




Treating Osteoporosis Without a Formal (T Score) Diagnosis

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Conflicts of Interest

- Clinical Endpoint Committee Chair, UCB


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Objectives:


1. Describe the utility and limitations of BMD and clinical risk scores in identifying individuals for treatment
2. Identify individuals who merit treatment consideration
 - without need for BMD measurement
 - despite non-osteoporotic T scores
3. Discuss practical strategies for risk stratification when BMD is impractical or unavailable

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Recent Clinical Scenarios

- 74-year-old woman with recent hip fracture.
- Primary Care Physician orders DXA and tells her it is “okay” (T -1.4)




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Recent Clinical Scenarios

- 80-year-old rural Veteran with humerus fracture,
- Nearest DXA 90 miles away – “will it change what you advise me?”




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Recent Clinical Scenarios

- 84-year-old man with multiple risk factors for fracture (prostate cancer, ADT, falls, dementia) living in nursing home
- DXA not practical

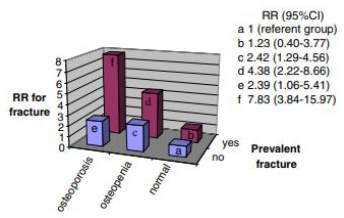


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BMD Useful for Predicting Fracture Risk

- Prospective cohort, Women aged 60-94
- 6-year follow-up



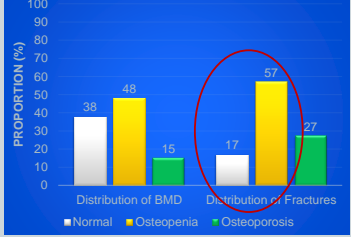
BMD Category	RR (95%CI)
a (referent group)	1
b	1.23 (0.40-3.77)
c	2.42 (1.29-4.56)
d	4.38 (2.22-8.66)
e	2.39 (1.06-5.41)
f	7.83 (3.84-15.97)

Osteoporosis Int (2006) 17: 1404–1409

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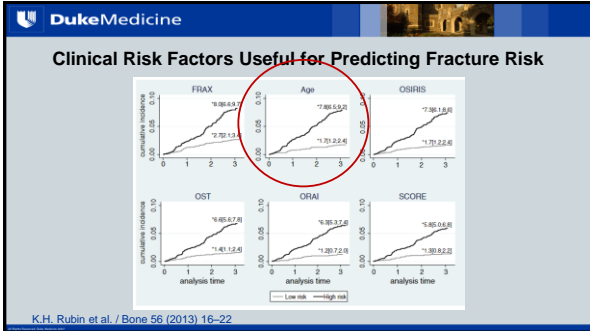
Limitations of BMD in Fracture Prediction



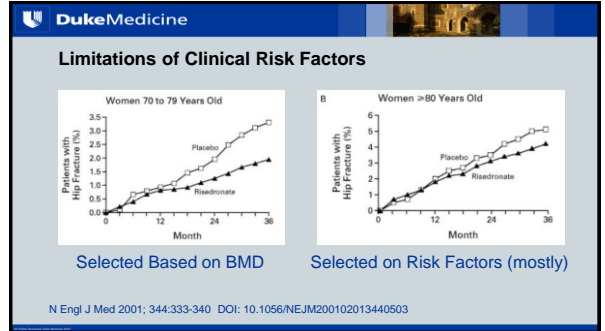
Category	Normal (%)	Osteopenia (%)	Osteoporosis (%)
Distribution of BMD	38	48	15
Distribution of Fractures	17	57	27

J Clin Densitom. 2017 Jul-Sep; 20(3): 444–450.

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When do Guidelines Suggest using Clinical Factors to Determine Treatment?

- After hip or vertebral fracture
 - Other countries may include other types
- For individuals with osteopenia
- When clinical risk factor score either very high or very low

<https://www.sheffield.ac.uk/NOGG/>

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Recent Clinical Scenarios


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Treating after Hip Fracture regardless of BMD

- Double-blind, placebo-controlled RCT
 - 2127 men and women, 148 clinical centers, 23 countries
- Treatment
 - Annual infusion of either ZOL 5 mg or placebo
 - Loading dose of vitamin D 75,000–125,000 IU
 - Calcium and vitamin D daily supplements
- Broad inclusion criteria
 - 58% T score > -2.5, 11% "normal"

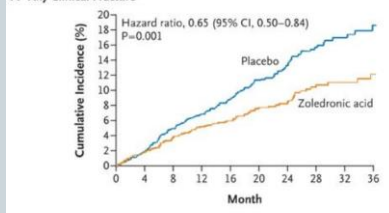


N Engl J Med 2007; 357:1799-1809

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A Any Clinical Fracture



Hazard ratio, 0.65 (95% CI, 0.50–0.84)
P=0.001

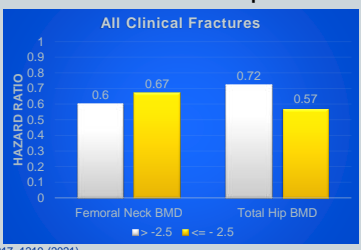
No. at Risk	0	4	8	12	16	20	24	28	32	36
Zoledronic acid	1065	1013	950	895	762	628	473	316	212	129
Placebo	1062	1010	947	884	742	611	443	305	190	119

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IV Zoledronic Acid after Hip Fracture

All Clinical Fractures



BMD Site	T > -2.5	T <= -2.5
Femoral Neck BMD	0.6	0.67
Total Hip BMD	0.72	0.57

Interaction P=0.95

Osteoporos Int 32, 1217–1219 (2021)


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Recent Clinical Scenarios

- 76-year-old woman with hip fracture, PCP measures BMD and tells her it is "okay" (T -1.4)

Treatment will reduce your 3-year risk of new fractures (and death) by approximately 1/3 regardless of your BMD



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Other Data Supporting Treatment in Osteopenia

- RCT 2000 women in Australia, Zol Q 18 month
 - Decreased fragility fractures 1/3, NNT = 15
 - Independent of prior fracture history
- Post-hoc analysis 3 RCTs Risedronate
 - Decreased fragility fracture 73% over 3 years


N Engl J Med 2018; 379:2407-2416 Osteoporos Int. 2008 May;19(5):681-6

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Recent Clinical Scenarios

- 80-year-old rural Veteran with humerus fracture,
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Value of DXA after Other Fracture Types

- N=230 Veterans ≥50 years with non-hip, non-spine fracture
- FRAX-BMI and FRAX-BMD
 - Treatment recommended Y/N by NOF guidelines
- Concordance, sensitivity, specificity, AUC
- Reclassification thresholds

Osteoporos Int 32, 467–472 (2021)

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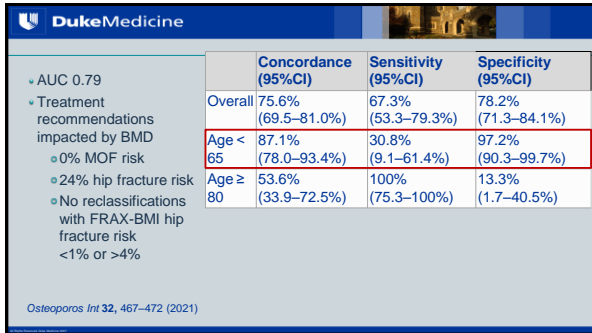
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- AUC 0.79
- Treatment recommendations impacted by BMD
 - 0% MOF risk
 - 24% hip fracture risk
 - No reclassifications with FRAX-BMI hip fracture risk <1% or >4%

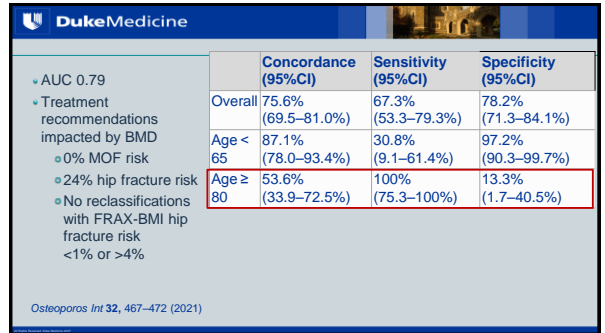
	Concordance (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)
Overall	75.6% (69.5–81.0%)	67.3% (53.3–79.3%)	78.2% (71.3–84.1%)
Age < 65	87.1% (78.0–93.4%)	30.8% (9.1–61.4%)	97.2% (90.3–99.7%)
Age ≥ 80	53.6% (33.9–72.5%)	100% (75.3–100%)	13.3% (1.7–40.5%)

Osteoporos Int 32, 467–472 (2021)

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Recent Clinical Scenarios

- 80-year-old rural Veteran with humerus fracture, nearest DXA 90 miles away – “Will it change what you advise me?”

DXA is unlikely to change our recommendations for you if your FRAX with BMI is:

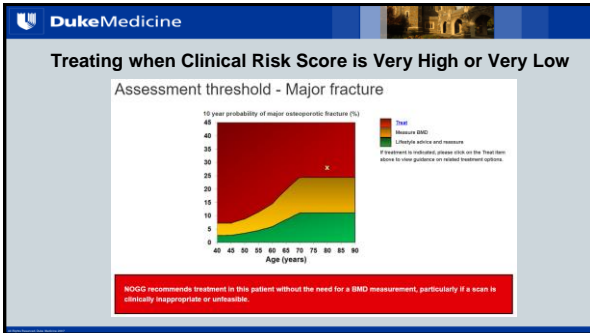
- (any age) >20% MOF or <1%/>4% hip
- (age ≥ 80) if you don't meet treatment threshold
- (age ≤ 65) if you do meet treatment threshold

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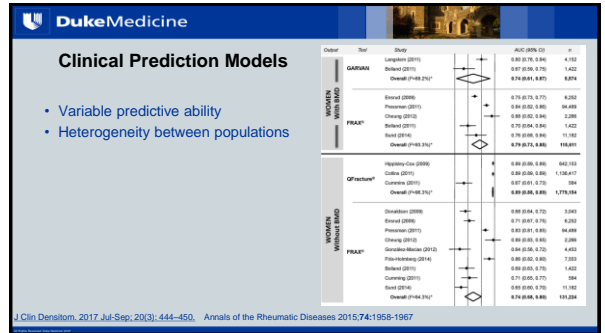
Recent Clinical Scenarios

- 84-year-old man with multiple risk factors for fracture (prostate cancer, ADT, falls, dementia) living in nursing home
- DXA not practical

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Fracture Risk Calculators

- FRAX <http://www.shef.ac.uk/FRAX>
 - Incorporates average life expectancy
 - BMI or BMD, sex, race, select comorbidities, family history
- Garvan nomogram <http://www.garvan.org.au/bone-fracture-risk/>
 - Australia, Canada
 - Age, BMD, and falls are major drivers

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Two Fracture Prediction Models

FRAX
3.5% Major, 1.5% Hip

Garvan
48.8% Any, 24.4% Hip

FRAX* VMO Fracture Risk Assessment Tool

Calculation Tool

QUESTIONS: 100% (10/10) Correct

1. Age (years) 65

2. Sex Male

3. Previous fracture No

4. Parental history No

5. Current smoking No

6. Rheumatoid arthritis No

7. Alcohol intake 10

8. Hip osteoporosis No

9. Hip fracture No

10. Hip fracture No

11. Hip fracture No

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99. Hip fracture No


100. Hip fracture No

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Issues with Fracture Prediction Models in Frail Older Adults

- FRAX may underestimate risk by not including
 - Falls
 - Age-related co-morbidities
- Garvan may overestimate risk by not including
 - Limited life expectancy
 - Race/ethnicity
- No models incorporate
 - Functional status
 - Environment (community, NH)
 - Multiple medications



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The "Geriatric Risk Adjustment"

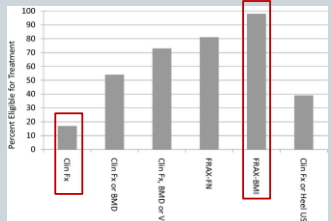
Condition	Fracture Risk
NH Residence	RR 4-10
Renal Impairment	RR 1.4 for every 10 cc/min decrease GFR
Parkinson's Disease	RR 2.5
Prostate Cancer	RR 2-4
Stroke	RR 2.5
Dementia	RR 1.6-2.5
Vitamin D Deficiency	RR 2.0

Looker et al, JBMR 2007; Melton et al, Movement Disorders 2006; Kanis J, Lancet 2002

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Selecting NH Residents for Treatment



Model	Percent Eligible for Treatment
Garvan	~15
Garvan + RAND	~55
Garvan + RAND + Fx	~70
FRAX + Fx	~80
FRAX + RAND	~105
Garvan + RAND + Fx + RAND + Fx	~40

JAGS 2012, 60(4):684-90

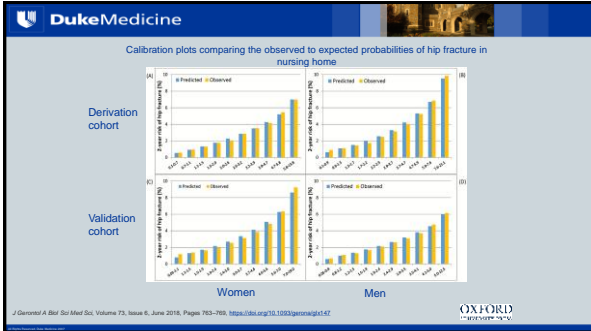
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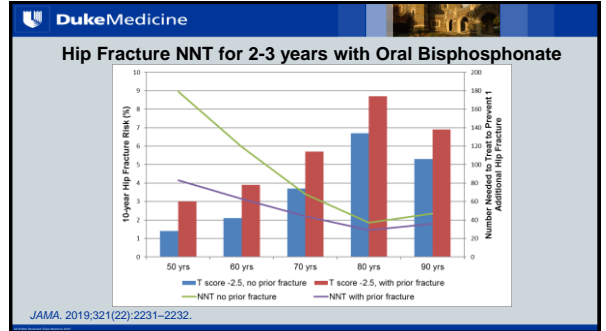
The FRail Tool <http://far-frail.hsl.harvard.edu>

- National Sample of Nursing Home Long-Stay Residents
- Routinely collected Minimum Data Set (MDS) data
- Predicts 2-year hip fracture risk
- Final model suggests **highest functioning** residents are at highest risk
 - Ambulatory or transfer independent
 - Continent
 - ADL independent
 - Cognitively impaired, wandering, distracted
 - SSRI, benzodiazepine, cholinesterase inhibitor, alpha blocker

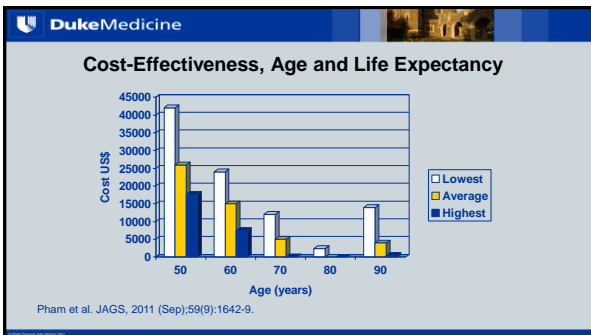
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Recent Clinical Scenarios

- 84-year-old man with multiple risk factors (prostate cancer, ADT, falls, dementia) living in nursing home, DXA not practical

Consider offering treatment if:

- Prior fracture
- FRAIL 2-year Hip Fracture >5%
- "Geriatric Adjusted" FRAX above NOF treatment threshold
 - Life expectancy >2 years
 - Ambulatory/transfer independent
 - Consistent with goals

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1. Describe the utility and limitations of BMD and clinical risk scores in identifying individuals for treatment
2. Identify individuals who merit treatment consideration
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 - despite non-osteoporotic T scores
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Thank you and Questions



Duke Gardens in the Spring

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