderly population-based data tell us regarding these questions?

The population-based study among elderly Lebanese aged 65−84 yr provided the following estimates:

a. *Prevalence of osteoporosis and of vertebral fractures.*
Lebanese men had higher mean BMD compared to women at all skeletal sites. Osteoporosis, defined as a T-score ≤ -2.5 at the total hip using NHANES gender-specific database, was significantly less prevalent in Lebanese men (23%) than in Lebanese women (33%) *(4)*. The prevalence of vertebral fractures in men was 11%, about half of what was observed in women (20%).

b. *BMD in patients with and without vertebral fracture.*
Men with prevalent vertebral fractures had higher mean BMD at all sites compared to women with prevalent vertebral fractures (Table 4), a finding that may be explained in part by differences in bone size. The RR for vertebral fracture per SD decrease in total hip BMD was similar in men and women: 1.59 (0.93; 2.71) vs 1.61 (1.16; 2.2) (Table 1). The ROC for BMD measurements of the hip to identify subjects with vertebral fractures was similar in both genders (Table 5).

c. *Effect of database selection (women vs gender specific) on the prevalence of osteoporosis and on BMD-fracture relationship.*
Using NHANES gender-specific reference for T-scores derivation in Lebanese men provided a higher prevalence of osteoporosis compared to the use of the NHANES female database (23% vs 5.1%). Similarly, the use of the Lebanese gender-specific database provided slightly higher prevalence of osteoporosis based on DXA, compared to the use of Lebanese female database (2.5% vs 1.9%). Thus, the use of a gender-specific database would increase sensitivity at the expense of specificity.

In subjects with vertebral fractures, the prevalence of osteoporosis was 39% when the NHANES gender-specific database was used vs 16.7% when the NHANES female database was used; again increasing sensitivity at the expense of specificity. Conversely, the prevalence of osteoporosis was similar whether using the Lebanese female or sex-specific database (11.1% in both cases). Finally, the RR of vertebral fracture per SD decrease in BMD was quite similar across databases: 1.43 (0.95−2.16) using the women's database vs 1.66 (0.93−2.94) using the gender-specific database.

The update of the guidelines for men recommends:

a. The use of a universal NHANES database for the hip and densitometer-based western reference database for the spine (consistent with the IOF recommendations), similar to recommendations in women, as per previous 2002 Lebanese Guidelines.

b. The database for T-score derivation is that of men.
Thus, the recommendations for men remain unchanged from 2002 guidelines.

Because fracture risk is the same for men and women at the same BMD, as demonstrated in the analyses of Johnell et al combining several large cohorts *(9)*, the use of absolute BMD (as opposed to T-score) in the WHO paradigm will resolve the dilemma of database selection in men *(38)*.

C. How Many Skeletal Site(s) Should Be Measured?

To address this question, one needs to consider the specific purpose for measuring BMD. Three possibilities arise:

a. Diagnosis of subjects with osteoporosis, based on BMD: A DXA-based BMD T-score ≤ -2.5 is the diagnostic threshold for osteoporosis *(15)*.

Table 4
Bone Mineral Density and T-scores[a] in Elderly Lebanese Subjects With and Without Vertebral Fractures

	Women			Men using men's database			Men using women's database		
	With fractures	Without fractures	*p*	With fractures	Without fractures	*p*	With fractures	Without fractures	*p*
Spine BMD	0.740 ± 0.1	0.776 ± 0.1	0.1	0.835 ± 0.1	0.893 ± 0.1	0.1	0.835 ± 0.1	0.891 ± 0.1	0.1
Total hip BMD	0.673 ± 0.21	0.743 ± 0.1	<0.001	0.792 ± 0.1	0.855 ± 0.1	0.05	0.792 ± 0.1	0.854 ± 0.1	0.06
Femoral neck BMD	0.570 ± 0.08	0.623 ± 0.1	<0.001	0.626 ± 0.09	0.674 ± 0.9	0.06	0.626 ± 0.09	0.673 ± 0.9	0.05
Spine T-score	-2.8 ± 1.1	-2.4 ± 1.3	0.07	-2.3 ± 1.5	-1.7 ± 1.3	0.1	NA	NA	NA
Total hip T-score	-2.5 ± 1.0	-1.9 ± 1.0	<0.001	-2.1 ± 1.2	-1.6 ± 0.9	0.06	-1.2 ± 1.3	$-0.7 (1.0)$	0.05
Femoral neck T-score	-3.2 ± 0.8	-2.7 ± 1.0	<0.001	-3.2 ± 0.8	-2.7 ± 0.8	0.05	-2.0 ± 0.8	$-1.5 (0.8)$	0.05

Note: p Values are for difference between subjects with and those without vertebral fractures. Values are mean $\pm$ SD.
Abbr: BMD, bone mineral density.
[a]T-score derived using NHANES for hip and densitometer database for spine and forearm.

Table 5
Sensitivity, Specificity, PPV, NPV and Area Under the Curve for Identifying Subjects at Risk for Vertebral Fractures Using 1 or 2 Skeletal Sites and a Gender-Specific Western Database

	Sensitivity	Specificity	PPV	NPV	ROC	95% CI
Women						
LS	59	49	19	85	0.59	0.49−0.68
TH	51	71	30	86	0.65	0.56−0.73
FN	80	37	23	88	0.65	0.56−0.73
TH and FN (average T)	64	56	26	86	0.65	0.57−0.74
LS, TH, and FN (average T)	59	50	20	85	0.63	0.53−0.73
LS, TH, and FN (lowest)	83	27	19	88	0.53	0.43−0.63
Men						
LS	46	68	16	91	0.60	0.43−0.76
TH	38	79	20	90	0.64	0.50−0.79
FN	83	31	14	93	0.67	0.53−0.80
TH and FN (average T)	66	61	19	93	0.66	0.52−0.80
LS, TH, and FN (average T)	40	68	14	89	0.60	0.44−0.75
LS, TH, and FN (lowest)	86	25	13	93	0.57	0.42−0.72
Overall						
LS	56	56	18	87	0.60	0.52−0.68
TH	48	74	27	87	0.65	0.58−0.72
FN	81	35	20	90	0.65	0.58−0.72
TH and FN (average T)	64	58	23	89	0.66	0.59−0.73
LS, TH, and FN (average T)	54	56	18	87	0.63	0.55−0.71
LS, TH, and FN (lowest)	84	26	17	90	0.54	0.46−0.62

Abbr: CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operator value; LS, lumbar spine; TH, total hip; FN, femoral neck.

b. Estimation of fracture risk to ultimately derive intervention thresholds: The latter are to be distinguished from the above diagnostic threshold.

c. Monitoring of BMD changes in response to therapy.

a. Diagnosis of subjects with osteoporosis

The BMD-based definition for osteoporosis developed by a WHO working group used a set of operational criteria that apply to postmenopausal Caucasian women *(15)*. Osteoporosis was defined as a T-score that is equal to or less than −2.5, based on measurements at the lumbar spine, hip using DXA, or forearm using single photon absorptiometry (SPA) *(15)*. This diagnostic threshold does not apply to non-DXA-based devices *(52−54)*. As an example, a woman aged 60 yr may have a T-score that varies between −0.7 and −2.5 depending on the technique and device used. The WHO working group did not specify which region of interest within a skeletal site should be used for diagnosis *(55)*.

b. Evaluation of fracture risk

It is generally agreed that for each SD decrease in BMD-fracture risk increases by 1.6−3.0-fold. This range is due to variations in the skeletal site used to estimate fracture risk (L2−L4, hip, forearm, etc.), variations in the standard deviations of BMD for that skeletal site by

densitometer, and variations according to the specific fracture outcome of interest (wrist, hip, or vertebral fracture). Risk estimates have been derived to evaluate fracture risk include global- or site-specific fracture risk estimates.

Global risk of fracture. The RR of developing an osteoporotic fracture anywhere in skeleton is the same 1.4−1.6/SD decrease in BMD as measured at any site in the skeleton *(13)*.

Site-specific fracture risk. Although site-specific fracture risk assessment can be estimated by measuring BMD at any skeletal site, the predictive value is higher if a site-specific assessment is conducted: for example, whereas spine, hip, and forearm all predict fracture risk at the hip and spine, the predictive value (RR/SD) is higher using a hip BMD for hip fracture and spine BMD for vertebral fracture *(5,12,13)*.

A large meta-analysis of 11 cohort studies from 1985 to 1994, which included 90,000 person-years and >2000 fractures and in which BMD was measured using central DXA, provided the following estimates for site-specific fracture risk *(13)*: RR/SD decrease in BMD; spine BMD for vertebral fractures 2.3 (1.9−2.8); femoral neck BMD for hip fractures 2.6 (2.0−3.5); and distal radius for wrist fractures 1.7 (1.4−2.0).

c. Monitoring BMD

The spine is the skeletal site most responsive to pharmacologic intervention and may be the best site to monitor the response to therapy *(56)*. Measuring 2 skeletal sites has the additional advantage of not losing the ability to monitor an individual site due to worsening osteoarthritis or fracture.

In addition, the following observations are relevant when making recommendations with regard to the number of skeletal sites to measure, whether it is for diagnosis of osteoporosis, fracture risk assessment, or monitoring:

1. Although there is a correlation in BMD between sites (typically $r = 0.4-0.6$), it is not perfect. Therefore, measuring only 1 site may underestimate a subject's osteoporosis risk *(53,57,58)*. However, measurement of multiples sites while increasing sensitivity would decrease the specificity of the test.

2. There is site specificity for BMD in predicting fractures. Risk estimates are higher using hip BMD for hip fracture and spine BMD for vertebral fractures, compared to the use of other skeletal when measuring BMD *(13)*. The situation may be different in the elderly, where hip BMD is a better predictor of vertebral fractures than spine BMD, due to degenerative changes (see below). Most studies have however evaluated the utility of the femoral neck, rather than total hip in fracture prediction.

3. At menopause, bone loss is greater at the spine than at the hip; measuring only hip BMD, therefore, may miss reduced bone mass at the spine particularly in younger postmenopausal women *(59,60)*.

4. Aging results in degenerative changes at the spine that may falsely increase BMD *(61,62)*. Scoliosis, extraskeletal calcification, and vertebral fracture may have the same effect. Measuring the hip in the elderly is therefore of particular importance.

5. Forearm: Some clinical conditions, such as primary or secondary hyperparathyroidism, may result in differential bone loss in the forearm *(63)*. In patients with these conditions, a forearm measurement is indicated. A forearm measurement is also indicated in the very obese patient, in whom a spine or hip measurement cannot be performed because of large size *(55)*.

Summary of International Guidelines Regarding Specification of Skeletal Site to be Measured

IOF Position

The IOF currently recommends the use of the hip to apply the WHO criteria for the diagnosis of osteoporosis (femoral neck or total hip), outlining that this skeletal site would also predict osteoporotic fractures as well as for any other skeletal sites *(35)*.

ISCD Position

The ISCD recommends measuring the spine and hip for all patients. Nondominant forearm is to be added if 1 of the above 2 skeletal sites cannot be used, if the patient has suspected hyperparathyroidism, or if the patient is obese. The updated recommendation from the ISCD Position Development Conference held in Vancouver in July 2005 is essentially unchanged and summarized as follows: ''The lowest BMD of either the PA spine or hip should be used to make the diagnosis of osteoporosis provided that the scans are technically valid… and low bone mass is not owing to some other localized pathology'' *(55)*. Total body bone mineral content (BMC) measurement is recommended in children *(64)*.

NOF Position

The National Osteoporosis Foundation (NOF) recommends measuring the hip. Indeed, NOF cost-effectiveness was all based on BMD measurement at the hip *(65)*.

Few studies have evaluated the discriminative ability of single vs multiple BMD measurements at several skeletal sites to either identify subjects with osteoporosis, or estimate fracture risk *(56−60,65,66)*.

Our group evaluated the discriminative ability of BMD measurements, when performed at the spine, hip, or both sites, in identifying elderly subjects with prevalent vertebral fractures in the population-based elderly sample *(67)*. The scans were reassessed independently by 2 ISCD-certified readers (AA, GE-HF), to exclude any artifactual effect of degenerative changes on BMD measurements at the spine, using the criteria proposed by the ISCD *(68)*. These were focal structural defect; unusual discrepancy in T-score between 2 adjacent vertebrae; and (3) lack of increase in BMC or bone area when proceeding caudally from L1 to L4. When scans of the spine were reassessed according to ISCD criteria, there was interreader disagreement in 71 cases (15%). The scans were judged unreadable in 50 women (16%) and 24 men (15%). The lumbar spine was assessable in its totality from L1 to L4 in only 91/301 women (30%) and 57/151 men (36%).

In both genders, there was no difference in mean lumbar spine BMD or lumbar spine T-score between subjects with and those without vertebral fractures (Table 4). Conversely, BMD and T-score values at the hip, both total hip and the femoral neck, were lower in subjects who had vertebral fractures than those who did not (Table 4, $p < 0.001$ in women, and $p = 0.05-0.06$ in men). In both genders, the best identification of subjects with a prevalent vertebral fracture, as assessed by the use of ROC curves, using T-scores at a single site, was obtained at the hip site (either total hip or femoral neck, Table 5), in the overall group and in both genders. The risk of vertebral fracture for each SD decrease in bone density, according to the skeletal site, before and after adjustment for age, is shown in Table 6. In both genders, the hip site had the best discriminative ability to identify subjects with vertebral fractures (Table 6). In women, the age-adjusted odds ratio (OR)/SD decrease in BMD for identifying a subject with a vertebral fracture was highest for the femoral neck, as follows: femoral neck OR = 1.79 (1.22−2.62), total hip OR = 1.58 [1.15−2.19], and for the spine OR = 0.99 (0.99−1.50) (Table 6). These estimates are consistent with similarly derived estimates for identifying patients with

Table 6
OR (95% CI) for Vertebral Fractures per SD Decrease in BMD,[a] Before and After Adjustment for Age

Site	Women		Men	
	OR (95% CI) Unadjusted for age	OR (95% CI) Adjusted for age	OR (95% CI) Unadjusted for age	OR (95% CI) Adjusted for age
Lumbar spine	1.30 (0.96; 1.7)	1.22 (0.91; 1.6)	1.39 (0.97; 2.1)	0.99 (0.89; 2.1)
Total Hip	1.78 (1.3; 2.4)	1.61 (1.16; 2.2)	1.65 (0.97; 2.7)	1.59 (0.93; 2.71)
Femoral neck	2.0 (1.4; 2.8)	1.98 (1.0; 3.9)	1.98 (1.0; 3.9)	1.91 (0.96; 3.8)

Note: There were 292 women 56 with vertebral fractures, and 157 men, 18 with vertebral fractures.
Abbr: OR, odds ratio; CI, confidence interval; SD, standard deviation; BMD, bone mineral density.
[a]T-score was based on the NHANES database for hip and densitometer database for spine and forearm.

vertebral fractures, from the placebo arm of the risedronate trial, mean age 69 yr *(69)*. Indeed, OR values of 2.47 (1.79−3.42) were obtained for the femoral neck and 1.84 (1.19−2.85) for the lumbar spine *(69)*. In our study, combining sites, that is, spine and hip, using either a mean T-score for both sites or the lowest T-score of both, did not improve the discriminative ability of DXA measurements to identify subjects with prevalent fractures (Table 6), similar to what has been previously reported *(69)*.

In summary, in the Lebanese elderly, mean age 74 yr, the usefulness of spine BMD measurements was limited. It could not be used in 15% of elderly men or women, and all 4 lumbar vertebrae could be used in only 1/3 of subjects due to degenerative changes and osteoarthritis, as previously reported *(70)*. Hip BMD, and specifically femoral neck BMD, showed better ability than spine BMD in identifying elderly subjects with prevalent vertebral fractures *(67)*.

Similarly, a much larger study evaluating 19,071 individuals from 6 prospective large population-based cohorts (68% women), revealed that global fracture risk, expressed as RR for any osteoporotic fracture/SD decrease in BMD, was similar when using the spine or the femoral BMD *(57)*, although higher fracture risk gradients were observed for hip fracture when using hip as opposed to spine BMD, confirming previous observations *(13)*. More importantly, the study concluded that the use of the lowest T-score of either spine or hip measurement did not further increase the predictive ability of BMD testing *(57)*, as demonstrated in the Lebanese elderly, although sensitivity increased at the expense of specificity *(57)*. This large cohort was relatively young, with a mean weighted age of 62 yr. Missing from such analyses was the predictive ability of combined BMD measures as opposed to hip only in predicting vertebral fractures, in this younger group of subjects at higher risk of vertebral compression fractures than of hip fractures *(57)*.

Finally, analyses from the Manitoba Bone Density Program, based on data in over 16,505 women, 50 yr of age or older, revealed that although age-adjusted fracture risk increased as the number of osteoporotic sites increased, the number of osteoporotic sites was no longer an independent predictor after total hip BMD was included in the model *(66)*.

It is therefore clear from the above studies that the measurement of spine in addition to hip BMD does not further improve the discriminative ability in predicting the risk of fractures, at least in elderly subjects. Similarly, measurement of both spine and hip, as opposed to hip only, does not improve the discriminative ability in predicting the patient at risk for any osteoporotic or for a hip fracture, even in a younger age group of men and women (age range 52−70 yr, mean age 62 yr). However, spine measurements have a better discriminative ability in detecting patients with vertebral fractures, in relatively younger patients *(13)*.

The following regarding selection of skeletal site for BMD measurement is recommended:

- Spine and hip for younger subjects <65 yr in whom degenerative changes are less likely and in whom, bone loss at the spine may exceed that at the hip.
- Hip only in elderly subjects >65 yr.
- Nondominant forearm is added in the following situations:
  o When 1 skeletal site cannot be used (arthritis, prosthesis, etc.).
  o When hyperparathyroidism is suspected.
  o When the patient is obese and exceeds the weight limit recommended by the manufacturer.

D. What Is the Relevance of Universally Used Risk Factors in the Lebanese?

As per ISCD recommendations, for spine, we recommend the use of L1−L4; and for the hip, the use of the lowest T-score of the 2 hip sites (total hip, femoral neck) *(56)*.

Clinical risk factors for fragility fractures that are partially or totally independent of BMD have been clearly recognized. Epidemiologically, only 44% of all nonvertebral fractures occur in women with a T-score below −2.5. This percentage is lower in men (21%). These findings underscore these risk factors, in both genders and in men in particular *(71)*.

Is the relationship between clinical risk factors and fracture similar in men and women?

The male cohort addressed some of these issues. These cohorts include around 6000 men in the United States *(72,73)*, 3000 men in Sweden *(9)*, and 2000 men in Hong Kong *(74)*. Participants were aged 65 yr and above, with independent ambulation and reflected the local community. The evidence available so far from these data suggests some gender-specific issues:

- Non-BMD factors may be more important in men than in women. The vast majority of men with fractures do not have BMD levels in the osteoporotic range.
- There is a wide variation in male femoral neck size and biomechanical properties ever after adjustment for height and weight and this may modulate BMD-fracture relationship.
- Weight loss is associated with bone loss, even in overweight men.
- Hormones levels: both free estradiol and free testosterone levels are correlated with fracture risk in men.

The strength of association between fracture and risk factors other than BMD may vary by risk factor *(75)*. For instance, the RR per unit change in body mass index (BMI) is similar in men and women in 12 prospective cohort studies *(76)*, whereas RR related to smoking is significantly higher in men *(77)*. Conversely, the evidence from the literature suggests gender similarities regarding common risk factors for osteoporosis including age, anthropometry, alcohol consumption, dietary calcium intake, and physical activity. The evidence for gender similarity in the RR of fracture with some variations in the strength of association for some risk factors has been documented in the European Prospective Osteoporosis Study *(78)*. In that study, the RRs of prevalent vertebral fracture in women were as follows:

- *Women*
  Age: 1.67 (1.46, 1.93) per decade
  Height loss: 1.06 (1.03, 1.10) per centimeter decrease
  Self-reported history of spine fracture: 7.52 (5.52, 10.23)
  History of other major fracture: 1.83 (1.46, 2.28)
  Body weight: 0.86 (0.79, 0.95) per 10-kg increase

- *Men*
  Age: 1.32 (1.18, 1.49) per decade
  Height loss: 1.06 (1.04, 1.09) per centimeter decrease
  Self-reported spine fracture: 5.05 (3.69, 6.90)
  History of other major fracture: 1.42 (1.12, 1.81)
  Body weight: 0.86 (0.79, 0.94) per 10 kg increase

The clinical determinants of fragility fracture including age, height loss, self-reported history of spine fracture, history of other major fracture, and body weight are similar between genders. The strength of association was also quite similar between genders for many of these clinical determinants. However, whether BMD-fracture relationship adjusted for clinical determinants other than age is similar in both genders remains debatable.

What does the Lebanese elderly data tell us regarding risk factors? Regarding clinical risk factors, age, height, weight, BMI, smoking, physical activity, dietary intake of dairy products, previous falls, previous fragility fracture, and family history of fragility fracture were studied in the Lebanese.

Correlation between prevalent vertebral fracture and age, height, physical activity, and previous fragility fracture was statistically significant in women in univariate analyses. Similar trends were found in men. Smoking did not predict osteoporosis in our population. This may be explained by a relatively small sample size. Alcohol was not included because the prevalence of alcohol consumption in our adult population is low and very low among the elderly.

In multivariate analysis using logistic regression with radiographic vertebral fracture as the dependent variable, significant predictors were age, self-reported fragility fracture, and total hip T-score in women. In men, only total hip T-score remained significantly correlated with prevalence of vertebral fracture. When osteoporosis was defined as a T-score ≤ -2.5 at any site, age and weight remained significant predictors in women but only weight was significant in men.

E. Recommendations in Premenopausal Women

Because of the wide use of densitometry testing in premenopausal women and of unindicated pharmacologic therapy in this group *(30)*, recommendations in premenopausal women were reiterated in this update.

Who to Test?

It is generally agreed that the relationship between BMD and fracture risk is an inversely exponential one. In postmenopausal women, as BMD decreases, fracture risk increases. There are no data available for such estimations in premenopausal women. Moreover, in healthy premenopausal women, the absolute 10-yr risk for a specific BMD is very low *(39)*. For all these reasons, the WHO T-score-based criteria are not applicable to premenopausal women *(15,64)*. The guidelines for premenopausal women are very conservative and essentially unchanged from the 2002 Lebanese Guidelines.

Diagnosis in Premenopausal Women
- The WHO BMD-based criteria for the diagnosis of osteoporosis should not be applied to premenopausal women.
- The diagnosis of osteoporosis may be considered if a premenopausal women has a low BMD with:
  ○ Secondary causes (e.g., glucocorticoid therapy, hypogonadism, hyperparathyroidism).
  ○ Risk factors for fracture.
  ○ A fragility fracture.

BMD testing is not indicated in apparently healthy premenopausal women.

When to Treat?

General or Universal Measures

The following universal measures are recommended independent of BMD measurement:

- Maintain a physically active lifestyle with adequate exposure to sunlight.
- Avoid smoking and high-alcohol intakes.
- Maintain a total dietary calcium intake of around 1.5 gm of elemental calcium in postmenopausal estrogen-deficient women or men >65 yr, as well as a vitamin D intake of 600−800 IU/d, even under the sun-drenched latitudes of Lebanon. Provide calcium and vitamin D supplementation to the elderly.
- Avoid a low weight <60 kg in men or <50 kg in women or a low BMI of <20 kg/m^2.
- The prevention of osteoporosis begins with optimal bone mass acquisition during growth and adolescence.

Pharmacological Interventions

Most approved pharmacologic therapies were studied exclusively in postmenopausal women; therefore, their efficacy in premenopausal women in large part is unknown. Thus, in the absence of any established treatment for normally menstruating premenopausal women with low bone density, such patients should be referred to specialized centers for investigation of underlying causes and advice on further management. Treatment should not be started in such patients before appropriate investigations and diagnoses are achieved.

There are no data on the use of antiresorptive therapies in normally menstruating premenopausal women with the exception of selective estrogen-receptor modulators and corticosteroid-induced osteoporosis. Bisphosphonates do prevent bone loss and may increase BMD in young women but their effect on fracture risk reduction in this group is unknown because of the lack of well-powered studies in this population (79). They may be used when the steroids are given at high doses and for a long period of time, especially in the presence of other fracture risk factors such as low BMD (79). Even in this case, such a treatment has to be put in a balance with the possibility of a future pregnancy and the risk of a potential harm inherent to such treatment. Indeed, long-term safety of bisphosphonates, either on bone or on fetal growth in a potentially child bearing group, is a concern. Selective estrogen-receptor modulators such as tamoxifen and raloxifene, decreases BMD in premenopausal women (80,81). Finally, available data on current treatments do not exceed 7−10 yr of use. Discontinuing pharmacologic therapy will result in a resolution of the bone preserving effect, if any, within months to years. So, it would be totally unclear as to what recommendations should be given after stopping treatment, if such treatment was to be given in premenopausal women. Because of all these considerations, the use of antiresorptive therapy in premenopausal women is not recommended.

To summarize, the population-based data in the Lebanese demonstrated the following:

- First, among Caucasian populations, the use of the NHANES database is associated with greater sensitivity for predicting prevalent radiographic vertebral fracture than a local population specific database.
- Second, our data do not provide evidence for the use of a female database in men, recognizing however that the numbers for the study in men were small to derive definite conclusions.
- Third, among common clinical risk factors, age, self-reported fragility fracture, and height were significant predictors of prevalent radiographic vertebral fracture among women with similar trends in men.

The above guidelines target specific points reinforcing or updating previous recommendations (1,2). Recommendations regarding guidelines not revisited herein remain unchanged. It is anticipated that the T-score anchored recommendations, on which the Lebanese guidelines and many other international osteoporosis guidelines were based will gradually be replaced by an absolute fracture risk assessment model incorporating risk factors with or without BMD (10,38). This forthcoming model spearheaded by the WHO initiative, under the leadership of Professor Kanis, is anticipated to provide a common platform for global fracture risk assessment, that is insensitive to database selection (because absolute BMD will be used) and can form the basis for the derivation of intervention thresholds that will incorporate the health priorities and financial constraints of individual countries (38).

The additional local Lebanese data detailed herein provide the evidence and rationale supporting the anticipated alignment with the WHO global fracture risk assessment model.

The Lebanese Guidelines are intended to provide a structural framework for high standards of care for the physician treating the patient at risk or with osteoporosis. They are not intended to supersede the ultimate decision of the practicing physician. In the case of rare and/or difficult cases, referral to an osteoporosis specialist is highly recommended. We anticipate continued periodic updates of these guidelines by the concerned societies under the leadership of OSTEOS and with continued support from the Ministry of Health and the WHO.

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