Executive Summary- Lebanese FRAX-Based Osteoporosis Guidelines 2013*

Marlene Chakhtoura, MD, Rafic Baddoura, MD, MPH and Ghada El-Hajj Fuleihan, MD, MPH.

National Task Force Members**

Ghada El-Hajj Fuleihan, MD, MPH, Rafic Baddoura, MD, MPH ,Asma Arabi, MD, MSc ,George Halaby, MD, Imad Uthman, MD, Jad Okais, MD, Ibrahim Salti, MD, PhD, Muheiddine Seoud, MD, Asaad Taha, MD, Naji Attallah, MD.

MOH Representatives to National Task Force

Abdel Rahman El Hout, MD, and Assaad Khoury, MD.

WHO Representative National Task Force

Alissar Rady, MD, MPH.

International Expert Advisory Panel

John A Kanis, MD, FRCP
Professor Emeritus
WHO Collaborating center for Metabolic Bone disorders
University of Sheffield, United Kingdom.

Michael McClung, MD, FACE, FACP
Associate Professor of Medicine
Founding Director
Oregon Osteoporosis Center, Portland

William Leslie, MD, FRCPC, MSc
Professor of Medicine and Radiology
University of Manitoba, Canada

Angela Cheung, MD, PhD, FRCP(C), CCD
Associate Professor in the Departments of Medicine, Health Policy Management and Evaluation, Public Health Sciences
Founding Director Centre of Excellence in Skeletal Health Assessment
University Health Network, Toronto

Address queries and correspondence to:
Ghada El-Hajj Fuleihan, MD, MPH
Professor of Medicine
Director Calcium Metabolism and Osteoporosis Program
WHO Collaborating Center for Metabolic Bone Disorders
American University of Beirut Medical Center
Beirut, Lebanon
Email: gf01@aub.edu.lb

* Presented at the Fourth Annual OSTEOS meeting held December 2-3, 2012.

**The Lebanese National Task Force for Osteoporosis and Metabolic Bone Disorders was established by Ministerial decree, by the Minister of Public Health Dr Mohammad Khalifeh, in March 2010. The charge of the Task Force is to establish a national program for osteoporosis, develop and disseminate national guidelines on osteoporosis and hypovitaminosis D, develop quality assurance protocols for bone mineral density (BMD) measurements and vitamin D assays, generate osteoporosis assessment and treatment protocols using national guidelines and assess disease burden using measures of morbidity and mortality.

Acknowledgements

This work was in part supported by grants from the Medical Resource Plan at the American University of Beirut and the Lebanese Council for National Scientific Research (CNRS).

The authors also wish to thank the international panel led by Professor John Kanis, and FRAX and osteoporosis guidelines experts Drs Michael McClung, William Leslie and Angela Cheung for their time, and insightful contributions, and the FRAX development team who helped develop FRAX Lebanon 2009 and its update January 2012, Drs Eugene McCloskey, Sheffield WHO Collaborating Center for Metabolic Bone Disorders, Sheffield, UK, and Helena Johansson, Department of Medical Biochemistry and Cell Biology, University of Gothenberg, Gothenberg, Sweden.

The authors thank the following presidents and constituents of the Lebanese societies for their time and input in reviewing and endorsing the current guidelines: Faycal El-Kak, MD, MSc (Lebanese Society for Osteoporosis and Metabolic Bone Disorders, OSTEOS); Charles Saab, MD (Lebanese Society of Endocrinology); Fayez Bitar, MD (Lebanese Society of Obstetrics and Gynecology); Assaad Taha, MD (Lebanese Association of Orthopedic Surgeons); Assaad Mhanna, MD, and Rami Chemali, MD (Lebanese Society of Radiology); Georges Merheb, MD (Lebanese Society of Rheumatology); Mona Osman, MD (Lebanese Society of Family Medicine); Zahi Helou, MD (Lebanese Society of Internal Medicine); Hasan Zeidan ,MD and Joseph Kahaleh , MD (Lebanese Society of General Practitioners). The authors wish to acknowledge Walid Ammar, MD, PhD, General Director Lebanese Ministry of Health; Mouin Hamzeh, PhD, General Director Lebanese National Council for Scientific Research for their support. They also thank Mr. Ali Hammoudi, for his efforts in developing Figures and Tables, formatting, and finalizing this document.

Abstract

FRAX was launched on-line in 2008 and FRAX Lebanon in September 2009. This update, the first taking advantage of FRAX Lebanon, revisited the initial set of national osteoporosis guidelines developed in 2002 and updated in 2007. This executive summary provides the rationale for the development of the Second Update for the Lebanese Guidelines for Osteoporosis Assessment and Treatment, and their final recommendations, otherwise known as the FRAX Based Lebanese Guidelines for Osteoporosis.

These guidelines retain four of the original definite indications on "Who to Test": presence of a fragility fracture, age older $\geq$ 65 years, bone demineralization by x-ray, chronic steroid therapy for a duration exceeding 3-6 months at doses exceeding the equivalent of a prednisone dose of 7.5 mg daily. Newly added is the indication of use of an aromatase inhibitor or chronic androgen deprivation therapy. For all other conditions, the recommendations are to run a fracture risk assessment (FRAX calculation) based on clinical risk factors, and to request a Bone Mineral Density (BMD) with DXA if the 10-year fracture risk estimate for overall fractures approaches 10%. For the determination of an intervention threshold, both a fixed and an age-dependent intervention threshold model were considered, and a hybrid model finally adopted. The hybrid model avoids treating a large proportion of young individuals at low risk for fractures, if one followed the age-dependent model adopted by the UK, and also avoids treating a very large proportion of older subjects, if one followed the fixed threshold model adopted by the US and Canada. Indications for “Who to Treat" retain the original indication of a history of fragility fracture, but with specification for the skeletal site, at the spine or hip, or the presence of $\geq$ 2 other fragility fractures. For subjects who have not experienced any fragility fracture, the intervention threshold is set at $\geq$ 10% for the 10-year overall risk of fractures for individuals up to age 70 years. For individuals above age 70 years, the threshold increases with age: 15% at 75 years, 21% at 80 years, 27% at 85 years, and 30% at 90 years. A BMD T-score $\leq$ -2.5, in the absence of additional risk factors, is no longer an indication for treatment by itself due to the very low estimated 10-year risk for fractures in such clinical scenarios (the 10-year overall risk of fractures is less than 10%, both in women up to age 70 years, and men up to age 90 years). These new guidelines, based on a case finding strategy incorporate important risk factors and take advantage of national hip fracture data to identify and treat high risk Lebanese individuals. They provide a major advance in the management of osteoporosis in Lebanon.

Lebanese FRAX based guidelines 2013- Executive Summary

Osteoporosis is a common disease. In women over 45 years of age osteoporosis accounts for more days spent in hospital than many other diseases, including diabetes, myocardial infarction and breast cancer. One in two women age 50 years will experience a vertebral fracture in their remaining lifetimes, and one in three women will experience a hip fracture – both of which result in substantial morbidity and mortality. Ten percent of hip fracture patients ultimately sustain a hip fracture affecting the contralateral hip, 20-40% die within the first year, and 30-50% lose functional independence. Many people with osteoporosis in the region, and indeed worldwide, lack access to care, and for those who do receive treatment, it is often fragmented and sub-optimal.

An individual's risk of developing chronic diseases, cancer and cardiovascular disorders, is dependent on disease-specific lifestyle and clinical risk factors. Risk prediction calculators, such as the PROCAM score, Reynolds' score, and the Gail model, incorporate the most important disease specific risk factors for cardiovascular diseases and breast cancer, and have played a central role in the identification and management of high risk individuals. Osteoporosis is no exception to this paradigm.

The WHO fracture risk assessment tool , FRAX®, is a computer-based algorithm introduced in 2008 (http://www.shef.ac.uk/FRAX) , developed to assist primary care providers in assessing a patient's fracture risk, identifying those at high risk, and thus facilitating decision making regarding pharmacologic therapies. It calculates the 10-year probability of a major fracture (hip, clinical spine, humerus or distal forearm) and, individually, the 10-year probability of hip fracture (1). Fracture probability is computed taking both the risk of fracture and the risk of death into account. The algorithm had been constructed using information derived from 9 population-based cohorts from around the world, including centers from North America, Europe, Asia and Australia, and was subsequently validated in 11 independent cohorts with a similar broad geographic distribution with in excess of 1 million individuals. Fracture risk can be calculated exclusively from clinical risk factors, or can be further refined by the inclusion of femoral neck Bone Mineral Density (BMD). The use of BMD in conjunction with clinical risk factors improves sensitivity for fracture prediction without adversely affecting specificity. Risk factors include age, body mass index and dichotomized risk factors comprising prior fragility fracture, parental history of hip fracture, current tobacco smoking, high alcohol consumption,

ever use of long-term oral glucocorticoids, rheumatoid arthritis, and other causes of secondary osteoporosis. Secondary causes of osteoporosis are type I (insulin dependent) diabetes mellitus, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (<45 years), chronic malnutrition, malabsorption and chronic liver disease.

Since its launch in 2008, FRAX® has resulted in a major paradigm shift in the assessment of the patient at risk for osteoporosis. It not only permits the use of clinical risk factors to decide who should have a BMD assessment, but also facilitates a case finding strategy by estimating absolute rather than relative fracture risk, and thus identifies high risk patients who should receive pharmacologic therapy. FRAX® takes into account population-specific life expectancy as well as hip fracture incidence rates, and has thus become the cornerstone for the development of national care pathway models, and encouraged many national and international organizations to revisit their previous osteoporosis guidelines based on information derived from FRAX (2-5).

FRAX has some limitations (2), such as not taking into account dose and duration impact of some risk factors on fracture risk. These include amount of smoking and alcohol consumption, steroid dose, number of prior fragility fractures, all of which are considered dichotomous in FRAX. It also does not take spine BMD into account. However, quantitative adjustments for some of these have been developed. For steroid use: at medium doses (prednisolone 2.5-7.5 mg daily or equivalent), the unadjusted FRAX value can be used, for low dose exposure (<2.5 mg daily of prednisolone or equivalent), the probability of a major fracture can be decreased by about 20% depending on age, and for high doses (>7.5 mg daily), probabilities can be upward revised by about 15% (6). FRAX underestimates major fracture risk when lumbar spine T-score is much lower than femoral neck T-score, and the FRAX derived estimate for a major fracture should be increased by one-tenth for each rounded T-score difference between the lumbar spine and femoral neck (7). Falls are not incorporated in FRAX model. In addition, FRAX is not applicable to young men and women with secondary osteoporosis. For full details, refer to a recent review (2). Notwithstanding these points, FRAX provides the most comprehensive, user friendly, population specific tool for fracture risk assessment to date, and is a major advance in osteoporosis care.

The advent of FRAX Lebanon, September 2009, has thus allowed a quantitative assessment of fracture risk in the Lebanese population, taking into consideration the impact of important risk factors. It has allowed, for the first time, objective assessment of the relevance of the original Lebanese guidelines, issued in 2002 (8) and updated in 2007 (9), re-evaluating them in their initial three categories: definite indications, less definite indications and no indications, regarding "Who to Test" and "Who to Treat ".

For on-line version of the 2002 and 2007 Lebanese Guidelines for Osteoporosis Assessment and Treatment please see below:

http://www.osteos.org.lb/admin/uploads/update-2007-pdf-foreword.pdf

http://www.iofbonehealth.org/sites/default/files/PDFs/National%20Guidelines/lebanese_guidelines.pdf

"Who To Test"

Recommendations for BMD testing have been issued by many organizations, including the National Osteoporosis Foundation (NOF), the International Society of Clinical Densitometry (ISCD), and Osteoporosis Canada. Their recommendations share many common indications and are in large part driven by older age ($\geq$ 65 years), the presence of fragility fractures, or of risk factors, medications, or medical illnesses associated with osteoporosis (see Appendix I). In contrast to the National Osteoporosis Guideline Group (NOGG) guidelines, neither the NOF nor the ISCD take advantage of the FRAX calculator.

In the 2002 Lebanese guidelines for Osteoporosis Assessment and Treatment, BMD testing was recommended to make decisions about pharmacological intervention, and these recommendations (except for presence of fragility fractures) were in large part driven by BMD results. The guidelines listed the following under definite indications for BMD testing: age 65 years in postmenopausal women as a major risk factor regardless of additional risk factors, as well as evidence of radiological demineralization, presence of vertebral deformity or fragility fracture, corticosteroid therapy for >3-6 months both in postmenopausal women and men, and the presence of hypogonadism in men. Other medical conditions or risk factors associated with bone loss were deemed as less definite indications.

The current FRAX-based update retained all indications that were listed under definite indications, with the exception of corticosteroid therapy, which along with less definite

indications was moved into a category guided by a FRAX calculation based on risk factors. This is somewhat akin to the updated American College of Rheumatologists (ACR) 2010 glucocorticoid guidelines (10). Subjects with a moderate overall 10-year risk for fracture based on risk factors (that is close to 10%) are recommended to have a BMD to further refine fracture risk. Therapy with aromatase inhibitors and androgen deprivation therapy was added. For a comparison of the 2002 and 2013 Lebanese guidelines for "Who to Test" see the summary Table below.

"When to Treat"

Several national organizations have revised their guidelines regarding osteoporosis therapies based on FRAX derived fracture risk estimates. They have either used a fixed intervention threshold based on a FRAX derived 10-year risk for a fragility fracture (e.g. NOF for USA and Osteoporosis Canada for Canada) or an age dependent variable threshold, such as developed in England (National Osteoporosis Guidelines Group, NOGG) and this model was adopted by other countries such as Switzerland (see Appendix II for details).

Definite indications, in the 2002 Lebanese guidelines, included the treatment of postmenopausal women and older men (>70 years) with a history of fragility fracture and low BMD, postmenopausal women and older men with either, a BMD T-score ≤-2.5, or on chronic glucocorticoid therapy, at doses exceeding 7.5 mg/day of prednisone equivalent, for more than 3-6 months.

In this FRAX based 2013 update, it was unanimously concurred by members of the national task force that treatment is definitely indicated in postmenopausal women and older men (≥ 50 years) with a history of one or more fragility fracture. The current update now also specifies the type/number of fragility fractures: one was to consider treatment in the presence of one classic osteoporotic fracture involving the spine (clinical or morphometric) or hip, but to require 2 or more fractures for other fragility fractures. This recommendation is identical to that in the Canadian guidelines (4) and aligned with the principle followed by the NOF and NOGG, with the exception that the US excludes fractures other than the spine and hip (11), whereas NOGG accepts all fragility fractures including a forearm fracture (12).

Conversely, the FRAX based guidelines now refute treating Lebanese subjects with a T-score ≤ -2.5 by itself, in the absence of additional risk factors, as a definite indication, both in men and women. Indeed, in Lebanese subjects, the 10-year overall risk for an osteoporotic fracture in

those with a BMD of -2.5 and no additional risk factors (see Figures 1 and 2) remains below 10% until women reach the age of 70 years and men the age of 90 years. This is explained by the fact that although the relative risk (RR) for fracture per Standard Deviation (SD) decrease in BMD is the same in Lebanese as other western populations (9), the absolute risk incurred is still low due to the low baseline incidence rate of hip fractures in the Lebanese population (13). Similarly, and for the same reasons, the absolute fracture risk incurred by other risk factors, such as intake of glucocorticoid therapy, or any other risk factor originally included under "less definite indications", would be lower in the Lebanese compared to subjects from western populations, and is again best estimated by calculating the FRAX derived risk of major fractures.

In conclusion, the only definite indication to treat retained from the original guidelines is the presence of a fragility fracture involving the spine or hip, or ≥ 2 fragility fractures for other fractures, both in postmenopausal women and older men (≥ 50 years). In all other instances, be it under previous definite or less definite indications, both in older men and women, one is to rely on the overall 10-year calculated FRAX estimate. However, even with this approach, one must still define the intervention threshold at which pharmacologic intervention would be indicated. The two major paradigms followed today are that of a fixed age-independent threshold, followed in the US by the NOF (11) and by Canada (4), or an age-dependent increasing threshold such as followed in the UK (12) and Switzerland (14).

In order to decide which paradigm to follow, both scenarios were examined to the Lebanese population and evaluated as follows.

Figure 1. 10-year fracture probability for major osteoporotic fracture (a) and for hip fracture (b) in Lebanese women with no risk factors with a BMI= 30kg/m² by age and T-score

a-

	T-score						
Age(y)	+1.0	0	-1.0	-2.0	-2.5	-3.0	-4.0
40	0.4	0.4	0.4	0.6	0.9	1.4	4.3
50	0.8	0.9	1.0	1.4	1.9	2.6	6.2
55	1.1	1.2	1.4	2.1	2.7	3.7	8.0
60	1.3	1.8	2.1	3.1	3.9	5.2	11
65	2.0	2.3	2.9	4.2	5.3	7.0	14
70	2.7	3.3	4.2	5.9	7.6	9.9	18
75	3.7	4.7	6.1	8.5	11	14	24
80	4.6	6.0	8.2	11	14	18	29
85	5.2	7.0	9.8	14	17	21	32
90	5.2	7.4	10	15	17	21	31

b-

	T-score						
Age(y)	+1.0	0	-1.0	-2.0	-2.5	-3.0	-4.0
40	0.0	0.0	0.0	0.2	0.4	0.8	3.8
50	0.0	0.0	0.1	0.3	0.6	1.2	4.5
55	0.0	0.0	0.1	0.5	0.9	1.6	5.4
60	0.0	0.1	0.2	0.7	1.2	2.1	6.7
65	0.0	0.1	0.3	1.0	1.7	2.9	8.2
70	0.1	0.2	0.6	1.5	2.5	4.1	11
75	0.2	0.5	1.1	2.5	4.0	6.1	14
80	0.5	1.0	2.0	4.1	5.9	8.7	18
85	1.0	1.9	3.5	6.4	8.5	12	21
90	2.2	3.6	5.8	9.1	11	14	22

Figure 2. 10-year fracture probability for major osteoporotic fracture (a) and for hip fracture (b) in Lebanese men with no risk factors with a BMI= 30kg/m² by age and T-score.

a-

	T-score						
Age(y)	+1.0	0	-1.0	-2.0	-2.5	-3.0	-4.0
40	0.3	0.4	0.5	0.7	1.1	1.7	5.4
50	0.6	0.7	0.9	1.4	2.0	2.9	7.4
55	0.8	0.9	1.2	2.0	2.6	3.8	8.9
60	1.1	1.3	1.7	2.6	3.4	4.7	9.8
65	1.3	1.5	2.0	3.2	4.1	5.5	10
70	1.6	2.0	2.6	4.0	5.1	6.6	11
75	2.1	2.6	3.4	5.2	6.5	8.1	13
80	2.6	3.3	4.3	6.3	7.7	9.4	14
85	3.0	3.8	5.0	7.1	8.5	10	14
90	3.4	4.4	5.7	7.7	9.0	11	14

b-

	T-score						
Age(y)	+1.0	0	-1.0	-2.0	-2.5	-3.0	-4.0
40	0.0	0.0	0.1	0.3	0.6	1.2	4.8
50	0.0	0.0	0.1	0.5	0.9	1.7	6.0
55	0.0	0.1	0.2	0.6	1.2	2.2	7.0
60	0.0	0.1	0.3	0.9	1.5	2.5	7.3
65	0.1	0.2	0.4	1.1	1.8	2.9	7.4
70	0.1	0.3	0.7	1.5	2.3	3.5	7.9
75	0.3	0.6	1.1	2.2	3.1	4.4	8.7
80	0.6	1.0	1.7	3.0	4.0	5.4	9.4
85	1.1	1.6	2.5	4.0	5.0	6.3	9.9
90	1.9	2.6	3.6	5.1	6.2	7.4	11

Applying NOGG to the Lebanese population. Since many guidelines recommend that women with a prior fragility fracture be considered for intervention, without the necessity for a BMD test (other than to monitor treatment), a prior fracture in women can be considered to carry a sufficient risk that treatment can be recommended. For this reason, the intervention threshold in women without a prior fracture can be set to be the equivalent of that for a woman with a similar age and a history of a prior fragility fracture, and no other clinical risk factors, at a fixed

country specific BMI, for example 25 kg/m² in England (15), and would therefore rise with age. The BMI used for FRAX Lebanon was 30 kg/m² as more representative of elderly Lebanese, as defined from population based studies. Table 1 illustrates the thresholds at which one would intervene using the NOGG model, starting at a 10-year overall fracture risk of 1.8% in a 50 year woman, to 4.4% at age 60, 9.7% at age 70 , 21% at age 80 and 30% at age 90. The corresponding proportion of women who would be treated would vary between 25-30% across all age categories (Table2) .This model would therefore result in over-treating a large proportion of women at low risk for fractures (below 10%) until age 70 years. It also would be too taxing financially at the public health level, as it would treat 25-30% of post-menopausal women, a treatment that is also not without its risks when started at such a young age.

Table 1. Ten-Year Probability of a Major Fracture in the Lebanese based on the NOGG model for Intervention Threshold, and the Upper and Lower BMD Assessment Thresholds

Age(years)	Intervention threshold (%)	Lower assessment threshold (%)	Upper assessment threshold (%)
50	**1.8**	0.8	2.2
55	**2.8**	1.3	3.4
60	**4.4**	2.1	5.2
65	**6.3**	3.2	7.6
70	**9.7**	5.1	12
75	**15**	8.5	18
80	**21**	13	25
85	**27**	17	32
90	**30**	20	36

Table 2. Proportion (%) of subjects in each age group, by gender, that have a probability for osteoporotic fracture above the threshold in NOGG (FRAX equivalent of a patient of same age, BMI 30 kg/m2, and with a fracture).

Age group	Proportion (%) that have a probability above the limit of a moving threshold NOGG like	
	Men	Women
50-55	4.5	26.3
55-60	3.3	28.5
60-65	2.4	30.4
65-70	2.7	33.0
70-75	3.4	30.0
75-80	4.8	30.5
80-85	6.5	28.2
85-	7.2	24.6

Applying a fixed threshold to the Lebanese. Two fixed thresholds, one set at 10% and another set at 20%, were considered. The cut-off of 10% is considered as moderate risk in the Canadian guidelines, and the cut-off of 20% is considered high risk in the Canadian guidelines and a definite indication to treat both in the Canadian guidelines and the US NOF guidelines. Applying these thresholds to women in the Lebanese population would result in a gradual increase in the proportion of subjects treated, as shown in Table 3. If one considers a threshold of 10%, the proportion of women who would be treated increased from 0.11% at age 50-55 years, to 1.3% at age 55-60 years, 5.7% at age 60-65 years, 18.8% at age 65-70 years, 42% at age 70-75 years and over 80% at age > 85 years. The proportion treated at age 65-70 years, corresponds to the proportion of women with prevalent morphometric vertebral fractures at age 72 years that is 19% (16). However, this model would treat very large proportions of subjects above age 70 years, increasing from 40% up to 80% by extreme old age. Conversely, the proportion of women who would be treated with a 20% threshold would be very low until age 70 years, the numbers being almost 0% at age 50-55 years, 0.04% at age 55-60 years, 0.44% at age 60-65 years, 2.8% at age 65-70 years, 10% at age 70-75 years and over 43% at age > 85 years. The corresponding proportions are also shown for men in Table 3. Considering a threshold of 10%, a low proportion of men would be treated until age 70-75 years, when it reaches 17.5% at 75-80 years, but then the proportions rise sharply reaching 37% at 80-85 years and 52% at 85+ years. This is to be put in the context of the observation that 13% of men with a mean age of 72 years have prevalent morphometric vertebral fractures (16). Considering a threshold of 20% would treat less than 1% of men until age 70-75 years, 10% at age 80-85 years, and 17% at age 85+.

Table 3. Proportion (%) of subjects at each age group, by gender, who have a 10-year overall probability for a major osteoporotic fracture above the pre-defined fixed thresholds of 10% and 20%.

Age group	Proportion (%) that have a probability above 10%		Proportion (%) that have a probability above 20%	
	Men	Women	Men	women
50-55	0.01	**0.11**	0.00	**0.00**
55-60	0.06	**1.3**	0.01	**0.04**
60-65	0.16	**5.7**	0.03	**0.44**
65-70	1.0	**18.8**	0.01	**2.8**
70-75	5.4	**41.5**	0.67	**9.8**
75-80	17.5	**62.8**	2.9	**22.5**
80-85	37.3	**77.4**	9.5	**35.8**
85-	51.8	**79.8**	17.3	**42.7**

Applying a hybrid model to the Lebanese. The NOGG model is very intuitive in light of its principle, namely commitment to treat women with fragility fractures, and by the same logic leads to commitment to treating any woman with a similar age and fracture risk. The problem when applied to the Lebanese population which has low baseline risk of fracture is that it would result in treatment of a large proportion/number of young women with very low projected baseline risk but potential long term side effects, as shown in Table 1, and would be prohibitive in term of costs . It was therefore decided, in view of above, to use a hybrid model that is NOGG-like for older woman aged > 70 years, the group at highest risk of fractures, and to use a fixed intervention threshold, selected at 10%, in younger subjects, age ≤ 70 years.

This hybrid model would allow for the smoothest transition in the proportion of subjects treated above and below that threshold (see Table 4). The proportions treated by age 70 years, 18.8%, is almost identical to the 19% proportion of Lebanese women with prevalent moderate or severe vertebral compression fractures based upon a population based study (16). It is also a close approximation of the risk in men at age 75-80 years (16). Such a hybrid model also ensures that an increasing proportion of subjects is treated, increasing from less than 6% at age 62 years, to 19% at age 67 years, and between 25-30% above age 70 years (see Table 5). The

same absolute intervention threshold is applied to men, since the effectiveness and cost effectiveness of intervention in men is broadly similar to that in women for equivalent risk (17-19). Finally, Table 5 summarizes the intervention thresholds coupled with the proportion of subjects treated for both genders in a hybrid model that uses 10% and 20% as fixed thresholds.

Table 4. Proportion (%) of each age group, by gender, that would be treated in the Lebanon hybrid model that used a fixed threshold at 10 % until 70 years, and Lebanon NOGG threshold after 70 years.

Age (years)	Intervention threshold (%)	
	Men	Women
	Fixed at 10%	
50-55	0.01	0.11
55-60	0.06	1.3
60-65	0.16	5.7
65-70	1.0	18.8
	NOGG model	
70-75	3.4	30.0
75-80	4.8	30.5
80-85	6.5	28.2
85-	7.2	24.6

Table 5. Intervention thresholds and proportions of women treated using 2 cut-off thresholds.

Age (years)	Intervention threshold (%)	Proportions above threshold (%)	
	Fixed at 10%	**10%**	**20%**
50	**10**		
52	**10**	**0.11**	**0.00**
55	**10**		
57	**10**	**1.3**	**0.04**
60	**10**		
62	**10**	**5.7**	**0.44**
65	**10**		
67	**10**	**18.8**	**2.8**
	NOGG Model	**NOGG model**	
70	**10**		
72	**12**	**30**	**30**
75	**15**		
77	**17**	**30**	**30**
80	**21**		
82	**23**	**28**	**28**
85	**27**		
87	**28**	**25**	**25**
90	**30**		

The FRAX Lebanon calculator is available online, http://www.shef.ac.uk/FRAX/tool.jsp, choose Middle East Africa, Lebanon. It is also available as an iPhone application. User friendly tables that incorporate Lebanese age and gender specific thresholds will be developed and circulated for use in clinics. For comparison of the 2002 and 2013 "Who to Treat" Lebanese guidelines see Summary Table below.

Treatment guidelines:

I-Preventive treatment:

-General measures to all as originally recommended in the 2002 (1) and 2007 (2) endorsed Lebanese guidelines and reemphasized in the upcoming 2013 vitamin D guidelines: (http://www.aub.edu.lb/FM/CMOP/Pages/LebaneseGuidelines.aspx)

-Regular weight-bearing exercise.
-Fall prevention.
-Avoid tobacco use and excess alcohol intake.
-Elemental calcium (including dietary intake) at 1200 mg/day.
-Vitamin D supplementation:
    -Desirable range 30-60 ng/ml.
    -The recommended vitamin D intake, as a maintenance regimen, is:
        -Children-adolescents: 15–25 µg (600–1000 IU) daily.
        -Adults under 50 years of age: 15–25 µg (600–1000 IU) daily.
        -High-risk* and older adults: 20–50 µg (1000–2000 IU) daily.

*High risk individuals are those with osteoporosis on pharmacologic therapy, with fractures, or conditions known to affect vitamin D metabolism or action: steroids, anticonvulsants, malabsorption, bypass surgery, cirrhosis and patients with secondary hyperparathyroidism.

A recent metaanalysis showed that calcium and vitamin D supplementation (in combination) reduce hip fractures by 19% (3).

II-Pharmacologic therapy targeted to high risk individuals:

According to the 2013 Lebanese FRAX-based osteoporosis guidelines high risk individuals are:
-Postmenopausal women and men ≥ 50 years with history of fragility fracture: Spine or Hip or ≥2 other fragility fractures.
-Individuals defined by the Lebanese guidelines based on age specific FRAX threshold. (http://www.aub.edu.lb/FM/CMOP/Pages/LebaneseGuidelines.aspx)

The below recommendations for pharmacologic interventions are based on the original 2002 Lebanese guidelines (1), incorporating additional information based on the following references (4-7).

-**Postmenopausal osteoporosis (PMO):**

- For menopausal women requiring treatment of osteoporosis, alendronate, risedronate, zoledronic acid and denosumab can be used as first-line therapies for prevention of hip, nonvertebral and vertebral fractures.
- For women 65 years or older with severe osteoporosis defined as a low BMD (T-score ≤–2.5) and a prevalent vertebral fracture, teriparatide can be used as a first-line therapy to reduce vertebral fracture risk.
- Other potential candidates for teriparatide include :
    - Postmenopausal women with very low BMD (T-score ≤ –3.5).
    - Postmenopausal women who sustain > 2 fragility fractures despite an adequate trial of bisphosphonates (1-year period).
- For early postmenopausal women (< 65 years of age) requiring treatment of osteoporosis, raloxifene can be used as a first-line therapy for prevention of vertebral fractures.
- For early postmenopausal women (< 60 years of age) requiring treatment of osteoporosis in combination with treatment for vasomotor symptoms, hormone therapy can be used as a first-line therapy for prevention of hip, nonvertebral and vertebral fractures.

-**Osteoporosis in men:**

- For men requiring treatment of osteoporosis, alendronate, risedronate and zoledronic acid can be used as first-line therapies for prevention of fractures.
- Teriparatide should be considered as a second-line therapy for men 65 years or older who have severe osteoporosis and prevalent fragility fractures.
- Testosterone is only indicated in men with a definite diagnosis of hypogonadism and under close expert medical supervision due to various complications.

-Glucocorticoid induced osteoporosis (GIOP):

- Recommendations are based on the American College of Rheumatology (ACR) 2010 guidelines (4) and Osteoporosis Canada guidelines (5) and summarized as below (Table 6):

Table 6. Treatment recommendations for GIOP:

	Daily Dose	Treatment [1,2]
Postmenopausal women and men ≥ 50	≥7.5 mg for > 3 months	Regardless of FRAX
	<7.5 mg for > 3 months	Medium/high FRAX risk*
	FRAX≤10%	If dose >7.5mg for >3 months*
	FRAX>10%	Treat all*
Premenopausal women and men <50	Treat ONLY if history of FRAGILITY fracture Others no recommendation was made by ACR	
Men and non-childbearing women	>5 mg for 1-3 months >3 months regardless of dose	Treat
Childbearing women	≥7.5 mg	Treat
	1-3 months or <7.5 mg	No consensus*

[1]FDA approved therapies for GIOP: alendronate, risedronate, zoledronic acid and teriparatide.

[2]Teriparatide is indicated in high risk individuals. High risk individuals are defined as postmenopausal women and men ≥ 50 years with high FRAX estimate as defined by FRAX Lebanon treatment thresholds, or premenopausal women and men < 50 years who have a history of fragility fracture and on a prednisone dose ≥7.5 mg daily for more than 3 months.

-Aromatase inhibitors and androgen deprivation therapy patients:

For women who are taking aromatase inhibitors and men who are undergoing androgen deprivation therapy, bisphosphonates (alendronate, risedronate, ibandronate , zoledronic acid) or Denosumab
should be considered .

Table 7.Fracture Risk Reduction in postmenopausal osteoporosis

Medication	Spine	Hip
Estrogen	✓	✓
Estrogen +Bazedoxifene	✓	✓
Raloxifene	✓	
Tibolone	✓	
Alendronate	✓	✓
Risedronate	✓	✓
Ibandronate	✓	
Zoledronic acid	✓	✓
Calcitonin	✓	
Denosumab	✓	✓
Strontium ranelate	✓	✓[3]
Teriparatide (PTH1-34)	✓	
PTH 1-84	✓	

[3]Only approved by EMEA (not FDA); post hoc analysis in high risk postmenopausal women ≥ 74 years and femoral neck T-score ≤-3 SD.

Table 8.FDA-Approved Medications:

Drug	PMO		GIO		Men
	Prevention	Treatment	Prevention	Treatment	
Estrogen	✓				
Calcitonin		✓			
Alendronate	✓	✓		✓	✓
Risedronate	✓	✓	✓	✓	✓
Ibandronate	✓	✓			
Zoledronic acid	✓	✓	✓	✓	✓
Raloxifene	✓	✓			
Denosumab		✓			
Teriparatide		✓		✓	✓

The potential benefits and risks of the prescribed agents should be discussed before therapy is initiated, to support informed decision-making.

Summary and Conclusions

Considerable effort has been dedicated over the last two decades, by various international scientific organizations, to the development and dissemination of Clinical Practice Guidelines, starting in the mid-eighties. However, to remain valuable, guidelines have to be current with recent scientific knowledge, and thus the need for periodic updates. For some guidelines, an arbitrary pre-scheduled date is set, while for others the update is implemented when new information becomes available. Guidelines for Osteoporosis are no exception, and Lebanon has paved the way for development and update of osteoporosis guidelines in the region, with updates every 5-6 years.

The Lebanese Guidelines for Osteoporosis Assessment and Treatment were first developed by a core of local and international experts in the spring of 2002, at a time when several other international guidelines were being developed, to provide a structural framework based on the evidence available then and build sound decision-making in the management of the patient at risk or with osteoporosis (8). The first Update in 2007 was undertaken to update several recommendations detailed in the original 2002 document, based on new relevant national and international data that became available at the time (9). Since its launch in 2008, FRAX® has resulted in a major paradigm shift in the assessment of the patient at risk or with osteoporosis, and resulted in an update of osteoporosis guidelines with the development of absolute fracture risk intervention thresholds by several National Osteoporosis Organizations (4, 11, 12, 14). These intervention thresholds were formulated at a country level and may thus vary by country for same age, BMI, and T-score.

FRAX Lebanon became available in September 2009, was based on data from the national hip fracture registry, and was updated based on updated mortality data in January 2012 by the FRAX development team (2, 16). FRAX Lebanon has made this second Update of the Lebanese guidelines a necessity. It allows a case finding strategy identifying high risk individuals, for whom to recommend pharmacologic therapy. Indications for “Who to Treat" retained the original indication of a history of fragility fracture, but with specification for the site, that is spine or hip, or ≥ 2 other fragility fractures. For subjects who have not experienced any fragility fractures, the intervention threshold is set at ≥ 10% for the 10-year overall risk of fractures for individuals up to age 70 years. For older individuals, the threshold increases with age: 15% at 75 years, 21% at 80 years, 27% at 85 years, and 30% at 90 years. A BMD T-score ≤ -2.5, in the absence of risk factors, is no more an indication to treat by itself, due to the very low estimated 10-year risk for

overall fractures , of less than 10% up to age 70 years in women, and 90 years in men. The Current 2013 FRAX-Based Lebanese Guidelines, based on a novel hybrid model, provide a logical framework, anchored on national hip fracture incidence data. These guidelines are meant to provide a structural framework developed for use by the physician treating the patient at risk for or with osteoporosis. The current Update tailors pharmacologic therapy to subjects at moderate to high risk, and avoids unnecessary treatment in low risk individuals, such as those with osteoporosis by bone mineral density and no other risk factors. The recommended FRAX derived intervention thresholds for the Lebanese cannot supersede nor replace clinical judgment, that needs to be judiciously used to fine tune such thresholds, upgrading or downgrading them based on clinical considerations, taking into account an individual patient's risk profile, risk factors not considered in FRAX, patient's preferences, and drug side effect profile, to name a few.

These FRAX-based recommendations were unanimously endorsed by all members of the National Task Force for Osteoporosis and Metabolic Bone Disorders, and are endorsed by concerned national scientific societies: Lebanese Society of Endocrinology ,Lebanese Society of Obstetrics and Gynecology , Lebanese Association of Orthopedic Surgeons ,Lebanese Society of Radiology, Lebanese Society of Rheumatology, Lebanese Society of Family Medicine, Lebanese Society of Internal Medicine, Lebanese Society of General Practitioners. Similar to the objectives of previous Lebanese Guidelines for Osteoporosis Assessment and Treatment, they are meant to provide a structural framework to guide 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. As with previous Lebanese osteoporosis guidelines, we anticipate periodic revisions of these guidelines, based on additional forthcoming data on osteoporosis locally, and our evolving knowledge about this under-recognized and under-treated disease.

"Who to Test": Comparison of 2002 and 2013 FRAX Based Guidelines

2002 and 2007 Lebanese Guidelines

Definite indications in postmenopausal (PM) women:

- ≥65 years: age as a risk factor (1/5 women ≥65 have vertebral fracture)
- Presence of vertebral deformity or fragility fracture
- Radiologic evidence of demineralization.
- Chronic corticosteroid (CS) therapy (>3-6 months)

Definite indications in men (>70 years):

- Presence of vertebral deformity or fragility fracture
- Hypogonadism
- Chronic corticosteroid (CS) therapy (>3-6 months)

Less definite indications in PM women:

- Medical conditions known to cause bone loss
- Other risk factors for bone loss: Low BMI, positive family history of hip fractures

No indications:

- Healthy cycling premenopausal women
- Men < 65 years

2013 FRAX Based Lebanese Guidelines

Definite indications both men and women:

- ≥65 years: age as a risk factor (1/5 women >65 have vertebral fracture, 13% of men)
- Presence of vertebral deformity or fragility fracture
- Radiologic evidence of demineralization
- Chronic corticosteroid therapy (>3-6 months)
- **Aromatase inhibitors or androgen deprivation therapy**

Previous Less definite indications in PM women and older men
Use FRAX Risk Factors to decide on BMD
If FRAX risk close to 10%, measure BMD to further refine risk assessment

Old No indications

Use FRAX with risk factors to reassure patient to low risk

"When to Treat": Comparison of 2002 and 2013 FRAX Based Guidelines

2002 and 2007 Lebanese Guidelines

Definite indications

- Postmenopausal women and older men (>70 years) with fragility fracture
- Postmenopausal women and older men and BMD T score ≤ -2.5
- Postmenopausal women and older men on CS and BMD T score ≤ -1.5

Less definite indications

- T- score between -1 and -2.5 (with/without risk factors, except for glucocorticoid induced osteoporosis (GIOP))

No indications

- T- score > -1
- Premenopausal normally cycling healthy women

2013 FRAX Based Lebanese Guidelines

Definite indications: regardless of FRAX and BMD

- Postmenopausal women and men (≥ 50 years) with history of fragility fracture: Spine, or Hip, or ≥ 2 other fragility fractures.

All Other conditions LISTED BELOW: use FRAX

- Postmenopausal women and men ≥ 65 years
- Women and men -2.5 ≤ T ≤ - 1.5 with/without risk factors including GIOP
- Women and men with T ≤ -2.5
- To reassure younger women and men about low risk despite low BMD (and/or with history of fractures)
  Risk Stratification: FRAX overall fracture risk

Cut-offs for treatment

Below age 70 years: Intervention threshold 10%
Age ≥ 70 years moving threshold as per Tables

Appendix I
National Recommendations for BMD Testing

National Guidelines of Indications for a Bone Mineral Density Test
http://www.nof.org/hcp/clinicians-guide

NOF Indications for BMD Testing:

- Women age 65 and older and men age 70 and older, regardless of clinical risk factors .
- Younger postmenopausal women, women in the menopausal transition and men age 50 to 69 with clinical risk factors for fracture.
- Adults who have a fracture after age 50
- Adults with a condition (e.g., rheumatoid arthritis) or taking a medication (e.g., glucocorticoids in a daily dose ≥ 5 mg prednisone or equivalent for ≥ three months) associated with low bone mass or bone loss

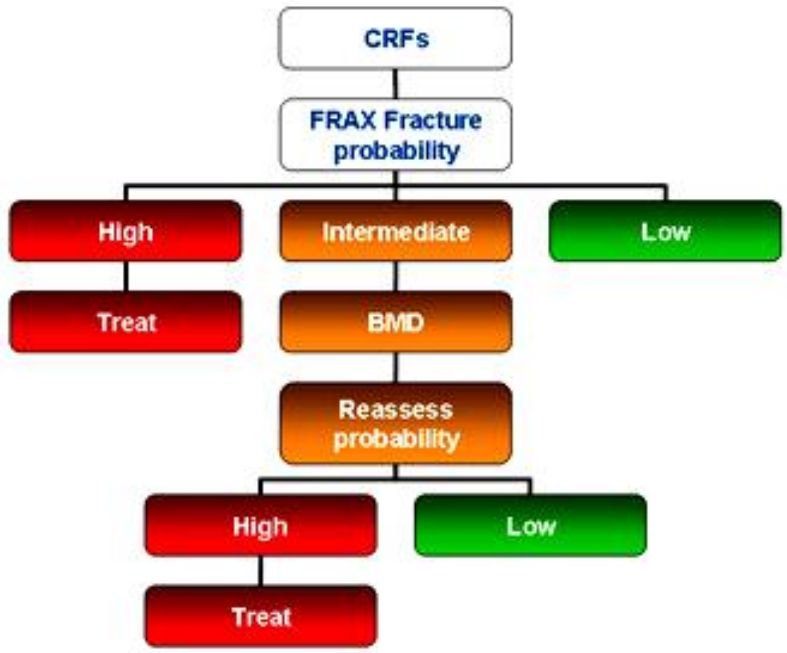
Medicare covers BMD testing for many individuals age 65 and older, including but not limited to:

- Estrogen deficient women at clinical risk for osteoporosis
- Individuals with vertebral abnormalities
- Individuals receiving, or planning to receive, long-term glucocorticoid therapy in a daily dose ≥ 5 mg prednisone or equivalent for ≥ three months
- Individuals with primary hyperparathyroidism
- Individuals being monitored to assess the response or efficacy of an approved osteoporosis drug therapy .

Osteoporosis Canada http://www.cmaj.ca/content/182/17/1864.full

Older adults (age≥50yr)	Younger adults(age <50yr)
Age ≥ 65yr (both women and men)	Fragility fracture
Clinical risk factors for fracture (menopausal women , men age 50-64yr)	Prolonged use of glucocorticoids
-Fragility fracture after 40yr	Use of other high risk medications
-Use of glucocorticoids	Hypogonadism or premature menopause(<45yr)
-Use of other high risk medications	Malabsorption syndrome
-Parental hip fracture	Primary hyperparathyroidism
-Vertebral fracture or osteopenia identified on Radiography	Other disorders strongly associated with rapid bone loss and/or fracture
-Current smoking	
-High alcohol intake	
-Low body weight (<60kg) or major weight loss(>10% of body weight at 25yr)	
-Rheumatoid arthritis	
-Other disorders strongly associated with Osteoporosis	

NOGG approach to BMD Testing
http://www.shef.ac.uk/NOGG/NOGG_Pocket_Guide_for_Healthcare_Professionals.pdf
http://www.shef.ac.uk/NOGG/NOGG_Executive_Summary.pdf



Subjects who should have a BMD are those in intermediate 10-year FRAX risk. The intermediate risk falls between the lower assessment and the upper assessment thresholds, and such subjects should be considered for testing with BMD using DXA and have their fracture probability

reassessed. The lower assessment threshold is set by FRAX for each age as 10-year probability of a major osteoporotic fracture for a woman with no risk factors, and the higher assessment threshold set for each age as 1.2 times the intervention threshold. The intervention threshold at each age is set at a risk equivalent to that associated with a prior fracture, as calculated by FRAX.

APPENDIX II

National Recommendations on Intervention Threshold for the Institution of Pharmacologic Therapies

United States: National Osteoporosis Foundation 2013 Clinician's Guide

The revised version of the National Osteoporosis Foundation's Clinician's Guide comes both as a publication and an App for iPhone and iPad (NOF 2013). Treatment recommendations include:

- Initiate pharmacologic treatment in those with hip or vertebral (clinical or asymptomatic) fractures.
- Initiate therapy in those with T-scores ≤ -2.5 at the femoral neck, total hip or lumbar spine by dual-energy x-ray absorptiometry (DXA), after appropriate evaluation.
- Initiate treatment in postmenopausal women and men age 50 and older with low bone mass (T-score between -1.0 and -2.5, osteopenia) at the femoral neck, total hip or lumbar spine by DXA and a 10-year hip fracture probability ≥ 3% or a 10-year major osteoporosis-related fracture probability ≥ 20% based on the U.S.-adapted WHO absolute fracture risk model (FRAX®; www.NOF.org and www.shef.ac.uk/FRAX).

Osteoporosis Canada 2010

Scientific Advisory Council of Osteoporosis Canada highlight that management of osteoporosis should be guided by an assessment of the patient's absolute fracture risk based on a validated fracture prediction tool (4). Tools validated in Canada (choice based on personal preference and convenience) include FRAX and CAROC (Joint initiative of the Canadian Association of Radiologists and Osteoporosis Canada), in which basal fracture risk is assessed based on age, sex, and femoral neck BMD (4). FRAX based risk-stratification in subjects who had initial BMD testing based on specific indications, as detailed above. In short, these include age≥ 65 years, presence of fragility fractures, intake of high risk medications, presence of secondary causes of osteoporosis, low body weight, and parental history of hip fractures (4).

Specific recommendations include:

- Pharmacologic therapy should be offered to patients at high absolute risk (> 20% probability for major osteoporotic fracture over 10 years).

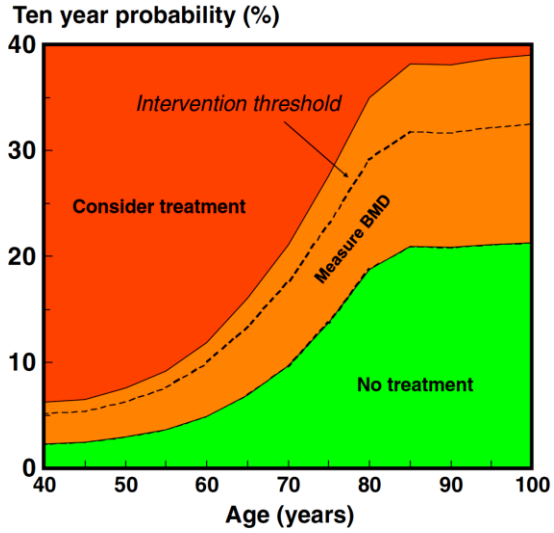
- Individuals over age 50 who have had a fragility fracture of the hip or vertebra and those who have had more than one fragility fracture are at high risk for future fractures, and such individuals should be offered pharmacologic therapy.
- For those at moderate risk of fracture, patient preference and additional risk factors should be used to guide pharmacologic therapy.

The UK NOGG Indications to treat are based on Case finding Strategy

Fracture risk should be assessed in postmenopausal women and in men aged 50 years or more with the risk factors outlined where assessment would influence management.

• Women with a prior fragility fracture should be considered for treatment without the need for further risk assessment although BMD measurement may sometimes be appropriate, particularly in younger postmenopausal women.

• In the presence of other clinical risk factors (CRFs), the 10-year probability of a major osteoporotic fracture (clinical spine, hip, forearm or humerus) should be determined using FRAX® (www.shef.ac.uk/FRAX, and see Figure below). Men and women with probabilities below the lower assessment threshold can be reassured. Those with probabilities above the lower assessment threshold but below the upper assessment threshold can be considered for testing with BMD using DXA and their fracture probability reassessed. Men and women with probabilities above the intervention threshold should be considered for treatment. The intervention threshold at each age is set at a risk equivalent to that associated with a prior fracture, as calculated by FRAX, and therefore rises with age. The proportion of women in the UK potentially eligible for treatment rises from 20-40% with age. The intervention threshold lies in between the lower assessment threshold (set by FRAX or each age as 10-year probability of a major osteoporotic fracture for a woman with no risk factors) and the higher assessment threshold (set for each age as 1.2 times the intervention threshold).



Intervention threshold represented by dotted line, lying between lower assessment threshold defining lower boundary of orange zone, and upper assessment threshold, defined by upper boundary of orange zone. These thresholds are based on the 10-year probability of a major fracture (in percent) based on data derived from 5 countries in EU France, UK, Germany, Italy, Spain. Adapted from Kanis et al, Osteoporos Int 2013.

References

1- Kanis JA, Johnell O, Oden A, Johansson H, McCloskey EV.FRAX™ and the assessment of fracture probability in men and women from the UK. Osteoporos Int. 2008;19: 385-397

2- Kanis JA, Hans D, Cooper C, Baim S, Bilezikian JP, Binkley N, Cauley JA, Compston JE, Dawson-Hughes B, El-Hajj Fuleihan G, Johansson H, Leslie WD, Lewiecki EM, Luckey M, Oden A, Papapoulos SE, Poiana C, Rizzoli R, Wahl DA, McCloskey EV; Task Force of the FRAX Initiative. Interpretation and use of FRAX in clinical practice. Osteoporos Int. 2011;22(9):2395-411.

3- Watts NB, Bilezikian JP, Camacho PM, Greenspan SL, Harris ST, Hodgson SF, Kleerekoper M, Luckey MM, McClung MR, Pollack RP, Petak SM; AACE Osteoporosis Task Force. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the diagnosis and treatment of postmenopausal osteoporosis. Endocr Pract. 2010;16 Suppl 3:1-37.

4- Papaioannou A, Morin S, Cheung AM, Atkinson S, Brown JP, Feldman S, Hanley DA, Hodsman A, Jamal SA, Kaiser SM, Kvern B, Siminoski K, Leslie WD; Scientific Advisory Council of Osteoporosis Canada. 2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary. CMAJ. 2010 ;182(17):1864-73.

5- Hans DB, Kanis JA, Baim S, Bilezikian JP, Binkley N, Cauley JA, Compston JE, Cooper C, Dawson-Hughes B, El-Hajj Fuleihan G, Leslie WD, Lewiecki EM, Luckey MM, McCloskey EV, Papapoulos SE, Poiana C, Rizzoli R; FRAX(®) Position Development Conference Members. Joint Official Positions of the International Society for Clinical Densitometry and International Osteoporosis Foundation on FRAX (®). Executive Summary of the 2010 Position Development Conference on Interpretation and use of FRAX® in clinical practice. J Clin Densitom. 2011;14(3):171-80.

6- Kanis JA, Johansson H, Oden A, McCloskey EV .Guidance for the adjustment of FRAX according to the dose of glucocorticoids. Osteoporos Int. 2010;22:809–816

7- Leslie WD, Lix LM, Johansson H, Oden A, McCloskey E, Kanis JA. Spine-hip discordance and fracture risk assessment: a physician-friendly FRAX enhancement. Osteoporos Int. 2011;22(3):839-47.

8- El-Hajj Fuleihan G, Baddoura R, Awada H, Okais J, Rizk P, McClung M. Lebanese guidelines for osteoporosis assessment and treatment: who to test? What measures to use? When to treat? LMJ 2002; 50:75-125

9- El-Hajj Fuleihan GH, Baddoura R, Awada H, Okais AA. First update of the Lebanese guidelines for osteoporosis assessment and treatment. LMJ 2007;55(4):176-91

10- Grossman JM, Gordon R, Ranganath VK, Deal C, Caplan L, Chen W, Curtis JR, Furst DE, McMahon M, Patkar NM, Volkmann E, Saag KG. American College of Rheumatology 2010 recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Care Res (Hoboken). 2010 Nov;62(11):1515-26

11- National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Washington, DC: National Osteoporosis Foundation; 2013.

12- Compston J, Cooper A, Cooper C, Francis R, Kanis JA, Marsh D, McCloskey EV, Reid DM, Selby P, Wilkins M; National Osteoporosis Guideline Group (NOGG). Guidelines for the diagnosis and management of osteoporosis in postmenopausal women and men from the age of 50 years in the UK. Maturitas 2009;62(2):105-8.

13- Sibai AM, Nasser W, Ammar W, Khalife MJ, Harb H, Fuleihan Gel-H. Hip fracture incidence in Lebanon: a national registry-based study with reference to standardized rates worldwide. Osteoporos Int. 2011;22(9):2499-506.

14- Association Suisse contre l'Ostéoporose: Recommandations 2010. ASCO. http://www.svgo.ch/content/documents/SVGO_Empfehlungen2010_V19April2010.pdf.

15- Kanis JA, McCloskey EV, Johansson H, Strom O, Borgstrom F, Oden A; National Osteoporosis Guideline Group. Case finding for the management of osteoporosis with FRAX-assessment and intervention thresholds for the UK. Osteoporos Int. 2008;19 (10):1395-408

16- Baddoura R, Arabi A, Haddad-Zebouni S, Khoury N, Salamoun M, Ayoub G, Okais J, Awada H, El-Hajj Fuleihan G. Vertebral fracture risk and impact of database selection on identifying elderly Lebanese with osteoporosis. Bone. 2007 ;40(4):1066-72.

17- Kanis JA, Adams J, Borgstrom F, Cooper C, Jonsson B, Preedy D, Selby P, Compston J .The cost-effectiveness of alendronate in the management of osteoporosis. Bone. 2008; 42:4–15.

18- Tosteson AN, Melton LJ 3rd, Dawson-Hughes B, Baim S, Favus MJ, Khosla S, Lindsay RL; National Osteoporosis Foundation Guide Committee. Cost-effective osteoporosis treatment thresholds: the United States perspective. Osteoporos Int. 2008 ;19(4):437-47.

19- Kanis JA, McCloskey EV, Johansson H, Cooper C, Rizzoli R, Reginster JY; Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and the Committee of Scientific Advisors of the International Osteoporosis Foundation (IOF). European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int. 2013;24(1):23-57.