Assessment and Management of Osteoporosis in Patients with Kidney Disease with Normal Kidney Function Treated with Prednisone

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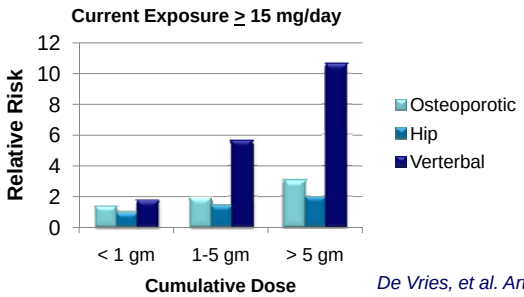
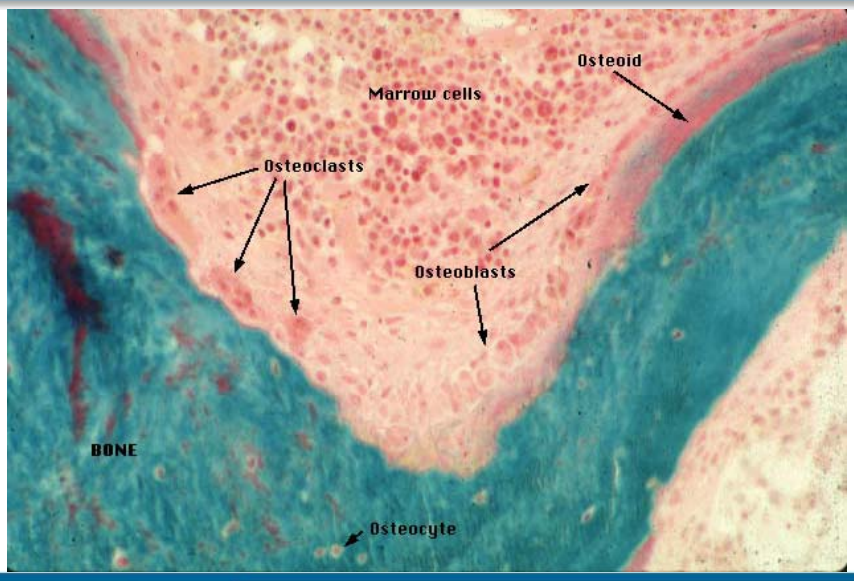
Glucocorticoid-Induced Osteoporosis

- Most common cause of secondary osteoporosis
- Associated with increased fracture risk
  - dose dependent; occurs rapidly after start of treatment
  - risk decreases abruptly after cessation of treatment



De Vries, et al. Arthritis Rheum 2007

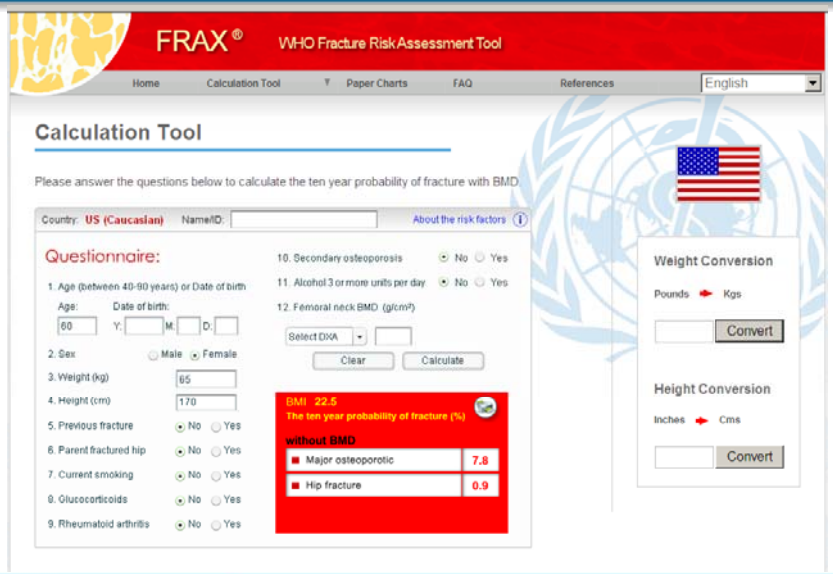
Remodeling in the Bone Multicellular Unit

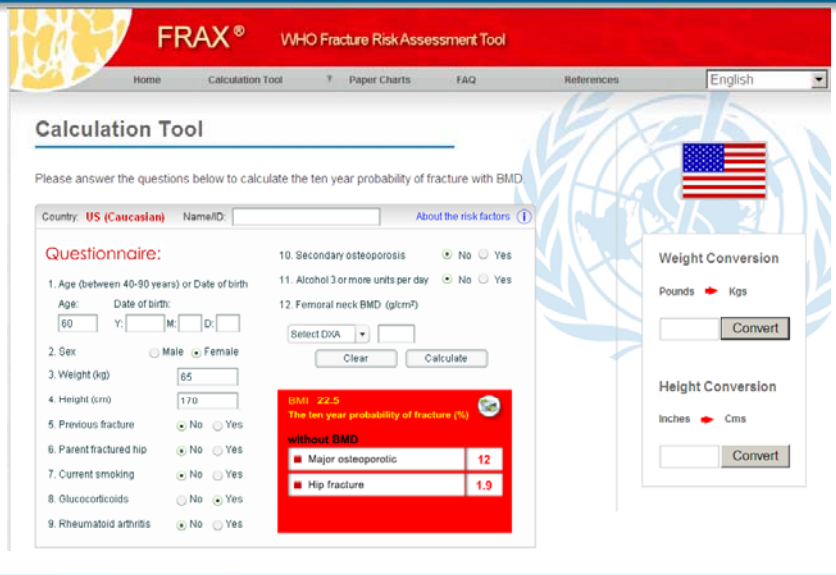


Glucocorticoid Effects

	GC
↓ **Bone Formation**	X
• Shift differentiation away from osteoblasts	
• Inhibit osteoblast activity	
• Promote osteoblast apoptosis	
↓ **Mechanosensors**	X
• Promote osteocyte apoptosis	
• Reduce angiogenesis	
↑ **Bone Resorption**	X
• ↑ RANKL and ↓ OPG activate osteoclasts	
↓ **Bone Resorption**	X
• Inhibit osteoclast actin ring formation	

FRAX


FRAX®
WHO Fracture Risk Assessment Tool
Home
Calculation Tool
Paper Charts
FAQ
References
English
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 40-90 years) or Date of birth
Age:
Date of birth:
60
2. Sex
Male
Female
3. Weight (kg)
65
4. Height (cm)
170
5. Previous fracture
6. Parent fractured hip
7. Current smoking
8. Glucocorticoids
9. Rheumatoid arthritis
10. Secondary osteoporosis
11. Alcohol 3 or more units per day
12. Femoral neck BMD (g/cm²)
Select DXA
Clear
Calculate
BMI 22.5
The ten year probability of fracture (%)
without BMD
Major osteoporotic
7.8
Hip fracture
0.9
Weight Conversion
Pounds
Kgs
Convert
Height Conversion
Inches
Cms
Convert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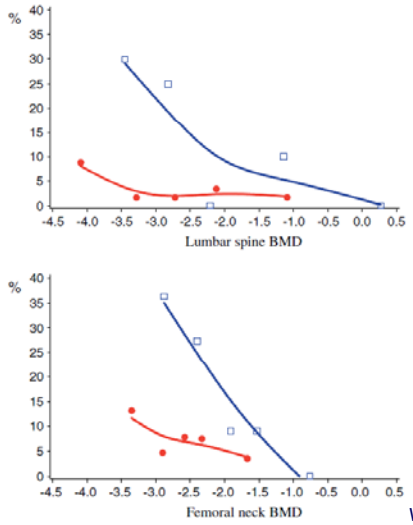
Calculate
BMI 22.5
The ten year probability of fracture (%)
without BMD
Major osteoporotic
12
Hip fracture
1.9
Weight Conversion
Pounds
Kgs
Convert
Height Conversion
Inches
Cms
Convert

GC Fracture Risk and BMD

Incidence of Vertebral Fractures



Van Staa, et al. Arthritis Rheum 2003

American College of Rheumatology 2010 Recommendations for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis*

***Reviewed and endorsed by the American Society of Bone and Mineral Research**

Arthritis Care & Research 2010

Determine Risk Category

- Low Risk: FRAX < 10% for 10 year major osteoporotic fracture
- Medium Risk: FRAX 10-20% for 10 year major osteoporotic fracture
- High Risk: FRAX > 20% for 10 year major osteoporotic fracture

The following may shift an individual to a greater risk category:

- Higher daily glucocorticoid exposure
- Higher cumulative glucocorticoid usage
- IV pulse glucocorticoid usage
- Declining BMD

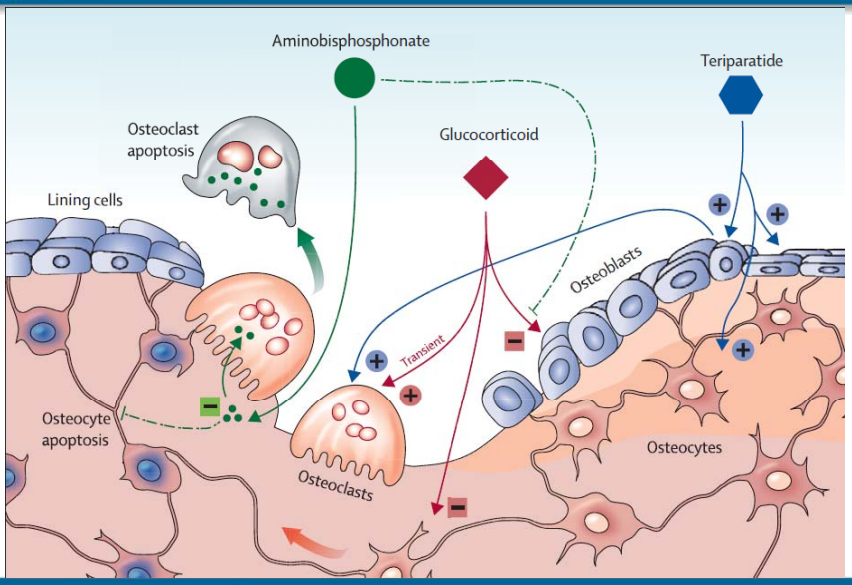
Lifestyle Modification & Assessment

- Weight-bearing activities
- Smoking cessation
- Avoidance of excessive alcohol intake (> 2 drinks per day)
- Nutritional counseling on calcium and vitamin D
- Assessment of prevalent fragility fractures and fall risk
- Baseline DXA
- Baseline height
- Baseline vitamin D level
- Consider radiographic imaging of the spine
- Calcium intake (supplement plus oral intake) 1,200-1,500 mg/day
- Vitamin D supplementation

Recommended monitoring

- **Consider serial BMD monitoring**
- **Consider annual serum 25(OH) vitamin D measurement**
- **Annual height measurement**
- **Assessment of incident fragility fracture**

Pharmacologic Therapy



Gennari & Bilezikian. Lancet 2009

Pharmacologic Therapy

Post-menopausal Women and Men age > 50 years

(Anticipated duration of GC therapy > 3 months)

Low Risk:

- If pred < 7.5 mg/day: no pharmacologic treatment recommended
- If pred ≥ 7.5 mg/day: alendronate, risedronate or zoledronic acid

Medium Risk:

- If pred < 7.5 mg/day: alendronate or risedronate
- If pred ≥ 7.5 mg/day: alendronate, risedronate or zoledronic acid

High Risk:

- If pred < 5 mg/day for ≤ 1 month: alendronate, risedronate or zoledronic acid
- If pred ≥ 5 mg/day for ≤ 1 month or any dose for > 1 month: alendronate, risedronate, zoledronic acid or teriparatide

Pharmacologic Therapy

Pre-menopausal Women and Men age < 50 years

No prevalent fragility fracture: Inadequate data for recommendation

Prevalent fragility fracture:

- **If 1-3 months of GC therapy and non-childbearing potential:**
  - If pred ≥ 5 mg/day: alendronate or risedronate
  - If pred ≥ 7.5 mg/day: alendronate, risedronate or zoledronic acid
- **If ≥ 3 months of GC therapy and non-childbearing potential:**
  - Alendronate, risedronate, zoledronic acid or teriparatide for any dose
- **If ≥ 3 months of GC therapy and childbearing potential:**
  - If pred ≥ 7.5 mg/day: alendronate, risedronate or teriparatide

The Children's Hospital of Philadelphia

Glucocorticoid-Induced Osteoporosis

- The assessment of GC effects on bone are confounded by the skeletal effects of the underlying disease
- Studies of GIO included:
  - Obstructive airway disease
  - Inflammatory bowel disease
  - Polymyalgia rheumatica
  - Systemic lupus erythematosis
  - Multiple sclerosis

Glucocorticoid and Cytokine Effects

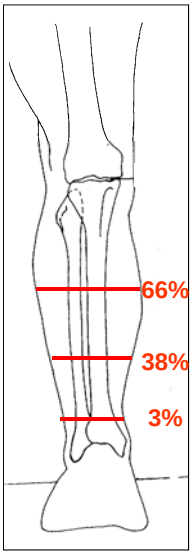
	GC	TNF-α
↓ Bone Formation	X	X
• Shift differentiation away from osteoblasts		
• Inhibit osteoblast activity		
• Promote osteoblast apoptosis		
↓ Mechanosensors	X	X
• Impair osteocytes		
↑ Bone Resorption	X	X
• ↑ RANKL and ↓ OPG activate osteoclasts		
↓ Bone Resorption	X	
• Inhibit osteoclast actin ring formation		

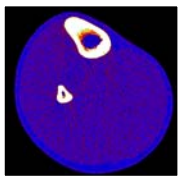
Steroid Sensitive Nephrotic Syndrome

- Characterized by proteinuria, edema, ↓ serum albumin, ↑ cholesterol, normal renal function
- Remits completely and quickly in response to high dose GCs (2 mg/kg/day)
- Relapses in the majority of children when the GCs are reduced, resulting in protracted, repeated courses of GCs
- Provides a model of GC effects in the absence of detectable underlying persistent inflammation
- DXA study did not demonstrate significant bone deficits in children with a median cumulative GC exposure of 23,000 mg

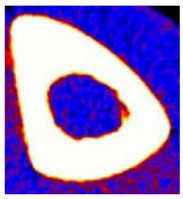
Leonard, et al. NEJM 2004

Peripheral Quantitative CT

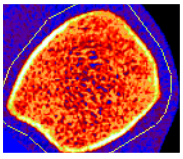




Muscle CSA

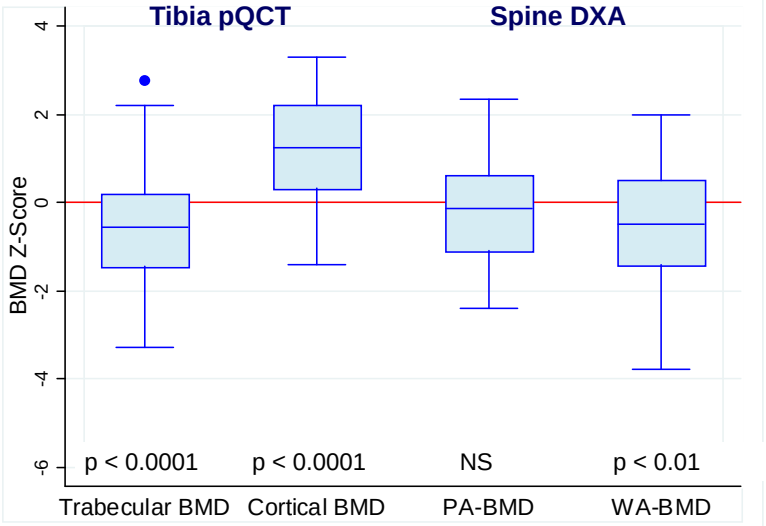


Cortical dimensions & compartment BMD



Trabecular compartment BMD

BMD in Steroid Sensitive NS



Wetzsteon, et al. J Bone Miner Res, 2009

pQCT Z-scores in SSNS

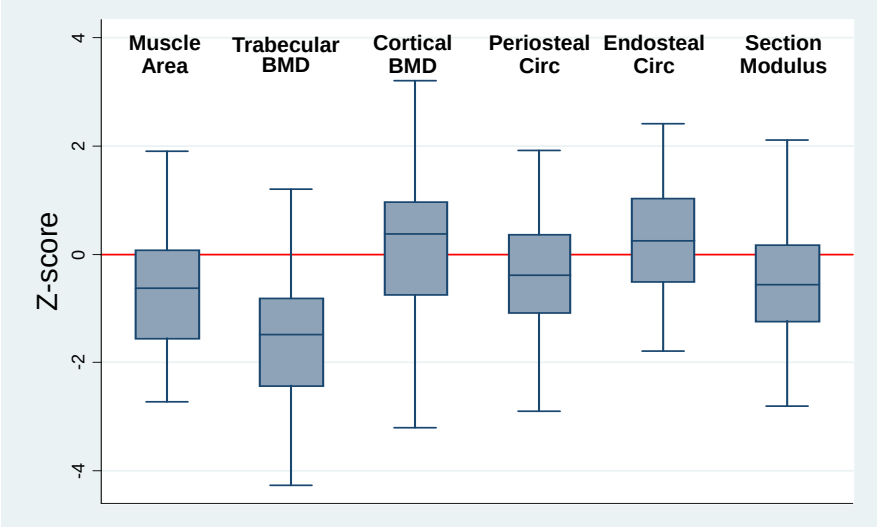
Z-score	SSNS	p-value	SSNS Adjusted for Muscle Z-score	p-value
Trabecular BMD	-0.60 (-0.89, -0.31)	< 0.0001	-0.69 (-0.97, -0.41)	< 0.0001
Cortical BMD	1.17 (0.89, 1.45)	< 0.0001	1.17 (0.89, 1.45)	< 0.0001
Cortical Content	0.60 (0.32, 0.87)	< 0.0001	0.38 (0.17, 0.59)	< 0.001
Cortical Area	0.37 (0.09, 0.66)	0.01	0.14 (-0.08, 0.35)	0.20
Muscle Area	0.34 (0.08, 0.61)	0.01		
Fat Area	0.56 (0.27, 0.84)	< 0.001		

Wetzsteon, et al. J Bone Miner Res, 2009

Crohn's Disease

- Chronic inflammatory bowel disease
- Insidious onset
- Results in abscesses, granulomas & fistulas
- 85% of children present with weight loss
- Growth failure and pubertal delay are common
- Treated with systemic glucocorticoids, steroid enemas, 5-ASA, methotrexate & immunomodulators
- Associated with fractures in children & adults

pQCT Z-scores in Crohn's Disease



Summary

- Glucocorticoid therapy is a common cause of osteoporosis, and is frequently under-recognized and under-treated.
- Glucocorticoids result in an early, transient increase in bone resorption and a sustained decrease in bone formation
- Rapid bone loss and increased fracture risk occur early in the course of glucocorticoid therapy, highlighting the importance of primary prevention in those at high risk of fracture
- Use of the FRAX tool will frequently underestimate the fracture probability in patients treated with glucocorticoids
- Bisphosphonates are the first-line therapy for the prevention of fracture in patients treated with glucocorticoids
- Glucocorticoids may have indirect beneficial effects on bone due to treatment of the underlying disease

Compston, J. Nat Rev Rheum 2010