Update of the Lebanese Osteoporosis Guidelines
Lebanese Society for Osteoporosis and Metabolic Bone Disorders

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As of 1999, the WHO has recognized osteoporosis as a major public health problem and included it on the priority list of non-communicable diseases. Because of the demographic explosion worldwide, osteoporosis is incurring increasingly heavier social and economic tolls on our societies.

International guidelines on osteoporosis have been put forth and further refined over the years, in light of the substantial body of evidence that accumulated from large prospective studies. In an effort to optimize the quality of care of osteoporosis in Lebanon, an initiative was launched in Beirut in the spring of 2002, and led to the development of the “Lebanese Guidelines for Osteoporosis Assessment and Treatment. These guidelines were endorsed by five Lebanese societies and the Eastern Mediterranean branch of the World Health Organization. The endorsing societies were the Lebanese Society of Endocrinology, the Lebanese Society of Obstetrics and Gynecology, the Lebanese Association of Orthopedics, the Lebanese Society of Radiology, and the Lebanese Society of Rheumatology. A dissemination effort was implemented in 2005 through 10 case-based interactive sessions conducted across Lebanon, in Beirut, Tripoli, Zahleh and Saida, and reaching over 500 physicians nationally, an effort that is currently under audit. The national guidelines effort was the nucleus for the foundation of the Lebanese Society of Osteoporosis and Metabolic Bone Disorders, OSTEOS, a multidisciplinary scientific society, and a member society of the Lebanese Order of Physicians.

The Lebanese Osteoporosis Guidelines were developed recognizing the need for periodic updates, in light of local and international evolving data. This first Update for the Lebanese Guidelines for Osteoporosis, revisits and re-enforces several recommendations detailed in the original Lebanese Osteoporosis Guidelines document, based on relevant national, as well as new international data. The national data presented herein is the fruit of a continued collaborative effort between investigators at the American University of Beirut and at the St Joseph University. The international data is presented by Professor John Kanis, the lead investigator spearheading the WHO initiative for osteoporosis global risk assessment. This Update lays the ground to align the Lebanese Guidelines for Osteoporosis with the WHO initiative on global fracture risk assessment. The support granted by the Lebanese Order of Physicians, the World Health Organization, and the Lebanese Ministry of Health are instrumental to the success of this national endeavor that aims at optimizing quality care in the field of osteoporosis in Lebanon.

Ghada El-Hajj Fuleihan, MD, MPH.

on the behalf of the founding members of OSTEOS.

## Agenda

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:45-9:15am</td>
<td>Registration</td>
</tr>
<tr>
<td>9:15-9:30am</td>
<td>Opening addresses</td>
</tr>
<tr>
<td>9:30-9:45am</td>
<td>Ghada El-Hajj Fuleihan, MD, MPH. Professor of Medicine. American University of Beirut.</td>
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<tr>
<td></td>
<td>The Lebanese Guidelines for Osteoporosis Assessment and Treatment. Historical perspective, achievements, goals. Introduction of OSTEOS.</td>
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<tr>
<td>9:45-10:15am</td>
<td>Juliet Compston, MD. Professor of Medicine and Consultant Cambridge University School of Medicine.</td>
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<td>Evidence-based guidelines for osteoporosis.</td>
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<tr>
<td>10:15-10:30am</td>
<td>Michael Mc Clung, MD. Associate Professor of Medicine. Director Oregon osteoporosis Center. Clinical perspective on osteoporosis guidelines evolution and practical issues at hand.</td>
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<tr>
<td>11:15-11:45am</td>
<td>Ghada El-Hajj Fuleihan, MD, MPH. Professor of Medicine. American University of Beirut. Update of the Lebanese Guidelines: which database to use and how many skeletal sites to measure?</td>
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<tr>
<td>11:45-12:00 noon</td>
<td>Coffee break:</td>
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<tr>
<td>12:15-12:30 pm</td>
<td>Rafic Baddoura, MD, MPH. Assistant Professor of Medicine. St Joseph University. Update of the Lebanese Guidelines: OP in men and risk factors for fracture risk assessment in Lebanon.</td>
</tr>
<tr>
<td>12:30-1:00 pm</td>
<td>Hassane Awada, MD. Professor of Medicine. St Joseph University. Update of the Lebanese Guidelines: BMD measurements in children and pre-menopausal women.</td>
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<tr>
<td>1:00-1:45 pm</td>
<td>John Kanis, MD, FRCP, FRCPath. Emeritus Professor, University of Sheffield, Director, WHO collaborating center for Metabolic Bone Diseases. The WHO initiative: Fracture risk assessment model.</td>
</tr>
<tr>
<td>1:45-2:15 pm</td>
<td>Open Discussion.</td>
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<tr>
<td>2:15 pm</td>
<td>Closing of the Scientific Program and perspective on the Update for the Lebanese Guidelines. Hassane Awada, MD,</td>
</tr>
<tr>
<td>2:30 pm</td>
<td>LUNCH at OLIVE AND OIL</td>
</tr>
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</table>
Juliet Compston is Professor of Bone Disease and Honorary Consultant Physician at Cambridge University School of Clinical Medicine. She obtained her medical degree at the Middlesex Hospital, London University, with a distinction in Medicine. Professor Compston is actively involved in research into metabolic bone disease. Her main interest is the cellular and structural pathophysiology of bone loss associated with osteoporosis and the effects of drugs on these changes. Current research interests also include the effects of glucocorticoids in bone and the role of megakaryocytes in bone remodelling.

Professor Compston is currently Vice-President and Chairman of the International Society of Bone Morphometry, Member of the Board of the International Osteoporosis Foundation (IOF), Member of the Committee of Scientific Advisors of the IOF, Project Leader and Chair of the European Commission / IOF Call to Action for Osteoporosis, Trustee of the Board of the National Osteoporosis Society (NOS), Member of the Advisory Scientific Board of the NOS, and Member of the Expert Advisory Committee to the Medicines and Healthcare Products Regulatory Agency (MRHA). She is a Member of Council of the European Calcified Tissue Society and a Board member of the International Bone and Mineral Society. She serves on the MHRA Working Party on Hormone Replacement Therapy and on the ASBMR Career Enhancement Awards review committee. She is a member of the ASBMR Women in Bone and Mineral Committee. She serves on the editorial board of Bone, Journal of Bone and Mineral Research, Osteoporosis International and the Journal of Clinical Endocrinology and Metabolism. She is a member of the Osteoporosis Guidelines Development Group for the National Institute of Clinical Excellence (NICE).

Her publications include approximately 200 peer reviewed original scientific papers, 50 invited reviews, 47 book chapters and 10 books.

Evidence-based guidelines are increasingly used in the management of osteoporosis and have the potential to produce high standards of clinical care across different sectors of the health service. The methodology underlying the development of guidelines has become increasingly sophisticated; the AGREE appraisal tool[1] defines many of the essential components of good guidelines, and consists of 23 key items in six domains, each of which is intended to capture a specific dimension of guidelines quality.

European guidelines currently advocate a case finding approach in which individuals are selected for bone densitometry on the basis of clinical risk factors. The majority of guidelines do not attempt to distinguish between those risk factors that are and are not independent of bone mineral density, nor do they consider interactions between different risk factors. North American guidelines uniformly recommend screening by bone densitometry in women aged over 65 years, a strategy that has been justified on the basis of its cost-effectiveness. Criteria for intervention in most guidelines are based on bone mineral density T-scores, sometimes with additional risk factors such as age and previous fragility fracture. In a number of guidelines, the presence of a fragility fracture is considered a sufficient indication for treatment and intervention without prior bone densitometry is also recommended for some individuals treated with oral glucocorticoids. None of the currently available guidelines use estimated fracture probability as a criterion for intervention.

Successful implementation of guidelines requires that they are accessible. Dissemination can be achieved electronically or in the written form; in either case, it is important that they are given sufficient publicity so that practitioners know of their existence. The use of guidelines in clinical practice is facilitated by implementation tools such as simple care pathways or algorithms, summary sheets and patient information sheets. Guidelines often have significant resource implications. In the case of osteoporosis, for example, more bone densitometry systems might be required, more bone specialists trained or greater expenditure budgeted for pharmacological interventions. These issues of cost are often a significant barrier to the full implementation of guidelines.

Assessment of the impact of guidelines on clinical practice requires audit. Ideally this should be performed before and after uptake of the guidelines; alternatively, repeated assessments of performance after the introduction of guidelines can be made. The audit process may also be useful in identifying problem areas in guideline uptake.
Evidence-based guidelines for osteoporosis

Why have guidelines?
- To provide a uniformly high standard of clinical care across healthcare sectors
- To provide cost-effective care
- To educate healthcare professionals

AGREE appraisal criteria: 6 domains
- Scope and purpose
- Rigour of development
- Stakeholder involvement
- Clarity and presentation
- Applicability
- Editorial independence

Current guidelines for osteoporosis
- Most rely predominantly on BMD to make treatment decisions and none currently use fracture probability
- Most do not distinguish between BMD-dependent and BMD-independent risk factors and interaction between risk factors is not considered
- Most do not incorporate health economic evaluation

Identification strategies in current guidelines
- North America
  - All women 255 yrs
  - Younger postmenopausal women with 1+ risk factor
- Europe
  - Women with at least one risk factor

Risk factors used for case finding: Canadian guidelines
- Major
  - Age
  - Previous fracture
  - Family history of fracture
  - Glucocorticoid therapy
  - Osteopenia on X-ray
  - Propensity to fall
  - Hypogonadism
  - Malabsorption
  - Primary hyperparathyroidism
- Minor
  - Rheumatoid arthritis
  - PH clinical
  - Hyperthyroidism
  - Anticoagulant therapy
  - Low dietary calcium intake
  - Current smoking
  - Alcohol abuse
  - Excessive caffeine intake
  - Low body weight
  - Heparin therapy

(from Brown et al, CMAJ 2002)

Intervention thresholds in current guidelines
- Most guidelines use T scores ≤-2.5 1 other risk factors
- NOF uses T score ≤-2
- Some use lower T score threshold if other risk factors are present
- Some use fracture alone (without BMD)
Osteoporosis Guidelines: Clinical Perspective

Osteoporosis is characterized as an impairment of bone strength due to low bone mass and other changes in the quality of bone that results in skeletal fragility and increased risk of fracture. Measurement of bone mineral density (BMD) is an important risk factor for fracture in older adults, and BMD is the basis of the WHO operational definition of osteoporosis in postmenopausal women. Clinical guidelines have been developed by many societies and organizations to assist practicing physicians in the identification of patients who would most appropriately be given drugs indicated for the prevention and treatment of osteoporosis. Not surprisingly, these guidelines have been based primarily on BMD values, expressed as standard deviation units or T-scores. This inevitably leads to debates about which database should be used in a specific gender, ethnic group or country. Without information about the relationship of BMD to fracture risk in a specific population, questions about which database to use cannot be resolved.

The BMD thresholds at which treatment is recommended is often modified by the presence or absence of risk factors. The inclusion of risk factors is quite variable among the guidelines, resulting in confusion and uncertainty among clinicians.

General measures to improve bone health, including nutrition and exercise, can generally be recommended to the entire adult population. However, expensive pharmaceutical agents – especially those with recognized side effects – should be targeted to patients in whom a clear treatment benefit will be realized. This is best accomplished by basing recommendations on fracture probability in individual patients and then selecting a level of risk at which treatment is both clinically beneficial and cost-effective. The WHO absolute fracture risk algorithm will provide the platform upon which those guidelines can be based. Having this algorithm available will be a major advance in our field and will be most useful in populations in which the relationship between bone density and fracture risk has been established.

Certain clinical problems will not be addressed by the WHO fracture risk strategy. This includes the management of premenopausal women and young men, patients receiving high doses of glucocorticoids or who have other secondary causes of bone loss and the management of women at the time of menopause when more rapid bone loss is anticipated. These situations will require additional clinical judgment in patient-specific strategies of management.
Osteoporosis Guidelines: Clinical Perspective

Guidelines for Osteoporosis: Clinical Perspective and Implications

Michael McChung, MD
Department of Medical Education
Providence Portland Medical Center
Director, Oregon Osteoporosis Center

Current Clinical Guidelines

- Almost all guidelines for when to use prescription treatments are based on BMD thresholds.
- Most patients with fractures do not have BMD values consistent with osteoporosis by the WHO criteria.
- Risk factors are used to identify patients for treatment who do not have osteoporosis.
- Substantial inconsistency exists among guidelines, leading to confusion and clinical paralysis.
- Patients at high risk are excluded from guidelines while some with low risk are included.

Postmenopausal Osteoporosis: Indications for Treatment in USA

<table>
<thead>
<tr>
<th>AMERICAN GUIDELINES</th>
<th>NOF ¹</th>
<th>AACE ²</th>
<th>NAMS ³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior fragility fracture</td>
<td>Vertebral or hip</td>
<td>Any fracture with low BMD</td>
<td>Vertebral only</td>
</tr>
<tr>
<td>T-score: - without RF</td>
<td>&lt;2</td>
<td>&lt;2.5</td>
<td></td>
</tr>
<tr>
<td>- with RF</td>
<td>&lt;1.5</td>
<td>&lt;1.5</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Risk factors</td>
<td>5 major &amp; additional</td>
<td>Several including risk of falling</td>
<td>Thin, family history, prior fracture</td>
</tr>
</tbody>
</table>

Impact of Implementing the WHO Absolute Risk Prediction Model

- Will not change the BMD-based diagnostic criteria for osteoporosis in postmenopausal women.
- The diagnostic category of “osteopenia” will no longer be relevant.
- It will shift treatment away from younger patients at low risk toward older patients with less BMD - who will more likely experience fracture protection with treatment.
- Since risk will be based on BMD values, the concerns about which database for T-scores to use will be lessened.
What Implementing the WHO Absolute Risk Prediction Model Will NOT Do

- Help manage premenopausal women
- Decide about treatment for early menopausal women
- Address treatment for women stopping estrogen therapy
- Make decisions for patients with secondary forms of bone loss
  - High dose glucocorticoid therapy
  - Aromatase inhibitors, GnRH agonists
- Aid in management of frail adults at risk for fall

Implementing Guidelines Based on Absolute Fracture Risk: Challenges

- Having the osteoporosis “experts” agree with this approach
- Having “bone density community” agree and understand
- Having the model available in an easily-used format
- Having physicians become familiar with fracture probability as basis for treatment recommendations
- Developing models to explain results to patients in an understandable way
- Documenting that treating patients based on this model are protected from fractures
Dr El-Hajj Fuleihan is Professor of Medicine and Founder and Director of the Calcium Metabolism and Osteoporosis Program at the American University of Beirut Medical Center. Dr El-Hajj Fuleihan obtained her MD degree in 1983 from the American University of Beirut, Lebanon. She completed her residency and fellowship at the New England Deaconess Hospital and Brigham and Women’s Hospital, Harvard Medical School, Boston, and received a master in Public Health from the Harvard School of Public Health.

Dr. El-Hajj Fuleihan’s major research interests revolve around calcium and bone metabolism, and women’s health issues. She is the lead investigator for several osteoporosis multi-center trials, protocols evaluating the epidemiology of osteoporosis in Lebanon, studies investigating the impact of hypovitaminosis D on musculoskeletal health, and trials evaluating the impact of bisphosphonates in preventing bone loss in patients with cancer.

Dr El-Hajj Fuleihan has extensively published on her topics of interest in numerous original publications, Editorials in the New England of Medicine, reviews, chapters in major reference texts such as “Principles of Bone Biology” and “The Parathyroids”, as well as in the CD Rom UpToDate. She was elected to the Alpha Omega Alpha Honorary Medical Society, and is the recipient of the National Institutes of Health Clinical Associate Physician Award, and of the Harvard-Sandoz Scholar in Medicine Award.

Dr El-Hajj Fuleihan has served on the Professional Practice Committee of the American Society of Bone and Mineral Research, she currently serves on the Scientific Advisory Committee of the International Society of Clinical Densitometry, and on the Ethics Advisory Committee of the American Society of Bone and Mineral Research. She also is a member of the Editorial Board of the following journals Journal of Clinical Endocrinology, and Metabolism, the Journal of Bone and Mineral Research and the Journal of Clinical Densitometry.

Dr El-Hajj Fuleihan is the lead investigator for several osteoporosis multi-center trials, protocols evaluating the epidemiology of osteoporosis in Lebanon, studies investigating the impact of hypovitaminosis D on musculoskeletal health, and trials evaluating the impact of bisphosphonates in preventing bone loss in patients with cancer.

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Which Database to Use and Which Skeletal Site to Measure?

Osteoporosis is identified as a major public health problem by the World Health Organization (WHO) (1). The proportion of individuals over the age of 65 yrs is projected to more than double in the next 30 yrs, a large proportion is from the Middle East-Africa and Asia, thus incurring substantial major medical, social and economic burdens on our societies.

The Lebanese Guidelines for Osteoporosis Assessment and Treatment, used evidence available until 2002, to address three questions: “who to test, what measures to use, and when to treat?” (3,4) The recommendations of the Lebanese guidelines regarding “who to test” and “when to treat” were anchored to T-scores (5), similar to many international guidelines, awaiting the WHO model for a global fracture risk assessment model (6). This global model would incorporate clinical risk factors and possibly bone mineral density (BMD) to derive 5 or 10 yr absolute fracture risk. In order to apply the WHO model to the Lebanese population, several points need to be validated:

* That the BMD-fracture relationship in the Lebanese (RR/SD decrease) is similar to western populations, and that the Lebanese fracture at the same BMD as western counterparts.

**That the measurement of only hip BMD is sufficient in fracture risk assessment, as recommended by the IOF and WHO.

*That the impact of major risk factors on fracture risk, used in the global model, is the same in the Lebanese.

In addition, based on several lines of evidence available in 2002, the Lebanese Guidelines recommended the use of a western normative database to derive T-scores. This recommendation, although consistent with the recommendation of the IOF, has not been applied consistently in Lebanon, resulting in major discrepancies in T-score based diagnoses of osteoporosis in Lebanon. We therefore tested the hypothesis that the choice of western BMD database is as good, if not superior, to the choice of a Lebanese database in identifying patients with osteoporosis.

Several of these points were examined in a population based study of elderly Lebanese (7), N=460, above age 65 years, who had BMD measurements of the spine and hip, and x-rays of the thoraco-lumbar spine. 13% of men and 18% of women had one or more vertebral compression fractures.

Fracture risk RR/SD: The RR for vertebral fracture/SD decrease was 1.58 [1.2-2.2] for hip BMD, and 0.99 [0.99-1.0] for spine.
BMD, estimates at the hip, but not the spine, being comparable to others in the literature, estimates were 1.8 [1.1 2.7] for hip BMD and 2.3 [1.9 2.3] for spine BMD. (8)

**Database selection:** In women, the sensitivity and the area under the ROC for picking up patients with prevalent vertebral fractures were higher when the Western database was selected ROC=0.61 at the hip, as compared to the Lebanese database ROC=0.57, but the NPP and the PPV did not differ between the 2 databases. A similar pattern was noted in men. Furthermore, the proportion of Lebanese women with a BMD-based T-score of osteoporosis were comparable to those obtained in western subjects matched for age, when a western, but not a Lebanese, database was used (9).

**Skeletal site selection:** The age adjusted OR/SD decrease in BMD for identifying a subject with a vertebral fracture was highest for the femoral neck the numbers were: 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]. These estimates are consistent with similarly derived estimates for identifying patients with vertebral fractures, from the placebo arm of the risedronate trial, 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 (8) Similarly, using the ROC curve as the criterion for best site to predict vertebral fractures revealed that the femoral neck was the best site with an ROC of 0.65, ROC for spine was 0.59, combining more than one site, or taking lowest, did not improve ROC further, similarly to what was previously reported (8).

In conclusion, the ability of BMD to predict prevalent vertebral fractures (RR/SD) is the same in Caucasians whether from Western countries, or from Lebanon. Our results also validate the recommendation of the use of the hip as the only skeletal site for fracture risk assessment in the elderly, and the IOF caution against the use of local databases, and favoring the use of universal standardized databases (8). This Update of the Lebanese Guidelines, based on analyses of data derived from a population based study of elderly Lebanese, lay the ground for aligning the Lebanese Guidelines with the global fracture risk model (8). The latter would calculate absolute fracture probability (2), either with or without the use of BMD, depending on the original risk stratification derived from clinical risk factors alone (8). Treatment could therefore be offered to those individuals identified as having a fracture probability greater than a certain threshold, a threshold that can vary between countries and societies depending on the availability of health resources based on cost-effectiveness analyses.

**References**

3. [http://www.osteofound.org/health_professionals/guidelines/guidelines_list.html](http://www.osteofound.org/health_professionals/guidelines/guidelines_list.html)
Update of the Lebanese Guidelines for Osteoporosis

Which Database and Which Skeletal Site?

Ghada El-Hajj Fuleihan, MD, MPH.
Professor of Medicine
American University of Beirut Medical Center

Lebanese Guidelines for Osteoporosis
Assessment and Treatment 2002

- Addressed three central questions: “Who to test, what measures to use and when to treat.”
- Recommendations anchored to DXA derived T-scores for elderly subjects (post-menopausal women and elderly men)
- Z-score for children and pre-menopausal women

http://www.osteobond.org/health_professionals/guidelines

Lebanese Guidelines for Osteoporosis
Assessment and Treatment 2002

- Recommended the use of a Universal NHANES database for hip and densitometer based Western database for spine, to derive T-scores.
- Recommended measuring spine and hip in all subjects, add the forearm in select situations:
  - Similar scheme suggested by ISCD
  - But: IOF, NOF and WHO: only one site that is hip

Which BMD normative database to use in the Lebanese?

Compare data in Lebanon and West regarding:
- Prevalence of OP using BMD data
- Prevalence of OP using fractures
- BMD-fracture relationship:
  - OR for fracture for each SD decrease in BMD,
  - Sensitivity, specificity: ROC curves for BMD in identifying Lebanese patients with vertebral fractures using Lebanese vs Western Database.

Prevalence of OP by BMD at THIg:
Lebanese & Swedish women

<table>
<thead>
<tr>
<th>Age</th>
<th>% Lebanese</th>
<th>% Swedish</th>
</tr>
</thead>
<tbody>
<tr>
<td>65-69 yrs</td>
<td>23%</td>
<td>20%</td>
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<tr>
<td>70-74 yrs</td>
<td>27%</td>
<td>27.9%</td>
</tr>
<tr>
<td>75-79 yrs</td>
<td>34%</td>
<td>37.5%</td>
</tr>
<tr>
<td>80-85 yrs</td>
<td>60%</td>
<td>47.2%</td>
</tr>
</tbody>
</table>

*Lebanese NHANES database bone density norms, 1999-2004
*Swedish, Copenhagen 2006-2009

Prevalence of vertebral fractures in elderly women
Lebanese and western data

[Graph showing prevalence of vertebral fractures]
Update of the Lebanese Guidelines for Osteoporosis

Age-Adjusted OR for VFX per SD vs. BMD*

<table>
<thead>
<tr>
<th>Site</th>
<th>Lebanese Elderly</th>
<th>Western*</th>
<th>Lebanese</th>
<th>Western*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LS</td>
<td>0.99</td>
<td>1.16</td>
<td>2.3</td>
<td>1.36</td>
</tr>
<tr>
<td>Hip</td>
<td>1.58</td>
<td>1.47</td>
<td>1.8</td>
<td>1.66</td>
</tr>
<tr>
<td>FA</td>
<td>1.58</td>
<td>1.47</td>
<td>1.7</td>
<td>-</td>
</tr>
</tbody>
</table>

*Gurvitz and BIANCHI, unpublished data, DVA, vinci
* Recker et al, Osteoporosis Int 2004, bone on 2005 version

WHO Global Absolute Fracture Risk Model
Risk Factors without or with BMD
- Age
- Prior fractures after age 50 yrs
- BMI
- Family history of hip fractures
- Cortisosteroid therapy
- Smoking
- ETOH > 2 units daily
- RA

Update of the Lebanese Guidelines for Osteoporosis and the WHO Initiative
- BMD fracture risk relationship in the Lebanese elderly, using a Western database, is similar to estimates used in WHO fracture risk assessment model.
- In elderly Lebanese subjects, measurement of the hip as the only skeletal site is most optimal for risk stratification.
- The impact of risk factors, used in the WHO model, on fracture risk in Lebanese is under implementation.
- The new population-based data provides evidence validating the application of the WHO global fracture risk assessment model to the Lebanese.

How many sites to measure?
- Fracture discrimination using BMD tested in a large population based sample of elderly, ages 65-85 yrs
- Hip was a better single predictor than the spine (using RR/SD and ROC curves).
- Adding the spine did not add to the discriminative ability to predict fractures (similar to data from Risedronate trial, Kanis et al. OI 2004)

“The issue is not just to detect disease but predict and impact outcome”
Osteoporosis in men still raises fundamental questions relative to bone mineral density and fracture relationship. From an epidemiological perspective it is well established that the incidence of fractures across age differs among genders at all sites, being significantly lower in men. It is also known that mean bone mineral density (BMD) is higher in men compared to women at all ages and it is also higher in men with fractures compared to women with fractures. However from an epidemiological perspective as well, dual-energy X-ray (DXA) based definition of osteoporosis as recommended by the WHO relies on the evidence obtained from women’s data in the National Health Assessment and Nutritional Evaluation Survey in the U.S.

Therefore, the use of DXA for fracture risk assessment this raises the following questions: Should we use gender specific reference database? Should we use population specific reference database? Is BMD-fracture relationship measured as the relative risk (RR) of fracture per standard deviation (SD) decrease in BMD similar in both genders?

- So far, data from the MrOS cohorts suggest the following:

- The risk of hip fracture is 10 times higher in men in the lowest quartile of hip DXA BMD compared to those in the highest quartile.

- The vast majority of men with fracture do not have BMD levels in the osteoporotic range.

- Dissimilarities exist in the BMD-fracture relationship between women and men.

- There is a very wide variation in male femoral neck size and biomechanical properties ever after adjustment for height and weight.

In our population, data from a cross-sectional survey on a population-based random sample of elderly people aged 65 to 85 years of age has shown the following:

- Using the NHANES database, the diagnostic performance of DXA for osteoporosis with vertebral fracture is better than using a local database. With the NHANES database and total hip T-score < -2.5 for osteoporosis diagnosis, sensitivity of DXA for prevalent vertebral fracture is 51.8% in women and 38.9% in men, while specificity is 71.5% in women and 79.9% in men.
• Using a population specific database, sensitivity is decreased to 24.6% in women and 11.8% in men, and specificity is slightly modified, being 89.4% in women and 99.3% in men. With a gender specific database that is using peak BMD in men to calculate the T-score in men, the diagnostic performance is even lower, sensitivity for osteoporosis dropping to 2.0%.

• Only slight difference was seen in RR per SD decrease in BMD between genders.

Osteoporosis
In Men

Male osteoporosis in Lebanon
Rafic Baddoura MD, MPH
Prevalence
BMD-fracture relationship
Clinical risk factors

Prevalence of vertebral fracture VF by gender, in the Lebanese elderly

<table>
<thead>
<tr>
<th>Gender</th>
<th>No. VF</th>
<th>VF</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>235</td>
<td>56</td>
<td>291</td>
</tr>
<tr>
<td>(%)</td>
<td>80.76</td>
<td>19.24</td>
<td>100.0</td>
</tr>
<tr>
<td>Men</td>
<td>134</td>
<td>18</td>
<td>152</td>
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<tr>
<td>(%)</td>
<td>68.16</td>
<td>31.84</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>369</td>
<td>74</td>
<td>443</td>
</tr>
<tr>
<td>(%)</td>
<td>83.30</td>
<td>16.70</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Characteristics of the elderly study population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All N=460</th>
<th>Women N=301</th>
<th>Men N=159</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>73.4 ± 6</td>
<td>73.4 ± 6</td>
<td>73.4 ± 6</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>70.4 ± 14</td>
<td>69.1 ± 15</td>
<td>71.7 ± 12</td>
<td>0.01</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>154.8 ± 6</td>
<td>150.4 ± 6</td>
<td>163.1 ± 6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>29.4 ± 6</td>
<td>30.5 ± 6</td>
<td>27.2 ± 3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of fracture yes/no (%)</td>
<td>25/75</td>
<td>25/75</td>
<td>25/75</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking current/ex-smoker (%)</td>
<td>30/30/40</td>
<td>30/28/47</td>
<td>32/40/28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Estimated time spent outdoors</td>
<td>4.2 ± 3.1</td>
<td>3.2 ± 3</td>
<td>6.6 ± 2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Update of the Lebanese Osteoporosis Guidelines

Osteoporosis in Men

Male osteoporosis in Lebanon
Rafic Baddour MD, MPH
Prevalence
BMD-fracture relationship
Clinical risk factors

Prevalence of vertebral fracture VF by gender, in the Lebanese elderly

<table>
<thead>
<tr>
<th>Gender</th>
<th>No. VF</th>
<th>VF (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>235</td>
<td>80.76</td>
<td>291</td>
</tr>
<tr>
<td>(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>134</td>
<td>68.16</td>
<td>152</td>
</tr>
<tr>
<td>(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>369</td>
<td>83.30</td>
<td>443</td>
</tr>
<tr>
<td>(%)</td>
<td></td>
<td></td>
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</tbody>
</table>

Characteristics of the elderly study population

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<thead>
<tr>
<th>Characteristic</th>
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<th>Women N=301</th>
<th>Men N=159</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>73.6±5</td>
<td>73.4±5</td>
<td>74.3±5</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>69.6±15</td>
<td>69.1±15</td>
<td>70.7±12</td>
<td>0.061</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>154±8</td>
<td>150±4</td>
<td>158±16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>29.4±6</td>
<td>30.5±6</td>
<td>27.2±3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of fracture (years (%))</td>
<td>29.7±1</td>
<td>25.7±3</td>
<td>48.5±2</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking (current smoker (%))</td>
<td>30±40</td>
<td>30±23</td>
<td>67±28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Estimated time spent outdoors</td>
<td>4.2±3.1</td>
<td>3.2±3</td>
<td>6.6±2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Dr Awada is Professor of Medicine, Head of the Division of Rheumatology at Hotel Dieu de France Hospital and Coordinator of the Department of Rheumatology at the Saint Joseph University of Beirut, Lebanon. He is also the Director of the Bone Mineral Measurement Unit at Hotel-Dieu Hospital.

Dr Awada obtained his MD degree as well as his Specialty in Paris, France, in 1984. He was Assistant Professor from 1984 to 1988, in the Rheumatology Department of Cochin Hospital.

Dr Awada was the founder of the Family Medicine Department and its Program Director from 1995 to 2005, at the Saint Joseph University, Beirut, Lebanon.

Dr Awada is a member of the Editorial Board of the Bone Joint Spine and the Middle East Edition of the Lancet.

Dr Awada’s major topics of interest are Osteoporosis, as well as Inflammatory Joint Diseases, mainly the Spondylarthropathies and Rheumatoid Arthritis. He is the first author or the coauthor of more than 40 articles in peer-review Journals. In the field of Osteoporosis, he participated to several multicentric studies about its epidemiology in Lebanon, calcium and vitamin D status, as well as the establishment, publication and dissemination of the “Lebanese Guidelines on Osteoporosis Assessment and Treatment”.

Osteoporosis in Premenopausal women

Who to test?
In healthy premenopausal women, the absolute 10 year risk for a specific BMD, is very low (1). There is no data available estimating fracture risk in relation with BMD in premenopausal women. Thus, the WHO T-score-based criteria are not applicable to premenopausal women (2). Comparing these patients to a reference population, using the Z-score, is more appropriate than using T-score (2,3). The use of a local database is also more appropriate than a western database, the comparison of a given BMD to the normal population of the same age being the only useful information in that situation. The studies available from our region revealed that peak BMD might be slightly lower than or equal to that of European and American Caucasians, possibly the result of differences in body size, chronic vitamin D deficiency, less physical activity, and genetic factors (4,5).

The assessment of BMD in premenopausal women might be needed in some severe secondary causes of osteoporosis, for example in women on high and prolonged treatment with corticosteroids or in patients with severe malabsorption or some endocrinopathies such as hyperparathyroidism or hypogonadism. BMD testing is not indicated in apparently healthy premenopausal women and a low BMD alone is not synonymous of osteoporosis in this population.

When to treat?

General or Universal Measures
Although few studies have addressed the specific topic of premenopause, physical active lifestyle, adequate calcium and vitamin intake, avoiding low weight, as well as addressing factors that increase bone resorption are recommended measures in premenopause, independently of BMD measurement.

Pharmacological Interventions
All known treatments were studied in postmenopausal women; therefore their efficacy in premenopausal women is unknown. Such patients with low BMD should be referred to specialized centers for investigation and advice. Treatment with anti resorptives, in premenopausal women, is not recommended.
Osteoporosis in Children

Who to test?

“Children are not simply small adults” (6); it may be dangerous to extrapolate the risk of bone fragility in children from adult data. There are few practice guidelines on BMD measurement in children. In the majority of clinical situations, the clinician must rely on clinical judgment to decide who needs bone densitometry. Early bone health may be compromised by several genetic or acquired childhood disorders, such as malabsorption, inflammation, immobilization, vitamin D insufficiency, glucocorticoids, as well as chemotherapy or organ transplantation.

Assessing pediatric bone health

The WHO criteria for osteopenia and osteoporosis are not appropriate for use in children, adolescents and young adults. The diagnosis of osteoporosis in a child requires, in addition to densitometric criteria, clinical findings such as a history of low impact fracture. Z score is the recommended score for use in children. The posteroanterior spine, then the whole body scans, are the preferred sites for BMD measurement (7,8).

When to treat?

Appropriate intake of calcium and vitamin D, as well as physical activity, balanced diet and healthy lifestyle are recommended in children and adolescents in order to reach a higher peak bone mass. Even in sunny countries such as in the Middle East, vitamin D insufficiency is prevalent in children (9). Drugs used to treat osteoporosis in adults are not necessarily appropriate for use in children.

References

BMD measurements in premenopausal women and in Children

2006 Recommendations
Who to test?
1. The WHO T-score-based criteria are not applicable to premenopausal women
2. No data on fracture-BMD relationship
3. No definite recommendations on who to test in the premenopause
4. Using Z-score is thus more appropriate than using T-score
   - Local reference data base

Vitamin D Levels

Assessment of Bone health in Children

Pharmacological Treatment
- Pharmacological treatment in premenopausal women is not recommended.
  - Efficacy of known drugs in premenopausal women is unknown.
  - Long-term safety of bisphosphonates, either on bone or on fetal growth, is a concern.
  - Anti-estrogen components, such as Tamoxifen, decreases BMD in premenopause.
  - Available data on current treatments do not exceed 7 to 10 years of use. What to recommend after?

- Premenopausal women with low BMD should be referred to specialized centers for appropriate evaluation and diagnosis.

Children Osteoporosis
Who to test?
- The clinician must consider how the information will influence his clinical management.
- Not enough data for a pediatric fracture threshold
- Factors contributing to that choice:
  - Disease severity
  - Age and duration of exposure to potentially harmful medication
  - Bone pain
  - Recurrent fractures
WHO Collaborating Centre for Metabolic Bone Diseases
University of Sheffield Medical School
Beech Hill Road, Sheffield S10 2RX, UK
Tel: 0114 285 1109/ Fax: 0114 285 1813

Education and qualifications
Surbiton County Grammar School
University of Edinburgh 1964-1970
BSc (Hons) 1st Class University of Edinburgh, 1967
MB ChB University of Edinburgh, 1970
MRCP (UK) Royal College of Physicians, Edinburgh, 1972
MA status University of Oxford, 1977
MRCPath Royal College of Pathologists, 1982
FRCP (London) Royal College of Physicians, 1984
MD University of Sheffield, 1985
FRCP (Edinburgh) Royal College of Physicians, 1986
FRCPath Royal College of Pathologists, 1992

Present appointments
Emeritus Professor, from 2003
Professor in Human Metabolism, University of Sheffield, from 1991.
Consultant Physician, Sheffield Area Health Authority, from 1979.
Physician in administrative charge of Metabolic Unit, Royal Hallamshire Hospital, from 1979.
Director, World Health Organisation Collaborating Centre for Metabolic Bone Diseases, from 1991.

Honorary appointments
Scientific Advisory Board, Paget’s Disease Foundation (USA), from 1986.
WHO Advisor on Osteoporosis from 1988.
Founder and Trustee, European Foundation for Osteoporosis and Bone disease (now the International Osteoporosis Foundation), from 1987.
Council and Founder Member: British Menopause Society, from 1989
Board Member, Health Council on Osteoporosis, from 1992
Board Member, International Bone and Mineral Society

Current Editorial appointments
Editor Bone 1990-
Editorial Board Journal of Bone and Mineral Research 1991-
Advisory Board Hormones & Metabolism 1987-
Advisory Board Revista Espanola de Enfermedades Ossias 1991-
Editorial Board Italian Journal of Mineral & Electrolyte Metabolism 1990-
Editorial Board Osteoporosis International 1990-
Editorial Board Trends in Endocrinology & Metabolism 1989-
Editorial Board Quarterly Journal of Medicine 1990-

Previous appointments
Medical Research Council Clinical Research Fellow, Renal Unit, Churchill Hospital and Metabolic Unit, Nuffield Orthopaedic Centre. October 1974 to July 1976.
Wellcome Senior Research Fellow in Clinical Science and Lecturer in Medicine, Nuffield Department of Medicine, University of Oxford. August 1976 to September 1979.
Senior Lecturer and later Reader in Human Metabolism, Department of Human Metabolism and Clinical Biochemistry, University of Sheffield, October 1979 to October 1991.

Research interests
Largely related to disorders of skeletal metabolism including osteoporosis, Paget’s disease of bone, hyperparathyroidism, renal osteodystrophy and neoplasia affecting the skeleton. Contributions to research include cell biology, histomorphometry of bone, assessment and treatment of bone disorders, guideline development, health technology assessment, epidemiology and health economics. Author of more than 500 papers, chapters and books on bone disease and metabolism since 1976.

Books published

*awarded the Royal Society of Medicine ‘best textbook’ of 1995.
The development of effective interventions for osteoporosis has had a significant impact on our ability to treat the disorder and decrease vertebral and non-vertebral fracture risk. A major problem that needs to be resolved is who best benefits from intervention, particularly in the absence of widespread screening policies with BMD. The resolution of the problem is to optimise fracture risk prediction which has been a major objective of the WHO Collaborating Centre at Sheffield. Risk factors for fractures have been identified from 12 prospective population-based cohorts comprising 250,000 person-years of observation with 3,500 osteoporotic fractures. Clinical risk factors that contribute to fracture risk independently of BMD include age, previous fragility fractures, a family history of fracture, rheumatoid arthritis, smoking, exercise, alcohol and the use of oral glucocorticoids. Their combined use with (or without) BMD enhances the sensitivity of fracture prediction without sacrificing specificity. The utility of the risk factors has been validated in the independent population-based cohorts of 230,000 individuals followed for 1.2 million person-years.

The ability to assess fracture risk from clinical risk factors permits intervention in men and women that is based not solely on BMD. Therefore, diagnostic thresholds for osteoporosis (based on BMD) differ from intervention thresholds. Because of the many techniques available for fracture risk assessment, the ten year probability of fracture is the desirable parameter to determine intervention thresholds. The setting of intervention thresholds is ultimately dependent on health economic considerations. When BMD is used as a test alone, an intervention threshold of –2.5 SD is cost-effective. In the presence of other independent risk factors less stringent criteria are appropriate so that intervention can be directed to individuals where hip fracture probability ranges from 2% to 10% (depending on age). These thresholds, derived from Sweden or the UK, require modification in different countries to take account of different costs and risks that vary markedly in different regions of the world.
Models for the Assessment of Fracture Risk

Cohorts studied

<table>
<thead>
<tr>
<th>EVOS / EPOS</th>
<th>Hiroshima</th>
<th>CaMoS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rochester</td>
<td>Sheffield</td>
<td>Rotterdam</td>
</tr>
<tr>
<td>Kuopio</td>
<td>Gothenburg I</td>
<td>Gothenburg II</td>
</tr>
<tr>
<td>EPIDOS</td>
<td>Dubbo</td>
<td>OFELY</td>
</tr>
</tbody>
</table>

n = 59,232 person-years = 249,898 % female = 74

Any fracture = 5,444 osteoporotic fractures = 3,495 hip fractures = 957

Ten year probability of hip fracture in Sweden

Risk factors for hip fracture in men and women
This event is supported by:

**Platinum Sponsor:**
Eli Lilly

**Gold Sponsor:**
Aventis-Sanofi
Merck Sharp and Dohme
Novartis

**Other Sponsors:**
Roche