OsteoporosisTrabecular Bone Score (TBS) for Fracture Risk Assessment

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Learning Objectives

- As a result of participating in this session, attendees should be able to:

  1. Describe the major studies that have examined the ability of TBS to predict fractures.
  2. Describe how TBS is used to adjust fracture probability.
  3. Describe when TBS has the greatest clinical impact on clinical management.

Case with questions

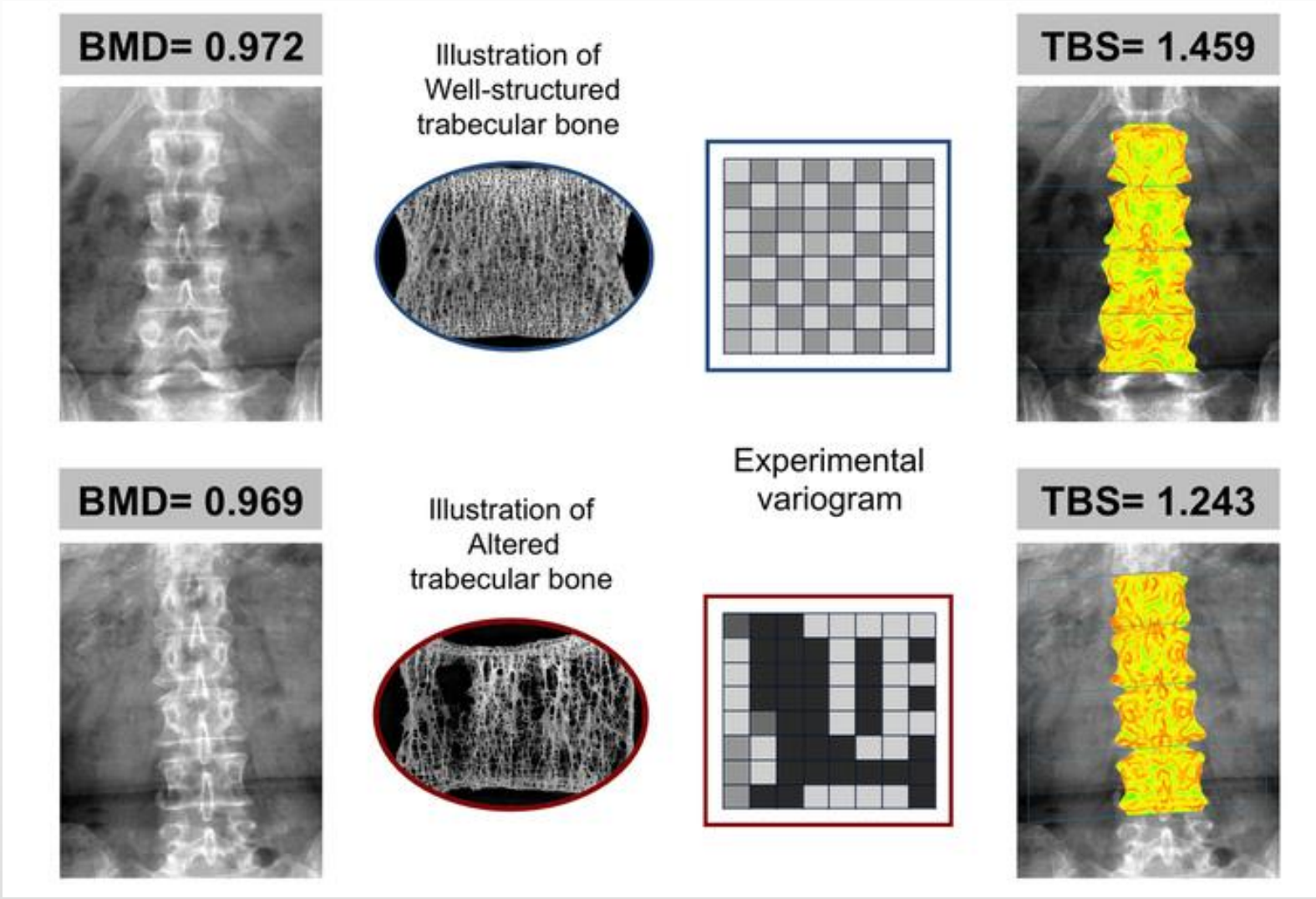
- For a woman with FRAX major fracture probability 15% and hip fracture probability 2.5%, what level of TBS would be required to exceed treatment thresholds?

What is TBS?

- TBS is a grey-level textural index derived from the lumbar spine DXA image by dedicated software
  - A high TBS correlates with a preserved bone structure
  - A low TBS correlates with a degraded bone structure

Silva et al. *JBMR 2014; 3:518.*

TBS Principles

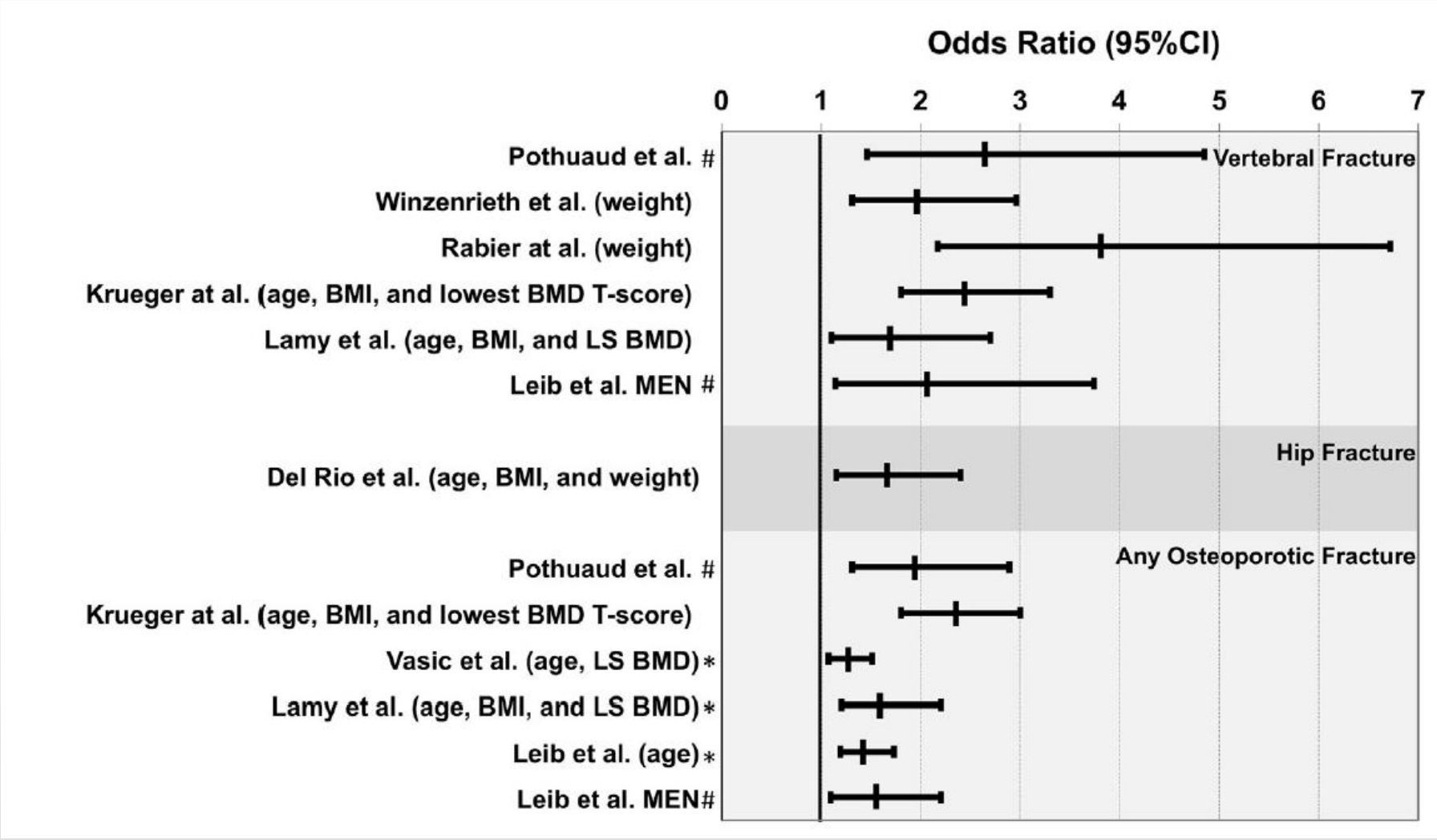


Silva et al. *JBMR 2014; Epub.*

What Does TBS Measure?

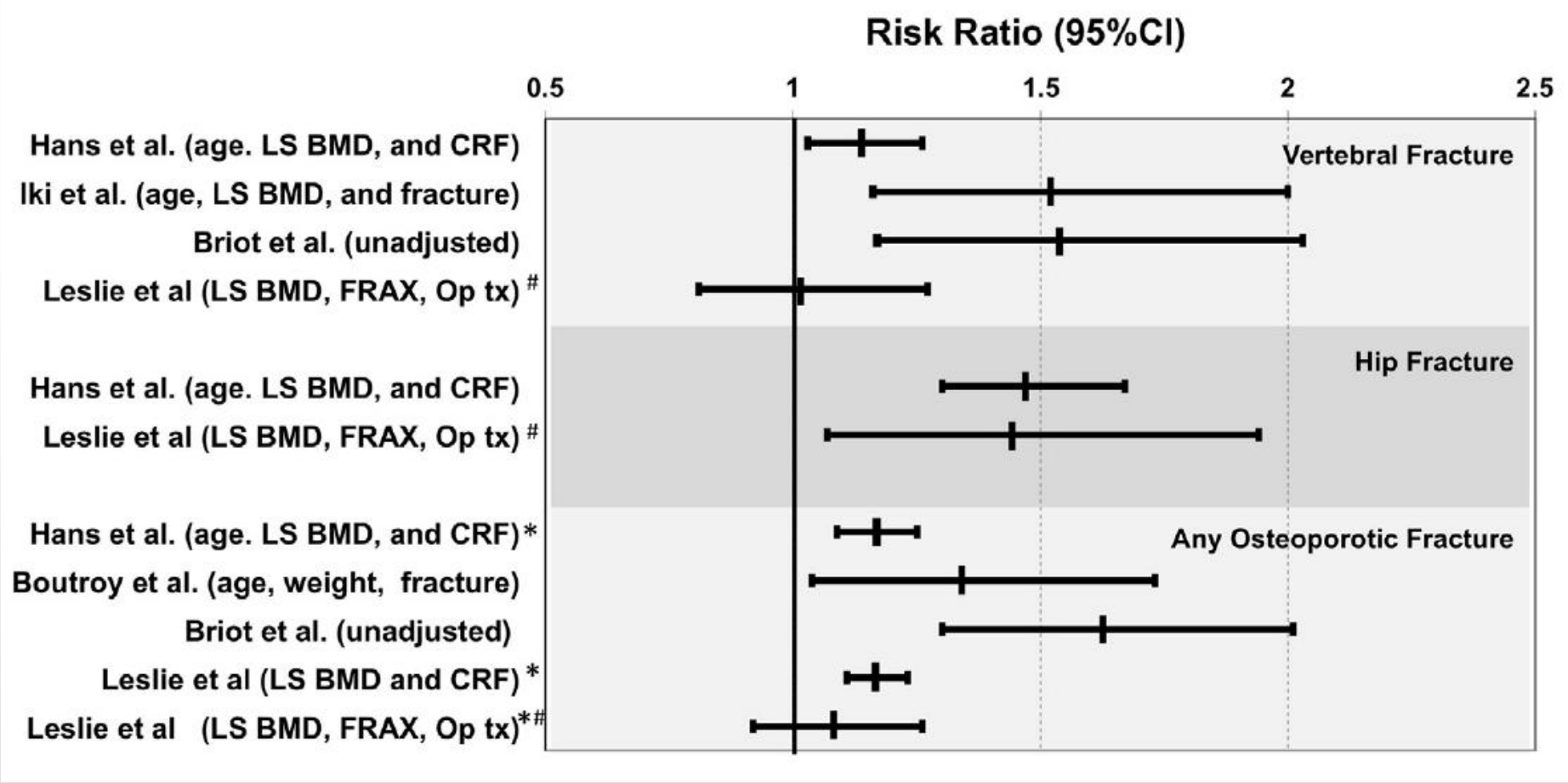
TBS is a novel texture measure – there is no independent gold standard – TBS measures TBS

Fracture Discrimination:
Cross-sectional Studies



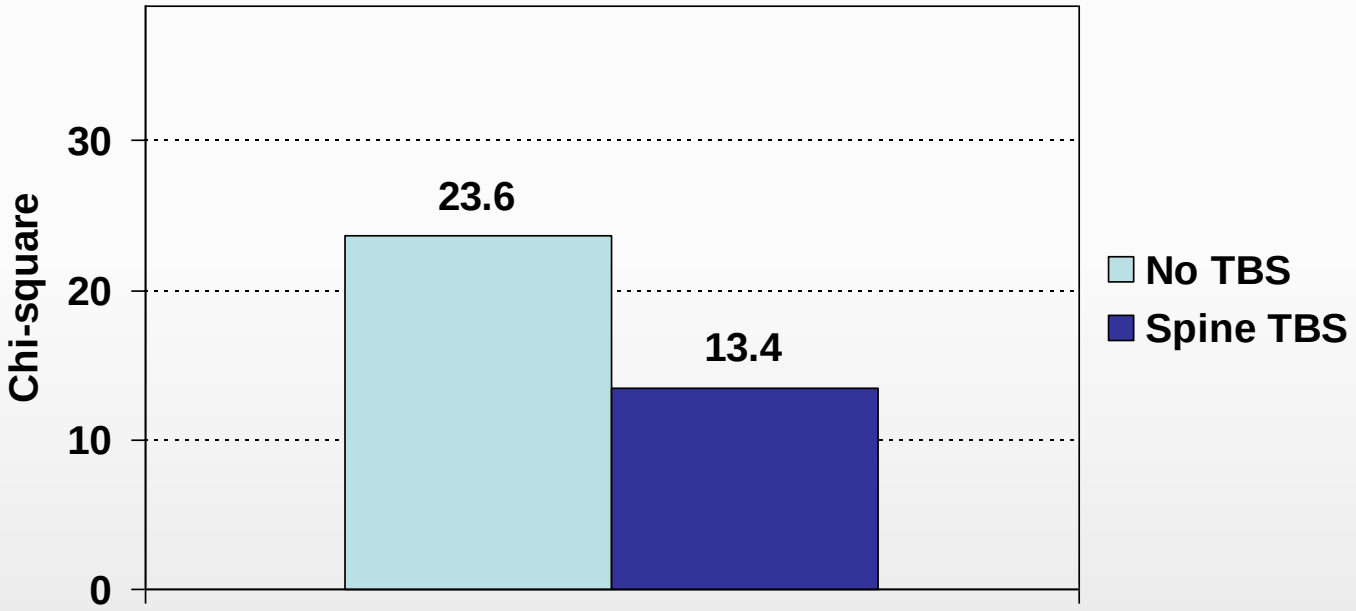
Silva et al. *JCD 2015; 18:309.*

Fracture Prediction:
Longitudinal Studies



Silva et al. ***JCD 2015; 18:309.***

Diabetes for Fracture Prediction*



LS TBS predicted fractures in those with diabetes (adjusted HR 1.27, 95%CI 1.10-1.46) and without diabetes (HR 1.31, 95%CI 1.24-1.38).

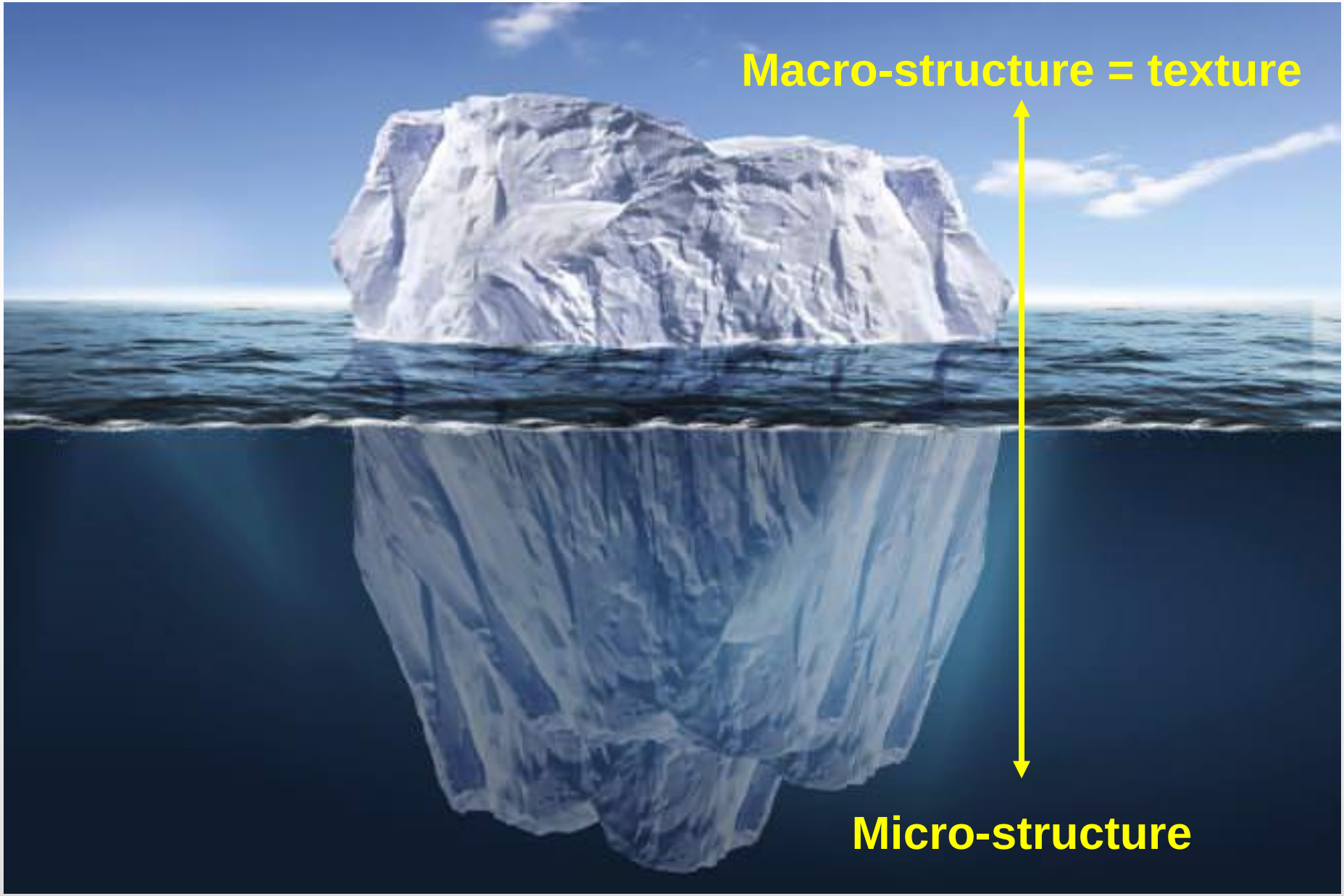
* Models adjusted for age, BMI, glucocorticoids, prior major fracture, rheumatoid arthritis, COPD, alcohol abuse and osteoporosis therapy.

Leslie WD et al. JCEM 2013.

The FDA Labeling for TBS

"TBS is derived from the texture of the DEXA image and has been shown to be related to bone microarchitecture and fracture risk. This data provides information independent of BMD value… The TBS score can assist the health care professional in assessment of fracture risk…"

FDA 510(k) Clearance in 2012


Macro-structure = texture
Micro-structure

How has the TBS algorithm changed?

- The original TBS algorithm had been optimized for women, but paradoxically gave lower TBS measurements in men than women
  - Image texture degrades with increasing adiposity. Adiposity in men tends to be more abdominal than in women, and a single TBS adjustment based upon BMI underestimates the effect of abdominal adiposity on the TBS measurement in men.
- The TBS algorithm was modified in version 2.x to address these technical issues, and became applicable to both women and men
  - The manufacturers of TBS software recommend that TBS not be used in individuals with BMI outside of the 15 – 37 kg/m2 range.

TBS: version 1.x v version 2.x

	Men (n=4348)	Women (n=47,736)
	Mean ± SD	Mean ± SD
Age (years)	64±12	63±11 *
BMI (kg/m²)	26.8±5.2	27.1±4.5 *
BMD L1-L4 (g/cm²)	1.128±0.200	1.047±0.181 *
Previous L1-L4 TBS (v1.7)	1.080±0.145	1.244±0.127 *
Updated L1-L4 TBS (v2.1)	1.360±0.132	1.318±0.123 *

* $p<0.001$

Leslie WD et al. ASBMR 2014

TBS: version 1.x v version 2.x

Pearson r with	Previous L1-L4 TBS (v1.8)	Updated L1-L4 TBS (v2.1)
	Men N=4348	
Age	-0.25*	-0.26*
BMI	-0.40*	0.01
BMD L1-L4	0.14*	0.25*
Previous L1-L4 TBS (v1.8)		0.77*
	Women N=47,736	
Age	-0.34*	-0.35*
BMI	-0.18*	-0.01
BMD L1-L4	0.33*	0.38*
Previous L1-L4 TBS (v1.8)		0.93*

* $p<0.001$

Leslie WD et al. ASBMR 2014

Only applies to GE/Lunar

TBS: version 1.x v version 2.x

Fracture prediction	Men (n=4348) AUROC [95%CI]*	Women (n=47,736) AUROC [95%CI]*
	Incident MOF Prediction	
L1-L4 BMD	0.637 [0.601-0.672]	0.662 [0.651-0.672]
Previous L1-L4 TBS (v1.8)	0.553 [0.515-0.591]	0.628 [0.618-0.638]
Updated L1-L4 TBS (v2.1)	0.574 [0.535-0.614]	0.640 [0.630-0.650]
Δ L1-L4 TBS (v2.1 – v1.8)	**0.021**	**0.012**
	Incident HF Prediction	
L1-L4 BMD	0.678 [0.602-0.754]	0.677 [0.656-0.698]
Previous L1-L4 TBS (v1.8)	0.623 [0.544-0.703]	0.679 [0.660-0.697]
Updated L1-L4 TBS (v2.1)	0.669 [0.585-0.753]	0.699 [0.680-0.718]
Δ L1-L4 TBS (v2.1 – v1.8	**0.046**	**0.020**

Leslie WD et al. ASBMR 2014

How is TBS accommodated in the FRAX algorithm?

Incorporating TBS into FRAX
33,352 women ≥40 years with baseline DXA

	Other OP fracture	Hip fracture	Mortality
TBS adjusted for	HR per 1 SD (95% CI)	HR per 1 SD (95% CI)	HR per 1 SD (95% CI)
time since baseline and age	1.35 (1.29-1.42)	1.48 (1.33-1.66)	1.32 (1.26-1.39)
FRAX CRFs	1.27 (1.20-1.33)	1.40 (1.25-1.57)	1.23 (1.17-1.29)
BMD	1.25 (1.18-1.31)	1.26 (1.12-1.42)	1.29 (1.23-1.35)
FRAX CRFs + BMD	**1.18 (1.12-1.24)**	**1.23 (1.09-1.38)**	**1.20 (1.14-1.26)**

McCloskey et al, 2015 , Calc Tissue Int

The TBS Adjustment for FRAX

Outcome: Hip fracture

The 10-year probability calculated with TBS is $\frac{100}{1+e^{-w}}$, where $W = 15.420 - 12.627 \times \text{TBS} - 0.194 \times \text{age} + 0.157 \times \text{TBS} \times \text{age} + 0.920 \times L$, $L = -\ln(100/p - 1)$, p is the 10-year probability calculated without TBS

Outcome: Major Osteoporotic Fracture

The 10-year probability calculated with TBS is $\frac{100}{1+e^{-w}}$, where $W = 5.340 - 4.213 \times \text{TBS} - 0.0521 \times \text{age} + 0.0393 \times \text{TBS} \times \text{age} + 0.897 \times L$, $L = -\ln(100/p - 1)$, p is the 10-year probability calculated without TBS

McCloskey et al, 2015 , Calc Tissue Int

Meta-Analysis of TBS

Cohort	N	Women (%)	Fup mean (max)	Age mean(range)	FN T-score mean (SD)	TBS mean (SD)	Incident Hip	Incident MOF
CaMos	**2863**	**70**	**4.7 (6.9)**	**69 (40-90)**	**-1.89 (1.07)**	**1.28 (0.11)**	**43**	**157**
FORMEN	1532	0	4.2 (6.1)	73 (65-90)	-0.98 (0.90)	1.27 (0.08)	2	20
GOS	597	0	5.0 (7.2)	69 (40-90)	0.52 (0.88)	1.29 (0.11)	8	30
JPOS	977	100	15.0 (16.7)	63 (50-80)	-1.62 (0.79)	1.31 (0.09)	27	114
MsOs HK	1953	100	8.8 (11.3)	73 (65-90)	-2.31 (0.79)	1.26 (0.08)	67	225
MrOS HK	1924	0	9.9 (12.2)	72 (65-90)	-1.44 (0.88)	1.28 (0.08)	61	132
MrOs Sweden	1781	0	5.3 (7.8)	77 (70-89)	-0.94 (0.91)	1.26 (0.11)	39	108
OFELY	496	100	11.5 (13.4)	67 (50-88)	-1.38 (0.77)	1.28 (0.10)	15	76
OPUS	937	100	5.9 (8.2)	66 (55-80)	-1.21 (0.91)	1.29 (0.10)	4	57
SOS	2364	100	1.6 (3.1)	74 (62-90)	0.19 (1.00)	1.24 (0.09)	17	65
Rotterdam RSI	914	100	3.5 (4.7)	74 (65-90)	-1.59 (0.78)	1.25 (0.10)	12	39
Rotterdam RSII	240	100	2.2 (4.5)	68 (59-88)	-0.15 (0.42)	1.27 (0.10)	0	4
SEMOF	524	100	2.8 (3.7)	76 (70-82)	-1.58 (0.84)	1.23 (0.11)	3	41
STRAMBO	707	0	5.4 (7.0)	72 (60-88)	-0.73 (0.94)	1.28 (0.10)	0	41
Total	**17809**	**59**	**6.1 (16.7)**	**72 (40-90)**	**-1.20 (1.21)**	**1.27 (0.10)**	**298**	**1109**

McCloskey EV et al: JBMR 2015.

Meta-Analysis of TBS for MOF

	Men + women GR (95% CI)	Men GR (95% CI)	Women GR (95% CI)
TBS (+age and time)	**1.44** (1.35-1.53)	**1.50** (1.36-1.66)	**1.40** (1.30-1.52)
TBS (+FRAX with BMD)	**1.32** (1.24-1.41)	**1.35** (1.21-1.49)	**1.31** (1.21-1.42)
FRAX with BMD [a]	**1.70** (1.60-1.81)	**1.80** (1.64-1.98)	**1.63** (1.50-1.77)
TBS adjusted FRAX with BMD [a,b]	**1.76** (1.65, 1.87)	**1.86** (1.70, 2.04)	**1.68** (1.55, 1.82)

[a] Time since baseline and age. [a] TBS adjustment from McCloskey CTI 2015.

McCloskey EV et al: JBMR 2015

Meta-Analysis of TBS for Hip

	Men + women GR (95% CI)	Men GR (95% CI)	Women GR (95% CI)
TBS (+age and time)	**1.44** (1.28-1.62)	**1.47** (1.23-1.75)	**1.42** (1.21-1.67)
TBS (+FRAX with BMD)	**1.28** (1.13-1.45)	**1.27** (1.06-1.53)	**1.29** (1.09-1.52)
FRAX with BMD [a]	**2.22** (2.00-2.47)	**2.34** (2.02-2.72)	**2.11** (1.81-2.45)
TBS adjusted FRAX with BMD [a,b]	**2.25** (2.03, 2.51)	**2.37** (2.04, 2.75)	**2.14** (1.84, 2.49)

[a] Time since baseline and age. [a] TBS adjustment from McCloskey CTI 2015.

McCloskey EV et al: JBMR 2015

Calculation Tool

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

Country: US (Caucasian) Name/ID: About the risk factors

Questionnaire:

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

   Age: 65 Date of Birth: Y: M: D:

2. Sex ○ Male ◉ Female

3. Weight (kg) 70

4. Height (cm) 165

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^2)

T-Score -2.4

Clear Calculate

BMI: 25.7

The ten year probability of fracture (%)

with BMD

Major osteoporotic	13
Hip Fracture	2.5

If you have a TBS value → Adjust with TBS

FRAX adjusted for TBS

WHO FRAX web site | What is TBS? | Calculation Tool | References | TBS web site | English

Calculation tool

Country:	US (Caucasian)
Name/ID:	-
Age:	65
Sex:	Female
BMI (kg/m²):	25.7

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

Lumbar Spine TBS: 1.16 Calculate

Attention: TBS values are accurate only for patients (women and men) with a BMI in the range [15 – 37 kg/m²]

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

Major Osteoporotic Fracture:	16
Hip Fracture:	3.3

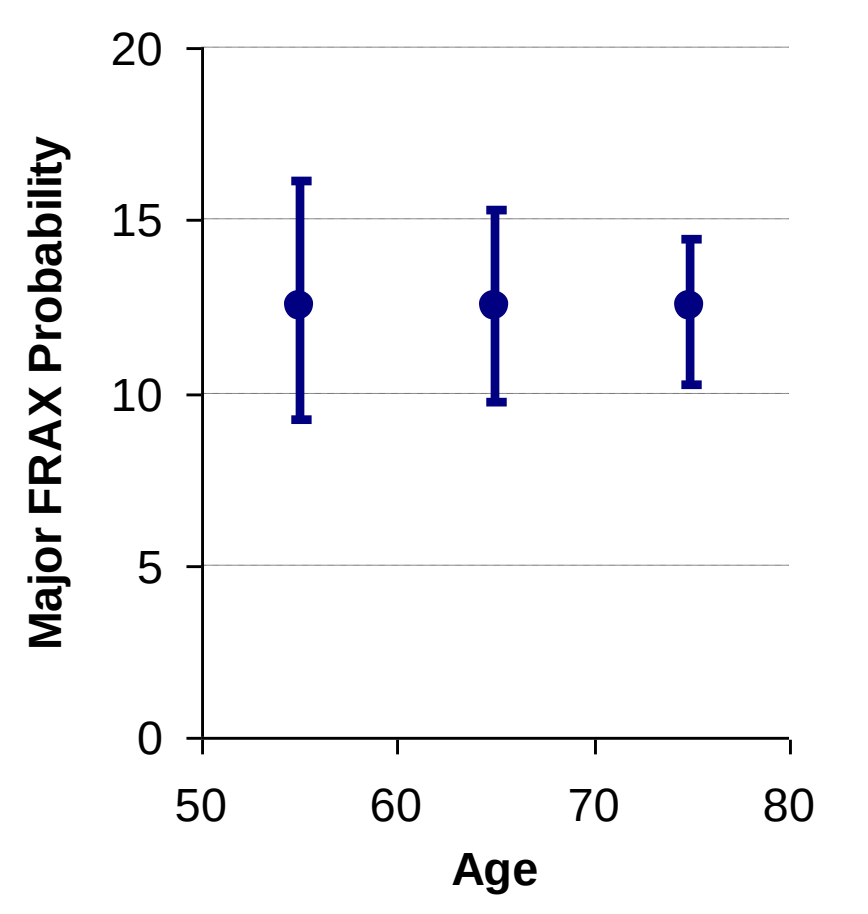
00000702

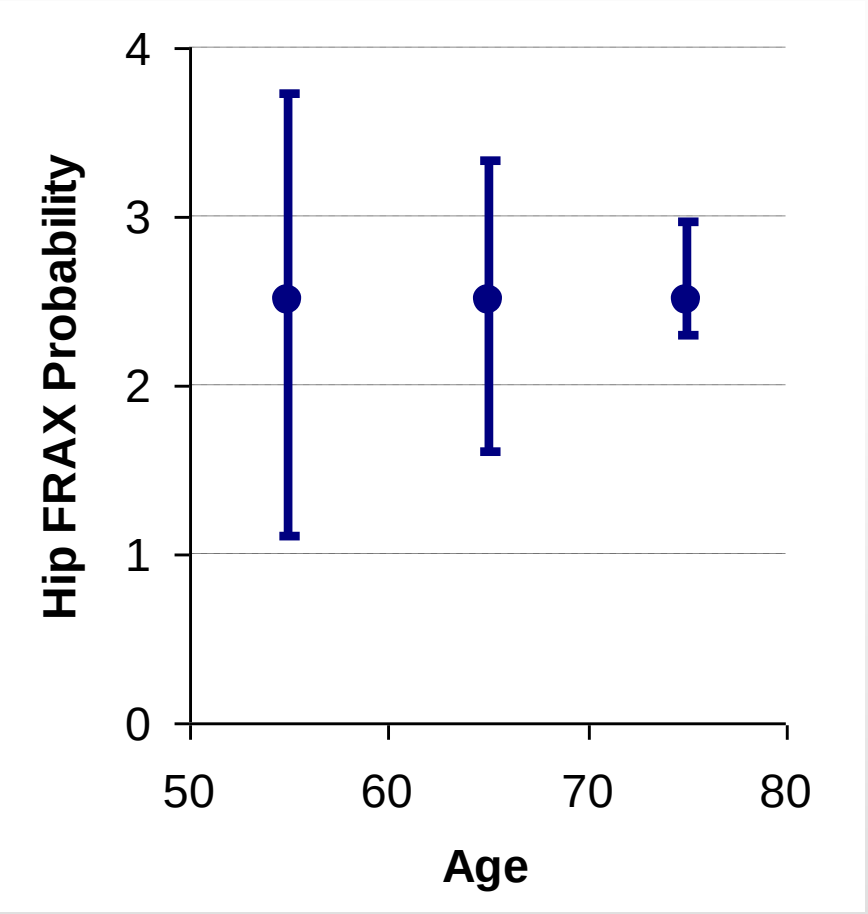
Individuals with fracture risk assessed since April 15, 2015

When does TBS have the greatest clinical impact on clinical management?

Effect of Age on the FRAX TBS Adjustment

TBS 1.160 (10th %ile) vs 1.470 (90th %ile)





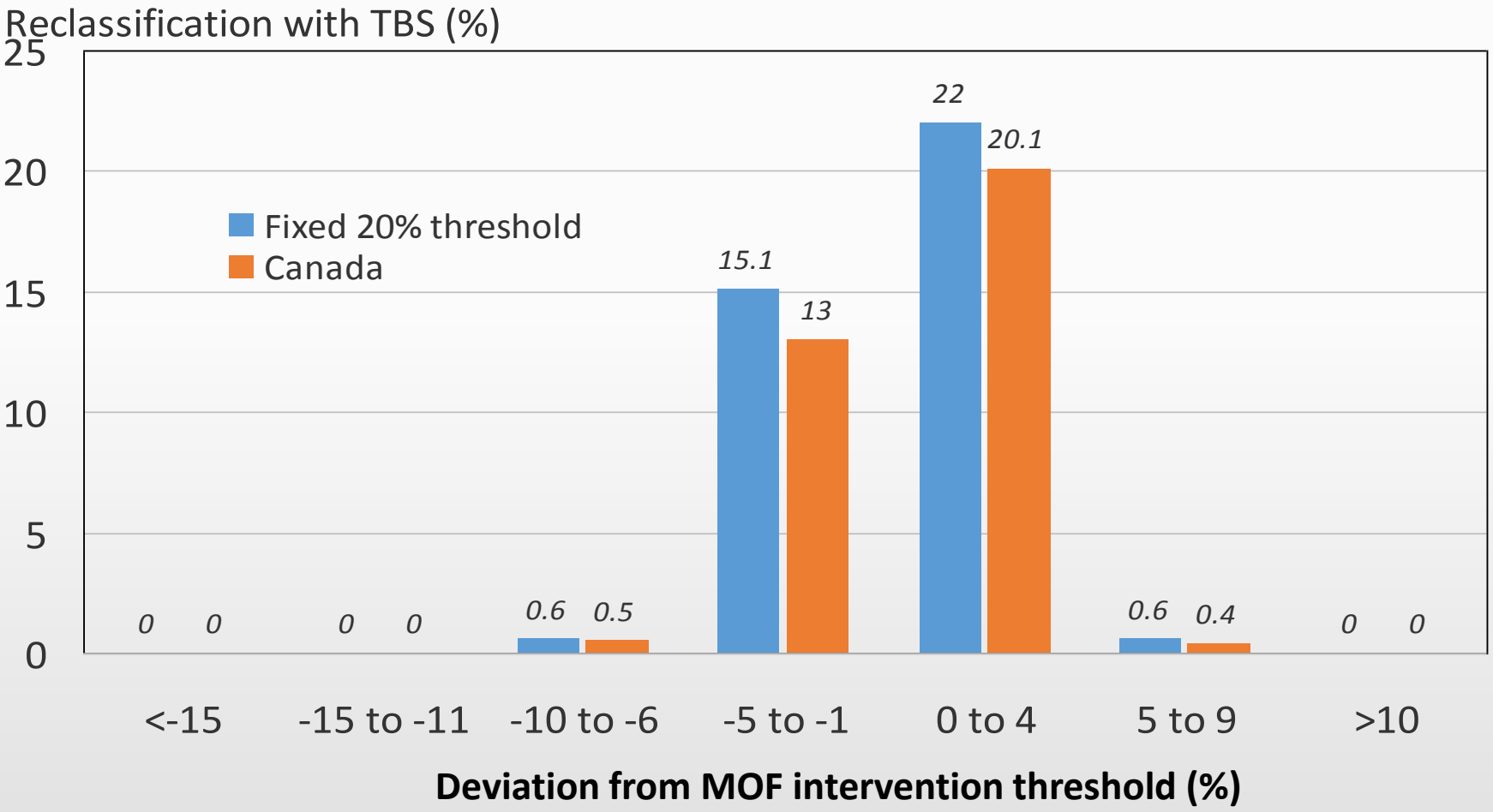
Net Reclassification Improvement (NRI) with FRAX TBS Adjustment

	MOF 20%	Canada
Reclassification		
All subjects	2.6%	2.3%
Close to cutoff [b]	17.5%	15.4%
NRI fractures	+1.4%***	+1.1%**
NRI non-fractures	-0.4%***	-0.3%***
NRI total all ages	+1.1%**	+0.8%*
NRI total age <65	+1.6%***	+1.2%**
NRI total age ≥65	+0.7%	+0.6%

* P<0.05, ** P<0.01, *** P<0.001

Leslie WD et al: ASBMR 2015.

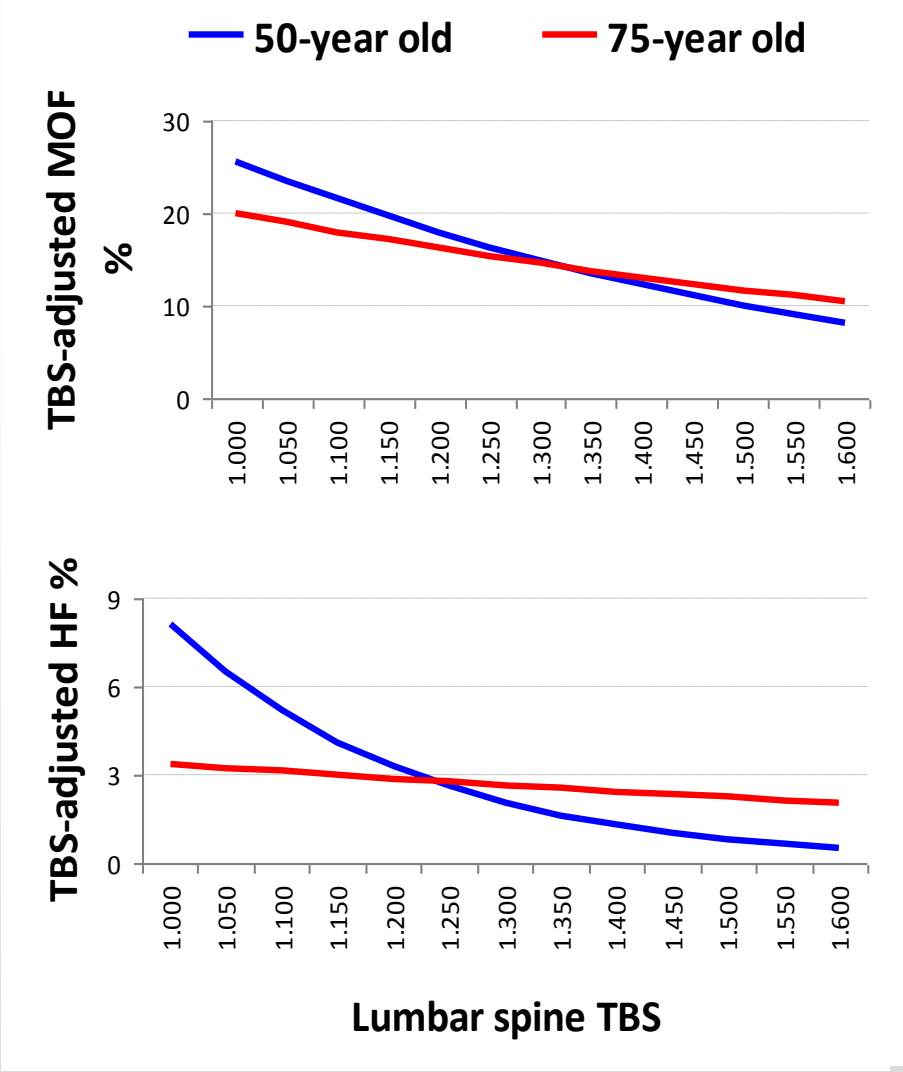
Reclassification with FRAX TBS Adjustment



Cases with questions

- For a woman with FRAX major fracture probability 15% and hip fracture probability 2.5%, what level of TBS would be required to exceed the treatment thresholds?

Woman MOF 15%, Hip 2.5%



Clinical Pearls ISCD Official Positions

- TBS is associated with
  - vertebral, hip and MOF fracture risk in postmenopausal women.
  - hip fracture risk and MOF risk in men over the age of 50 years.
  - MOF risk in postmenopausal women with type II diabetes
- TBS should not be used alone to determine treatment recommendations in clinical practice.
- TBS is not useful for monitoring bisphosphonate treatment in postmenopausal women with osteoporosis.
- TBS can be used in association with FRAX and BMD to adjust FRAX-probability of fracture in postmenopausal women and older men