EDITORIAL

In the spirit of fulfilling one of its major goals, namely continuing medical education, the Lebanese Medical Journal in this special supplement, the 5th in this series of special issues, contains proceedings of the Regional Densitometry Workshop that took place in Beirut on April 20th 2002 and the resulting National Practice Guidelines regarding the use of bone mineral density testing.

These practice guidelines were reviewed and unanimously approved by the five national major scientific societies of specialties that commonly deal with densitometry use.

The organizers of this landmark meeting, Drs Ghada El Hajj Fuleihan, Rafic Baddoura, Hassane Awada, Jad Okais and Paul Rizk, the guest expert Dr Michael McClung, the Presidents of the Lebanese Societies of Endocrinology, Rheumatology, Orthopedics, Radiology and Obstetrics and Gynecology, and their scientific committees are all to be commended on a splendid job, the fruits of which are presented herein. Also I would like to express my gratitude to Dr. Ghada El Hajj Fuleihan for having kindly accepted to be the guest editor of this special issue and for the excellent work she did for it.

We trust that this first set of National Practice Guidelines published in the LMJ will undoubtedly reinforce quality care and optimize management of patients seeking attention for skeletal health matters.

Adel E. BIRBARI
Editor in Chief
FOREWORD

Osteoporosis is a major public health problem projected to have an increasingly heavier social and economic toll in view of the demographic explosion of the aging population worldwide in general, and in developing countries including in the Middle East in particular. The World Health Organization has listed osteoporosis as a major item on the list of non-communicable diseases, that account for 60% of mortality worldwide.

Because bone mass or bone mineral density is the strongest single predictor of osteoporotic fracture, both the International Consensus Panel on Osteoporosis (1993) as well as the National Institute of Health Consensus Panel on Osteoporosis (2001) have used the term bone mass or bone density in their definition of osteoporosis. The World Health Organization working group has proposed several years ago an operational definition of osteoporosis based on bone mineral density derived cut-offs.

Because of the increasing recognition of osteoporosis as a disease and demand for identification of a larger number of subjects at risk, densitometry technology has undergone substantial growth as well as changes over the years. A plethora of instruments are therefore available on the market to-date, with a myriad of validated and not validated technologies, as well as a diversity of databases from which fracture risk assessment could be derived, justifiably and not so-justifiably depending on the specific instance. The Middle East in general and Lebanon in particular has not escaped this global phenomenon, that added to uncertainties regarding the status of densitometry use amongst practicing physicians. Thus guidelines regarding densitometry testing have been put forth and further refined over the years in the light of the substantial body of evidence that has accumulated from prospective studies evaluating risk factors and fracture risk, and from large randomized controlled trials evaluating the safety and efficacy of various osteoporosis treatment strategies.

On April 20, 2002, in an effort to further optimize the quality of care in osteoporosis nationally, a group of experts convened and presented regional data on osteoporosis, and provided guidelines based on the review of the evidence behind currently published guidelines on densitometry use as put forth by several organizations including the World Health Organization, The National Osteoporosis Foundation, the International Osteoporosis Foundation, the American Association of Clinical Endocrinologists, the Canadian Medical Association and the North American Menopause Society. This local meeting was a collaborative effort between several Lebanese Scientific Societies and the Eastern Mediterranean Regional Office of the World Health Organization. The resultant guidelines, the document justifying such guidelines and the proceedings of this meeting are detailed in this special supplement of the Lebanese Medical Journal. These guidelines were unanimously endorsed after careful evaluation by the Lebanese Society of Endocrinology, the Lebanese Society of Obstetrics and Gynecology, the Lebanese Society of Orthopedics, the Lebanese Society of Radiology and the Lebanese Society of Rheumatology, and the Eastern Mediterranean Regional Office of the World Health Organization.

We would like to thank the Presidents and constituents of the societies for the time and input in reviewing and endorsing the current guidelines: Ibrahim Salti, MD, PhD, Paula Atallah, MD, Georges Halaby, MD, Pierre Najm, MD and Charles Saab, MD (Lebanese Society of Endocrinology); Georges Kaadeh, MD, Muhieddine Seoud, MD and Jihad Ezzedine, MD (Lebanese Society of Obstetrics and Gynecology); Raja Shaftari, MD, and Assaad Taha, MD (Lebanese Society of Orthopedics); Georges Rouhana, MD and Naji Atallah, MD (Lebanese Society of Radiology); Abdel Fattah Masri, MD and Said Atweh, MD (Lebanese Society of Rheumatology); Ussama El-Khatib, MD, PhD (Eastern Mediterranean Regional Office of the World Health Organization). Special thanks to Professor Eric Orwoll, Oregon Health Sciences University, for his thoughts on guidelines for men.

Such guidelines have been put forth to provide a framework around which sound clinical decision-making can be built. They are not meant to supercede the prerogative of the practicing physician making decisions and treating an individual patient, nor are they meant as rigid yardsticks to measure standard of care. Rather, they are meant to provide a platform for an evidence-based approach to osteoporosis management based on data available to-date. Such guidelines will undoubtedly continue to be refined as our knowledge base on this challenging silent disease keeps evolving globally, regionally and last but not least nationally.

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### Bone Mineral Density (BMD) Measurement Guidelines 2002

**Endorsed by**
- Lebanese Society of Endocrinology
- Lebanese Society of OBGYN
- Lebanese Society of Orthopedics
- Lebanese Society of Radiology
- Lebanese Society of Rheumatology
- WHO Eastern Mediterranean Region

### Rationale for BMD use: The Evidence

- BMD predicts fractures
- BMD can be measured accurately and safely
- BMD cannot be deduced from clinical data
- BMD influences treatment choice
- Treatment reduces fractures
- BMD measurement thus indirectly reduces fractures

*NOF JBMR 1989; 4:Supplement 2*

### BMD Measurement: The Issues

- Who to test?
- What measures to use?
- When to treat?

### Recommandations sur la mesure de la densité minérale osseuse (DMO) 2002

**Agréées par**
- les Sociétés Libanaises d’Endocrinologie
- d’Obstétrique et de Gynécologie
- d’Orthopédie
- de Radiologie
- de Rhumatologie
- et le Bureau de l’OMS de la Méditerranée orientale

### Utilité de la mesure de la DMO

- La DMO prédit les fractures (risque relatif)
- La DMO est mesurable avec précision et sans risque
- Les données cliniques ne permettent pas de prédire la DMO
- La DMO influence la décision thérapeutique.
- Des traitements peuvent réduire l’incidence des fractures
- La DMO indirectement diminue l’incidence des fractures

*NOF JBMR 1989; 4:Supplement 2*

### DMO: Les questions qui se posent

- Quels sujets tester ?
- Quelles mesures choisir ?
- Quand traiter ?
GUIDELINES

BMD Testing Strategy
The Evidence

La Densitométrie Osseuse
Les données et les preuves

Who to treat?

• “The more general use of BMD measurement may be costly but it is less costly than indiscriminate and frequently expensive treatment” (WHO)

• A case-finding strategy of high-risk patients in whom BMD is expected to be low is recommended. BMD results assist in clinical decision-making, and treatment is to be cost-effective

Qui tester?

• “La mesure de la DMO dans la population générale est certes coûteuse mais sûrement moins qu'un traitement non ciblé” (OMS)

• La mesure de la DMO doit rester cependant une aide à la décision clinique et au choix du traitement le plus adapté en termes de coût-efficacité

BMD and fracture risk

• Evidence-based information on fracture reduction is available in high-risk patients, i.e. those with BMD T-score < – 2.5 or with prevalent spine fragility fractures.

• Most abundant data is in Caucasian elderly postmenopausal women

• There are some fracture data in patients on corticosteroid therapy, mostly postmenopausal women

DMO et risque de fracture

• La diminution de l'incidence des fractures par les traitements inhibiteurs de la résorption osseuse est établie chez les sujets à haut risque: ceux qui ont déjà eu une fracture de fragilité et ceux dont le T-score est < – 2.5

• Les données concernent essentiellement la femme ménopausée et âgée dans les populations caucasiennes

• Certaines données existent également sur l'ostéoporose cortico-induite chez la femme ménopausée
BMD Testing in Postmenopausal Women
Definite Indications

- > 65 years: age as a risk factor
- Presence of vertebral deformity or fragility fracture
- Radiologic evidence of demineralization
- Chronic corticosteroid therapy (> 3 months)

Mesure de la DMO chez la femme ménopausée
Indications certaines

- Femme de plus de 65 ans: l’âge comme facteur de risque
- Une déformation vertébrale ou fracture de fragilité
- Une déminéralisation radiologique
- Traitement par corticostéroïdes > 3 mois

BMD Testing in Postmenopausal Women
Less Definite Indications

- If < 65 years, with or without other risk factors such as low body weight < 50 kg or BMI < 20 kg/m²
- Medical conditions known to cause bone loss: Hyperparathyroidism, hyperthyroidism, anticonvulsant use, renal insufficiency, chronic liver disease, etc.

Mesure de la DMO chez la femme ménopausée
Indications sans preuves suffisantes

- La femme ménopausée de moins de 65 ans avec ou sans facteurs de risque surajoutés comme par exemple un poids < 50 kg ou un IMC < 20 kg/m²
- La femme ménopausée ayant une ostéoporose secondaire: hyperparathyroïdie, maladie de Cushing, traitements anti-convulsifs, insuffisance rénale, insuffisance hépatique chronique, etc.

BMD Testing in Pre-menopausal Women
Definite Indications

- NONE

Mesure de la DMO chez la femme pré-ménopausée
Indications certaines

- AUCUNE
BMD Testing in Pre-menopausal Women

Less Definite Indications

- Systemic corticosteroids for > 3 months
- Medical conditions known to cause bone loss: hyperprolactinemia, hyperparathyroidism, hyperthyroidism, anticonvulsant use, Cushing’s disease, renal insufficiency, chronic liver disease, etc.

BMD Testing in Pre-menopausal Women

No Indication

- In healthy normally cycling pre-menopausal women

BMD Testing in Men

Definite Indications

- Vertebral deformity or fragility fracture
- Chronic corticosteroid therapy > 3 months
- Hypogonadism

Mesure de la DMO chez la femme pré-ménopausée

Indications sans preuves suffisantes

- Un traitement par corticostéroïdes > 3 mois
- Affections médicales susceptibles d’influencer le turnover osseux: hyperparathyroïdie, Cushing, hyperprolactinémie, insuffisance rénale, insuffisance hépatique chronique, traitement anti-convulsif, etc.

Mesure de la DMO chez la femme pré-ménopausée

Absence d’indication

- La femme en bonne santé apparente

Mesure de la DMO chez l’homme

Indications certaines

- Antécédents de fracture de fragilité ou déformation vertébrale
- Traitement par corticostéroïdes > 3 mois
- Hypogonadisme
BMD Testing in Men
Less Definite Indications

- Radiologic evidence of demineralization
- Alcohol abuse
- Medical conditions known to caused bone loss: hyperprolactinemia, hyperparathyroidism, use of anticonvulsants, Cushing’s disease, renal insufficiency, chronic liver disease, etc.

BMD Testing in Men
No Indication

- Healthy men

Decision-Making

- In difficult and/or unusual cases, referral to a specialist is strongly recommended
- In difficult cases the decision on who to test and when to treat remains at the discretion of the specialist

Mesure de la DMO chez l’homme
Indications sans preuves suffisantes

- Déminéralisation radiologique
- Alcoolisme chronique
- Hyperparathyroïdie, maladie de Cushing, insuffisance rénale, insuffisance hépatique chronique, etc.

Mesure de la DMO chez l’homme
Absence d’indication

- L’homme en bonne santé apparente

Décision clinique

- Dans les cas difficiles, l’avis du spécialiste est fortement recommandé
- Dans les cas difficiles, la décision de mesurer la DMO et de traiter reste à la discrétion du spécialiste
What measures to use?

What Technology to Use?

Central DEXA (Dual Energy X-ray Absorptiometry)
- Accurate and precise
- Most validated measure for BMD fracture relation
- The one on which WHO T-scores cut-off were developed

Why to use DEXA?
- One on which risk assessment is based:
  RR/SD decrease, but more practically absolute risk (5-yr, or 10-yr)
- One on which guidelines are based: NOF, IOF, NAMS, AACE, ISCD, etc.
- All RCT treatment efficacy data based on central DEXA

Quelles mesures choisir ?

Quelle technique adopter ?

Absorptiométrie des Rayons-X à Double Energie (DEXA):
- La mesure de la DMO est exacte et précise
- La validation des études de la relation entre la DMO et les fractures a été réalisée par DEXA
- La valeur seuil du T-score de l’OMS a été développée sur DEXA

Pourquoi le DEXA ?
- L’évaluation du risque relatif (RR) de fracture a été réalisée sur DEXA : RR/par diminution d’une DS de la DMO. Actuellement l’estimation du risque absolu à 5 ans ou 10 ans est envisagée.
- Les recommandations faites par NOF, IOF, NAMS, AACE, ISCD, etc., sont basées sur la DEXAcentrale
- L’efficacité des traitements par des études randomisées a été établie avec la DEXAcentrale
### Alternative Technologies

- Alternative devices e.g. Quantitative Ultra-Sounds (QUS) could be used if absolute fracture risk measure can be readily derived (5-year or 10-year).
- QUS cannot use T-score: age at which T-score of – 2.5 is reached by QUS is > 95 years.
- T-score non applicable to non-central DEXA devices.
- Reject non-established devices: devices where accuracy and precision issues are in question will lead to patient mismanagement and jeopardize quality of clinical care.

### Which DEXA Databases?

The Western gender-specific database: T-score or BMD
- Caucasians should have same BMD fracture relation.
- WHO T-score cut-offs are based on Caucasian Western database (spine and hip) for postmenopausal women.
- Changing to local and different databases without validation will lead to patient misclassification and mismanagement.
- Local databases need validation of BMD-Fracture relationship.

### Which Skeletal Sites?

- Spine (L1-L4) and hip (proximal femur)
  - Sites of which WHO T-score is based (1994)
  - Measure both because they are not always congruent.
  - Spine more sensitive to intervention: monitoring.
  - Spine may be affected by DJD, less is hip.
  - Hip is best predictor of hip fractures.

### Techniques alternatives

- Les appareils à ultrasons (US) seront utiles lorsqu’ils fourniront un risque absolu de fracture à 5 ans ou 10 ans.
- La valeur seuil du T-score < – 2.5 est non-applicable avec les appareils à US: ce seuil n’est atteint que vers l’âge de 95 ans.
- Le T-score n’est pas applicable pour les appareils de DEXApériphérique.
- Il faut rejeter les mesures obtenues avec des appareils DEXA dé faible précision ou reproductibilité car ils conduisent à des erreurs diagnostiques et thérapeutiques.

### Quelle base de données en DEXA ?

- La relation entre la DMO et l’incidence fracturaire devrait être la même dans toutes les populations caucasiennes.
- La valeur seuil de – 2.5 pour le T-score proposé par l’OMS est validée uniquement sur une population caucasienne de femmes postménopausées.
- L’utilisation d’une courbe non validée peut, dans l’état actuel des données, conduire à un diagnostic erroné et donc à une indication thérapeutique inappropriée.
- Une étude de la relation entre la DMO et l’incidence fracturaire doit donc être conduite sur la population locale afin de valider l’utilisation des données de DMO locales.

### Quels sites osseux ?

- Le rachis lombaire (L1-L4) et le fémur proximal.
- Les sites sur lesquels le T-score a été établi en 1994 par l’OMS.
- Il faut mesurer les deux car il ne sont pas toujours concordants.
- Les vertèbres sont plus rapidement sensibles au traitement.
- La mesure des vertèbres est affectée par l’arthrose alors que l’arthrose de hanche affecte rarement le résultat.
- La DMO du fémur proximal prédit le mieux les fractures de hanche.
**How to Monitor Therapy**

*If the treating physician decides to monitor the patient, it is recommended to:*

- Measure patient on same machine, same device
- If switching, always perform careful cross-calibration
- When using cross-calibration, confidence in assessing significance of change is less
- Measure same skeletal site: no switching Right-Left

**Quel suivi thérapeutique ?**

*Si le médecin décide de suivre la progression de la DMO, les recommandations sont:*

- Répéter la mesure de la DMO sur la même machine
- En cas de changement de machine, une cross-calibration est nécessaire
- En cas de cross-calibration, la précision est moindre et l’appréciation du changement plus délicate
- La mesure du site osseux sera réalisée toujours du même côté de l’hémicorps: gauche ou droit

**How to Monitor Therapy**

- Use the compare feature for BMD: do not compare T-scores, compare BMD
- We cannot compare T-scores across machines: different databases, different ROI, etc.
- Strict QA: follow manufacturer guidelines, scan mode, acquisition, ROI, etc.

**Quel suivi thérapeutique ?**

- Ne pas comparer des T-scores mais comparer les chiffres absolus de DMO
- On ne peut pas comparer des T-scores de différentes machines: les bases de données et les zones d’intérêt sont différentes.
- Avoir une assurance qualité dans la procédure: suivre les recommandations du fabricant sur la zone d’intérêt, le mode, les contours...

**Quality Assurance**

- Phantom plot: look out for calibration shift (relocation, change X-ray tube, maintenance) or drift (room conditions, power supply, aging tube)
- Do not use manufacturer phantom based precision
- Derive center specific precision based on in-vivo data to assess significance of change over time

**L’assurance qualité**

- Pour la calibration reposant sur le fantôme, mesurer la dérive quotidienne de la courbe et surveiller les changements qui peuvent être dûs au repositionnement de la machine, aux changements de stabilité du courant électrique ou de la température du local
- Ne pas utiliser la précision sur fantôme « in vitro » comme une précision pour la pratique « in vivo »
- Pour plus de précision dans le suivi thérapeutique, chaque centre devrait réaliser une étude de précision « in vivo »
When to Treat?

Pharmacologic Intervention: The Evidence

- All clinical trial fracture data are limited to elderly postmenopausal women, usually > 65 years with osteoporosis by BMD (T-score < −2.5) or with prevalent fractures.
- No clinical trial fracture data in pre-menopausal women.
- No clinical trial fracture data in men.

Quand faut-il traiter?

Traitements pharmacologiques: Les faits

- L’efficacité de réduction du risque des fractures est uniquement prouvée chez des femmes ménopausées, âgées en moyenne de plus de 65 ans, avec un T-score < −2.5 DS ou une fracture de fragilité.
- Il n'y a pas d'étude de réduction des fractures chez les femmes non ménopausées.
- Il n'y a pas d'études de réduction des fractures chez l'homme.
Recommendations on When to Treat

- Universal measures in all, as early as possible
- Pharmacological treatment in high risk patients

Universal Measures

- Daily Ca intake around 1000 mg as well as vitamin D intake of 600 to 800 IU, even under our latitudes
- Physically active lifestyle
- Avoid smoking and high alcohol intakes
- Address factors that stimulate resorption or inhibit formation
- Promote falls prevention in the elderly

Pharmacologic interventions in postmenopausal women

Definite indications

- Postmenopausal women with fragility fracture and a low BMD
- Postmenopausal women T-score < −2.5
- Postmenopausal women on corticosteroid therapy (> 3 months) and T-score < −1.5

Recommendations thérapeutiques

- Mesures générales à prendre le plus tôt possible
- Traitements pharmacologiques chez les patients à haut risque de fracture.

Mesures générales

- Calcium > 1000 mg par jour
- Vitamine D: 600 à 800 UI par jour
- Poursuivre un exercice régulier
- Arrêt du tabagisme et de l’alcoolisme
- Agir sur les facteurs qui favorisent la résorption et/ou inhibent la formation osseuse
- Prévenir les chutes chez les personnes âgées

Traitements pharmacologiques chez la femme ménopausée

Indications certaines

- Femme ménopausée ayant une fracture de fragilité et une diminution de la DMO
- Femme ménopausée avec un T-score < −2.5 DS
- Femme ménopausée sous cortisone (> 3 mois) et T-score < −1.5
Pharmacologic interventions in postmenopausal women

- T-score between –1 and > –2.5 (with/without risk factors)

Pharmacological intervention in men*

- Men with fragility fractures and low BMD
- Men > 70 years with T-score < −2.5
- Chronic use of glucocorticoids > 3 months and T-score < −1.5

* Recommendations in men are less evidence-based than in postmenopausal women

Les indications incertaines

- Femme ménopausée avec un T-score entre –1 et –2.5 avec ou sans facteur de risque

Les indications certaines

- Homme avec fracture de fragilité et une diminution de la DMO
- Homme de plus de 70 ans avec un T-score < −2.5 DS
- Traitement glucocorticoïde > 3 mois et T-score < −1.5

* Les recommandations chez l’homme sont moins factuelles que chez les femmes ménopausées

Les indications incertaines

- Facteurs de risque et T-score entre −1 et −2.5 DS
- Homme de moins de 70 ans avec un T-score < −2.5 DS

* Les recommandations chez l’homme sont moins factuelles que chez les femmes ménopausées

**Guidelines**
Anti-resorptive therapy is definitely not indicated in:

- Normal healthy pre-menopausal women with low bone mass (–2.5 < T-score < –1)
- Normal healthy men with low bone mass (–2.5 < T-score < –1)

Middle East Densitometry Workshop
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Who to test?
What measures to use?
When to treat?

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Traitements pharmacologiques
Absences certaines d’indication

- Une femme en pré-ménopause normalement réglée avec une diminution de la DMO (–2.5 < T-score < –1) ne doit pas recevoir de traitement anti-résorption osseuse
- Un homme avec une diminution de la DMO (–2.5 < T-score < –1) ne doit pas recevoir de traitement anti-résorption osseuse

Atelier densitométrie osseuse pour la Méditerranée orientale
20 avril 2002

Quels sujets faut-il tester?
Quelles mesures choisir?
Quand faut-il traiter?

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PRACTICE GUIDELINES ON THE USE OF BONE MINERAL DENSITY MEASUREMENTS
WHO TO TEST ? WHAT MEASURES TO USE ? WHEN TO TREAT ?
A Consensus report from the Middle East Densitometry Workshop

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WHO TO TEST ?

When the question is “to test or not test” using bone mineral density (BMD) one could anticipate the answer is not straightforward. As with any diagnostic procedure, indications should be linked to clinical decision-making and this has to do with issues of sensitivity, specificity, predictive value, and balance between health and economic consequences of false positive and false negative results. Moreover targeting osteoporosis adds some peculiarities to the analytical process. The outcome is a probability, i.e. the risk of fracture and the test is a quantitative measure with an arbitrary cut-off threshold value [1-3].

Clinical decision-making [4] can occur in the setting of either initiating or monitoring therapy. In the first situation, two approaches are identified, mass screening or targeting high-risk population [5-6]. The latter is currently the main policy by cost-effectiveness considerations using evidence-based knowledge about osteoporosis. Therefore the question of who to test for BMD can be first approached as of who is at high risk of fracture. The difficulty comes however from the very objective of BMD testing that is to estimate the risk of fracture [7].

Regarding the risk of fracture, epidemiological evidence supports the role of multiple risk factors for fracture, commonly classified into bone and none bone related determinants (see Table I). The latter are related to the risk of falls namely locomotor problems and environment characteristics and the former to bone strength determinants including bone density and bone quality [8-14].

So far bone density remains the most important determinant of fracture in terms of relative risk, that we can estimate with enough confidence using DEXA technology and that is amenable to modification through pharmacological interventions [15-19].

However, in practice we are dealing with two different estimations of the risk of fracture, the absolute risk or remaining lifetime risk [20] and the relative risk [21]. The lifetime risk is the probability of sustaining a fracture over life expectancy which is higher for early postmenopausal than for late postmenopausal women. The relative risk is the ratio of the probability of sustaining a fracture when the risk factor is present compared to probability of sustaining a fracture when the risk factor is absent. Relative risk is higher for late postmenopausal than early postmenopausal women [22-23].

Besides BMD simple clinical variables could be identified as determinants of fracture risk based on epidemiological data [24]. However these variables poorly predict BMD [25]. Therefore BMD testing remains the cornerstone in the evaluation of the risk of fracture. Guidelines have been developed to select people at high risk of fracture based on those simple clinical variables [26-29].

Since guidelines necessarily reflect health system patterns one might anticipate several guidelines to be published. Literature review provides guidelines reports from the American National Osteoporosis Foundation [27], the American Association of Clinical Endocrinologists [30], the American College of Rheumatology [31], the North American Menopause Society [32], the US Preventive Services Task Force [33-34], the International Society of Clinical Densitometry [28], the Osteoporosis Society of Canada [29], the European Foundation for Osteoporosis now known as IOF [35-36], the Australian National Consensus Conference [37] and WHO [1].

Despite the apparent diversity of recommendations, common and simple clinical variables associated with increased fracture risk constitute the core set of the clinical decision making rule of proposed guidelines. However their diagnostic value might be different. This issue has been recently addressed in an original contribution [38], where the diagnostic value of the NOF guidelines

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was compared to four other clinical decision rules [39-42] based on simple clinical criteria identified through MEDLINE search excluding decision aids based on regression models or involving detailed questionnaires. The study concluded to the superiority of Simple Calculated Osteoporosis Risk Estimation (SCORE) and Osteoporosis Risk Assessment Instrument (ORAI) methods, compared to the NOF recommendations in terms of sensitivity and specificity. The strength of the study rises from the database on which the comparison was made, that is a population based community sample from the Canadian Multi-center Osteoporosis Study [42]. However this might not apply to other populations and yet remains the issue of cost effectiveness that reflects health system priorities and practices. As an indicator, BMD testing cost and reimbursement differ widely across national health systems and as a consequence access to BMD testing may be dependent on patterns of health care provision [1].

Until further progress can be made in the validation of widely applicable rules [42-43], we recommend the use of a core set of clinical variables that are accepted universally to select individuals at high risk of fracture to whom BMD testing will help clinical decision making and therefore add value to health outcomes.

RECOMMENDATIONS FOR WHO TO TEST

FOR WOMEN, the core set of clinical risk factors includes menopausal status, age, weight, past history of fragility fracture and steroid therapy. Therefore we recommend the following:

a. In postmenopausal women, regardless of age, BMD testing is definitely indicated if:
   a. There is evidence of radiological demineralization.
   b. Vertebral deformity or fragility fracture is present.
   c. Corticosteroid therapy for > 3 months is contemplated.

In postmenopausal women, in the absence of the conditions above, age is an important issue and we recommend the following:

Σ In late postmenopausal women (aged 65 years and above) BMD testing is definitely indicated regardless of clinical risk factors to make a decision about pharmacological intervention.

In early postmenopausal women (age less than 65 years), BMD testing is less definitely indicated, and can be considered in conditions associated with increased fracture risk such as maternal history of fragility fractures, low body weight (Wt < 50 kg or BMI < 20 kg/m²) or conditions associated with secondary causes of bone loss, since the likelihood of identifying subjects with osteoporosis is higher. These medical conditions associated with bone loss, include premature menopause < 45 years, asymptomatic primary hyperparathyroidism, hyperthyroidism, chronic renal failure, chronic liver disease, malabsorption, and use of anticonvulsants, etc.

π In premenopausal women with medical conditions known to be associated with bone loss BMD is less definitely indicated in clinical decision making regarding these conditions. These conditions include: anorexia nervosa, asymptomatic primary hyperparathyroidism, hyperthyroidism, chronic renal failure, chronic liver disease, malabsorption, use of anticonvulsants, etc.

In apparently healthy premenopausal women, BMD testing is definitely not indicated since the prevalence of low BMD is rare and the safety and efficacy of pharmacological intervention is not established.

FOR MEN although epidemiological data is less abundant, however recent evidence suggests a similar BMD fracture relationship and BMD response to anti-resorptive agents in men as in women [44-49]. However, the evidence is less definite. We suggest that the following set of clinical risk factors for fracture in men is to be considered. These include past history of fragility fracture, chronic steroid therapy, hypogonadism, alcohol abuse, demineralization, low weight and medical conditions associated with bone loss. The main difference would be that the efficacy of osteoporosis therapies is less established in men and the incidence rate of fracture is lower in men compared to women. Therefore, testing in men would be recommended on less definitive grounds. Until further information on the epidemiology of osteoporosis in men becomes available, we recommend the following:

a. BMD is definitely indicated in the presence of vertebral deformity or fragility fracture, hypogonadism or chronic steroid therapy.

Σ BMD is less definitely indicated in the case of alcohol abuse, low weight, radiologic evidence of demineralization, medical conditions that are associated with bone loss such as hyperparathyroidism, renal insufficiency, chronic liver disease, and anticonvulsant use.
BMD testing is definitely not indicated in healthy men in the absence of clinical risk factors. However, these recommendations represent general guidelines. For difficult and unusual cases referral to a specialist is strongly recommended. Deciding who to test and how to treat is then left to the discretion of the expert.

WHAT MEASURES TO USE?

What measures to use to assess BMD?
1. To evaluate the risk of fracture.
2. To monitor response to therapy.
In order to adequately address that question, the following four issues need to be covered:
   a. BMD and fracture risk
   b. Which technique and device?
   c. Which parameter (BMD/T-score) and which database?
   d. Which skeletal site to measure?

1. What measures to use to assess the risk of fracture

a. Bone Mineral Density as a strong predictor of fracture: the evidence
   Before we discuss which measures to use to assess the risk of fracture, let us review two widely recognized definitions of osteoporosis.
   1. “A systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fractures.” International Consensus Definition 1993 [50].
   2. “A skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture. Bone strength reflects the integration of two main features: bone density and bone quality.” NIH Consensus Development Panel 2001 [51].

WHO WORKING GROUP OPERATIONAL DEFINITION OF FOSTEO - POROSIS IS BASED ON BMD

Bone mass or BMD are recurrent terms in the above two definitions, that were coined almost a decade apart. This is due to the fact that over the last twenty years abundant data has accumulated, establishing BMD as one of the strongest, if not the strongest predictor of fractures. As a matter of fact, it is a stronger predictor of fracture, than cholesterol is a predictor of coronary artery disease (CAD), and is at least as good as hypertension is a predictor of stroke. This was the main reason why the World Health Organization working group developed an operational definition for osteoporosis based on BMD. Although the BMD fracture relationship is an exponential one, a specific BMD-based cutoff was chosen for osteoporosis diagnosis: a BMD T-score (number of SD below peak bone mineral density) below –2.5 [1]. Such a cutoff value identifies approximately 30% of postmenopausal women as having osteoporosis using measurements made at the spine, hip, or forearm. This percentage is approximately equivalent to the lifetime risk of fracture at these sites” [1]. Indeed, Melton et al recently demonstrated that the proportion of postmenopausal women who have a BMD T-score < –2.5 at the femoral neck, spine, forearm, or at any of these three sites corresponds to the same proportion of women with a lifetime risk of hip, spine, wrist, or any of these three fractures, respectively [52-53]. This –2.5 T-score cutoff only applies to postmenopausal Caucasian women and only to DEXA densitometry measurements [1, 54].

MEASURES VALIDATING THE USE OF BMD TO PREDICT FRACTURES

The rationale for the use of BMD in fracture prediction is validated by the following observations:
1. Biomechanical testing in the laboratory supports a strong relationship between BMD and bone strength as assessed by failure load, etc. [55].
2. Ample epidemiologic data from longitudinal studies such as the Study of Osteoporotic fractures, the EPIDOS study, the Rochester study, the Rotterdam study, and the Hawaii Osteoporosis study documenting BMD to be a strong predictor of fractures. Indeed, for each SD decreases in BMD the RR of fracture is 1.7-3, depending on the fracture type, the skeletal site, and the device being used [56-65].
3. An evaluation of the large randomized controlled trials using pharmacologic treatment reveals that BMD increments account for a significant proportion of the variance in vertebral fracture risk reduction [66-71]. However, the proportion of variance in fracture reduction that is explained by BMD changes has varied widely depending on the study [66-67, 69-71]. Although measurement of bone mineral density only captures one aspect of bone strength, since there is no additional readily measure of bone quality to date, bone mineral density remains a pivotal tool in the diagnosis of patients at risk for fracture.

b. Which device and technique to use?

There are multiple devices on the market to measure bone mineral density in the central or the peripheral skeleton. The techniques used in these devices are also different. The main techniques available today are dual energy x-ray absorptiometry (DEXA), single energy x-ray absorptiometry (SXA), quantitative computerized tomo-graphy (QCT) and ultrasonometry (QUS).
Technical issues

X-ray technology as DEXA or SXA: uses ionizing radiation and measures areal density (bone mineral content/area), this can be affected by size, growth, etc. DEXA can be used to measure BMD at the central as well as peripheral skeleton. Central DEXA is the yardstick to which all measures are compared (see section on validation of techniques used below). Central devices measure BMD at the spine, hip, forearm and total body. Peripheral devices are based on single energy (SXA) or dual energy (pDEXA) technology and measure BMD at the forearm or calcaneus’s (SXA) or at the finger, toe, heel, forearm (pDEXA) [72].

Quantitative computerized tomography (QCT): uses ionizing radiation and measures true volumetric as opposed to areal density such as measured by SXA and DEXA. QCT can be used for central measurements at the spine, and a special QCTis available to measure volumetric density at the forearm (pQCT). Recent advances in spiral CT and recent automated software make hip measurement also feasible. A major drawback of central QCT is high radiation exposure, doses reaching 40 times that of a DEXA. Although QCT does offer high sensitivity in detecting osteoporosis and excellent fracture discrimination in cross-sectional studies there are no longitudinal studies relating QCT BMD measures to fracture risk. Furthermore, the standard T-scores do not apply well to QCT, therefore caution must be exercised in interpretation of results.

Quantitative ultrasound (QUS): this technology uses sound waves, measures speed of sound and broadband ultrasound attenuation that can then yield calculated parameters (e.g. stiffness, etc. [73]). Both the directly measured and the derived parameters are lower in the patient with osteoporosis. Similarly to QCT, T-scores also do not apply to QUS.

Validation of the technique used

DEXA: is by far the most widely accepted technology and one that is most well validated by all three criteria listed above. It is the technique with which we have the most information and is the gold standard today. It has very good accuracy and excellent precision in expert hands (see below), and incurs low radiation exposure. DEXA is FDA approved for the diagnosis of osteoporosis. Indeed, the biomechanical data was mostly obtained using DEXA, most epidemiologic studies establishing the close relationship between fracture risk and BMD used DEXA [59-60, 63, 74]. Similarly, the data from the randomized controlled trials linking treatment efficacy to fracture outcome, exclusively used DEXA (as opposed to pDEXA or SXA) as an intermediary measure for efficacy, as required by the FDA.

pDEXA, SXA: Data from the NORA study of over 200,000 women screened across the United States with a wide variety of devices demonstrates a significant relationship between BMD as assessed by any of these techniques/devices (SX A, pDEXA, DXA) and fracture risk, with variations in the risk measure depending on the device [64, 75].

QUS: Several prospective studies such as the SOF study, EPIDOS and the NORA studies, have demonstrated a direct correlation between QUS measured and derived parameters and fracture risk [61-62, 64]. However, it is the calculated QUS parameters and not the directly measured ones that are used to calculate T-scores, and therefore by inference fracture risk.

QCT: Two studies have recently demonstrated the ability of QCT and pQCT to predict risk of vertebral fracture for the former, and spine, hip and global fracture for the latter [76-77]. However, QCT is to be considered of experimental value compared to DEXA. QCT also incurs the highest radiation exposure, around 40X that of a DEXA.

Accuracy and precision

Key characteristics to be considered in the choice of a device to be used to diagnose and monitor a clinical condition.

The main critical characteristic to be considered in the choice of a technique/device to diagnose a condition is its accuracy: how close the measure is to what it is supposed to measure. In this instance, this can be evaluated by measuring BMD/BMC of a bone specimen using the different techniques and devices and comparing that to the actually measured bone mineral content by ashing that specimen afterwards. This was carefully studied and the accuracy for various devices/techniques listed above varies between 3-6%, it may be slightly higher for both QCT and pQCT, with a range of 8-15% [78-79]. Precision (reproducibility) on the other hand is the most important variable to consider when using a technique to monitor therapy [79-82], see section below “What measures to use to monitor the patient”.

Central DEXA technology is the most established technology in which the BMD-fracture relationship has been validated in longitudinal studies, and the one with which WHO T-score based cutoffs have been established. FDA approved central DEXAbased densitometry devices are therefore the preferred method of choice for evaluating fracture risk, when available. Alternative measures that could be used are QUS, pDEXA, QCT, or other validated devices. However, non-validated DEXA like devices are to be avoided in view of their poor accuracy and their probable poor precision.
c. Which parameter, which device and which databases

It is generally agreed that the relationship between BMD and fracture risk is an inversely exponential one, as BMD decreases fracture risk increases; expressed differently, for each SD decrease in BMD fracture risk almost doubles. This assessment was derived from several large epidemiologic studies conducted mostly in Caucasian populations: SOF in the United States [83], Rotterdam study in the Netherlands [74]; EPIDOS in France [63]; The Hawaii Osteoporosis study in Hawaii [56], although some scarcer data is available with other races.

To-date, fracture risk can either be expressed in one of two ways:

1. An absolute risk, lifetime or 5-year risk, for a specific BMD at a certain age (since age is another independent predictor of fractures) such as provided in the Rotterdam study [74].
2. More commonly but in less practical terms as RR/SD decrease. Therefore an individual with a T-score of $-3$ has a fracture risk that is twice that of an individual with a T-score of $-2$. The latter assessment is less useful in the clinical setting as it expresses risk in relative rather than absolute terms, the latter being a much more clinically applicable and relevant risk assessment tool [59-60, 63, 83-84].

Very few studies have expressed absolute fracture risk as a function of BMD such as the Rotterdam study [74]. However, since absolute BMD in gm/cm$^2$ may vary depending on central DEXA manufacturer, appropriate conversions are to be implemented prior to the ability to use such data [85]. In view of the paucity of absolute fracture risk data published, 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-offs for the diagnosis of osteoporosis are applicable only to central DEXA generated data in postmenopausal Caucasian female subjects only. Conversely, T-score derived from other technologies such as pDEXA, QUS and QCT are not comparable to DEXA derived T-scores for multiple reasons including differences in what is measured with these technologies, differences in normative databases and the lack of agreed upon diagnostic criteria [86-87]. Work in progress between committees from the NOF, the ISCD and ASBMR with the goal of deriving T-score equivalents that vary depending on the device, to estimate fracture risk may help partially resolve this issue. Alternatively, other algorithms are currently being evaluated to estimate absolute 5 (or 10)-yr fracture risk using absolute BMD adjusting for variation in densitometer types (DEXA, U/S, pDEXA, etc.).

The second issue of relevance in our part of the world is how to use the BMD-fracture data expressed in the European and American Caucasians to our part of the world, the Middle East. That really gets to the question of how do absolute BMD/fracture curves compare across populations within the same racial category, for our purposes, Caucasians. A comparison of absolute BMD vs fracture risk across populations of the same race would be needed to evaluate that question. Such data is just not available to-date for populations from the Middle East. Therefore, resorting to T-score was the next available strategy, to assess fracture risk in individuals in the Middle East. This would be sound if the following two conditions were met:

1. We assume that the absolute BMD/fracture relationship is overall the same in all Caucasians regardless of the population. There is no reason to-date to think otherwise.
2. We use the appropriate device and database in which the BMD-fracture relationship and therefore T-score cut-off was derived. These would be a central DEXA device and a Caucasian postmenopausal female normative database.

Let us turn to the data available to us to-date from the region trying to address that issue. Peak BMD has been studied mostly in non-population based [88-90] and in population-based samples [91-92]. The studies available from our region reveal peak BMD in these subjects may be slightly lower than (in 4 studies) or equal to (in one study) that of European and American Caucasians, possibly due to differences in body size, chronic vitamin D deficiency or less physical activity [89, 93-94]. The prevalence of vertebral fractures in postmenopausal women and hip fracture rates are comparable to data for Western counterparts [95-98]. Finally, mean BMD in hip fracture in Lebanese subjects is comparable to mean BMD in hip fracture subjects from the West [99-100]. The latter information suggests that the absolute BMD-fracture relationship may be the same in our region as it is in the West. The situation may very well be different in other races i.e. Asians, African-Americans, etc.

In view of the above observations, the application of Western standards for the diagnosis and assessment of fracture risk in Caucasian subjects from the Middle East are prudent, until additional forthcoming data from the region becomes available. This is consistent with the recommendations from the International Osteoporosis Foundation [35]. Therefore, we recommend the use of central DEXA devices and Western databases (for e.g. NIANES, etc.) for the derivation of T-scores to assess...
fracture risk, or absolute BMD/fx risk data such as provided in the Rotterdam study after appropriate transformation of the data to obtain comparable densitometry units (see above). Any other practice will result in a tendency to erroneously diagnose osteoporosis and wrongly estimate fracture risk. WHO T-score based criteria are not applicable to non-Caucasian postmenopausal women, to premenopausal women, to men, to children and non-Caucasians. They are also not applicable to other technologies such as QCT, pQCT, QUS, pDEXA and SXA.

Algorithms are currently being evaluated to use information gathered from non-central DEXA devices to estimate absolute 5-year or 10-year fracture risk, however such data is not readily available yet.

d. Which skeletal sites to measure?

It is generally agreed that the relationship between BMD and fracture risk is an inversely exponential one, as BMD decreases fracture risk increases; expressed differently for each SD decrease in BMD fracture risk increases by 1.5-2.8 folds. This range is due to variations in the skeletal site used to estimate fracture risk (L2-L4, hip, forearm, etc.) and the specific fracture for which the risk is predicted (wrist, hip, or vertebral fracture).

Global risk of fracture: Several studies have established that the global relative risk of fracture, relative risk of developing an osteoporotic fracture anywhere in the skeleton is the same 1.4-1.6/SD decrease in BMD as measured at any site in the skeleton [84].

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: e.g. whereas spine, hip and forearm all predict fracture risk at the hip and spine, hip BMD is the best predictor of hip fracture and spine BMD is the best predictor of vertebral fracture [59-60, 83-84].

Central DEXA: RR/SD decrease in BMD from a meta-analysis of 11 prospective cohort studies, 1985-1994, 90,000 person-years, > 2000 fractures [84].

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]
Distal radius for wrist fractures: 1.7 [1.4-2.0]

How many skeletal sites to measure?
1. Although there is correlation in BMD between one site and the other (r = 0.4-0.6), it is not perfect. Therefore measuring only one site may underestimate a subject’s osteoporosis risk [87, 101-103].
2. Hip BMD is the best predictor of hip fracture, spine BMD is the best predictor of vertebral fractures, as outlined in the previous section.
3. At the menopause, accelerated bone loss takes place more so at the spine than at the hip. So measuring only a hip BMD may miss the lower bone mass at the spine [102].
4. Aging results in degenerative changes at the spine that may falsely increase BMD by 0.5-1SD [104-105]. Measuring the hip in the elderly is of particular importance.
5. The spine site is the most responsive skeletal site to pharmacologic intervention and may be important in monitoring a patient [69].
6. Forearm: Some clinical conditions such as primary or secondary hyperparathyroidism may lower forearm BMD the most [106]. In such instances a forearm measurement is indicated. A forearm is also indicated in the very obese patient in whom a spine or hip cannot be performed due to large size.

EFFO POSITION (NOW IOF): In a position paper the European Foundation for Osteoporosis has suggested measuring only one skeletal site for the young patient (spine, hip, or forearm) and the hip only in the elderly as it best predicts the occurrence of the most important fracture, and avoids running into the problems of DJD of the spine [35].

ISCD POSITION: ISCD forum July 2001. Measure spine and hip for all patients, non-dominant forearm is to be added if one of the above two skeletal sites cannot be used, if the patient has suspected hyperparathyroidism, or if the patient is obese. Total body BMC measurement is recommended in children.

NOF: NOF analyses for cost-effectiveness were all based on BMD measurement at the hip.

Although it is controversial whether measurement of more than one skeletal site improves our discriminative ability in predicting the patient at risk for fractures, a two-site central DEXA measurement is preferred for the above-mentioned reasons.

We therefore recommend following the guidelines of the ISCD (ISCD Syllabus, Version 4, Jan 2002) for skeletal site selection:
* Spine and hip for all patients.
* Non-dominant forearm is added in the following situations:
  One skeletal site cannot be used : arthritis, prosthesis, etc.
  Hyperparathyroidism is suspected
  The patient is obese
* For spine the use of L1-L4 is recommended, and for the
hip ISCD suggests the use of the lowest T-score of all 3 hip sites total, femoral neck, trochanter.

2. What measures to use to monitor the patient?

A complete and detailed overview of that topic is provided in the ISCD Clinical track syllabus, Version 4, January 2002.

a. Skeletal sites to monitor BMD change over time and what is a significant change

b. Interval time for repeating BMD to assess response to therapy.

The purpose of this discussion is not to advise whether a patient (whether on therapy or not) should have serial BMD measured, but rather once the decision is made to repeat BMD measurements which skeletal sites should be used, and when should the follow-up scan take place.

In order to assess change over time the following conditions should be met:

1. The same skeletal site as measured on the same device, not just same model, should be used. In the event of a change in the machine, careful cross-calibration is mandatory.
2. Absolute BMD, rather than T-scores should be used.
3. Cannot compare T-score on scans performed on different manufacturers due to differences in normative databases [92, 107] and differences in identifying ROI (e.g., L1-L4 vs. L2-L4; differences in algorithm used to define ROI for femoral neck).
4. The ROI of BMD sites being compared should be identical and the area should be within 2% between the two duplicates, otherwise the comparison of areal BMD is not valid.
5. Strict adherence to manufacturer guidelines for position and analysis are of utmost importance.
6. The skeletal site to be chosen for monitoring BMD change over time is one that has the highest precision ($\leq 1\%$), is the most responsive to change with treatment, and is the least affected by potential artifacts. The spine definitely fulfills the first two criteria [81-82]. In case of DJD of the spine, the total hip (rather than femoral neck, better precision less affected by rotation) is the next preferred site. The forearm is unlikely to show changes over time due to its lower bone turnover.
7. Center specific precision data should be available. Ideally such precision (duplicate BMD scans on the same patient, performed on over 30 individuals few days apart) should be calculated in each center, on their own machines, in the population being evaluated, namely postmenopausal women. Indeed, we have demonstrated that same day precision is better than different day precision, and precision derived from osteoporotic patients is worse than in normal subjects [82]. Use of in-vitro precision based on phantom duplicate measurements, provided by the densitometer manufacturers and used by the densitometry software to assess significance of changes in an individual over time should be discouraged. Indeed, these estimates are not applicable to the real clinical situations but are unfortunately used by many centers.
8. The mean SD (rather than CV) derived from all duplicate scans is calculated, and the root mean square average for the entire group is then calculated by summing the square of the SD, then dividing by the number of patients (e.g., $N = 30$), and then taking the mean square root MSR [79].

### TABLE I

**BONE AND NON-BONE RELATED RISK FACTORS FOR FRACTURES**

<table>
<thead>
<tr>
<th>A. BONE RELATED RISK FACTORS</th>
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<tbody>
<tr>
<td>White or Asian women (Genetic factors)</td>
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<tr>
<td>Low BMD ($&lt; -2.5$)</td>
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</tr>
<tr>
<td>Extensive epidemiologic data demonstrate that fracture risk increases progressively as bone density decreases (quite a doubling of fracture risk for one standard deviation decrease under peak bone mass). Maternal history of hip fracture Early menopause Prolonged amenorrhea Preexisting fracture Low trauma fracture since age 45 Thin body build Chronic CS use (?6 months) Medical conditions predisposing to osteoporosis (see Table II) High bone turnover</td>
<td></td>
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<table>
<thead>
<tr>
<th>B. NON-BONE RELATED RISK FACTORS</th>
<th></th>
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<tbody>
<tr>
<td>Age $&gt; 65$</td>
<td></td>
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<tr>
<td>Propensity to falls Medications : anxiolytics, sedatives Neurologic disorders leading to altered vision/proprioception</td>
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</table>

**SMOKING, ALCOHOL USE AND PHYSICAL INACTIVITY ARE LESS STRONG RISK FACTORS.**
9. A change over time is real if it exceeds the Least Significant Change (LSC), a number derived from the precision, preferably calculated from SD from duplicates rather than CV%. LSC is calculated as $2.77 \times MSR$ of the data, with a 95% confidence interval [79]. Even in the centers with the best precision, one should not repeat BMD before 1.5-2 years, unless one expects accelerated bone loss such (see below).

### b. Interval time for repeating BMD to assess response to therapy

The interval of time is determined by the expected change in BMD over time (the latter depends on type of therapy and specific skeletal site), the center derived LSC. Mean Treatment Interval = LSC/expected change/year [79]. This implies that even in expert centers with an MSR of 1, LSC of 2.77, and an expected mean change in BMD of 0.03 gm/cm$^2$, repeating a BMD before 1.5-2 years is not indicated. The interval time is obviously shorter in cases of anticipated fast increments and/or decrements in BMD (as seen post-oophorectomy, post GnRH therapy, with high doses chronic corticosteroid therapy, or with bone anabolic therapies) in which instances the interval may be as short as six months to a year.

To conclude, if the decision is to monitor a patient, it is strongly recommended to evaluate the patient ideally on the same device, not just same model, with strict QA measures for scan acquisition and analysis. This includes choice of scanning mode, choice of site, ROI, and the derivation of center specific patient based precision data for the skeletal site of interest, to determine a center specific LSC measure and therefore significance of a change in an individual patient. The skeletal site we recommended for monitoring is the spine, the hip can be used instead in select situations or in addition. Monitoring interval depends on the center specific LSC data and expected changes in BMD in each patient/year. Usually, follow-up scans should not be done before 1.5-2 yrs.

### WHEN TO TREAT?

Over the last decade there has been an effort to expand guidelines from “who to test” to “who and when to treat” using the body of evidence provided by the large randomized osteoporosis trials with the solid endpoints of osteoporotic fractures. With the increasing evidence for a relatively rapid rate of treatment onset and offset for these interventions, there has been a move away from long-term preventive strategies towards the use of shorter-term therapy in high risk individuals as outlined below and in public health decisions.

### TABLE II

<table>
<thead>
<tr>
<th>CAUSES OF OSTEOPOROSIS/OSTEOPENIA*</th>
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<tbody>
<tr>
<td>Genetic</td>
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<tr>
<td>White or Caucasian</td>
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<tr>
<td>Maternal family history</td>
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<tr>
<td>Thin body habitus</td>
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<tr>
<td>Genetic polymorphisms:</td>
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<tr>
<td>Vitamin D receptor, COLA1, Estrogen receptor</td>
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<td></td>
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<tr>
<td>Lifestyle/Nutritional</td>
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<tr>
<td>Smoking</td>
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<tr>
<td>Excessive alcohol</td>
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<tr>
<td>Prolonged amenorrhea</td>
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<tr>
<td>Inactivity/Prolonged immobilization/Spaceflights</td>
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<td></td>
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<tr>
<td>Medical Conditions</td>
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<tr>
<td>Endocrine</td>
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<td>Anorexia nervosa</td>
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<td>Hypogonadism</td>
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<td>Hypercortisolism</td>
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<td>Hyperparathyroidism</td>
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<td>Hypercalcita</td>
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<td>Prolactinomas</td>
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<td>Thyrotoxicosis</td>
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<tr>
<td>Diabetes</td>
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<tr>
<td>Connective tissue/Rheumatologic</td>
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<tr>
<td>Osteogenesis imperfecta</td>
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<tr>
<td>Scurvy</td>
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<tr>
<td>Ehlers-Danlos syndrome</td>
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<tr>
<td>Ankylosing spondylitis</td>
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<tr>
<td>Rheumatoid arthritis</td>
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<tr>
<td>Process affecting the marrow</td>
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<tr>
<td>Multiple myeloma</td>
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<tr>
<td>Leukemia, lymphoma</td>
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<tr>
<td>Anemias - sickle cell disease, thalassemia</td>
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<tr>
<td>Gastrointestinal (GI) diseases</td>
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<tr>
<td>Cystic fibrosis</td>
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<tr>
<td>Post-gastrectomy</td>
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<tr>
<td>Primary biliary or alcoholic cirrhosis</td>
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<tr>
<td>Malabsorption/Sprue</td>
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<tr>
<td>Crohn’s disease</td>
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<tr>
<td>Others</td>
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<tr>
<td>Post-transplantation</td>
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<tr>
<td>Renal failure chronic</td>
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<td></td>
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<tr>
<td>Drugs</td>
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<tr>
<td>Anticonvulsants</td>
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<tr>
<td>Cyclosporine</td>
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<tr>
<td>Chemotherapy</td>
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<tr>
<td>Glucocorticoids</td>
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<td>GnRH agonists</td>
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<tr>
<td>Heparin</td>
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<tr>
<td>Methotrexate</td>
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<td>Excess thyroid hormone</td>
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</table>

lished guidelines or reviews on that topic [27, 35, 108-111]. The pivotal randomized controlled trials that are responsible for the switch in the treatment strategies will also be highlighted in this overview.

Definition of prevention and treatment strategies and the evidence for intervention

- **Prevention** is defined by primary prevention, i.e. prevention of bone loss in early postmenopausal women without established osteoporosis i.e. with BMD T-score between – 1 and – 2.5.
- Prevention studies are conducted with a primary end-point of BMD, not fracture. Indeed, in these women the absolute risk of fracture is very low and thus, within the relatively short time frame of the majority of these studies, anti-fracture efficacy cannot be tested. As with any preventive treatment, prevention of osteoporosis should be cost-effective and easy to use in large populations.

- **Treatment** is defined as reduction in fracture risk in postmenopausal women with established osteoporosis (BMD T-score below – 2.5, with or without a previous prevalent fracture). Usually, the much higher risk of fragility fracture in the treatment populations, in late (older) postmenopausal women, enables assessment of anti-fracture efficacy.

To help evaluating known evidence related to these interventions, the Royal College of Medicine established the following grading of evidence. (Grading of evidence levels as well as tables I and II are taken from the Royal College of Medicine Guidelines, updated in July 2000 [112]. The United States Preventive Services Task Force as well as the Osteoporosis Society of Canada have also recently reviewed osteoporosis treatment efficacy as well as issued clinical guidelines for osteoporosis screening [34, 113].

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<thead>
<tr>
<th>Grade</th>
<th>Spine</th>
<th>Non-vertebral</th>
<th>Hip</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>A</td>
<td>B</td>
<td>B</td>
</tr>
<tr>
<td>nd</td>
<td>nd</td>
<td>nd</td>
<td>nd</td>
</tr>
</tbody>
</table>

Grade A: Meta-analysis of randomized clinical trials (RCT) or at least one RCT. At least one well designed controlled study without randomization. Valid cohort study for prognosis or risk assessment purpose.

Grade B: At least one other type of well designed quasi-experimental study. Well-designed non-experimental descriptive studies (comparative, correlation or case-control studies).

Grade C: Expert committee reports/opinions and/or clinical experience of authorities.

Among risk factors for osteoporosis, some may be modified through behavioral or environmental interventions (see Tables I and II) whereas others may be targets for pharmacological intervention. It has been suggested that an adequate work-up to rule out secondary causes of osteoporosis could include a 24-hour urinary calcium, serum calcium and serum PTH to all postmenopausal women with osteoporosis, and a TSH in those on chronic supplementation [114].

---

**TABLE III**

### EFFECT OF INTERVENTIONS ON THE PREVENTION/REDUCTION OF POSTMENOPAUSAL BONE LOSS

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>A</td>
</tr>
<tr>
<td>Vitamin D + Calcium</td>
<td>A</td>
</tr>
<tr>
<td>Physical exercise</td>
<td>A</td>
</tr>
<tr>
<td>Cessation of smoking</td>
<td>B</td>
</tr>
<tr>
<td>Reduced alcohol consumption</td>
<td>C</td>
</tr>
<tr>
<td>HRT</td>
<td>A</td>
</tr>
<tr>
<td>Alendronate</td>
<td>A</td>
</tr>
<tr>
<td>Raloxifene</td>
<td>A</td>
</tr>
<tr>
<td>Risedronate</td>
<td>A</td>
</tr>
<tr>
<td>Calcitriol</td>
<td>A</td>
</tr>
<tr>
<td>Cyclic Etidronate</td>
<td>A</td>
</tr>
<tr>
<td>Tibolone</td>
<td>A</td>
</tr>
</tbody>
</table>

**TABLE IV**

### ANTI-FRACTURE EFFICACY OF INTERVENTIONS IN THE TREATMENT OF POSTMENOPAUSAL OSTEOPOROTIC WOMEN

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Grade</th>
<th>Spine</th>
<th>Non-vertebral</th>
<th>Hip</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>A</td>
<td>B</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Vitamin D</td>
<td>nd</td>
<td>B</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Vitamin D + Calcium</td>
<td>nd</td>
<td>A</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Physical exercise</td>
<td>nd</td>
<td>B</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Hip protectors</td>
<td>-</td>
<td>-</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>HRT</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Alendronate</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Raloxifene</td>
<td>A</td>
<td>nd</td>
<td>nd</td>
<td></td>
</tr>
<tr>
<td>Risedronate</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Calcitriol</td>
<td>A</td>
<td>B</td>
<td>B</td>
<td></td>
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<tr>
<td>Cyclic Etidronate</td>
<td>A</td>
<td>B</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Calcitriol</td>
<td>A</td>
<td>A</td>
<td>nd</td>
<td></td>
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<tr>
<td>Tibolone</td>
<td>nd</td>
<td>nd</td>
<td>nd</td>
<td></td>
</tr>
</tbody>
</table>

nd: not demonstrated
a) General or universal measures

There are many possible non-pharmacological interventions that might decrease the number of osteoporotic fractures, but not all have been subjected to definite assessment.

Strategies with observational data or trials with surrogate end-points include:

- provision of a diet which maintains normal body weight throughout life and provides a total elemental calcium intake (from dietary and supplemental sources) of some 1000 mg/day from late childhood to midlife; and 1500 mg after age 65 years;
- encouragement of a physically active lifestyle;
- avoidance of smoking and of high alcohol intake;
- promotion of vitamin D supplementation with 600-800 IU of vitamin D per day and/or regular time spent outdoor in the elderly;
- fall prevention programs in the elderly and use of hip-protectors in those at very high risk of falls.

b) Pharmacological interventions

The aim of osteoporosis management is to reduce the incidence of both vertebral and hip fractures. Consistent anti-fracture efficacy is demonstrated in postmenopausal women with established osteoporosis for:

- Radiographic and clinical vertebral fractures with Alendronate, Risedronate and Raloxifene [115-119].
- Clinical non-spine fracture with Alendronate and Risedronate [115-118].
- Hip fractures in community-dwelling women with Alendronate and Risedronate [115, 120].
- Post-hoc analyses demonstrated the efficacy of bisphosphonates in the prevention of morphometric vertebral fractures in postmenopausal women treated with corticosteroid-induced bone loss, see below [121-123].
- Data on anti-fracture efficacy in men is very scarce [124-125].
- There is no data on the use of antiresorptive therapies in normally cycling premenopausal women, since use of such therapy in this group of women is unwarranted.

As to whether efficacy on fracture risk is demonstrated with bisphosphonates in postmenopausal women with unknown or low bone density has been answered in two studies. In the osteopenic arm of the FIT study [126], and in the elderly arm of the HIP study [120] there was no evidence of anti-fracture efficacy in non-osteoporotic women (T-score higher than –2.5). In studies with both Alendronate and Risedronate, BMD increased to the same extent in osteopenic as well as in osteoporotic women, but a significant decrease in fractures could be demonstrated only in osteoporotic women.

There is, albeit less abundant, evidence-based data for anti-fracture efficacy of intranasal CT and Etidronate in postmenopausal women [127-130]. Hormone replacement therapy was supported with strong evidence from the Women’s Health Initiative as an efficient mean to prevent hip fracture. However, the increased risk of breast cancer and cardiovascular mortality may offset the benefits observed on bone [131].

Anti-fracture efficacy of Ca/D has been demonstrated for spine, non-vertebral and hip fractures, only in nursing homes and in elderly individuals with low intakes of these nutrients at baseline [132-133]. However, in most randomized controlled trials over the last decade, pharmacological agents other than Ca and Vitamin D provide benefits beyond those of calcium and vitamin D, as Ca/D have been the treatment strategy in the “placebo” arm of most of these trials.

A direct comparison of the relative anti-fracture efficacy of the various osteoporosis therapies is not possible. However, the overwhelming evidence for anti-fracture efficacy is from studies using second-third generation bisphosphonates such as Alendronate and Risedronate, where over 15,000 patients have been enrolled in their respective randomized controlled trials.

Four randomized controlled trials have demonstrated the efficacy of bisphosphonates in the maintenance of bone mass in patients on chronic corticosteroid-therapy whether used in a primary prevention mode, (that is when bisphosphonate therapy is instituted at the start of steroid therapy), for Etidronate, and Risedronate [121, 123] or in secondary prevention mode, (that is when bisphosphonate therapy is instituted after patients have been on chronic steroid treatment), for Alendronate and Risedronate [122, 134]. Post-hoc analyses in these studies also demonstrated the efficacy (or trend for efficacy) of Etidronate, Risedronate and Alendronate in the prevention of morphometric vertebral fracture in the subgroup of postmenopausal women only [121-123].

c) Treatment strategies guidelines published to date

Since the early nineties, and with the increasing evidence for a relatively rapid rate of treatment onset and offset for these interventions, there has been a move away from long-term preventive strategies towards the use of shorter-term therapy in high risk individuals. In addition, pharmacological interventions are expensive and should, therefore, be targeted to those at highest risk of fracture in order to be most cost-effective. Treatment guidelines are uniformly anchored to-date around DEXA-based BMD–T-scores.

Universal measures are recommended in all of the population, especially in women with osteopenia or osteoporosis, as they are cost-effective and safe. Further-
more, most of the guidelines published to-date favor pharmacologic intervention in high risk individuals as defined with T-score < – 2.5 or a T-score < – 2 in the presence of additional independent risk factors for fracture [27, 32, 35]. These would include high on the list prevalent fracture at entry and glucocorticoid use. Indeed, the number needed to treat to prevent a vertebral fracture in older postmenopausal women with a low T-score at entry and prevalent fractures varies between 9 and 20 depending on the study [115, 117-119, 131, 135]. Similar analyses conducted in older postmenopausal women with a BMD T-score at entry of less than 2.5 but without fractures, is calculated at 35 for Alendronate and 45 for Raloxifene [115, 119]. In contrast, subgroup analyses of the FITtrial revealed that the number needed to treat to prevent a vertebral fracture, even in older postmenopausal women, increases from 35 if the T-score at study entry is < – 2.5, to 59 if the entry T-score is between – 2 and – 2.5, and is as high as 363 for older postmenopausal women with entry T-score between – 1.6 and – 2 [115].

Despite increasing awareness of people as well as physicians about osteoporosis and its related complications, a high percentage of people with osteoporotic fractures remain untreated [98, 136]. This paradox between scientific data and current clinical practice is common worldwide [136], in particular in our country where, as shown in a recent study, no more than 5% of people over 50 with a fracture were receiving anti-resorptive treatments [98].

d) In conclusion

The only patients in whom fracture prevention with pharmacological intervention has been proven are those at high risk of fracture : elderly postmenopausal women with preexisting fracture, or with BMD T-score lower than – 2.5, or postmenopausal women on chronic glucocorticoid therapy, albeit with more limited evidence. Treating young postmenopausal women who do not have osteoporosis for several years with anti-resorptive therapy preserves bone density but does not seem to be associated with reduction in spine or hip fractures. Therefore, the timing of the institution of pharmacological intervention in that subgroup after menopause remains to be determined.

Treatment of acute vertebral fracture

Treatment of acute and chronic pain related to vertebral fractures depends on specific measures and not on anti-osteoporotic drugs. These measures include painkillers, NSAIDs, bed rest, back support and soft massages as well as mild exercises for subacute and chronic pain. Calcitonin also has additional analgesic effects. Verteboplasty, that is injection of intravertebral metacylate, can be helpful to alleviate morbidity from vertebral fractures in case of prolonged pain or refractory conditions. It should not be routinely used as its safety and long-term effects are unknown [137].

RECOMMENDATIONS
FOR WHO AND WHEN TO TREAT

UNIVERSAL MEASURES are recommended independently from BMD measurement
• Maintain a physically active lifestyle with adequate exposure to sunlight.
• Avoid smoking and high alcohol intakes.
• Maintain a total dietary calcium intake around 1.5 gm of elemental calcium in postmenopausal estrogen deficient women or men > 65 years, as well as vitamin D intake of 600 to 800 IU/day, even under our latitudes. Provide calcium and vitamin D supplementation in the elderly.
• Avoid a low weight < 60 kg in men or 50 kg in women or a low Body Mass Index BMI < 20 kg/m².
• The prevention of osteoporosis begins with optimal bone mass acquisition during growth. Factors hindering bone mass acquisition, such as malnutrition, should be considered, identified, and addressed during childhood.
• Address known factors that stimulate bone resorption or inhibit bone formation, including hypogonadism, primary hyperparathyroidism, hyperthyroidism and hypercortisolism.
• Develop fall prevention awareness and programs in the elderly. Hip protection and/or soft floor covering in elderly environment.

PHARMACOLOGICAL INTERVENTION is warranted in high-risk individuals. BMD assessment is pivotal in clinical decision-making regarding pharmacological interventions.
Specifically it is definitely indicated in postmenopausal women with:
• BMD T-score < – 2.5.
• Prevalent fragility fractures when further documented with low BMD.
• On chronic corticosteroid therapy with BMD T-score < – 1.5.

No clear evidence is available to demonstrate the efficacy of pharmacological intervention in postmenopausal women with – 2.5 < T-score < – 1. No treatment (in addition to universal measures) is indicated if BMD T-score > – 1.
In premenopausal women
All known treatments were studied in postmenopausal women. Their efficacy in premenopausal women is unknown. Thus, in the absence of any established treatment for normally cycling premenopausal women with low bone density, such patients should be referred to specialized centers for investigation of possible underlying causes and advice on further management. Treatment should not be started in such patients before appropriate investigations and diagnoses are achieved.

In men
Given the few number of studies done in men osteoporosis, no definite recommendation other than universal measures can be given for men. These universal measures as outlined above include reversal of conditions associated with bone loss. Preliminary data from one trial only suggest treatment efficacy of high risk individuals with Alendronate.

Treatment is probably indicated in men:
- with prevalent fragility fractures when further documented with low BMD
- > 70 years and BMD T-score < -2.5
- on chronic (> 3 months) corticosteroid therapy and a BMD T-score < -1.5.

It is less clearly indicated in men:
- with -1 < T-score < -2.5 in the presence of risk factors
- < 70 years and with a T-score < -2.5

The above guidelines, were endorsed by the five major Lebanese scientific societies, the Lebanese Society of Endocrinology, the Lebanese Society of Obstetrics and Gynecology, the Lebanese Society of Orthopedics, the Lebanese Society of Radiology, and by the Eastern Mediterranean Regional Office of the World Health Organization. They are meant to provide a structural framework to be used by the physician treating the patient at risk for or with osteoporosis. They are certainly not meant 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.

ACKNOWLEDGEMENTS

The authors would like to thank Mrs Michele Valligny for her tireless efforts in coordinating the editing, formatting and printing of this document for the Lebanese Guidelines on Osteoporosis Assessment and Treatment.

REFERENCES


90. El-Desouki M. Bone mineral density of the spine and femur in the normal Lebanese population. Lebanese Medical Journal 2002 • Volume 50 (3) 103.


The Middle East Densitometry Workshop

April 20, 2002
Gefinor Rotana Hotel
Beirut, Lebanon

Who to test?
What measures to use?
When to treat?

In collaboration with:
The Lebanese Society of Endocrinology
The Lebanese Society of Orthopedics
The Lebanese Society of Radiology
The Lebanese Society of Rheumatology
WHO Eastern Mediterranean Branch
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Professor of Medicine
St Joseph University, Beirut, Lebanon

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Associate Professor of Medicine
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Associate Professor of Medicine
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Non-Communicable Diseases
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Director Oregon Osteoporosis Center
Professor of Medicine
Portland Medical Center
Portland, Oregon, USA
Middle East Densitometry Workshop  
April 20, 2002

- Who to test?  
- What measures to use?  
- When to treat?

## Session I

**Chairperson**  
Abdel Fattah Masri, MD.  
President Lebanese Society of Rheumatology

**Welcome Introduction**  
15 min

**BMD-fracture relationship: what is the evidence?**  
An insight from geographic variations in BMD and fracture epidemiology  
Michael McClung, MD.  
45min (10min Q/A)

**BMD in the Middle East:**  
Implications for fracture risk assessment  
Ghada El Hajj Fuleihan, MD, MPH.  
45min (10min Q/A)

COFFEE BREAK  
40min

## Session II

**Chairperson**  
Naji Atallah, MD.  
Treasurer Lebanese Society of Radiology

**Indication for BMD testing:**  
Current practice in the Western world  
Rafic Baddoura, MD, MPH.  
35min (10min Q/A)

**BMD testing in Lebanon**  
Rafic Baddoura, MD, MPH.  
35min (10min Q/A)

LUNCH BREAK  
90min
Session III  15:00-16:45

Chairperson
Sami Azar, MD.
President-Elect Lebanese Society of Endocrinology

Intervention to prevent/treat osteoporosis:
Review of current guidelines (NOF, IOF, AACE, ISCD,...)
Michael McClung, MD.  35min (10min Q/A)

Importance of QA in BMD testing
Hassane Awada, MD.
Ghada El Hajj Fuleihan, MD, MPH.  20min (10min Q/A)

WHO Middle East
Agenda for BMD testing policy
Oussama Khatib, MD, PhD.  20min (10min Q/A)

COFFEE BREAK  15min

Session IV  17:00-18:30

Chairperson
Habib Latiri, MD.
WHO Representative

Workshop/consensus on BMD  17:00-18:00
Participation of
The Lebanese Society of Endocrinology
The Lebanese Society of Orthopedics
The Lebanese Society of Radiology
The Lebanese Society of Rheumatology
WHO Middle East

Wrap-up/closing  18:00-18:30
**BMD-Fracture Relationship: What is the Evidence?**

An Insight from Geographic Variations in BMD and Fracture Epidemiology

**Michael McClung, MD.**

Low bone mineral density (BMD) is a risk factor for fractures of the spine and hip. However, other major determinants of fracture risk include age, previous fractures, skeletal geometry, body size and falls. The interplay of these various risk factors differs markedly between spine and hip fractures and among different populations of people.

Spine fractures are the quintessential osteoporotic (low BMD) fractures. Across different populations of older women, the relationship between absolute BMD values and vertebral fracture risk appears to be very similar. (Data regarding these relationships in men are inadequate for comparisons to be made.) This observation suggests that a common database, as opposed to racial, regional or national databases, should be used to calculate T-scores, to estimate fracture risk and to determine thresholds for treatment.

In contrast, substantial differences are observed between BMD and hip fracture risk among different populations of women. Asian women have lower BMD than do Caucasian women but have variably lower hip fracture rates. The hip fracture incidence among African American women is lower than predicted by racial differences in BMD. This indicates that BMD alone is inadequate to predict the risk of hip fracture across populations, and that other risk factors (especially hip geometry, body size and physical fitness) must be included, along with BMD, in the clinical estimate of hip fracture risk. It is probable that the specific contribution of low BMD to hip fracture risk is similar among various populations, but that this risk is modified to very different extents by the other determinants of risk. This means that BMD - no matter how it is expressed or how T-scores are calculated - will never adequately account for population differences in hip fracture risk. Rather than develop different racial or national BMD databases upon which T-scores are based, population-specific information and data about the non-BMD risk factors must be gathered. Models combining BMD with these other risk factors need to be developed to estimate hip fracture risk. We will then move from the use of T-scores alone toward more appropriate estimates of absolute fracture risk as thresholds for patient evaluation and especially for pharmacological intervention.
Osteoporosis in the Middle East

Ghada El-Hajj Fuleihan, MD, MPH.

Osteoporosis is a major public health problem worldwide to-date. Although it is projected that the magnitude of the problem may be even larger in the developing countries including those in the Middle East, such projection is however based on several assumptions. This paper will evaluate the above conclusion. In order to achieve that the following will be reviewed:

1. BMD in various groups/populations from the Middle East: Cross-sectional data.
2. Prevalence of osteopenia and osteoporosis in our populations using the WHO operational definition for osteoporosis
3. Fracture prevalence data
4. BMD-fracture relationship: BMD in hip fracture patients

Peak BMD is a major determinant of BMD and therefore fractures in later life. Several studies have demonstrated that young healthy subjects from the region have a BMD that is 3-10% lower than the published Western norms, depending on the study, gender, skeletal site and type of densitometer. Body size differences may account for some of these differences. These decrements in BMD seem to be sustained at older ages, potentially inferring a higher fracture risk in the elderly. Using the WHO operational definition of osteopenia/osteoporosis, the prevalence of osteopenia ranges between 37-66% at the lumbar spine and 47-54% at the femoral neck in female subjects after age 50 years depending on the study; whereas for osteoporosis these numbers are 28-33% for the spine and 6-18% for the hip, respectively. The overall prevalence of spontaneous clinical fractures in women after age 50 years, is estimated to vary between 11-17%; a study of morphometric vertebral fractures estimates a prevalence of 20-22% after age 60 years. Finally, mean BMD in hip fractures subjects is comparable if not identical to mean BMD in hip fracture patients from the US/Europe, however they seem to occur at a slightly younger age. Limited data on hip fracture incidence also suggests that it is comparable to that from the Western world.

In conclusion, BMD in subjects from the region is slightly lower than that of US/European counterparts when matched for age and gender. Although fracture estimates are comparable, this seems to be possibly explained by their occurrence at a younger age. Therefore, the burden of osteoporosis in the Middle East is comparable to the Western world, and can only be expected to increase based on the steady increase in our aging population.
Indication for BMD testing: 
Rationale from the Western World

Rafic Baddoura, MD, MPH.

Bone densitometry is one of the most powerful clinical tools in the diagnostic evaluation of the patient with or at high risk for osteoporosis, thus allowing the appropriate choice of therapeutic strategies. As early as 1989, the National Osteoporosis Foundation Scientific Advisory Board has put forth its first set of Clinical Indications for BMD measurements. This was the result of early observations that demonstrated the following: BMD predicts fractures, BMD can be measured safely and accurately, clinical risk factors alone do not accurately predict BMD, information about BMD influences choice of therapy, treatment of osteoporosis affects fracture outcomes, and therefore BMD measurements should lead to fracture reduction. Since then, abundant information has come through confirming these points as summarized throughout this meeting. Furthermore, meta-analyses of several large randomized controlled trials have shown since then that the further the BMD increments, the lower is the risk of fractures. In this paper the currently published western guidelines for densitometry testing are reviewed.

The WHO: recommends BMD had in patients with radiographic evidence of osteopenia or vertebral deformity; loss of height or thoracic kyphosis; previous low trauma fracture; and the presence of risk factors such as prolonged steroid therapy, hypogonadism in either sex, hyperthyroidism or hyperparathyroidism, low BMI < 19 kg/m², low calcium intake.

The NOF: recommends BMD to be measured in the following groups of women: women< age 65 with one or more risk factors (family history, personal history of fractures, smoking, weight<57 kgs); all women > 65 years; postmenopausal women with fractures; women considering therapy if BMD influences the decision; women on HRT for prolonged periods.

The EFO: now IOF: recommends BMD measurement in patients with radiographic evidence of osteopenia or deformity, previous fragility fracture, significant height loss or kyphosis, presence of strong risk factors, and monitoring therapy.

The ISCD: recently came out with its recommendations as follow: all women >65 years, all men >70 years, anyone with a fragility fracture, anyone with a disease or condition associated with osteoporosis, anyone considering therapy for osteoporosis based on BMD, anyone on prolonged HRT therapy.

The AACE: in 1996 adopted the older NOF guidelines from 1989 and gave its revised recommendations in 2001. BMD is recommended in peri- or postmenopausal women, in women with x-ray findings of osteoporosis, in women on long term glucocorticoid therapy, in peri- or postmenopausal women with hyperparathyroidism. In women on osteoporosis treatment for monitoring response to therapy.

The principle behind all of the above commonly shared recommendations is that of a cost-effective case-finding strategy using risk factors that predict low BMD in order to identify the high risk individuals in whom identification and treatment will result in a significant reduction in future fractures, whereas the role of prevention in the younger perimenopausal women is not established.

1. Genant et al. Osteoporos Int 1999; 10:259-
3. Kanis et al. Osteoporos Int 1996; 6:256-
4. ISCD Bone Densitometry Forum 2001; JCD in press
INTRODUCTION: Bone mineral density (BMD) measurement using Dual Energy X-ray Absorptiometry (DEXA) is the core of osteoporosis diagnosis and management (1). Disease definition is based on DEXA-based BMD assessment as well as decision to treat (2). However, technology costs and access are significant barriers to screening policies for osteoporosis and justify the efforts to identify at high risk populations to achieve the cost-effective case identification (3). Published clinical decision rules addressing this issue have to be challenged methodologically before gaining large adherence from health professionals and authorities (4).

OBJECTIVES: The aims are to characterize demographically and clinically referred population for BMD testing and to evaluate BMD diagnostic performance by international standards.

MATERIAL AND METHOD: Our sample is driven from referred population for BMD testing in three hospital-based osteoporosis units during fall 2001. Subjects were submitted a questionnaire collecting information about age, gender and known risk factors for osteoporosis. Using W.H.O. definition of osteoporosis we evaluated the diagnostic performance of clinical variables for case identification and compared the actual performance with propose theoretical models.

RESULTS: Sample size is 722 with 95.0% females. Mean (SD) age is 58.5 (11.0) for females and 56.5 (16.9) for males. The overall proportion of individuals >=65 years is 31.2% in females and 38.9% in males. Proportion of post-menopausal women is 83.4% (573/687 women) and mean (SD) age at menopause is 46.6 (5.6). Prevalence of common osteoporosis risk factors is as follows:

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low weight defined as less than 70kg</td>
<td>57.3%</td>
</tr>
<tr>
<td>Current smoking</td>
<td>34.6%</td>
</tr>
<tr>
<td>Early menopause defined as less than 45 years of age</td>
<td>24.7%</td>
</tr>
<tr>
<td>Personal history of fracture after a fall</td>
<td>21.3%</td>
</tr>
<tr>
<td>Family history of osteoporotic fracture in first-degree relatives</td>
<td>18.9%</td>
</tr>
<tr>
<td>Oral steroid therapy</td>
<td>10.9%</td>
</tr>
</tbody>
</table>

384 women are tested for diagnosis as compared to treatment evaluation among others and 306 (79.7%) were post-menopausal. Based on W.H.O definition, prevalence of osteoporosis in post-menopausal women is 37.6%, 25.5% and 17.7% using spine, radius and hip BMD values respectively. Using hip BMD for case definition, osteoporosis is significantly associated with all common risk factors. Corresponding sensitivity (Se) and specificity (Sp) are the following:

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Se</th>
<th>Sp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;=65 years</td>
<td>62.3</td>
<td>73.4</td>
</tr>
<tr>
<td>Low weight defined as less than 70kg</td>
<td>77.1</td>
<td>91.5</td>
</tr>
<tr>
<td>Current smoking</td>
<td>98.4</td>
<td>98.0</td>
</tr>
<tr>
<td>Early menopause defined as less than 45 years of age</td>
<td>50.8</td>
<td>89.1</td>
</tr>
<tr>
<td>No prior estrogen use</td>
<td>18.0</td>
<td>85.4</td>
</tr>
</tbody>
</table>

Using NOF guidelines, the Osteoporosis Risk Assessment Instrument and the weight criterion, percent of post-menopausal women at high risk of osteoporosis in our target population would be 47.7%, 60.5% and 56.5% respectively.

CONCLUSION: Subject selection for osteoporosis case identification using DEXA may be improved provided common risk factors are taken along with consensus guidelines.

Main issues to be discussed.
Who are those who benefit from DEXA bone density measurement?
What is our diagnostic performance using DEXA?
Where do we stand compared to NOF, IOF and literature recommendations?
The objective of managing patients with or at risk for osteoporosis is to prevent or minimize the occurrence of new fractures. We can identify patients at high fracture risk on the basis of their BMD, their history of previous fractures, their age and other important determinants of fracture risk. Therapies exist to preserve or even increase bone density and to reduce the incidence of both vertebral and hip fractures. The main challenge today for clinicians is to determine in which patients our new therapies are most appropriate.

Although our current anti-remodeling drugs prevent bone loss in men and postmenopausal women regardless of age or BMD, the only patients in whom fracture protection has been documented are those at high current risk of fracture - those with previous spine fractures or BMD values consistent with osteoporosis. The clinical utility and cost effectiveness of treating high-risk patients is clear. However, the rationale and need for treating women at lower risk is much less certain. Treating young postmenopausal women who do not have osteoporosis for up to 6 years with estrogen or bisphosphonates preserves bone density but is not associated with a reduction in spine or hip fractures. These data demonstrate that pharmacological therapy to prevent fractures in low-risk populations will require many years before fracture protection is afforded, and that the use of bone-specific agents to prevent osteoporosis is neither cost effective nor necessary.

Clinical guidelines for osteoporosis management in the United States have evolved over the past 4 years in recognition of the evidence from clinical trials that our therapeutic resources should be aimed at individuals with recognized risk factors for fracture rather than at preventing those risk factors. The various guidelines are consistent in recommending that women with fragility vertebral fractures be treated. The NOF guidelines of 1998 suggested treating all women with BMD T-scores < -2 and other women with T-scores of less than -1.5 and another risk factor. The AACE guidelines, published in 2000, proposed treating women with T-scores < -2.5 or lower and those with values < -1.5 and other risk factors. Both the NOF and ACCE guidelines suggest treating all women with a fragility fracture. Most recently, the guidelines of the North American Menopause Society (Menopause, March 2002), recommend treating women with T-scores of -2.5 or lower and those with other risk factors and low BMD (T-score lower than -2). The NAMS guidelines do not suggest treating all women with non-spine fragility fractures but rather that these women undergo evaluation including BMD testing, and that those non-spine fractures be treated as a risk factor to modify the BMD threshold at which treatment be considered. These most recent US guidelines have moved toward the recommendations of the European osteoporosis community that has always had a more conservative approach toward treatment, restricting pharmacological therapy to patients known to have osteoporosis.

We now define osteoporosis as a risk factor for fracture - not as a patient who has had a fracture. Consequently, treating patients to prevent osteoporosis would be analogous to treating patients with lipid-lowering drugs to prevent hyperlipidemia - a strategy that is not accepted except in very high-risk patients.

Guidelines for osteoporosis management are moving toward risk-based intervention thresholds. This is similar to the recent guidelines for lipid-lowering therapy that recommend therapy at different levels of serum cholesterol depending on the individual's other risk factors. Only is this way will our treatments be used most effectively and efficiently to reduce the burden of osteoporotic fractures.
Importance of Quality Assurance (QA) in BMD Testing

Hassane Awada, MD.
Ghada El-Hajj Fuleihan, MD, MPH.

B one densitometry technology has undergone fast changes over the last decade, with dual energy X-ray absorptiometry as the gold standard measure. In the clinical setting, densitometry is used in the following situations:
1. The diagnostic evaluation of the patient with or at risk for osteoporosis
2. In the monitoring of such patients

D ensitometry in the diagnostic evaluation of a patient at risk or with osteoporosis.
A key characteristic to be considered in the choice of a study in the management of osteoporosis is its accuracy: how close is the measurement to what it is supposed to measure, (ie how close is measured BMC to actual BMC determined by ashing the bone) and how well does BMD predict fractures? Accuracy error has been measured on all devices available and is better for DXA than it is for QCT, ranging between 4-10% depending on the skeletal site. Because QUS does not really measure BMC, it is not possible to define the accuracy of that technique. QA data from phantom measurements allows detection of machine drifts or shifts that affect accuracy. As to fracture prediction, DXA is undoubtedly the most validated measure to-date. Indeed, BMD as measured by DXA predicts failure load, BMD is one of the strongest predictors of fractures, and as BMD increases fracture risk decreases. For those reasons the WHO working group on osteoporosis proposed cut-offs based on DXA derived BMD T-scores to diagnose osteoporosis. These T-score cut-offs do not apply to other densitometry technologies. However in order for DXA to fulfill its function, strict adherence to manufacturer's guidelines in scan acquisition and analysis are of utmost importance. Furthermore, adherence to FDA approved densitometers will in great part insure excellent accuracy.

D ensitometry in the monitoring of the patient at risk for or with osteoporosis
P recision (reproducibility) is the most important characteristic to consider in the choice of a technique to monitor a patient's progress. Precision of a measure reflects its ability to reproduce the same result on repeat (duplicate) measurements, in the event of absence of a real biological change, provided the test is conducted in an identical situation. Indeed, any changes exceeding the precision error by a certain magnitude, otherwise called least significant change (LSC, see below) are likely to reflect true biological changes. Sources of precision error include the machine itself, but more importantly changes in technicians, inconsistencies in patient positioning, choice of ROI, scan mode, and scan analysis, as well as artifacts and some biological variations. The precision of the instrument should be assessed continuously in each center, and derived from situations identical to the clinical situation in which the test is performed: on osteopenic/or osteoporotic patients ideally measured few days apart. It should not be based on phantom measurements. This allows the assessment of significance of changes in an individual over time.

T he 95% CI for the LSC=2.77X precision error =2.77X RMS SD.
T ime interval at which a LSC can be detected = LSC/expected change/year.

S trict adherence to quality assurance measures is critical to the sound use of densitometry. Failure to do so will undermine the validity of the densitometry study and therefore the quality of clinical care delivered.
Agenda for BMD Testing Policy

Dr Oussama Khatib, MD-PhD.

With the advent of quantitative techniques to measure bone mineral content a little more than a decade ago, our ability to quantify changes in bone mass and assess osteoporosis has markedly improved. The relation between bone density and fracture is important, and an estimate of bone mineral density can provide an effective assessment of fracture risk. It is thus possible to choose a value for bone mineral density that defines the presence of osteoporosis. According to World Health Organization (WHO) criteria, two diagnostic thresholds of bone density for Caucasian women, which are based on distribution of skeletal mass in young healthy individuals.

- **Normal**: A value of bone mineral within 1 SD of young adult reference mean (t-score > 1.0) is considered normal.
- **Low** bone mass (Osteopenia): A value of bone mineral more than 1SD below the young adult mean but less than 2.5 SD below this value (-1.0 > t-score > -2.5). Low bone mass is visualized as a risk factor for fracture.
- **The** term osteoporosis is used to designate bone mass value more than 2.5 standard deviations (SD) below the young adult mean (t-score < -2.5).
- **Severe** (established) osteoporosis: A value for bone mineral 2.5 SD or more below the young adult in the presence of one or more fragility fractures.

Suitable diagnostic cut-off values for non-Caucasian women and for men are less secure. It has been suggested that a similar absolute value for bone mineral density to that used in women can be taken as a cut-off point for the diagnosis of osteoporosis in men, that is, a value 2.5 SD below the average for adult pre-menopausal women. It is necessary to be recognized that cut-off values are arbitrary and may differ according to sites measured, race, and type of equipment. Because of this difficulty in accurate measurement and standardization between instruments and sites, controversy still exists among experts regarding the use of the above-mentioned criterion in non-DXA devices. Similarly, it is to be stressed that the use of locally generated databases is not validated and should be avoided.
Satellite Symposium
Monroe Hotel 7:00 - 9pm
April 19, 2002

Osteoporosis:
from the Evidence to the Clinical Practice

Case study 1: 7:30-8:10 pm
Post-menopausal osteoporosis
Ghada El-Hajj Fuleihan, MD, MPH.

Case study 2: 8:10-8:30 pm
Glucocorticoid-induced bone loss
Michael McClung, MD.

Case study 3: 8:30-9:00 pm
Osteoporosis in men
Michael McClung, MD.

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