Identifying High Risk Individuals in the Management of Osteoporosis

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Please download the “Socrative” student version from Google Play or Apple Itunes

Room number: optimal

Case Discussion I-1

50 yr old Female Chinese

- Fell down a flight of stairs. Comminuted wrist fracture.
- No F/H of Osteoporosis;
- Perimenopausal;
- Weight 56 kg. Height 156 cm.
- No steroid use,

Would you order a BMD?

A. Yes because she has osteoporotic fracture
B. Yes because her OSTA is moderate risk
C. No because her OSTA is low risk
D. No because her fracture is due to fall from height

What is the most cost effective way to diagnose osteoporosis?

New Definition of Osteoporosis

"Osteoporosis is defined as a skeletal disorder characterized by compromised ***bone strength*** predisposing to an increased risk of fracture."

Bone strength = **bone density** + **bone quality**

Bone density: grams of mineral/area (volume)

Bone quality: architecture, turnover, damage accumulation, and mineralization

NIH Consensus Development Conference on Osteoporosis, 2000.

Bone Density

骨质密度

(g/cm^2 or g/cm^3)

DXA hip & spine

Others:

- DXA forearm or heel
- SXA forearm or heel
- US heel, tibia or multisite
- QCT spine

Bone Quality

骨品质

- Architecture 骨结构
- Turnover 骨翻折
- Microfractures 微型骨折
- Mineralisation 骨钙含量

Most well-defined & validated;

Widely used in epidemiology;

Extensive use in treatment trials: entry, monitoring

Z SCORE

The number of standard deviations above or below the mean of an age and gender matched population

T SCORE

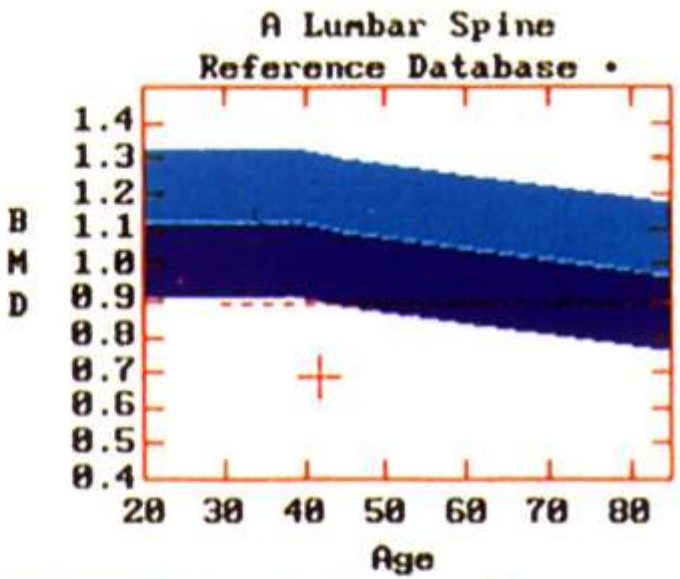
The number of standard deviations above or below the mean peak bone mass of the population

WHO DEFINITION OF OSTEOPOROSIS

T SCORES

- > -1 NORMAL
- -1 TO -2.5 OSTEOPENIA
- < -2.5 OSTEOPOROSIS

FRACTURE = ESTABLISHED OSTEOPOROSIS



BMD(L2-L4) = 0.681 g/cm^2

Region	BMD	T(30.0)		Z	
N/A					
L2	0.703	-3.55	64%	-3.47	65%
L3	0.705	-3.62	64%	-3.53	64%
L4	0.640	-4.59	56%	-4.50	56%
L2-L4	0.681	-3.94	61%	-3.86	62%

◆ Age and sex matched
T = peak bone mass
Z = age matched

Consequences of Fracture

- Hip fracture
  - mortality of 26% in the first year
  - Of the survivors, 9 % were bedridden and
  - 24 % wheelchair bound*
- Vertebral fracture
  - may be associated with back pain, disability or physical deformity
  - increase in mortality related to frailty, comorbities and an increased risk of pneumonia
  - A history of vertebral fracture is associated with an increased risk of a subsequent fragility fracture.

*Ann Acad Med Singapore 1994; 23:876-8.

The most cost effective way to diagnose osteoporosis:

1. Have you ever had a fragility fracture?
2. Look out for kyphosis and height loss

How to pick up (asymptomatic) osteoporosis

BMD everyone

BMD if at risk

Age

50-65 yr	~10%
> 65 yr	~30%

+

Risk factors

- age
- weight
- past fracture
- family history
- illness
- smoking
- etc

Already had fracture

Osteoporosis Self-assessment Tool for Asians (OSTA)
Postmenopausal Female

Model with only 2 variables

Age (years) - Weight (kg) =

More than 20	high risk
0 to 20	Moderate risk
Less than 0	low risk

A Simple Tool to Identify Asian Women at Increased Risk of osteoporosis, LKH Koh et al Osteoporosis Int (2001) 12:699-705

Risk Stratification

Risk level	% of all women	% with osteoporosis
Low	40%	3%
Medium	52%	15%
High	8%	61%

High sensitivity
Low specificity

SnNout (negative, rule out)
SpPin (positive, rule in)

Case Discussion I-1

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Case I-1

- BMD
  - Spine T score -1.8
  - Hip T score -1.5

What would you do next?

A. Calculate FRAX
B. Start pharmacotherapy
C. Do nothing

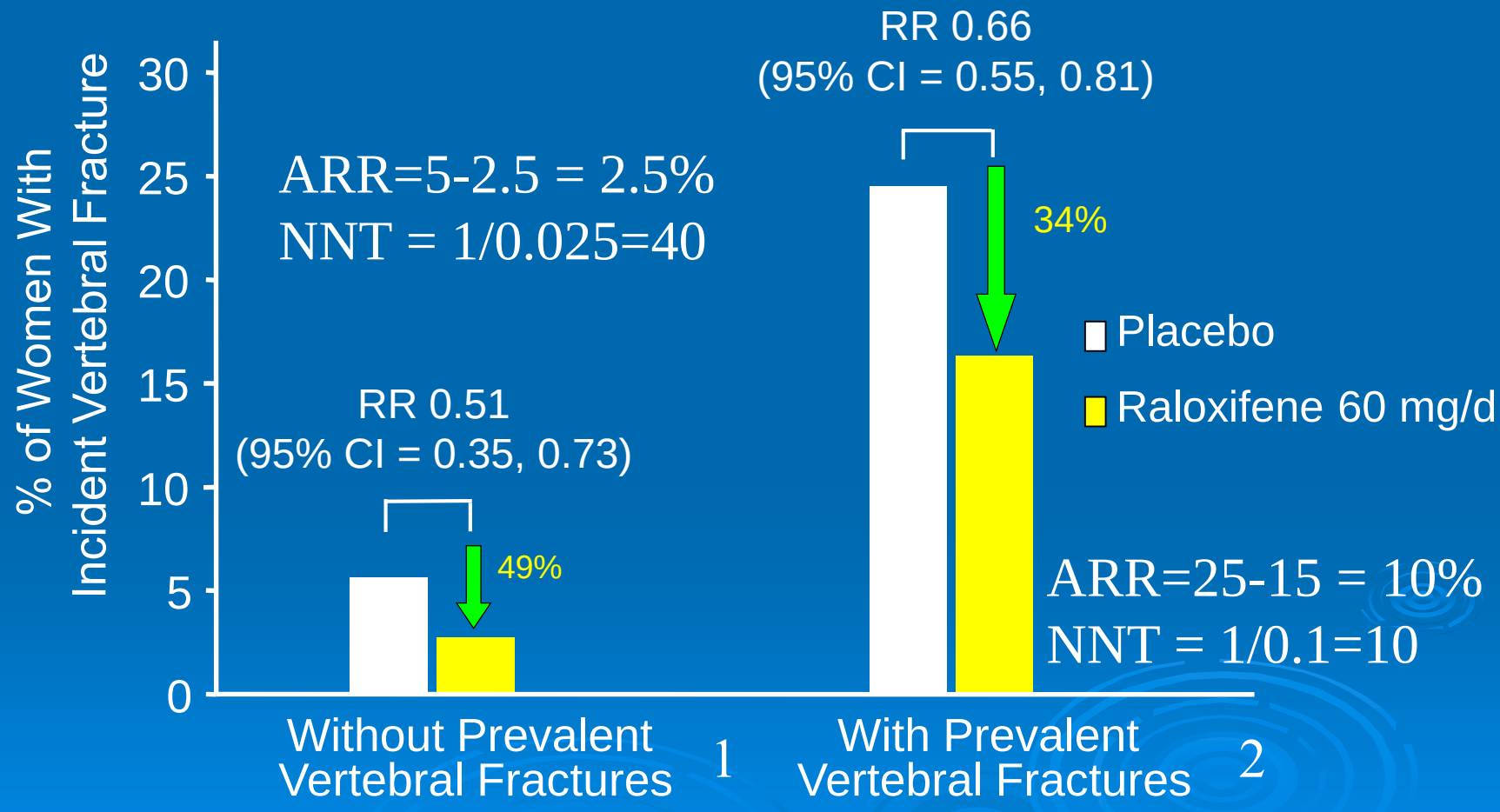
When to start treatment for osteoporosis ?

Factors to consider in decision to treat

Factors	Tend to treat if	Tend to defer if
Fracture risk	high	low
Past fracture	present	absent
BMD	lower (T-score <-2.5)	higher
Age	older (e.g. >65 years)	younger
Risk for falls / bone loss	high	low

Effect of Raloxifene in Women With or Without Existing Fractures

MORE Trial - 4 Years



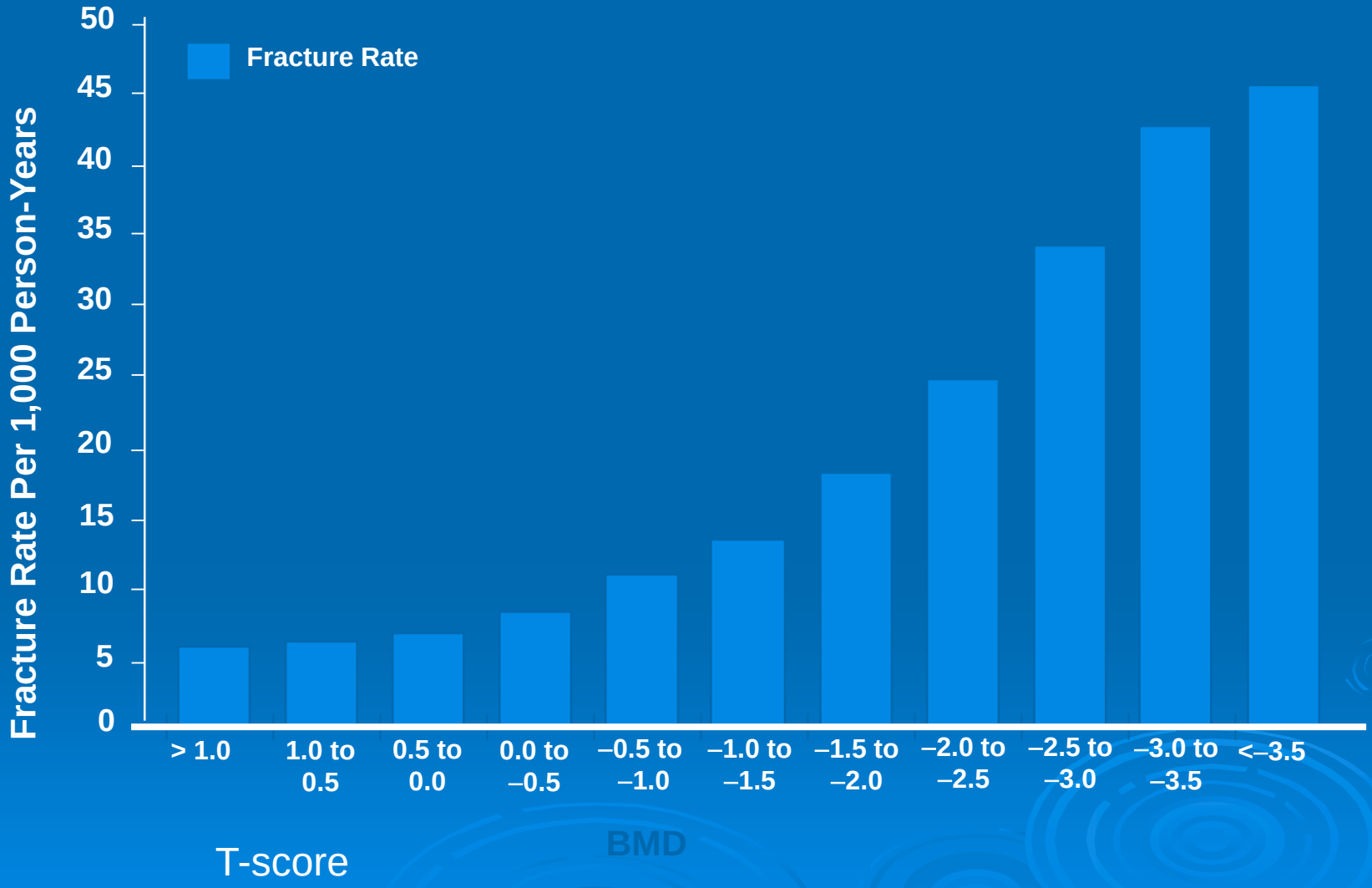
Eastell R, et al. *J Bone Miner Res*. 2000;15(suppl 1):S229.

NORA

Fracture Rates by T-score

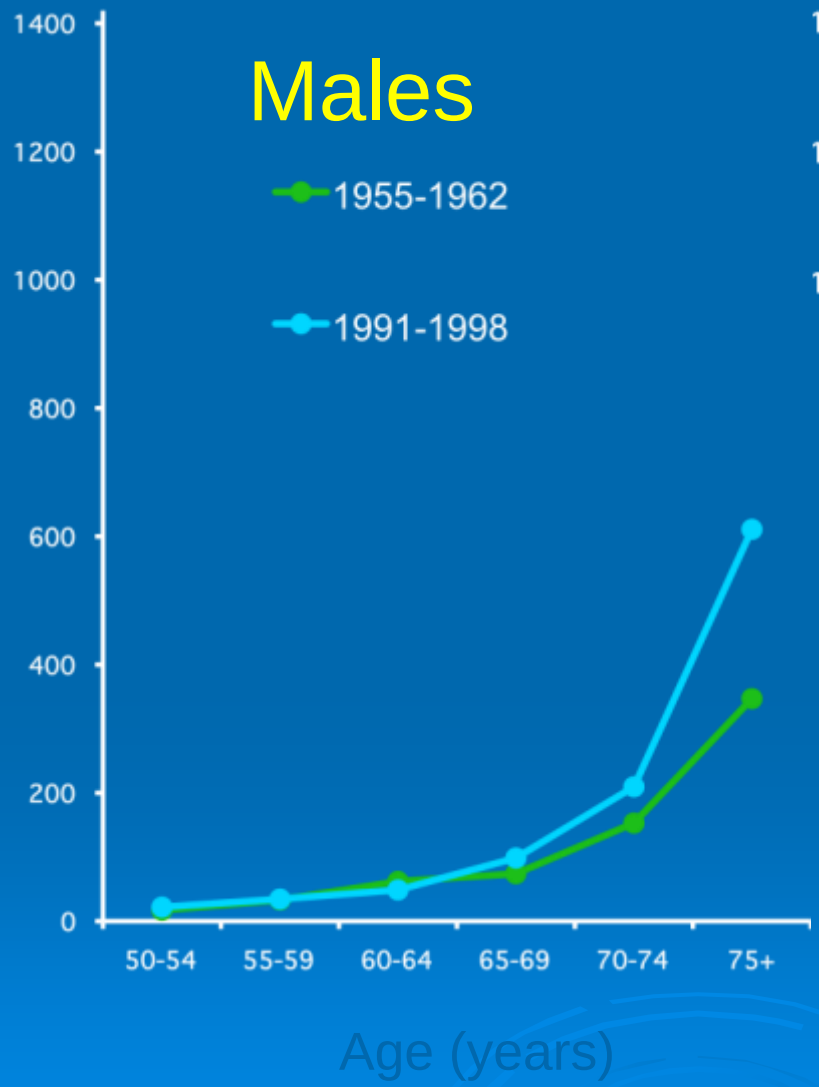
n Fx=2,259

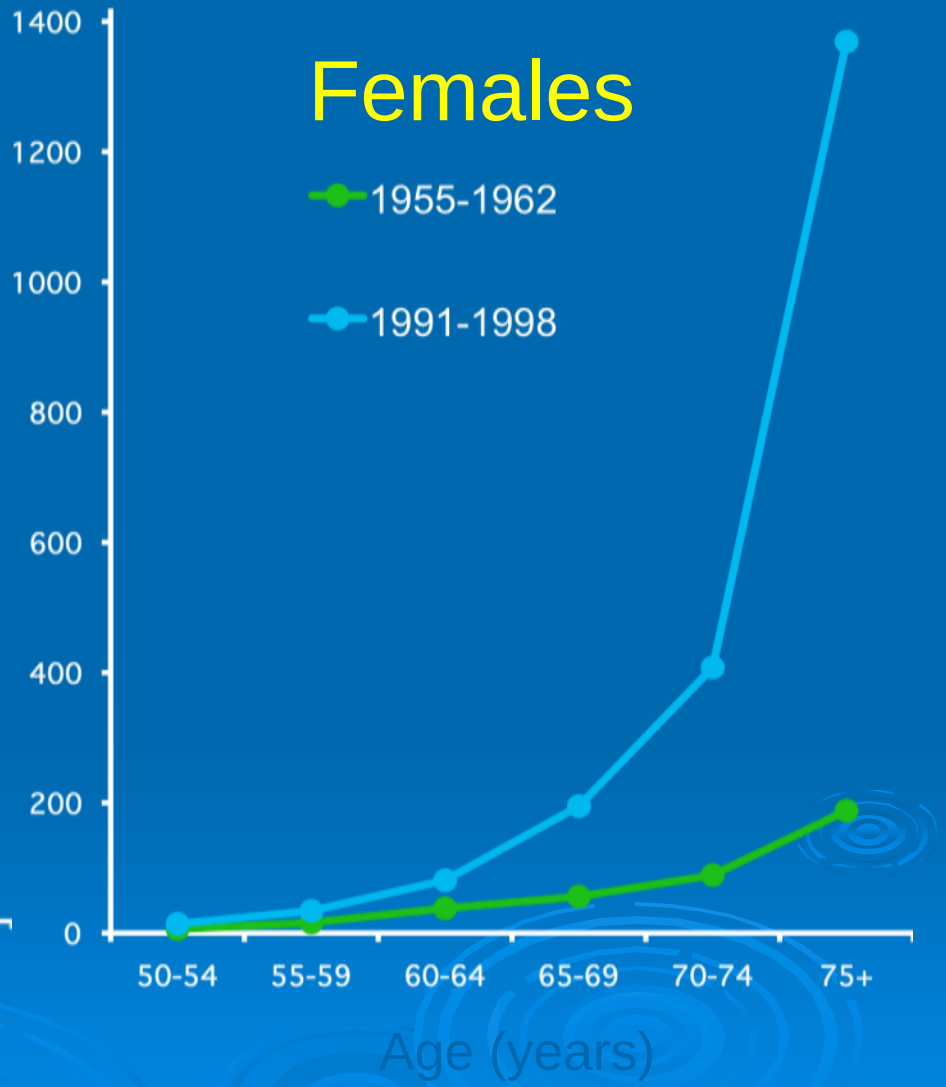
1-Year Follow-Up



Siris ES et al. Bone Mineral Density Thresholds for Pharmacological Intervention to Prevent Fractures. Arch Intern Med 2004; 164. In Press.

Hip Fractures in Singapore





Wong, Clin Orthop 1966; LKH Koh, Osteoporos Int 2001

Welcome to FRAX

www.sheffield.ac.uk/FRAX/

Home - MedNet | Curriculum Review | Apple | Rheumatology - som | .Mac | Amazon | Apple | BibleGateway.com: A | CMH110 Epidemiolo | Other Bookmarks

FRAX® WHO Fracture Risk Assessment Tool

Home | Calculation Tool | Paper Charts | FAQ | References | English

Welcome to FRAX®

The FRAX® tool has been developed by WHO 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® models have been developed from studying population-based cohorts from Europe, North America, Asia and Australia. In their most sophisticated form, the FRAX® 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® 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).

Web Version 3.2

View Release Notes

Links

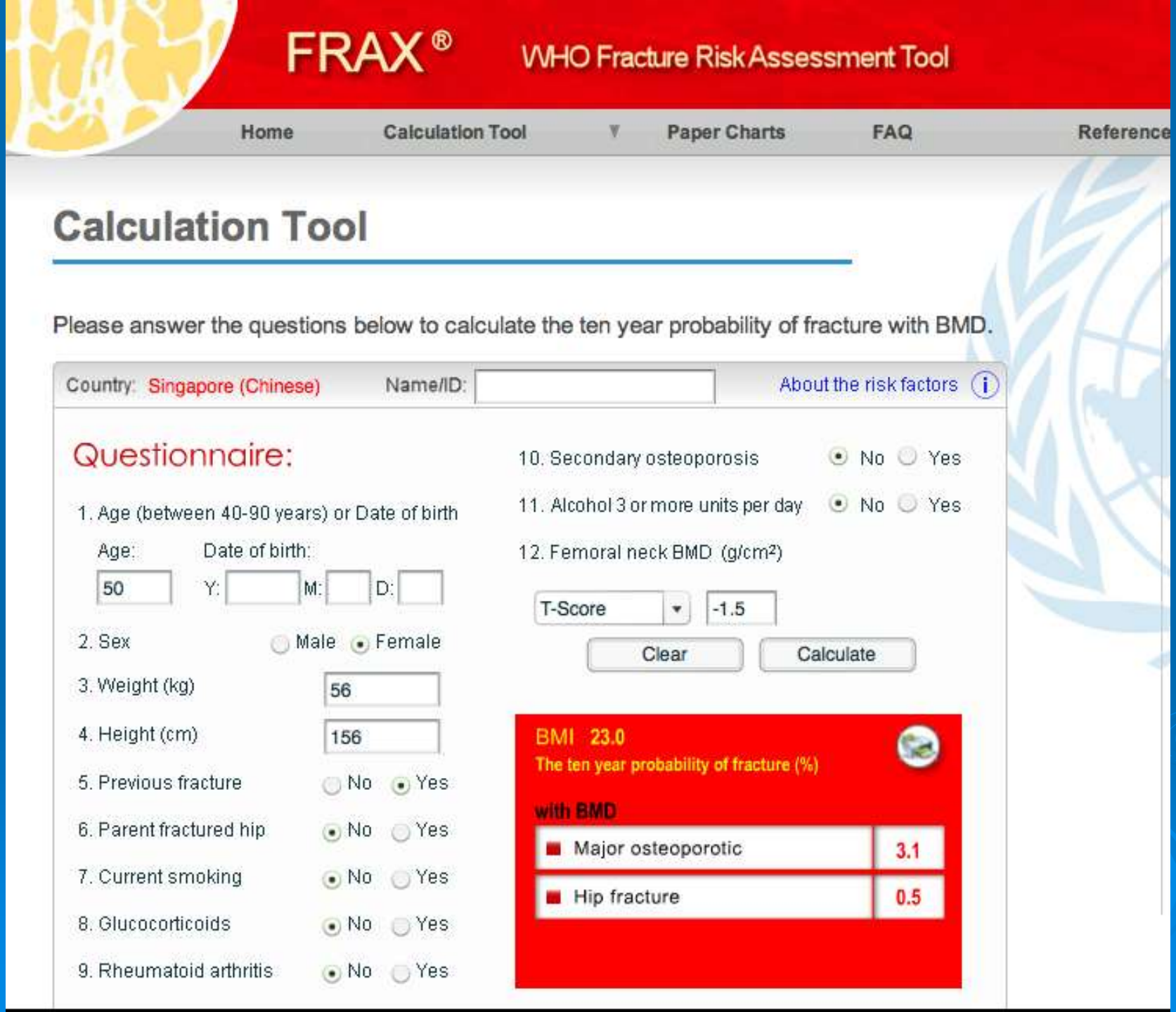
www.iofbonehealth.org

www.nof.org

www.jpof.or.jp

www.esceo.org

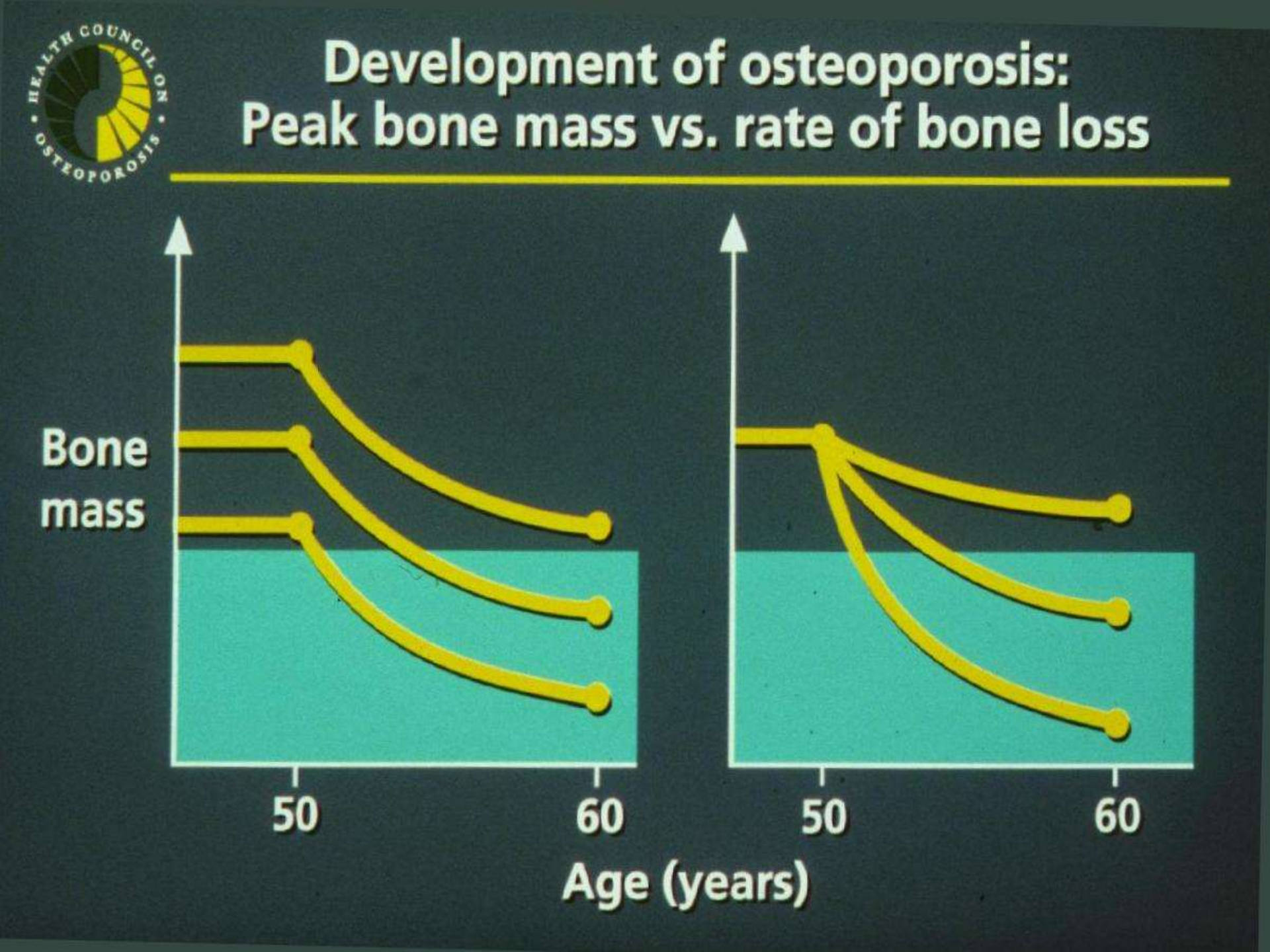
FRAX available as iPhone App


FRAX®
WHO Fracture Risk Assessment Tool
Home
Calculation Tool
Paper Charts
FAQ
Reference
Calculation Tool
Please answer the questions below to calculate the ten year probability of fracture with BMD.
Country: Singapore (Chinese)
Name/ID:
About the risk factors
Questionnaire:
1. Age (between 40-90 years) or Date of birth
Age:
Date of birth:
50
Y:
M:
D:
2. Sex
Male
Female
3. Weight (kg)
56
4. Height (cm)
156
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 per day
No
Yes
12. Femoral neck BMD (g/cm²)
T-Score
-1.5
Clear
Calculate
BMI 23.0
The ten year probability of fracture (%)
with BMD
Major osteoporotic
3.1
Hip fracture
0.5

What would you do next?

A. Start pharmacotherapy
B. Healthy lifestyle advise
C. Do nothing

Development of osteoporosis: Peak bone mass vs. rate of bone loss



Efficacy of population-based preventive approaches

Intervention	BMD	Vertebral fracture reduction	Hip fracture reduction
Dietary calcium	B	B	B
Calcium (± vitamin D) supplements	A	A	A
Exercise	A	B	B
Smoking cessation	B	B	B
Reduced alcohol intake	C	C	B

Case Discussion II-1

- Mdm FSY, 66 year old teacher, menopause since age 51, came to you with complaint of low back pain after a fall.
- Maternal history of hip fracture
- No other risk factors for osteoporosis
- Weight 56 kg, height 156 cm

Would you order a BMD?

A. Yes because she has osteoporotic fracture
B. Yes because her OSTA is moderate risk and she has maternal history of hip fracture
C. No because her OSTA is low risk

Case II-2

- BMD
  - Spine T score -1.8
  - Hip T score -1.5
- Lumbar spine X ray

What would you do next?

A. Calculate FRAX
B. Start pharmacotherapy
C. Do nothing

FRAX® WHO Fracture Risk Assessment Tool

Home | Calculation Tool | Paper Charts | FAQ | Reference

Calculation Tool

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

Country: Singapore (Chinese) Name/ID: About the risk factors

Questionnaire:

1. Age (between 40-90 years) or Date of birth
   Age: 66 Date of birth: Y: M: D:
2. Sex ○ Male ◉ Female
3. Weight (kg) 56
4. Height (cm) 156
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 per day ◉ No ○ Yes
12. Femoral neck BMD (g/cm²)
    T-Score -1.5

Clear Calculate

BMI 23.0

The ten year probability of fracture (%)

with BMD

Major osteoporotic	11
Hip fracture	1.5

What would you do next?

A. Start pharmacotherapy
B. Healthy lifestyle advise
C. Do nothing

FRAX® WHO Fracture Risk Assessment Tool

Home | Calculation Tool | Paper Charts | FAQ | References

Calculation Tool

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

Country: Singapore (Chinese) Name/ID: About the risk factors

Questionnaire:

1. Age (between 40-90 years) or Date of birth
   Age: 66 Date of birth: Y: M: D:
2. Sex ○ Male ● Female
3. Weight (kg) 56
4. Height (cm) 156
5. Previous fracture ○ No ● Yes
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8. Glucocorticoids ● No ○ Yes
9. Rheumatoid arthritis ● No ○ Yes
10. Secondary osteoporosis ● No ○ Yes
11. Alcohol 3 or more units per day ● No ○ Yes
12. Femoral neck BMD (g/cm²)
    T-Score -1.5

Clear Calculate

BMI 23.0

The ten year probability of fracture (%)

with BMD

Major osteoporotic	18
Hip fracture	2.5

What would you do next?

A. Start pharmacotherapy
B. Healthy lifestyle advise
C. Do nothing

Which drug will you choose?

A. Oral bisphosphonate
B. IV bisphosphonate
C. Strontium Ranelate
D. SC Denosumab
E. SC Teriparatide

How to counsel patients on treatment options?

IPOET
Individualised Patient Osteoporosis Education Tool

听而易忘

见而易记

做而易懂

Tell me and I forget.

Teach me and I remember.

Involve me and I learn

Benjamin Franklin

Case Discussion III-1

- Mdm TAL, 75 year old retired seamstress, previous history of L2 vertebra fracture, recently discharged from hospital for hip fracture
- Maternal history of hip fracture
- No other risk factors for osteoporosis
- Weight 56 kg, height 156 cm

Would you order a BMD?

A. Yes because she has osteoporotic fracture
B. Yes because her OSTA is moderate risk and she has maternal history of hip fracture
C. No because her OSTA is low risk
D. No, just start pharmacotherapy

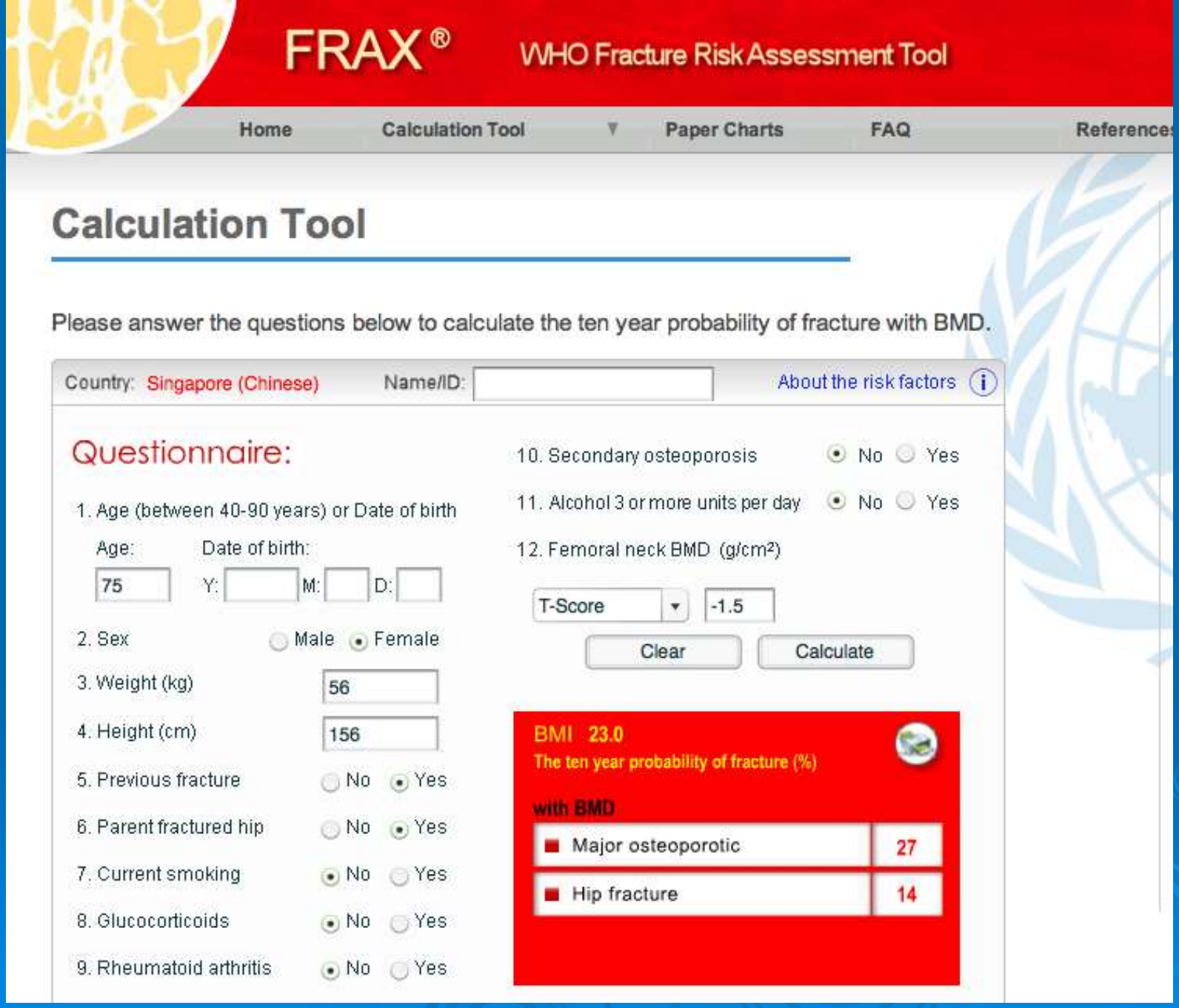
Case III-2

- BMD
  - Spine T score -1.8
  - Hip T score -1.5

  - FBC, creatinine normal
  - ALP slightly high, corrected calcium slightly low

What would you do next?

A. Calculate FRAX
B. Check her 25 OH- vitamin D
C. Start pharmacotherapy
D. All of the above



25 OH- Vitamin 10 ug/L (normal > 30 ug/L)

What would you do next?

1. Start pharmacotherapy
2. Replete her with vitamin D
3. Healthy lifestyle advise
4. All of the above

Which drug will you choose?

A. Oral bisphosphonate
B. IV bisphosphonate
C. Strontium Ranelate
D. SC Denosumab
E. SC Teriparatide

Which drug will you avoid if the patient has reflux oesophagitis?

A. Oral bisphosphonate
B. IV bisphosphonate
C. Strontium Ranelate
D. SC Denosumab
E. SC Teriparatide

Which drug will you choose if the eGFR is < 30 ml/min?

1. Oral bisphosphonate
2. IV bisphosphonate
3. Strontium Ranelate
4. SC Denosumab
5. SC Teriparatide

What do we do if patients cannot tolerate oral bisphosphanates? How do we manage osteoporotic patients with renal impairment?

What do you have to do before giving SC denosumab or IV bisphosphonate therapy?

A. Check creatinine and 25 OH vitamin D levels
B. Replete vitamin D
C. Give calcium supplement if patient is renal impaired
D. All of the above

Grades of Recommendations for *Therapeutic* Interventions

Drug	Benefit in BMD	Vertebral fracture reduction	Non-vertebral fracture reduction	Hip fracture reduction
Alendronate	A	A	A	A
Risedronate	A	A	A	A
Zoledronate	A	A	A	A
Strotium Ranelate	A	A	A	A*
Denosumab	A	A	A	A
Parathyroid hormone (Teriparatide)	A	A	A	-
Raloxifene	A	A	A*	-
Ibandronate	A	A	A*	-
Calcitonin	A	A	B	B
Calcitriol	A*	A*	A	-
Alfacalcidol	A	A	-	-

Treatment Considerations

- Amino-bisphosphonates
  - Reflux oesophagitis (IV route will negate this, e.g. zoledronate)
  - Renal impairment (CCT < 35 ml/min)
- Strontium Ranelate
  - Renal impairment (CCT<30 mL/min)
- Teriparatide
  - Moderate to severe renal impairment
- Denosumab (RANKL inhibitor)
  - Severe renal impairment (CCT < 10ml/min)
- Raloxifene (SERM)
- Vitamin D analogue

Before Starting Treatment

- Creatinine (eGFR) or CCT
- Calcium, albumin
- 25 Vitamin D level (3000 U D3 for 2 to 3 months for every 5 ug/L deficiency)
- FBC
- ESR
- Other test if secondary causes suspected

QUESTION AND ANSWER

Patient TAL expresses concern about ONJ and atypical femoral fracture, what will you do next?

A. Avoid using anti-resorptives, just prescribe calcium and vitamin D
B. Avoid using bisphosphonates, just prescribe other osteoporosis medications
C. Explain risk versus benefit of each class of medication
D. Insist patient follow the doctor advice, as doctor knows best

Osteonecrosis of Jaw/ atypical femoral fracture risk

Risks vs. Benefits?

Treatment Adverse Effects

- Amino-bisphosphonates
  - Atypical fracture (1 in a 1000 to 4000)
  - Osteonecrosis of jaw, < 1 in 100,000 for use in osteoporosis
- Strontium Ranelate
  - Serious skin reaction (1 in 8,000)
  - IHD
- Teriparatide
  - Osteosarcoma in animal study, not proven in human
- Denosumab (RANKL inhibitor)
  - Skin infection (4 in 1000)

Benefits vs Risks

- Consider a patient with moderate risk of fracture:
  - All site – 20%
  - Hip – 3%
- Benefit of treatment
  - All site fractures reduce by 8%, NNT = 1:12
  - Hip fracture reduce by 1%, NNT = 1:100
- Risk of various serious complication
  - Numbers needed to harm about 1 in 1000
- Review for risk factors for atypical fractures and intervene with appropriate measures if risk factors are present may be useful in our patients as well.

Mdm Tan has been treated with oral bisphosphonates for 4 years, she is keen to stop her medication, what will be your advice?

A. Evaluate her fracture risk and consider stopping medication if fracture risk is low
B. Insist that she continue her medication as osteoporosis is a life long disease
C. Allow her to stop medication as she is exercising autonomy
D. Switch her to another osteoporosis medication

Rational of using medication long term.

Drug holiday, is it valid? Can/Should we give longer?

The long term use of osteoporosis medication does it result in higher fracture risk?

Those patients who are approaching 5 years do we stop them?

Switch to which medication?

Treatment beyond 5 years

- The jury is still out on risk vs benefit of routine treatment with alendronate (or other bisphosphonates) beyond 5 years.
- It will have to be individualised to the patient's risk of fracture vs the harm of atypical fracture.
- FRAX may be use to predict fracture risk even when the patient is already on treatment.
- Therefore, if the ten year total risk of fracture is still over 20% or if there is a previous vertebra fracture, it will be appropriate to continue treatment.

Mdm Lee has been treated with oral bisphosphonates for 2 years, her repeat BMD has declined by 3% in the spine and NOF, what will be your advice?

A. Evaluate her for secondary osteoporosis
B. Check her compliance and adherence to the osteoporosis medication
C. Treat her with the same medication for one more year, then repeat BMD
D. Switch her to another osteoporosis medication

How do we define treatment failure?
How do we manage such cases?

Treatment Failure

- When BMD fail to improve after an adequate course of medication, with exclusion of poor compliance and adherence, and secondary causes of osteoporosis.
- Evaluate the underlying cause and intervene appropriately
- Switching to 6 monthly or once yearly treatment options may be useful

Practice Improvement

- Check creatinine level
- Check and replete vitamin D levels
- Supplement calcium in those who are renal impaired
- Empower patient with simple information on benefits and risk of therapy
- Watch out for thigh pain, especially patients with other risk factors for atypical fractures

The Missing Ingredient

Adherence to all to the above strategies

Chronic Disease Management Program

Conclusion

- Fractures due to osteoporosis is a potentially life threatening condition
- OSTA formula is a cost effective way to screen female for risk of low DXA BMD
- Healthy lifestyle interventions to prevent osteoporosis is likely to be cost effective
- Osteopaenic patients should be categorised into high risk or low risk for fractures using FRAX before deciding on treatment
- Selecting patients with high 10 year life time risk of fracture for treatment and ensuring their adherence is the most cost effective treatment strategy
- Involve patients with decision on management with simple to understand information

Some Words of Wisdom
金玉良言

- There are three grades of doctors
  - The superior treat the system, the average treat the patient, the inferior treat the illness
  - The superior treat pre illness, the average treat the illness, the inferior treat the complications
  - The superior listen, the average observe and the inferior investigate
- 医有三品,
  - “上 医医国,中医医人,下医医病”
  - “上医医未病之病,中医医欲病之病,下医医已病之病”
  - “上医听声,中医察色, 下医诊脉”

医圣孙思邈《千金要方》
Doctor sage Sun Si Miao