

## **Executive Summary- Lebanese FRAX-Based Osteoporosis Guidelines 2013**

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

On behalf of

### **National Task Force for Osteoporosis and Metabolic Bone Disorders 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 to 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](mailto:gf01@aub.edu.lb)

**WHO To TEST:**

**Definite indications in 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

**All other indications in postmenopausal women and older men**

Use FRAX Risk Factors to decide on BMD.

If FRAX risk estimate based on risk factors is close to 10%, measure BMD to further refine risk assessment.

**WHO To TREAT:**

**Definite indications: regardless of FRAX and BMD**

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

**All Other conditions LISTED BELOW: use FRAX and treat at age-specific cut-offs**

- Postmenopausal women and men ≥ 65 years
- Women and men  $-2.5 \leq T \leq -1.5$  with/without risk factors including GIOP
- Women and men with  $T \leq -2.5$
- To reassure younger women and men about low risk despite low BMD (and/or with history of fractures)

Risk Stratification: FRAX overall fracture risk

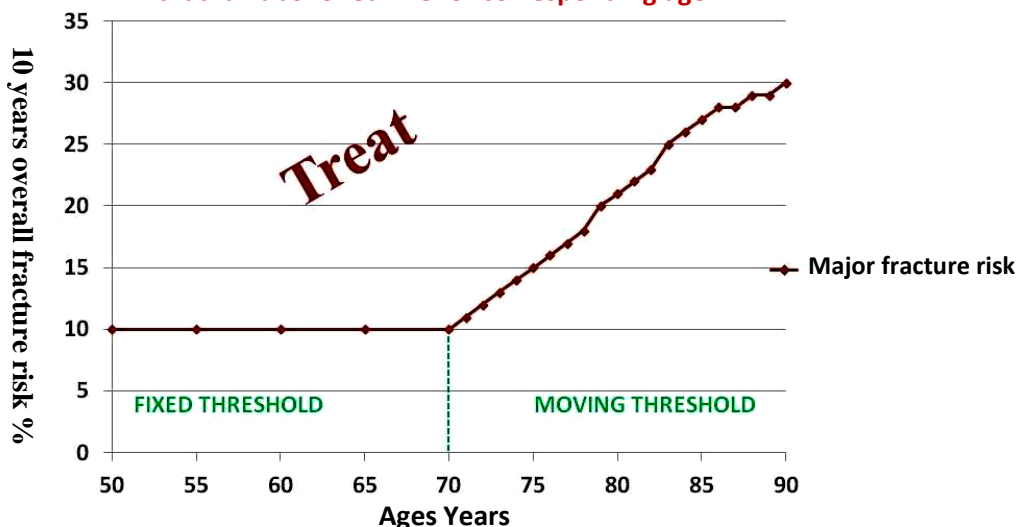
**Cut-offs for treatment**

Below age 70 years: Intervention threshold 10%.

Age ≥ 70 years moving threshold as per Table:

Age (years)	Intervention threshold (10%)
70	10
75	15
80	21
85	27
90	30

**Treat anyone with calculated 10 year overall fracture risk that fall above red line for corresponding age**



## **WHAT to TREAT WITH?**

### **I-Prevention 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 meta-analysis 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  $\geq$  50 years with history of fragility fracture: Spine or Hip or  $\geq$ 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  $\leq$ -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  $\leq -3.5$ ).
- 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 :

	Daily Dose	Treatment <sup>1,2</sup>
<b>Postmenopausal women and men <math>\geq 50</math></b>	$\geq 7.5$ mg for > 3 months	Regardless of FRAX
	<7.5 mg for > 3 months	Medium/high FRAX risk*
	FRAX $\leq 10\%$	If dose >7.5mg for >3 months*
	FRAX>10%	Treat all*
<b>Premenopausal women and men &lt;50</b>	Treat ONLY if history of FRAGILITY fracture Others no recommendation was made by ACR	
<b>Men and non-childbearing women</b>	>5 mg for 1-3 months >3 months regardless of dose	Treat
<b>Childbearing women</b>	$\geq 7.5$ mg	Treat
	1-3 months or <7.5 mg	No consensus*

\*ACR

<sup>1</sup>FDA approved therapies for GIOP: alendronate, risedronate, zoledronic acid and teriparatide.

<sup>2</sup>Teriparatide is indicated in high risk individuals. High risk individuals are defined as postmenopausal women and men  $\geq 50$  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  $\geq 7.5$  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 1. Fracture Risk Reduction in postmenopausal osteoporosis**

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

<sup>3</sup>Only approved by EMEA (not FDA); post hoc analysis in high risk postmenopausal women  $\geq 74$  years and femoral neck T-score  $\leq -3$  SD.

**Table 2. 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.*

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