

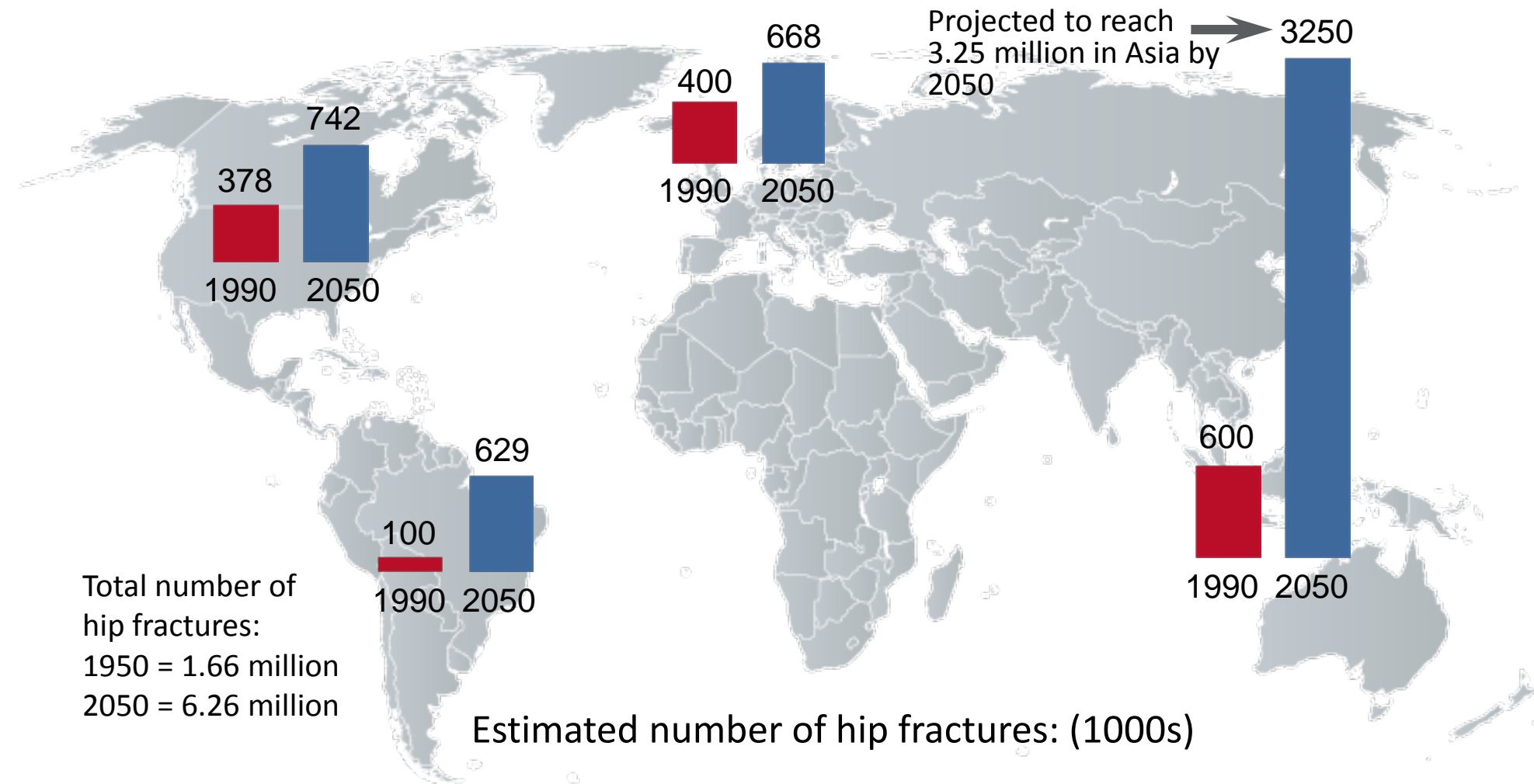
# Risk stratification In Osteoporosis

**Mohammad Hossein Dabbaghmanesh**  
**Professor of internal medicine, Endocrinologist**  
**Internal Medicine Institute**  
**Endocrine and Metabolism Research Center**

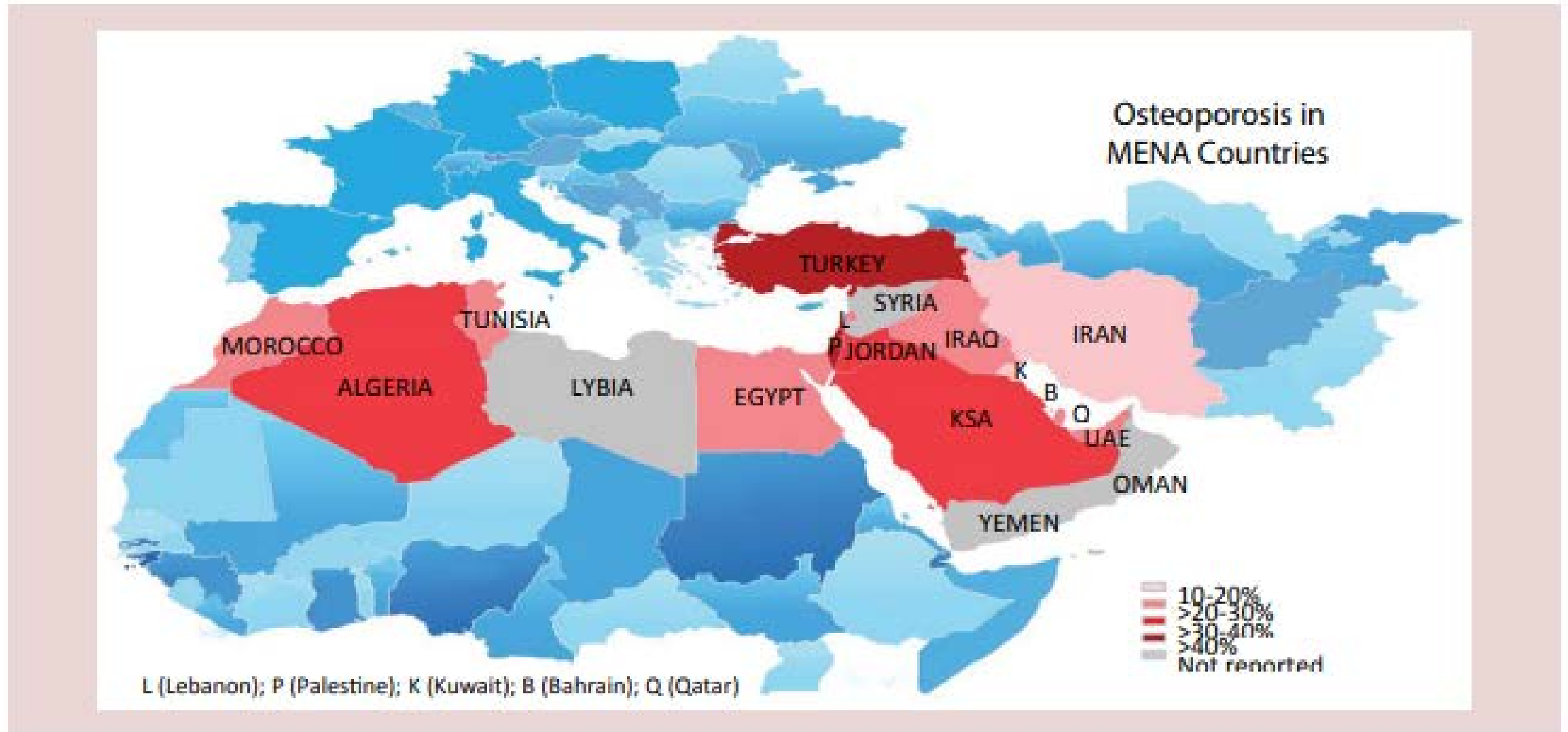
# Osteoporosis Prevalence and Incidence Worldwide

- **Prevalence:** Over 200 million people worldwide have osteoporosis
- **Incidence:** Hip fractures projected to increase substantially by 2050:
  - 240% in women
  - 320% in men
- Even if no increase in the age-adjusted hip fracture rate, the number of hip fractures will increase from 1.7 million in 1990 to 6.3 million in 2050

# Projected Worldwide Increase in Hip Fracture Number



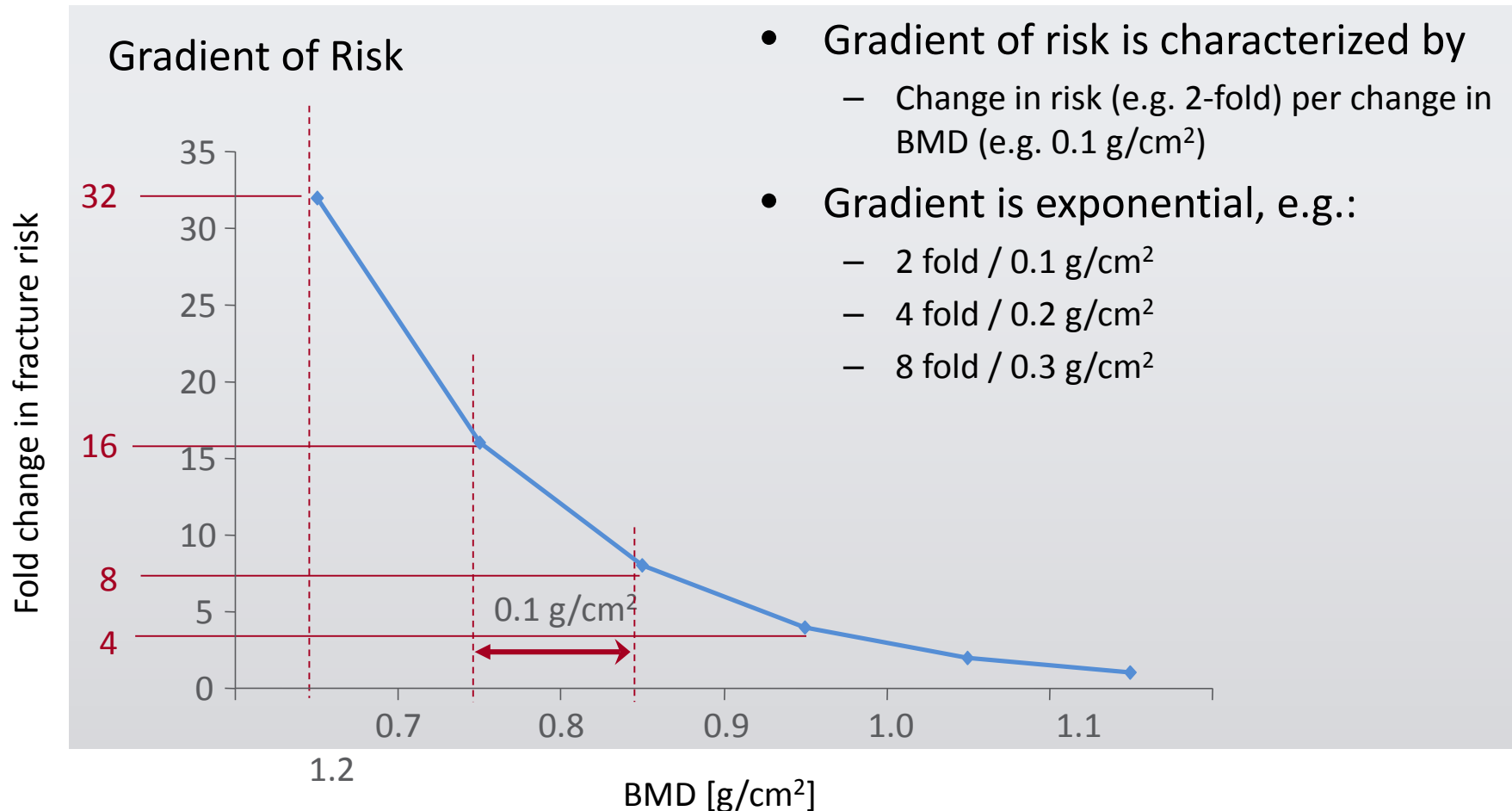
# Osteoporosis Prevalence in adult Females in MENA region



# Fracture Prevalence and Incidence in Middle east

- Iran accounts for **0.85%** of the global burden of hip fractures and **12.4%** of the burden of hip fractures in the Middle East
- In Iran, there were **50 000** hip fractures in 2010, and **62 000** are reached for 2020
- The disease burden is expected to increase with the projected rise in the aging population, with over 35% of people exceeding the age of 50 years.
- In the next few decades, the number of fragility fractures will likely double or even quadruple in MENA region countries

# Fracture Risk Increases Exponentially with Declining BMD



# Diagnosis of osteoporosis by DXA

The T-score compares an individual's BMD with the mean value for young normals and expresses the difference as a standard deviation score

	<b>T-score (SD)</b>
Normal	Equal to -1.0 or higher
Low Bone Mass (Osteopenia)	Between -1.0 and -2.5
Osteoporosis	Equal to -2.5 or lower
Severe Osteoporosis	Equal to -2.5 or lower with fracture

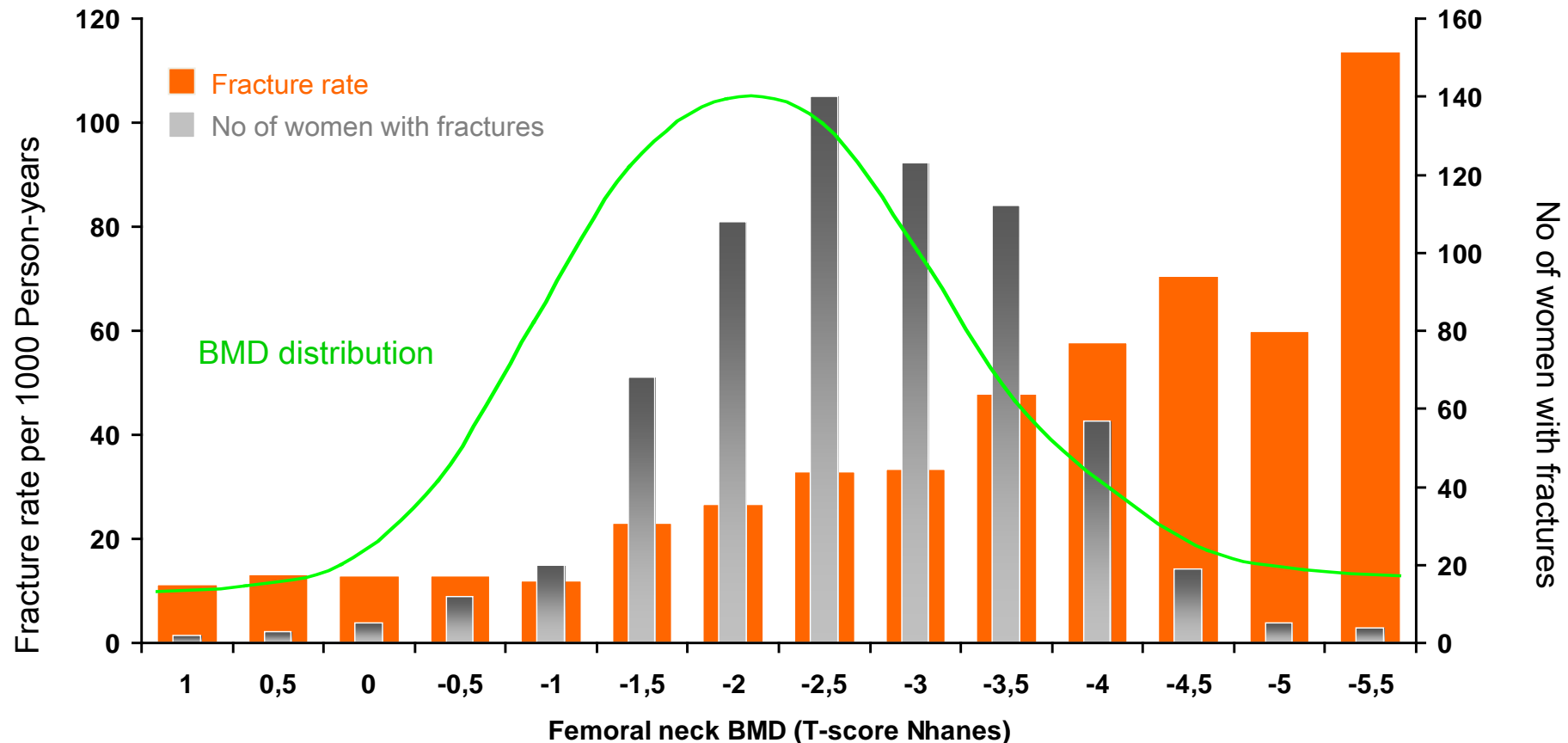
World Health Organization. Technical Report Series 843; WHO, Geneva.1994.

Kanis JA et al. J Bone Miner Res. 1994;9:1137.

# BMD Overlaps in Women With and Without Fracture

EPISEM study; 6862 postmenopausal white women  $\geq 70$  years, randomly selected from population based listing

Mean f/u of 3.2 yrs. 678 OP fractures (hip, distal forearm, proximal humerus)

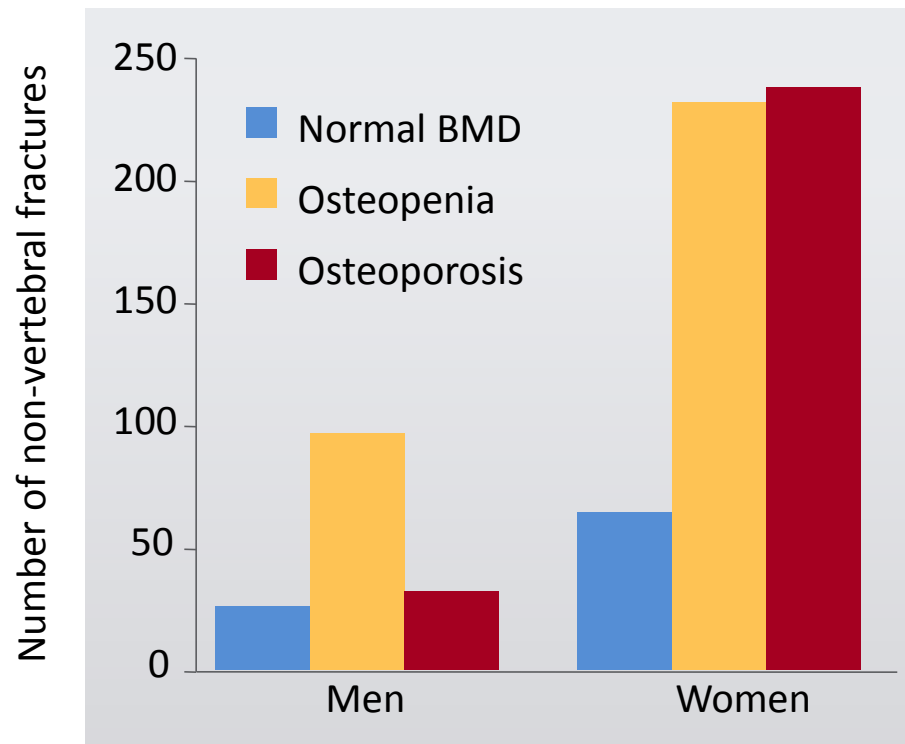


Courtesy of D Hans & MA Krieg – Adapted from the EPISEM Study  
Presented at the SSR, Lausanne, CH, September, 2009 and ASBMR, Philadelphia 2006



# Basing Treatment Decisions Solely on T-score Will Miss Over Half of Those Who Will Fracture

- Numerically More Fractures Occur in Those Without Osteoporosis by T-score (Only 44% of women and 21% of men who sustain non-vertebral fractures have osteoporosis by BMD)



5794 participants in the Rotterdam study;  
Mean follow-up 6.8 yrs  
FN BMD at baseline

# Bone Density and Fracture Risk

- Bone mineral **density** is important determinant of bone **strength**
- Bone **strength** is important predictor of fracture **risk**
- But we need to consider clinical risk factors in addition to BMD

**Fracture Risk Assessment**

```
graph TD; A[Fracture Risk Assessment] --> B[Intervention Thresholds]; B --> C[Evaluation/Discussion]; C --> D[Treatment]; D --> E[Follow-up];
```



**Intervention Thresholds**



**Evaluation/Discussion**



**Treatment**



**Follow-up**

# Multiple Fracture Risk Factors Exist

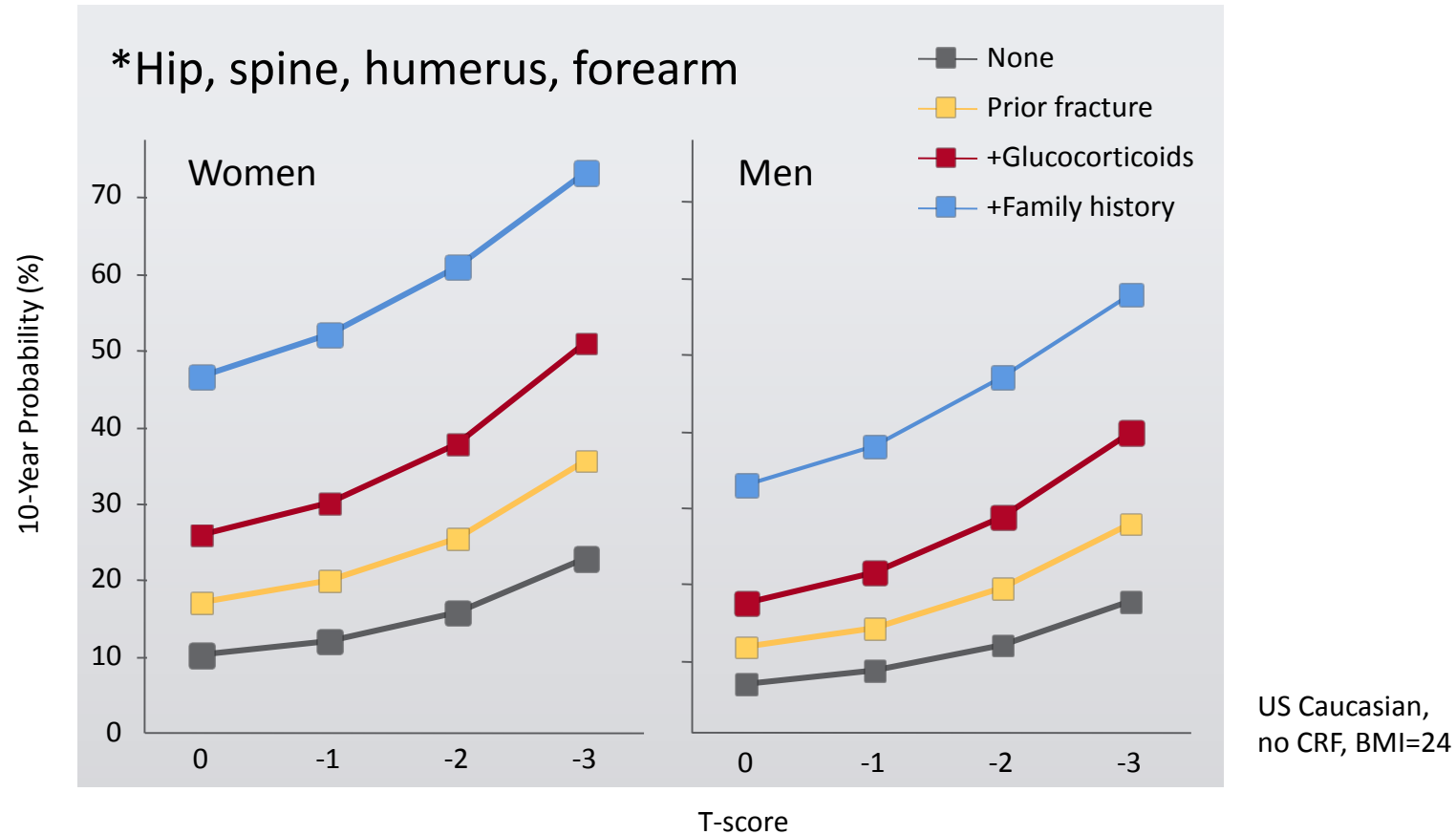
## Which Ones to Use?

- Age
- Prior fracture
- Low body weight
- Weight loss
- Inactivity
- Glucocorticoids
- Hyperparathyroidism
- Diabetes type 1
- Anorexia
- Gastrectomy
- Gender (female)
- Current smoking
- Low sunlight exposure
- Family Hx of fracture
- Surgical menopause
- Low calcium intake
- Hyperthyroidism
- Diabetes type 2
- Rheumatoid arthritis

# Criteria Required for Risk Factors in the FRAX<sup>®</sup> Model

- Validated in multiple populations
- Easily accessible by primary care practitioners
- Be intuitive, rather than counterintuitive, to medical care
- Contribute to risk that is amenable to the therapeutic intervention proposed

# Combining Risk Factors Improves Osteoporotic Fracture\* Prediction



# Cohorts Studied to Generate the WHO Fracture Risk Assessment Tool

- Twelve studies world-wide
  - EVOS/EPOS, Hiroshima, CaMoS, Rochester, Sheffield, Rotterdam, Gothenberg I, Gothenberg II, Dubbo/DOES, EPIDOS, Kuopio, OFELY
- N = 59,232; 74% female
- Person years = 249,898
- Osteoporotic fractures = 3,495
- Hip fractures = 957
- Validated in 11 cohorts; over 1 million person years

# WHO Assessment of Absolute Fracture Risk - FRAX<sup>®</sup>



# FRAX<sup>®</sup> Risk Factors Estimate 10-year Risk of Fracture

- Age (40-90), sex and clinical risk factors
- BMI
- Prior fragility fracture
- Parental history of hip fracture
- Current tobacco smoking
- Ever long-term use of glucocorticoids
- Rheumatoid arthritis or other secondary causes
- Alcohol intake 3 or more units daily

## Welcome to FRAX<sup>®</sup>

The FRAX<sup>®</sup> tool has been developed to evaluate fracture risk of patients. It is based on individual patient models that integrate the risks associated with clinical risk factors as well as bone mineral density (BMD) at the femoral neck.



Dr. John A Kanis  
Professor Emeritus,  
University of  
Sheffield

The FRAX<sup>®</sup> models have been developed from studying population-based cohorts from Europe, North America, Asia and Australia. In their most sophisticated form, the FRAX<sup>®</sup> tool is computer-driven and is available on this site. Several simplified paper versions, based on the number of risk factors are also available, and can be downloaded for office use.

The FRAX<sup>®</sup> algorithms give the 10-year probability of fracture. The output is a 10-year probability of hip fracture and the 10-year probability of a major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture).

### Clarification

The University of Sheffield launched the FRAX tool in 2008. At that time the University hosted the The World Health Organisation (WHO) Collaborating Centre for Metabolic Bone Diseases (1991-2010), and the FRAX tool is based on data generated from that centre. However, FRAX was neither developed or endorsed by WHO. Any references to the 'WHO tool' or to the WHO Collaborating Centre after it finished its work in 2010 are incorrect.

### FRAX Desktop Application

Click here to view the applications available



### Web Version 4.3

View Release Notes  
UDI:  
(01)05065010474000(8012)4.3



### Links

[www.iofbonehealth.org](http://www.iofbonehealth.org)



[www.nof.org](http://www.nof.org)



[www.jpof.or.jp](http://www.jpof.or.jp)



[www.esceo.org](http://www.esceo.org)



45322637

Individuals with fracture risk assessed since  
1st June 2011



## Welcome to FRAX<sup>®</sup>

The FRAX<sup>®</sup> tool has been developed to evaluate fracture risk of patients. It is based on individual patient models that integrate the risks associated with clinical risk factors as well as bone mineral density (BMD) at the femoral neck.



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- Asia
- Europe
- Middle East & Africa
- North America
- Latin America
- Oceania
- Abu Dhabi
- Botswana
- Ethiopia
- Iran**
- Jordan
- Kuwait
- Lebanon
- Morocco
- Palestine
- Qatar
- Saudi Arabia
- South Africa
- Syria
- Tunisia
- Zimbabwe

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[www.iofbonehealth.org](http://www.iofbonehealth.org)



[www.nof.org](http://www.nof.org)



[www.jpof.or.jp](http://www.jpof.or.jp)



[www.esceo.org](http://www.esceo.org)



45322552

Individuals with fracture risk assessed since  
1st June 2011



## Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: Iran Name/ID:  [About the risk factors](#)

**Questionnaire:**

1. Age (between 40 and 90 years) or Date of Birth  
 Age:  Y:  M:  D:

2. Sex  Male  Female

3. Weight (kg)

4. Height (cm)

5. Previous Fracture  No  Yes

6. Parent Fractured Hip  No  Yes

7. Current Smoking  No  Yes

8. Glucocorticoids  No  Yes

9. Rheumatoid arthritis  No  Yes

10. Secondary osteoporosis  No  Yes

11. Alcohol 3 or more units/day  No  Yes

12. Femoral neck BMD (g/cm<sup>2</sup>)  
 Select BMD

**BMI: 25.0**  
 The ten year probability of fracture (%)

without BMD	
Major osteoporotic	4.8
Hip Fracture	0.7

[Print tool and information](#)



### Weight Conversion

Pounds kg

### Height Conversion

Inches cm

**00227349**

Individuals with fracture risk assessed since 1st June 2011



## Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: Iran Name/ID:  [About the risk factors](#)

**Questionnaire:**

1. Age (between 40 and 90 years) or Date of Birth  
 Age:  Y:  M:  D:

2. Sex  Male  Female

3. Weight (kg)

4. Height (cm)

5. Previous Fracture  No  Yes

6. Parent Fractured Hip  No  Yes

7. Current Smoking  No  Yes

8. Glucocorticoids  No  Yes

9. Rheumatoid arthritis  No  Yes

10. Secondary osteoporosis  No  Yes

11. Alcohol 3 or more units/day  No  Yes

12. Femoral neck BMD (g/cm<sup>2</sup>)  
 T-Score

**BMI: 25.0**  
 The ten year probability of fracture (%)

with BMD	
Major osteoporotic	5.3
Hip Fracture	0.7

If you have a TBS value, click here:

[Print tool and information](#)



### Weight Conversion

Pounds kg

### Height Conversion

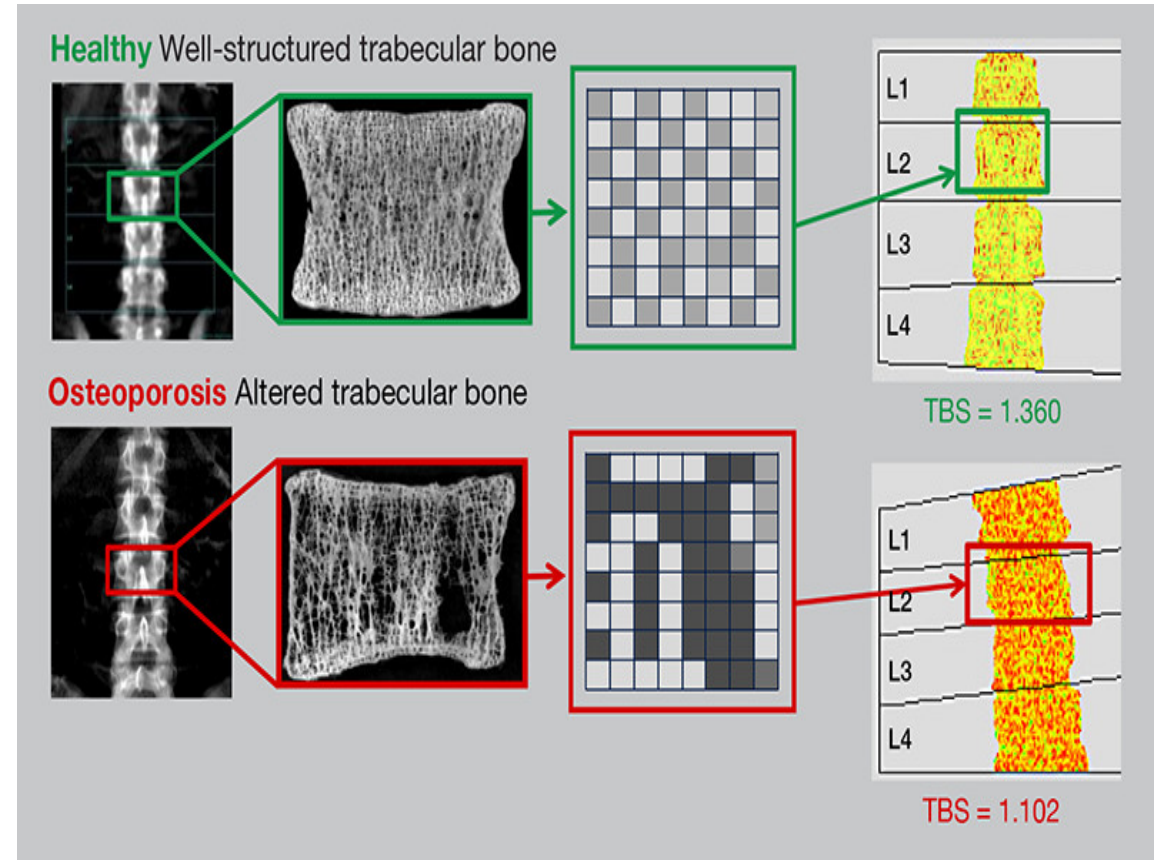
Inches cm

**00227349**

Individuals with fracture risk assessed since 1st June 2011

# Assessing trabecular microstructure noninvasively via DXA: TRABECULAR BONE SCORE (TBS)

- Analytical tool that performs novel gray-level texture measurements on lumbar spine DXA images
- Low TBS is consistently associated with an increase in the prevalence and incidence of fractures.
- may be used as an adjunct to BMD measurements and FRAX variables to improve fracture prediction
- may have a role in the assessment of fracture risk in secondary osteoporosis.



## Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: **Iran** Name/ID:  [About the risk factors](#)

### Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth  
 Age:  Date of Birth: Y:  M:  D:

2. Sex  Male  Female

3. Weight (kg)

4. Height (cm)

5. Previous Fracture  No  Yes

6. Parent Fractured Hip  No  Yes

7. Current Smoking  No  Yes

8. Glucocorticoids  No  Yes

9. Rheumatoid arthritis  No  Yes

10. Secondary osteoporosis  No  Yes

11. Alcohol 3 or more units/day  No  Yes

12. Femoral neck BMD (g/cm<sup>2</sup>)  
 T-Score

**BMI: 25.0**  
 The ten year probability of fracture (%)  
 with BMD

Major osteoporotic	<b>5.3</b>
Hip Fracture	<b>0.7</b>

If you have a TBS value, click here:

[Print tool and information](#)



### Weight Conversion

Pounds  → kg

### Height Conversion

Inches  → cm

**00227349**

Individuals with fracture risk assessed since 1st June 2011



## Calculation tool

Country:

Name/ID:

Age:

Sex:

BMI (kg/m<sup>2</sup>):

Please enter the Trabecular Bone Score to compute the ten year probability of fracture adjusted for TBS

**DXA device manufacturer:**

**Lumbar Spine TBS:**



Attention: TBS values are accurate only for patients (women and men) with a BMI in the range [15 – 37 kg/m<sup>2</sup>]

The 10 year probability of fracture (%)  
 Adjusted for TBS



Major Osteoporotic Fracture: **6.2**

Hip Fracture: **0.7**

**00047231**

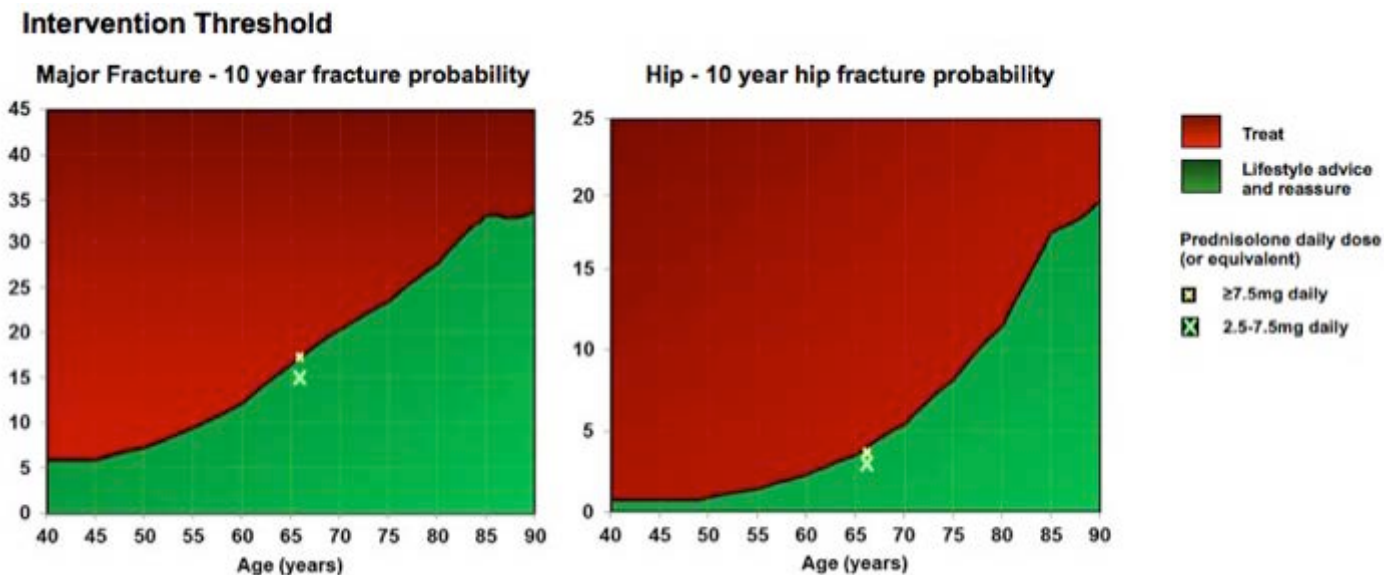
Individuals with fracture risk assessed since April 15, 2015

# Adjustment of FRAX Based on Glucocorticoid Dose

Can be done manually as follows:

Glucocorticoid dose	Adaptation	
	Major fractures	Hip fractures
Low (<2.5 mg)	-20%	-35%
Medium (2.5-7.5 mg)	0%	0%
High ( $\geq 7.5$ mg)	+15%	+20%

Or automated via FRAX in the UK as below:



# Adjustment of FRAX Based on Hip-Spine Discordance

- Effect of LS-FN T-score discordance assessed in Canadian Manitoba BMD database (study population of 36,368)
- 15% had lumbar spine BMD at least 1 SD lower (i.e., 1 T-score) than at the femoral neck
- For every rounded T-score difference of 1 unit adjust FRAX risk of major osteoporotic fracture (MOF) up or down by 10%
  - Example: FN T-score = -1.5, LS T-score = -3.5
  - Difference = 2 units; increase MOF by 20%
  - MOF risk = 18% ➔ adjusted risk = 18% x 1.2 = 21.6%

# Discover the advantages of FRAXplus®

FRAXplus® allows you to modify a probability result derived from conventional FRAX estimates of probabilities of hip fracture and major osteoporotic fracture with knowledge of:

- Recency of osteoporotic fracture
- Higher than average exposure to oral glucocorticoids
- Information on trabecular bone score (TBS)
- Number of falls in the previous year
- Duration of Type 2 diabetes mellitus
- Concurrent information on lumbar spine BMD
- Hip axis length (HAL)

**Caveat :** There is no evidence base available to inform on the accuracy of multiple adjustments. Pragmatically, any adjustment should be made for the most dominant factor, i.e., that which is likely to have the greatest clinical relevance for the estimated probability.

Recency of osteoporotic fracture



Information on trabecular bone score (TBS)



High exposure to oral glucocorticoids



Falls history



Type 2 diabetes mellitus



Hip axis length



Concurrent data on lumbar spine BMD





## Calculation Tool

Please answer the questions below to calculate the ten-year probability of fracture with or without BMD.

Continent  Country

Name/ID

About the risk factors

Individuals with fracture risk assessed since 1st June 2011: 215958

## Questionnaire

1. Age (between 40 and 90 years) or Date of Birth

2. Sex

Female  Male

3. Weight

kg  kg/cm

4. Height

cm

5. Previous Fracture

YES

6. Parent Fractured Hip

NO

7. Current Smoking

NO

8. Glucocorticoids

NO

9. Rheumatoid arthritis

NO

10. Secondary osteoporosis

NO

11. Alcohol 3 or more units/day

NO

12. Femoral neck BMD

T-score

Calculate

Clear

BMI: 25 with BMD

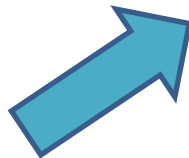
### THE TEN-YEAR PROBABILITY OF FRACTURE

Major osteoporotic 5.3%

Hip 0.7%

Adjust your results, try FRAX plus®

[What does FRAX plus® do? Click here](#)



# Adjust your results with FRAX plus®

Please select one of the available adjustment algorithms:

Adjust probability according to recent fractures



Adjust probability according to the dose of oral glucocorticoids



Adjust probability according to TBS value



Adjust probability according to duration of diabetes



Adjust probability according to recent falls



Adjust major osteoporotic fracture probability according to differences between femoral neck and lumbar spine BMD T-scores



Adjusting FRAX hip fracture probabilities according to the hip axis length (HAL)



Only available if BMD included in the FRAX calculation.

Hip axis length

 mm

Adjust probability

**Fracture Risk Assessment**



**Intervention Thresholds**



**Evaluation/Discussion**



**Treatment**



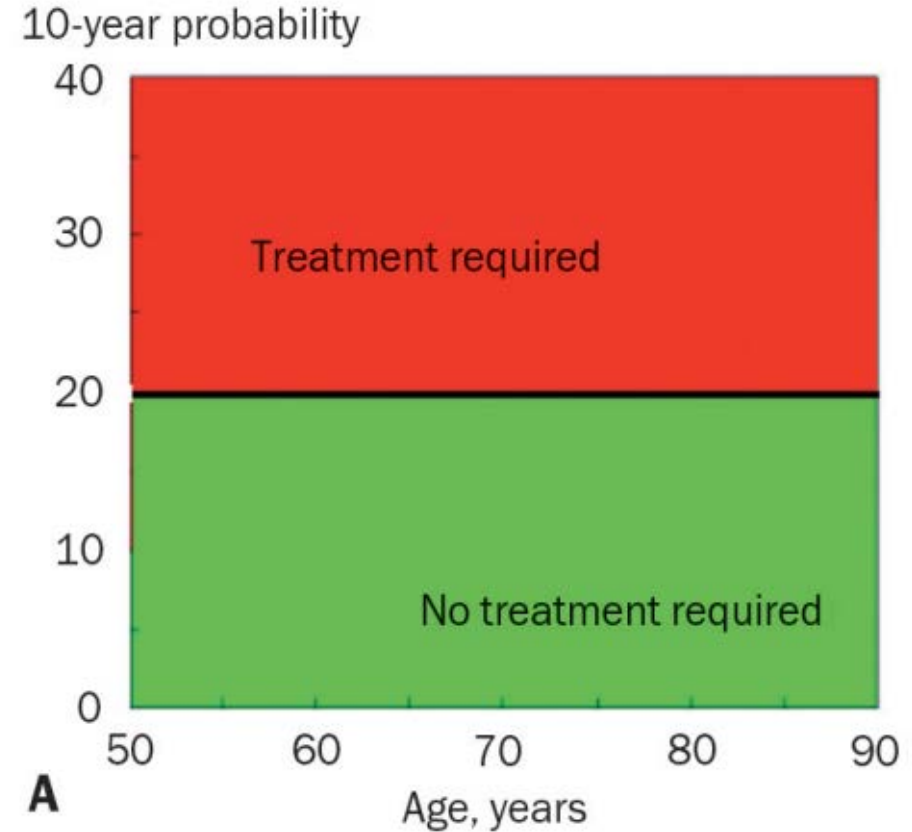
**Follow-up**

# FRAX-based Fixed Intervention Thresholds

The National Osteoporosis Foundation (NOF) popularized Fixed ITs in the US, recommending a 20% cut-off for major osteoporotic fractures and 3% for hip fractures.

In the USA, a HF IT of 3% and a MOF IT of 20% were deemed as cost-effective for intervention.

Due to the vast heterogeneity in epidemiologic and economic characteristics between countries, intervention thresholds should be country specific



# Guidance From NOF 2014 and AACE 2020:

## Whom to Treat

- After exclusion of secondary cause, treat postmenopausal women and men age  $\geq 50$  yr who have:

### Osteoporosis

#### Clinical

- Hip or spine fracture

*OR*

#### BMD by DXA

- T-score  $\leq -2.5$  in spine, femoral neck, total hip, or 1/3 radius

### Osteopenia/Low Bone Mass

#### BMD by DXA

- T-score between -1.0 and -2.5

*AND*

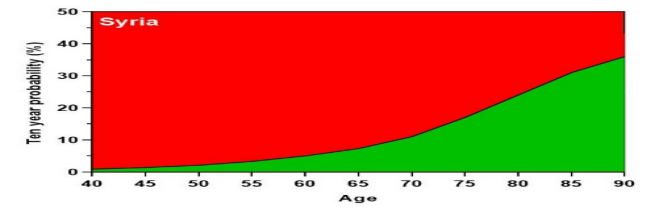
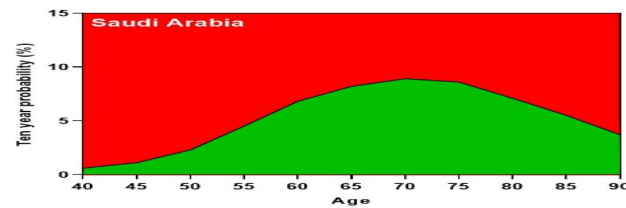
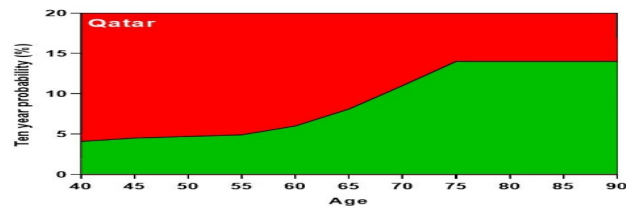
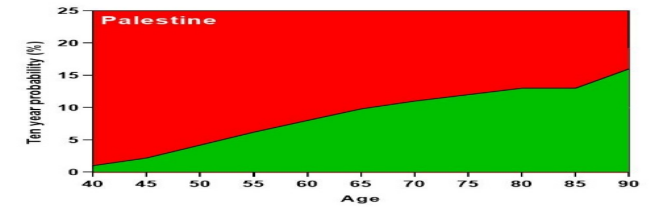
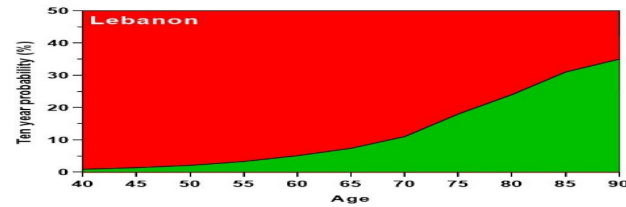
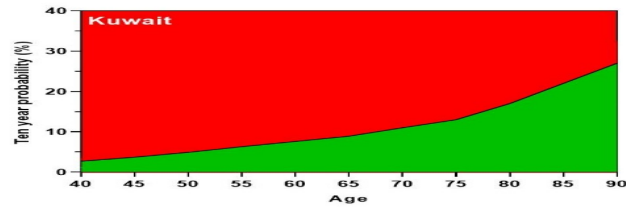
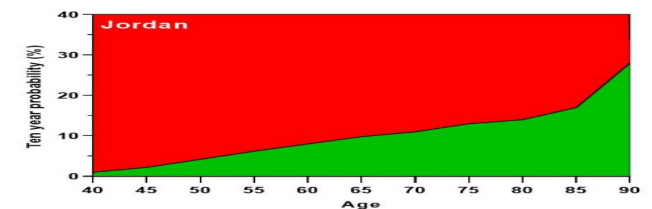
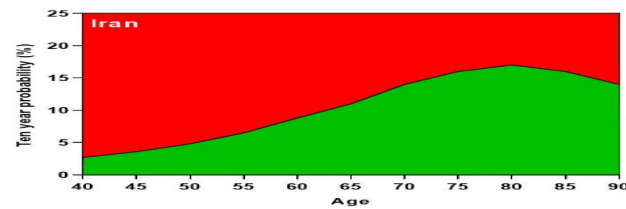
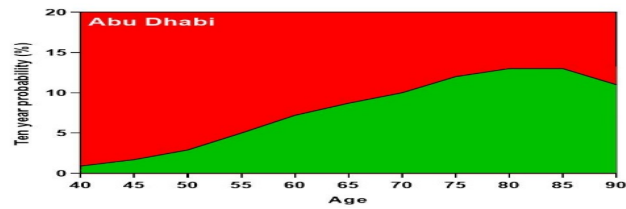
#### FRAX 10-Yr Fracture Risk

- $\geq 3\%$  for hip
- $\geq 20\%$  for major osteoporotic-related fracture

		High Risk	Very High Risk
Treatment algorithm	stratification of the patient according to the risk of fragility fracture	<ul style="list-style-type: none"> <li>▪ Previous fracture (vertebral or hip)</li> <li>▪ T-score <math>\leq</math> -2.5</li> <li>▪ T-score <i>between</i> -1.0 and -2.5 + FRAX high risk</li> </ul>	<ul style="list-style-type: none"> <li>▪ Recent fracture (less than 1 year)</li> <li>▪ Fracture during osteoporosis-approved treatment</li> <li>▪ Multiple fractures</li> <li>▪ T-score very low (<math>\leq</math>-3.0)</li> <li>▪ High risk of falls or history of recurrent falls</li> <li>▪ FRAX very high risk</li> <li>▪ Fractures during treatment with drugs that are deleterious to the bone</li> </ul>
	For all patients	<p>Evaluated for causes secondary osteoporosis</p> <p>Correct calcium and vitamin D deficiency</p> <p>Education on lifestyle measures, fall prevention, benefits, and risk of medications</p>	
	Pharmacological treatment	<ul style="list-style-type: none"> <li>▪ alendronate</li> <li>▪ denosumab</li> <li>▪ risedronate</li> <li>▪ zoledronate</li> <li>❖ Alternate therapy: ibandronate, raloxifene</li> </ul>	<ul style="list-style-type: none"> <li>▪ teriparatide*</li> <li>▪ romosozumab*</li> <li>▪ denosumab</li> <li>▪ zoledronate</li> <li>❖ Alternate therapy: alendronate, risedronate</li> </ul>

- Many Middle Eastern Countries face hindrances in the BMD assessment due to a lack of densitometry devices and high costs
- Fracture risk assessment tools have revolutionized osteoporosis management by allowing physicians to select patients for therapy based on their absolute fracture risk instead of relying solely on bone mineral density

# Intervention thresholds as set by FRAX-based 10-year probability (%) of a major osteoporotic fracture for the nine Middle Eastern countries with out availability of bone densitometry

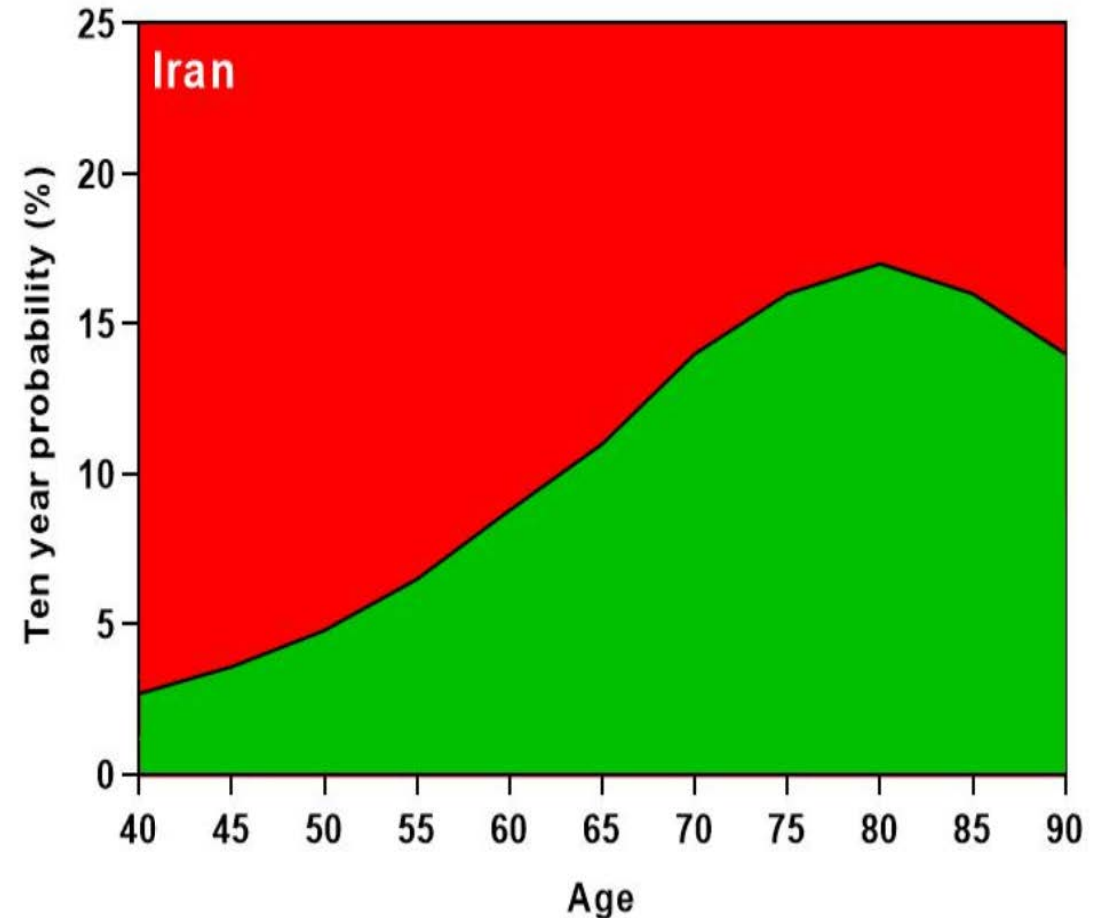


\*We have developed age-specific intervention thresholds for the Middle Eastern countries where FRAX models are available

# Iran Age-specific FRAX Based Intervention Thresholds

We have developed age-specific intervention thresholds for the Middle Eastern countries where FRAX models are available, which will make it easier for clinicians to use the tool.

- The intervention threshold was set as a woman's 10-year fracture probability if she has a body mass index (BMI) of  $25.0 \text{ kg/m}^2$  and a history of previous fracture without bone mineral density (BMD) and other clinical risk factors.





# Iran Age-specific FRAX Based Intervention Threshold

## Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: Iran Name/ID:  [About the risk factors](#)

**Questionnaire:**

1. Age (between 40 and 90 years) or Date of Birth  
 Age:  Date of Birth: Y:  M:  D:

2. Sex  Male  Female

3. Weight (kg)

4. Height (cm)

5. Previous Fracture  No  Yes

6. Parent Fractured Hip  No  Yes

7. Current Smoking  No  Yes

8. Glucocorticoids  No  Yes

9. Rheumatoid arthritis  No  Yes

10. Secondary osteoporosis  No  Yes

11. Alcohol 3 or more units/day  No  Yes

12. Femoral neck BMD (g/cm<sup>2</sup>)  
 Select BMD

**BMI: 25.0**  
 The ten year probability of fracture (%)  
 without BMD

Major osteoporotic	22
Hip Fracture	11

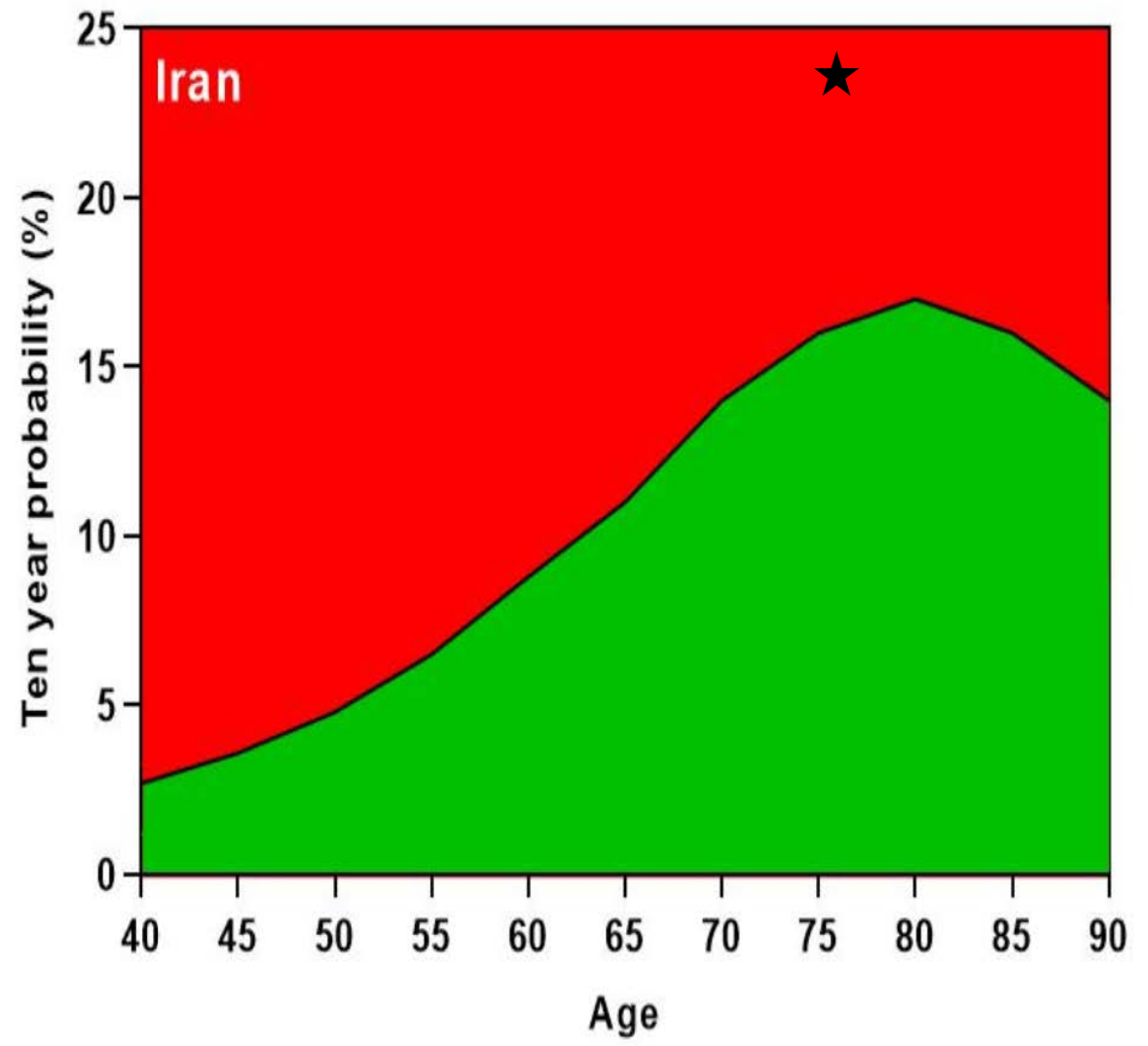


**Weight Conversion**  
 Pounds  kg

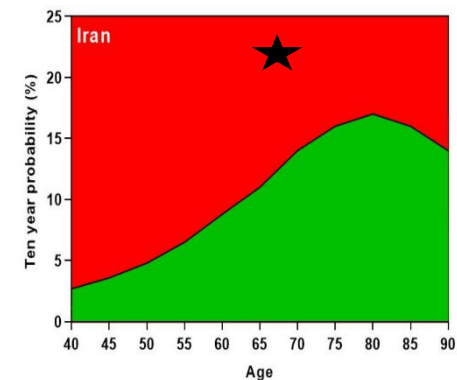
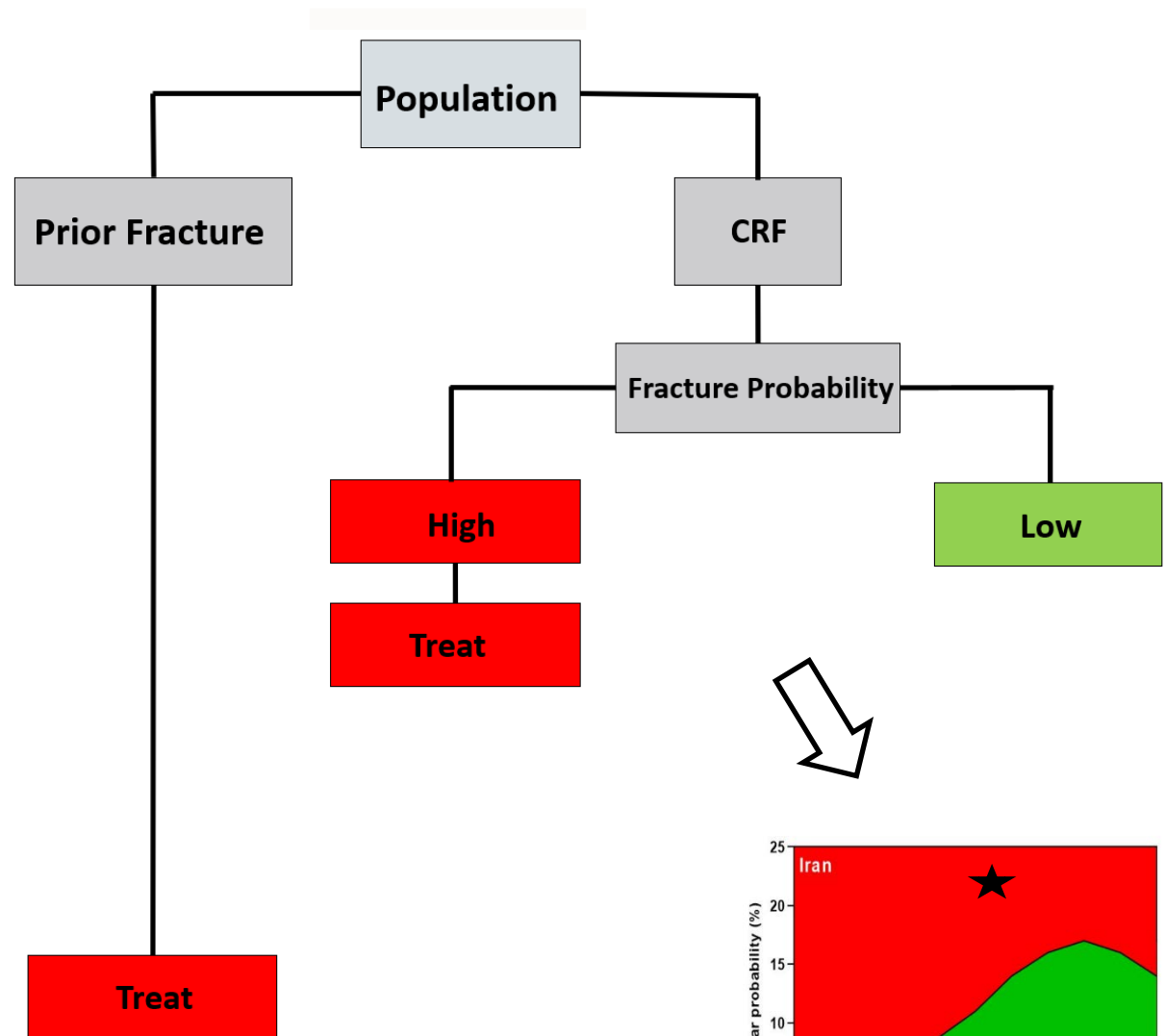
**Height Conversion**  
 Inches  cm

00227768  
 Individuals with fracture risk assessed since 1st June 2011

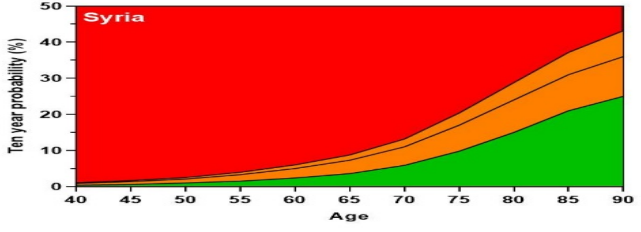
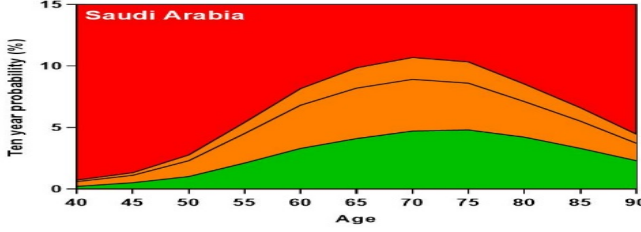
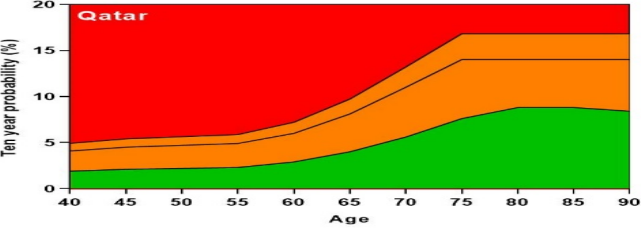
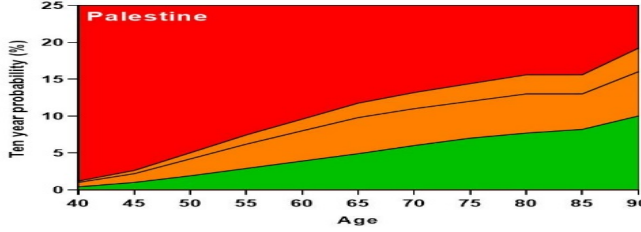
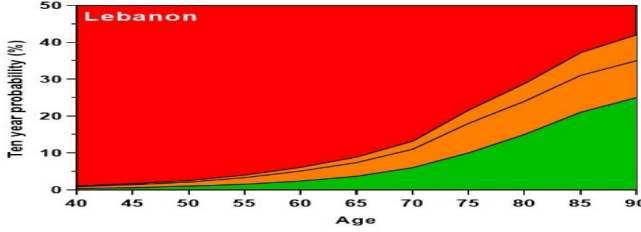
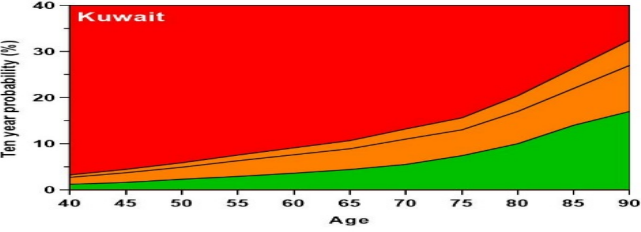
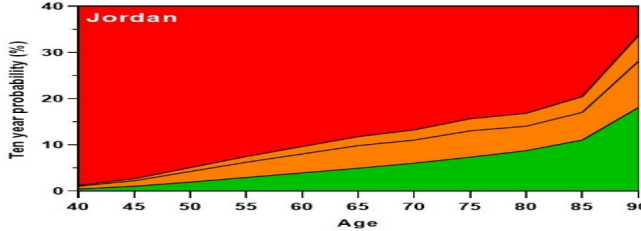
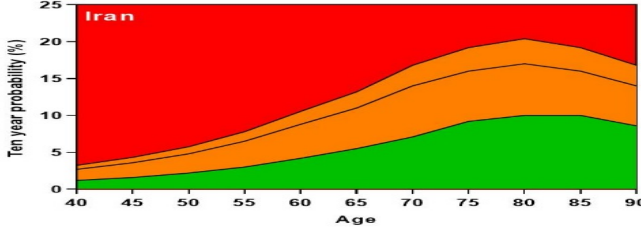
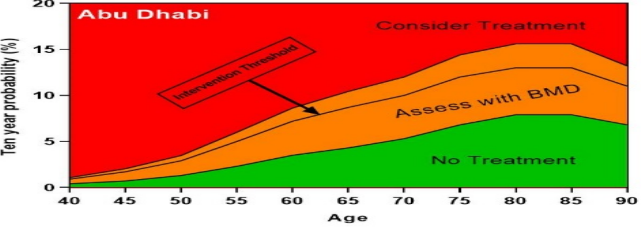
Print tool and information



- When bone densitometry is unavailable, reassurance may be provided for those with probabilities below the intervention threshold, and no other clinical considerations and treatment can be considered for those with fracture probabilities above the intervention threshold.



# Assessment thresholds as set by FRAX-based 10-year probability (%) of a major osteoporotic fracture for the nine Middle Eastern countries when bone densitometry is available



# Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: **Iran** Name/ID:  [About the risk factors](#)

### Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth  
 Age:  Date of Birth: Y:  M:  D:

2. Sex  Male  Female

3. Weight (kg)

4. Height (cm)

5. Previous Fracture  No  Yes

6. Parent Fractured Hip  No  Yes

7. Current Smoking  No  Yes

8. Glucocorticoids  No  Yes

9. Rheumatoid arthritis  No  Yes

10. Secondary osteoporosis  No  Yes

11. Alcohol 3 or more units/day  No  Yes

12. Femoral neck BMD (g/cm<sup>2</sup>)  
 Select BMD

**BMI: 30.9**  
 The ten year probability of fracture (%)  
 without BMD

Major osteoporotic	<b>7.4</b>
Hip Fracture	<b>1.5</b>



### Weight Conversion

Pounds ➔ kg

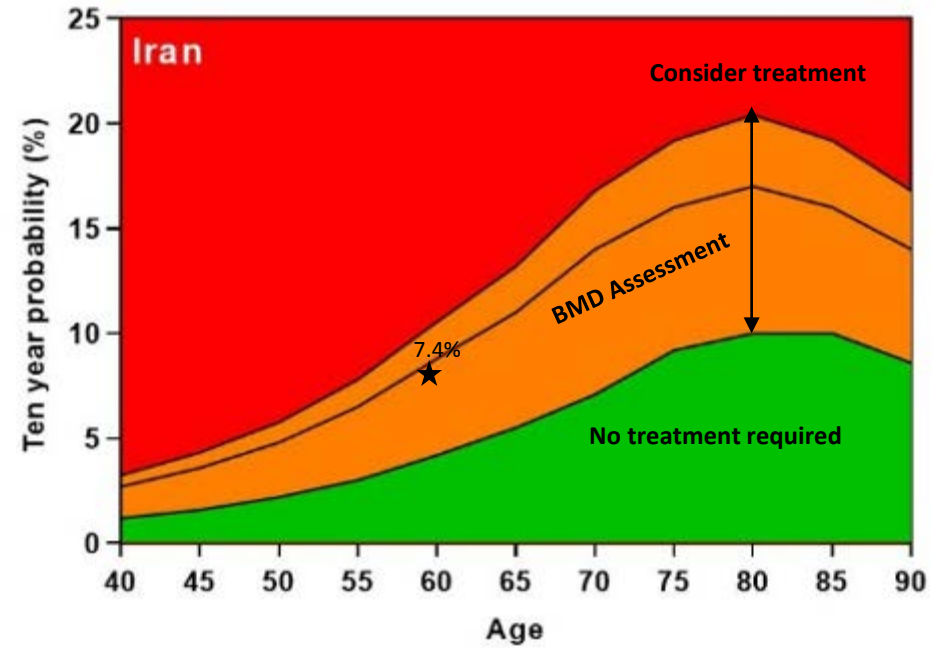
### Height Conversion

Inches ➔ cm

**00227768**

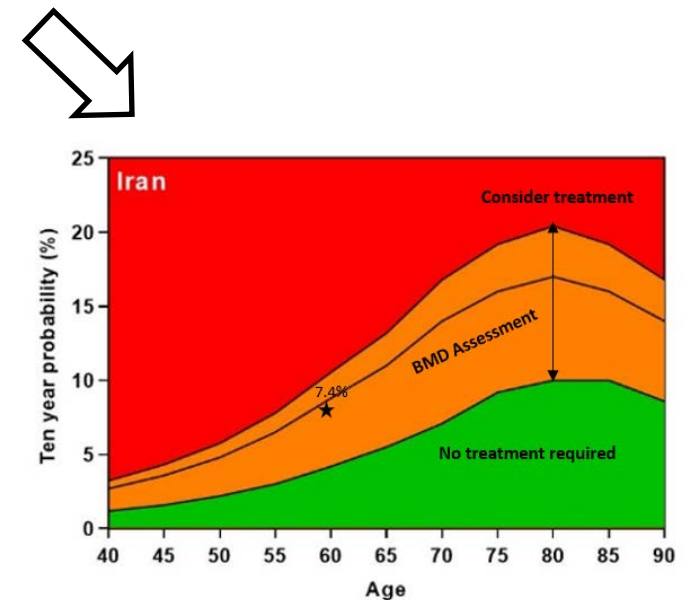
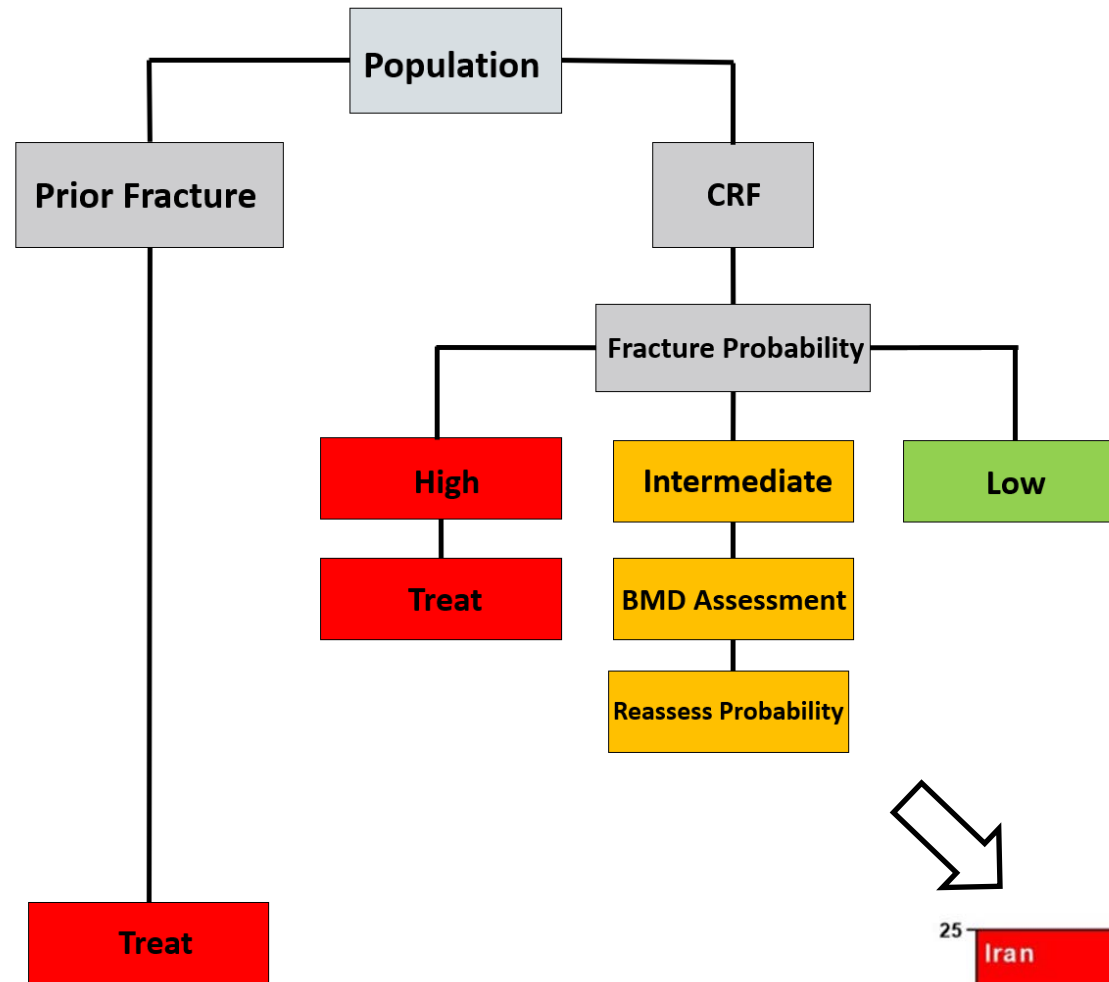
Individuals with fracture risk assessed since 1st June 2011

[Print tool and information](#)



Slide credit: [clinicaloptions.com](http://clinicaloptions.com)

- However, if BMD measurements are available and there are no other clinical considerations, reassurance may be given to men and women with probabilities below the lower assessment threshold.
- Those with probabilities above the upper assessment threshold can be considered for treatment
- those with probabilities between the lower and upper assessment thresholds can be considered for bone densitometry using dual-energy X-ray absorptiometry, with their fracture probability reassessed afterward.



**Fracture Risk Assessment**



**Intervention Thresholds**



**Evaluation/Discussion**

**Treatment**



**Follow-up**