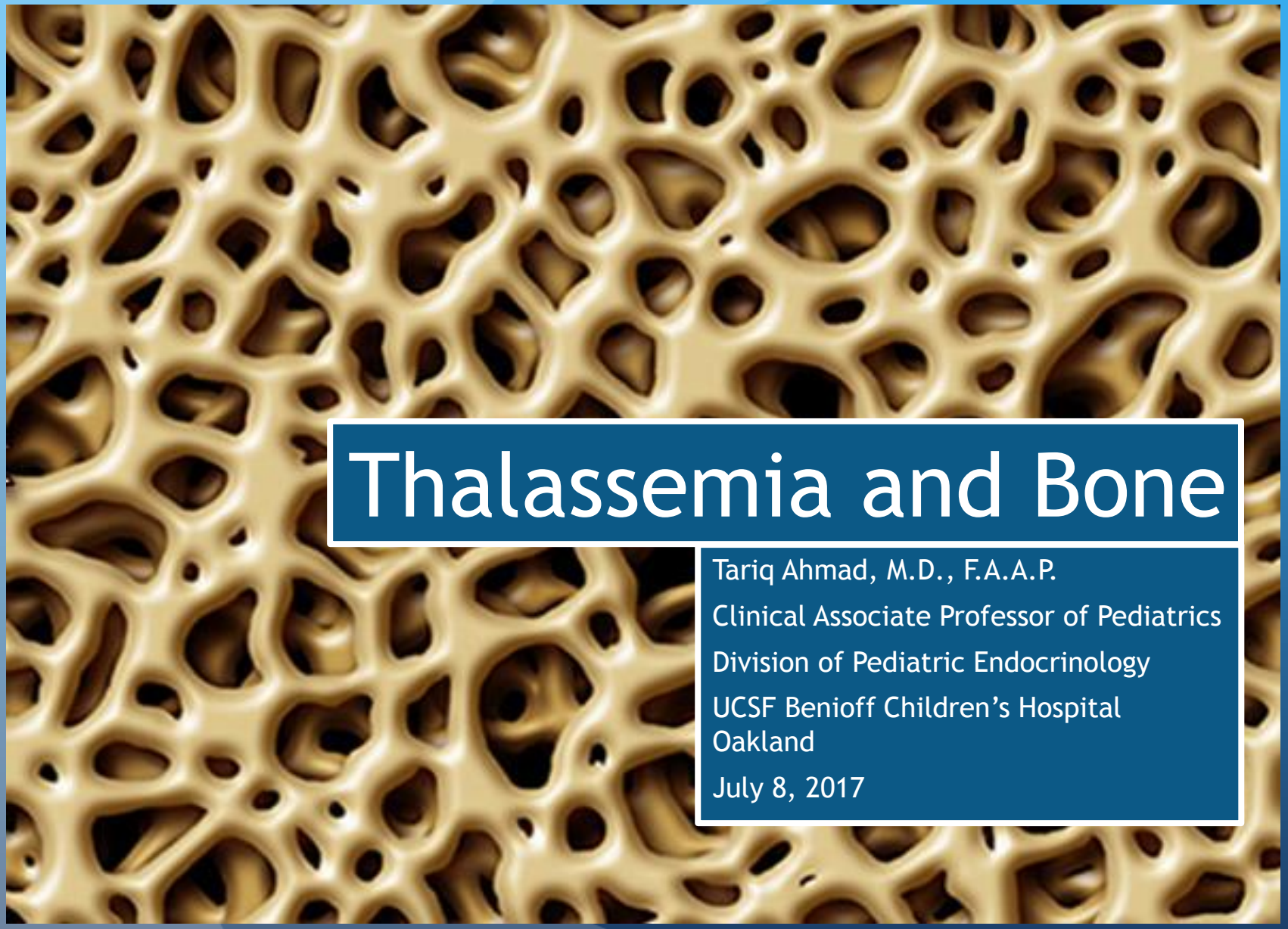

Thalassemia and Bone

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Division of Pediatric Endocrinology

UCSF Benioff Children's Hospital Oakland

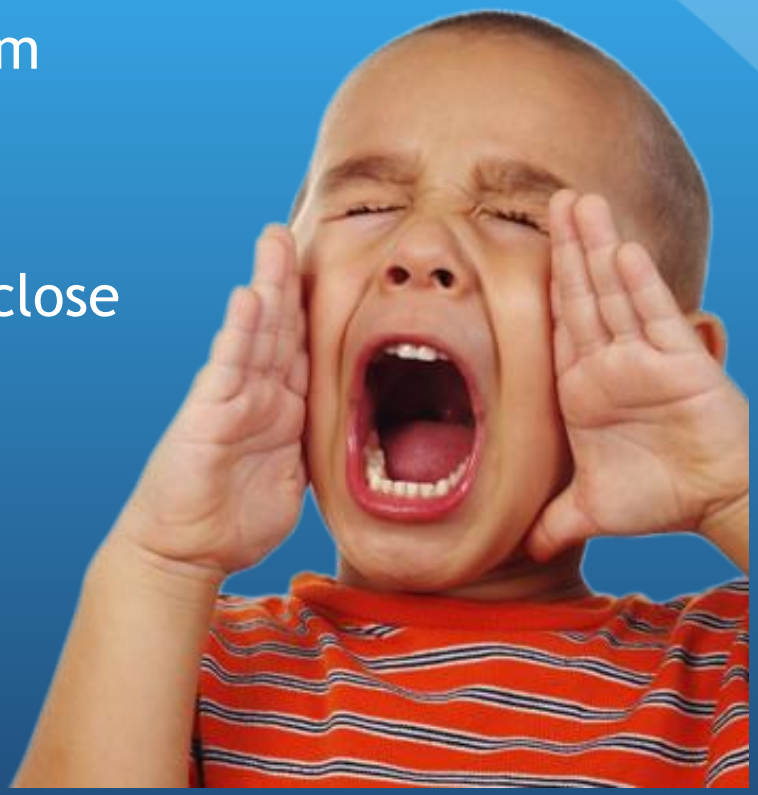
July 8, 2017

Quick Shout Out

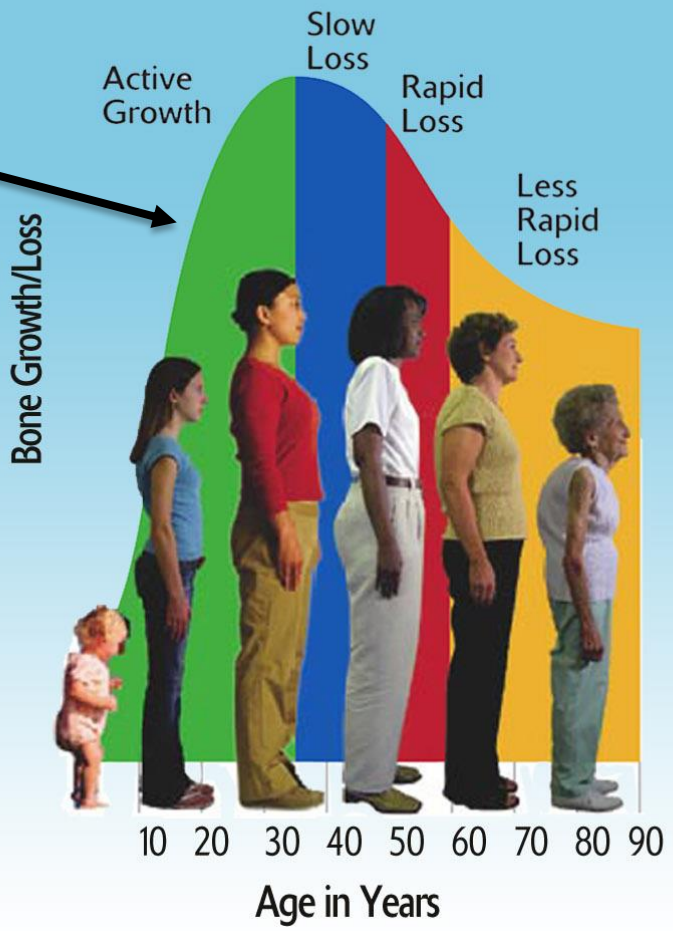
UCSF Benioff Children's Hospital Oakland

Northern California Comprehensive Thalassemia Center

- Dr. Mona Al Mukaddam
- Dr. Ellen Fung
- I have nothing to disclose



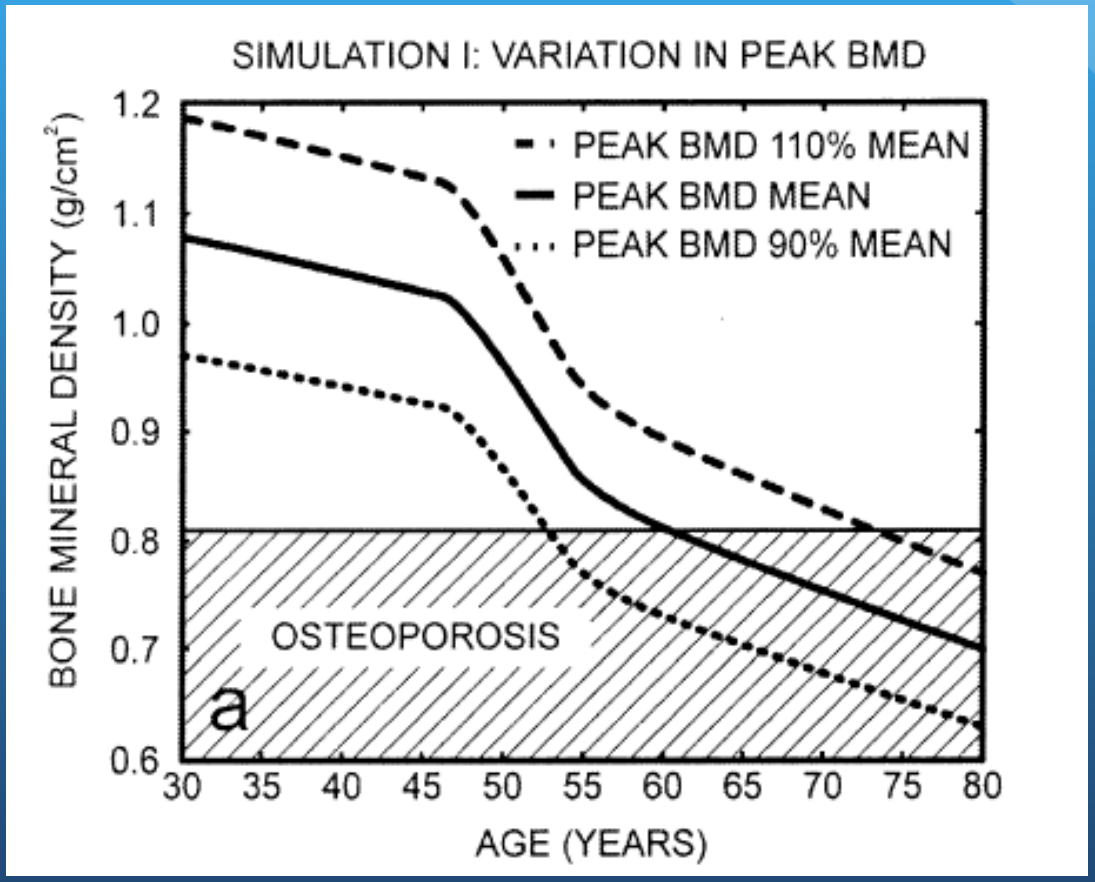
Inactivity, Poor Nutrition Chronic Disease, etc.



The "Bone Bank" Is Built in Childhood

Adapted from US Surgeon General's Report. 2004.

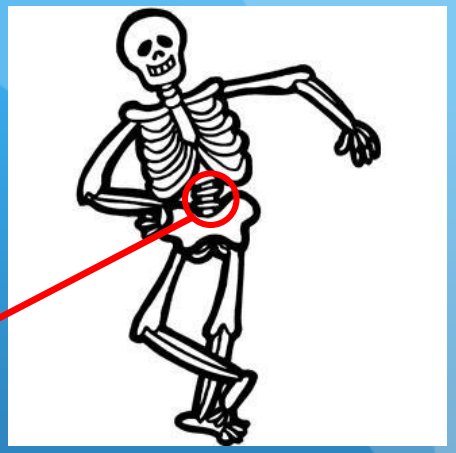
Effects of Peak Bone Mass



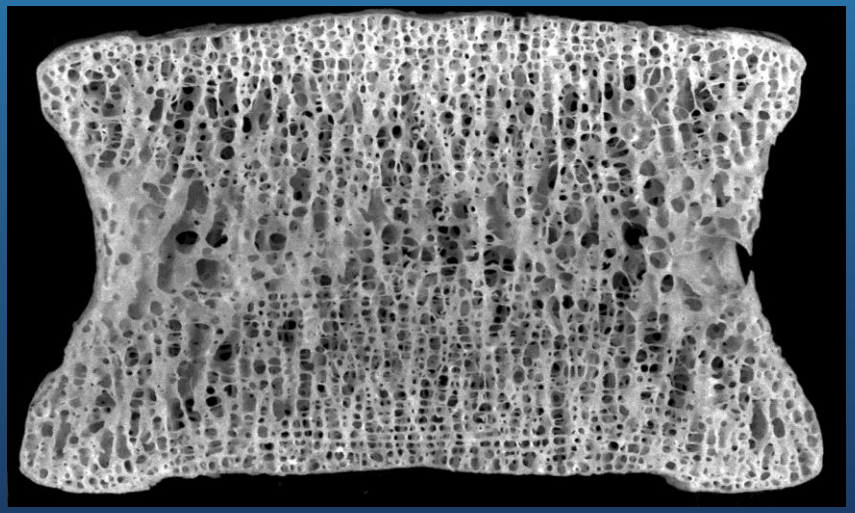
Hernandez CJ et al Osteo Inter 2003

What is unhealthy bone?

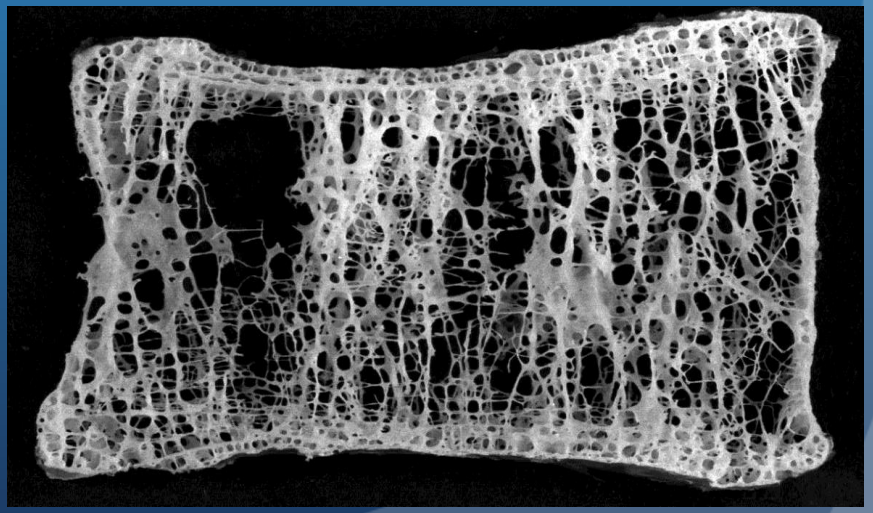
- Bone that is low in density
- Bone that is weak
- Bone that is at high risk of breaking



Normal

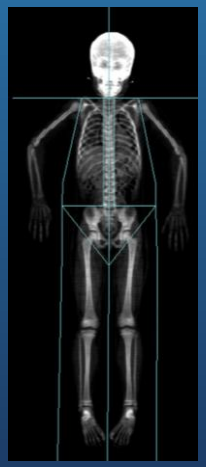


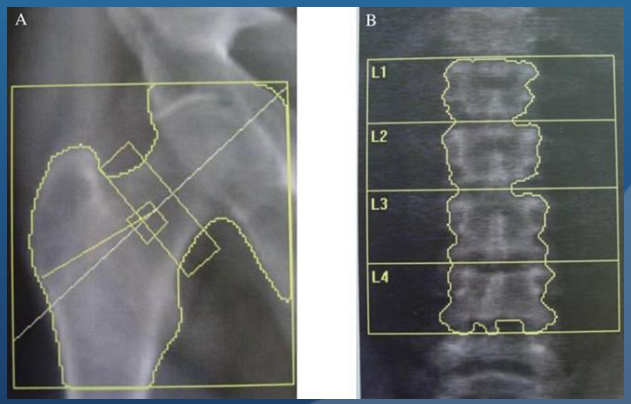
Severe Osteoporosis



Dual Energy X-Ray Absorptiometry (DXA)

- Non-invasive, very low dose of radiation (2 – 5 µSv), 10 s – 1.5 min





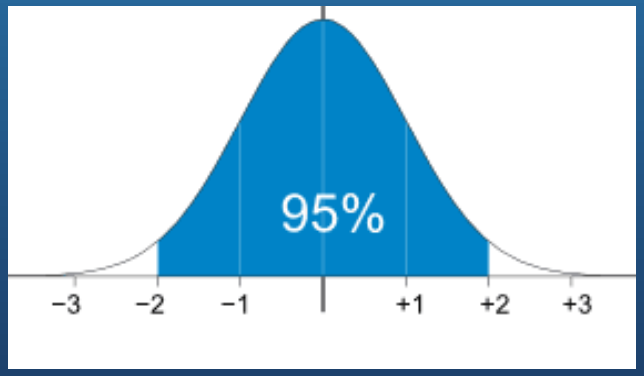
Dual Energy X-Ray Absorptiometry (DXA)

- Non-invasive, very low dose of radiation (2 – 5 µSv), 10 s – 1.5 min

Source	Effective Dose Equivalent (mSv)
Natural Radiation Sources	
Natural background radiation at sea level	3,000 per year
Roundtrip transcontinental airplane flight	60
QCT	
Peripheral QCT (Stratec 2000)	< 0.01
Spine QCT	30 – 100
Hand-wrist x-ray	1
Ultrasound	0

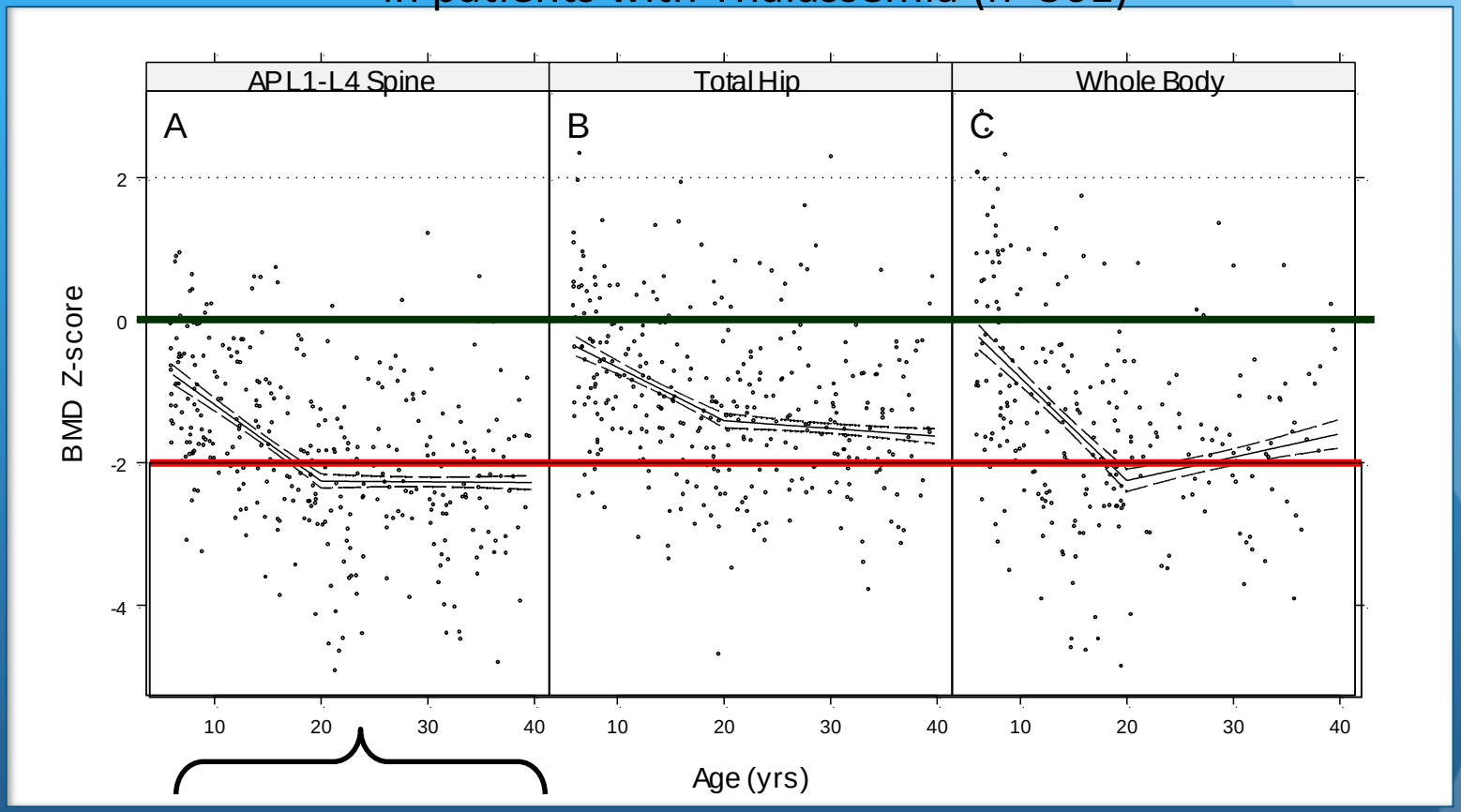
Dual Energy X-Ray Absorptiometry (DXA)

- Non-invasive, very low dose of radiation (2 – 5 µSv), 10 s – 1.5 min
- Measures the bone mineral density (BMD) and compares it to a normative database of people of similar age, ethnicity and gender
- Z-score ≤-2.0 below what is expected for their age



Pediatric Normative Data are Available down to age 3 yrs

Bone Density Z-Scores Decline with Age in patients with Thalassemia (n=361)



Spine Z <-2.0 **9% for 6 - 10 yrs**
44% for 11 – 19 yrs
61% for > 20 yrs

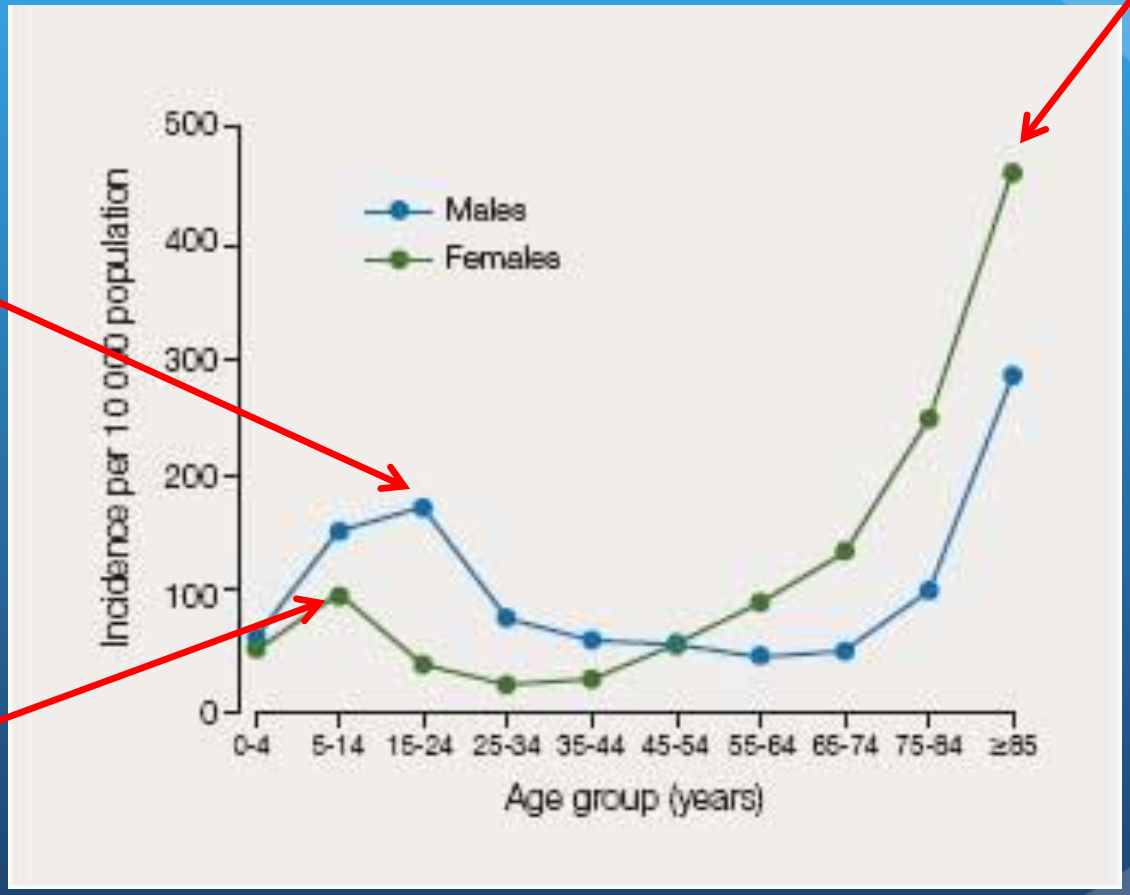
Vogiatzi M et al JBMR, 2009;24:3:543-57

Fracture rates in the general population

~ 4.5 %

~ 1.75 %

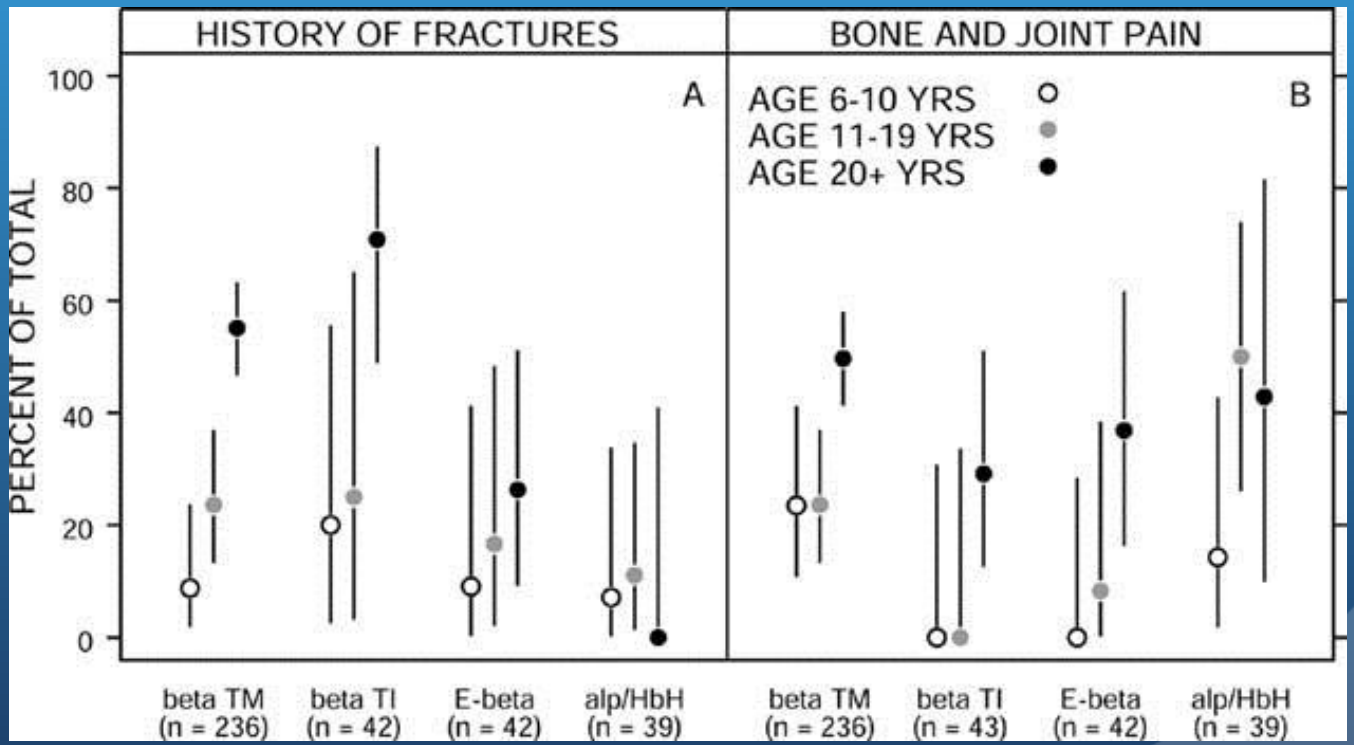
~ 1 %



Landin et al 1997

Fractures and Bony Pain in Thalassemia

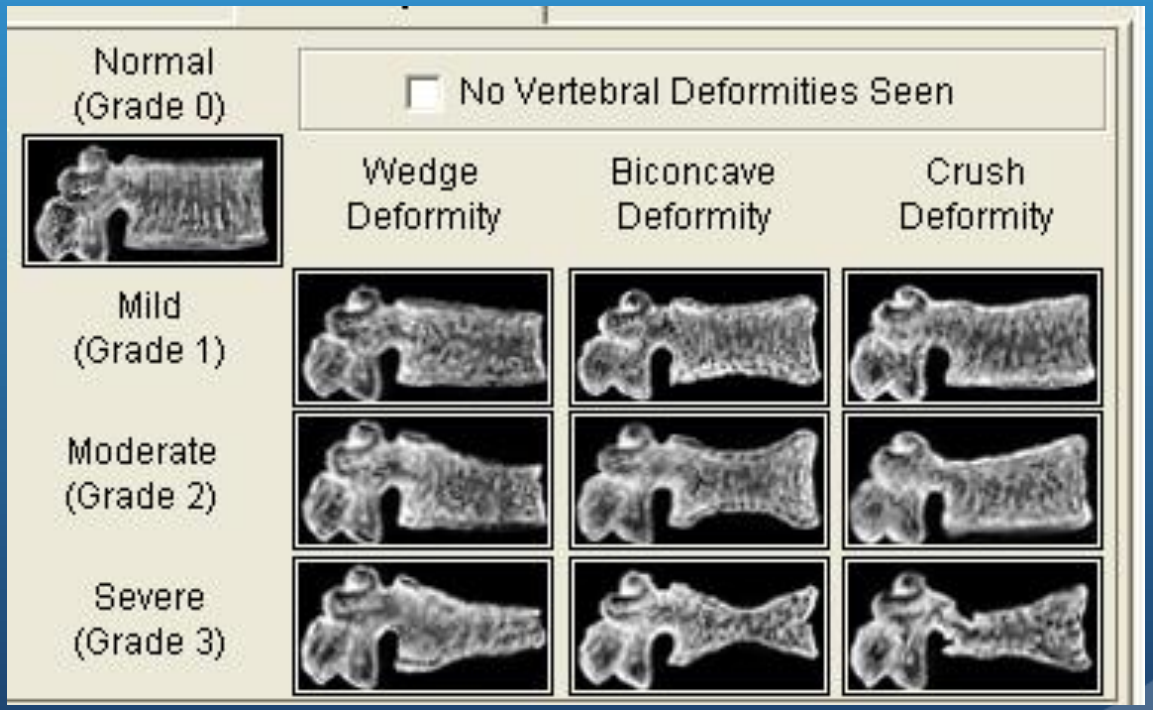
~30% had fractures among all groups
Risk of fractures higher age>20



Vogiatzi JBMR 2009

Vertebral Fracture Assessment Scans on DXA

- Genant Scale used to access vertebral abnormalities and graded from mild to severe



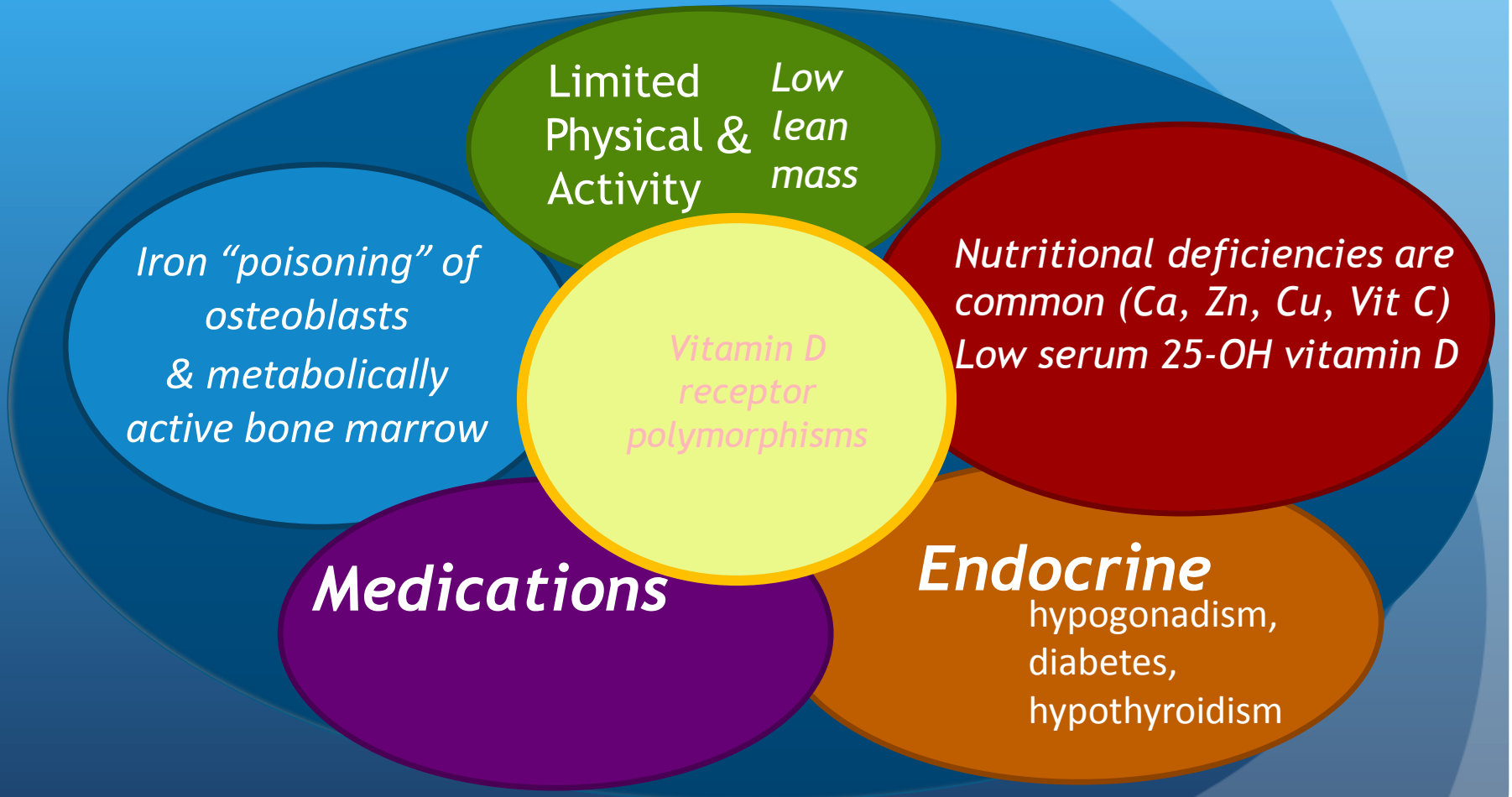
Genant HK J Bone Miner Res 1996;11:984-6

What can we do?

- Early screening and prevention is key
- DXA starting at age 10

Modifiable Contributors to Suboptimal Bone Health

In Patients with Thalassemia



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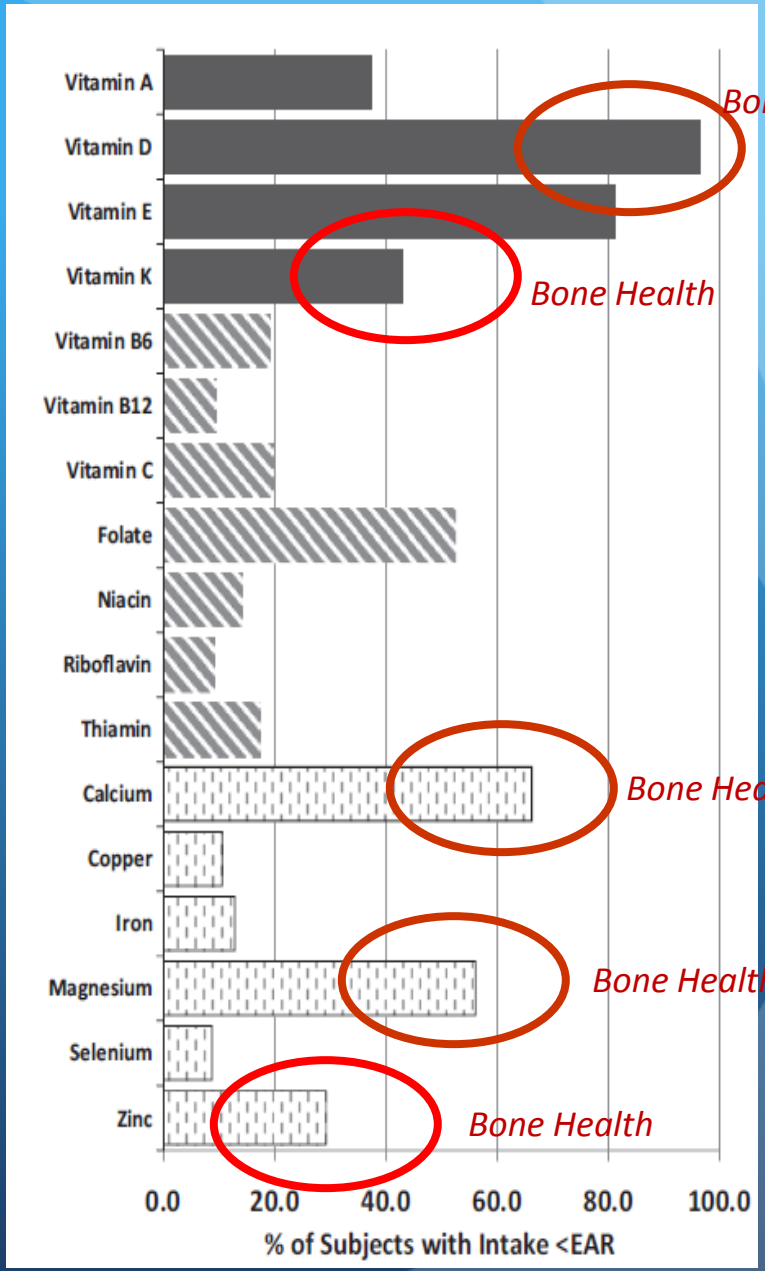
Sadat-Ali M. et al. Indian J Med Sciences, 2008;62:193-98.
Fung EB et al. Bone 2011:48:1305-12
Haidar R et al Bone 2011;48:425-32.

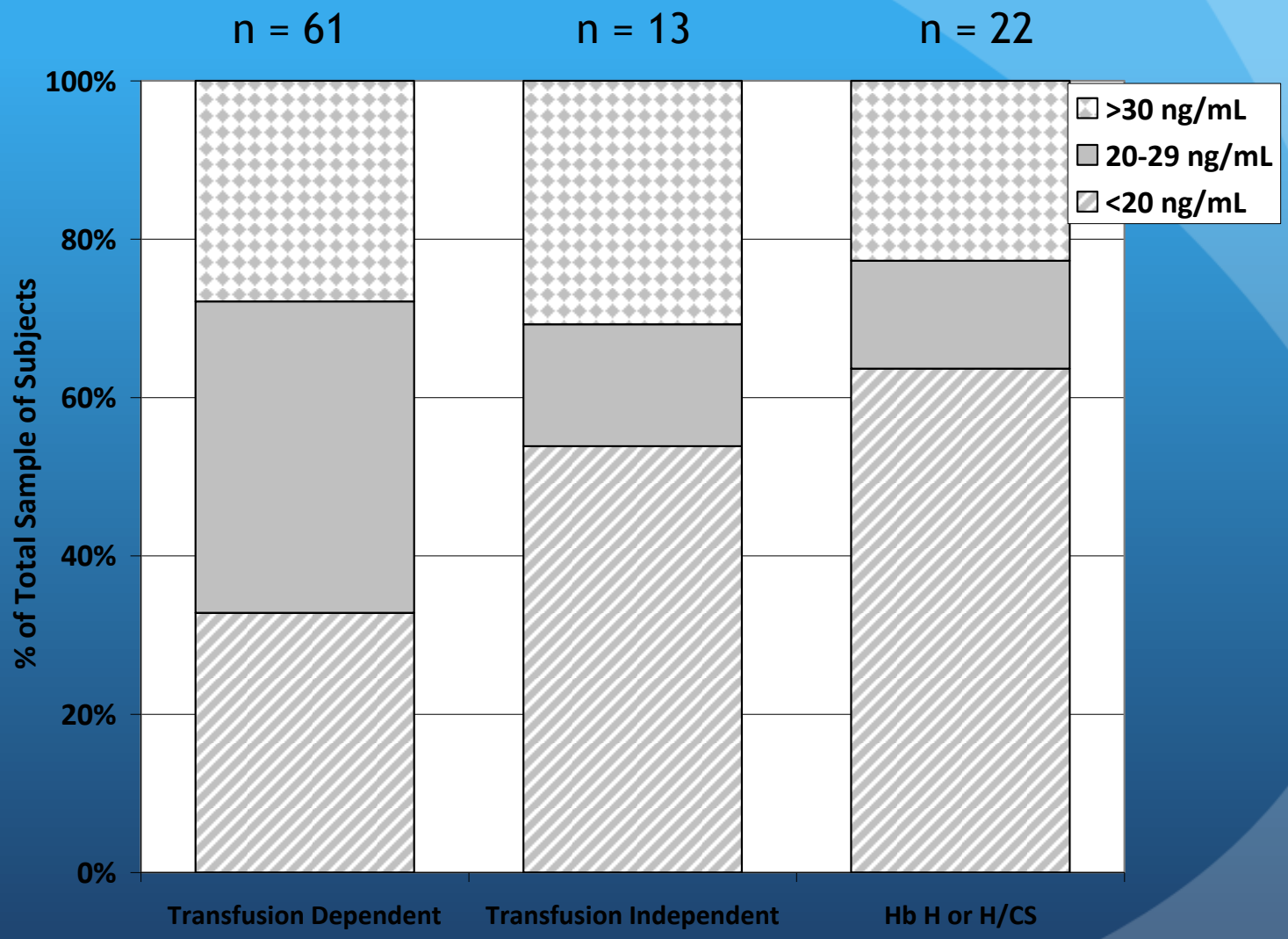
Dietary Survey in thalassemia

North American Patients
n=221
48% male
51% Asian
19.7 ± 11.3 yrs
78.8% with beta thal
90% transfused



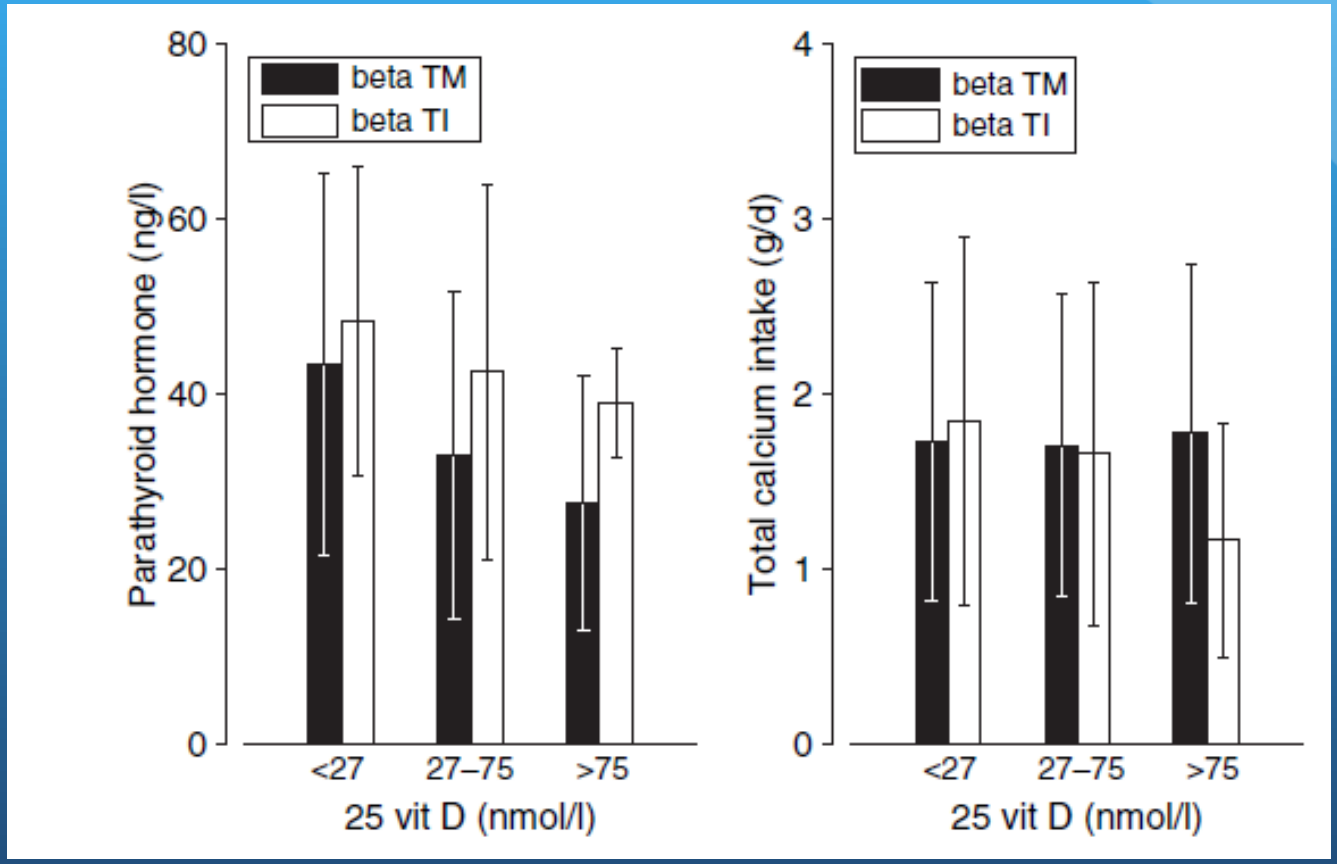
Fung EB et al, JAND 2012

Vitamin D Deficiency in Thalassemia



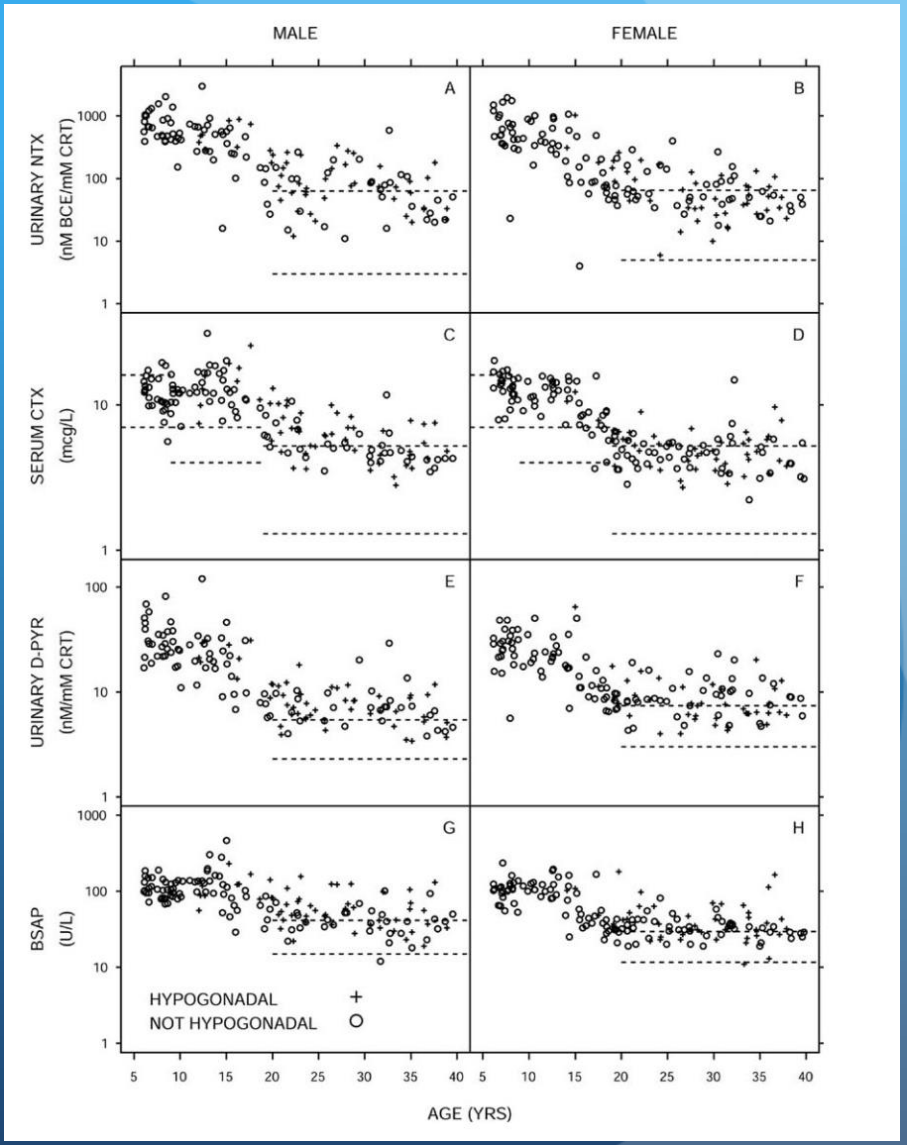
Fung EB et al, Amer J Heme 2011

Vitamin D & Parathyroid Hormone



Vogiatzi BJH 2009

- Players of bone building
  - 25(OH) Vitamin D
  - 1,25 (OH)2 Vitamin D
  - Calcium
  - Osteocalcin
  - Alkaline phosphatase
  - Phosphorus
  - Magnesium
  - Zinc
- Markers of bone resorption
  - n-telopeptides
  - Deoxypyridinoline



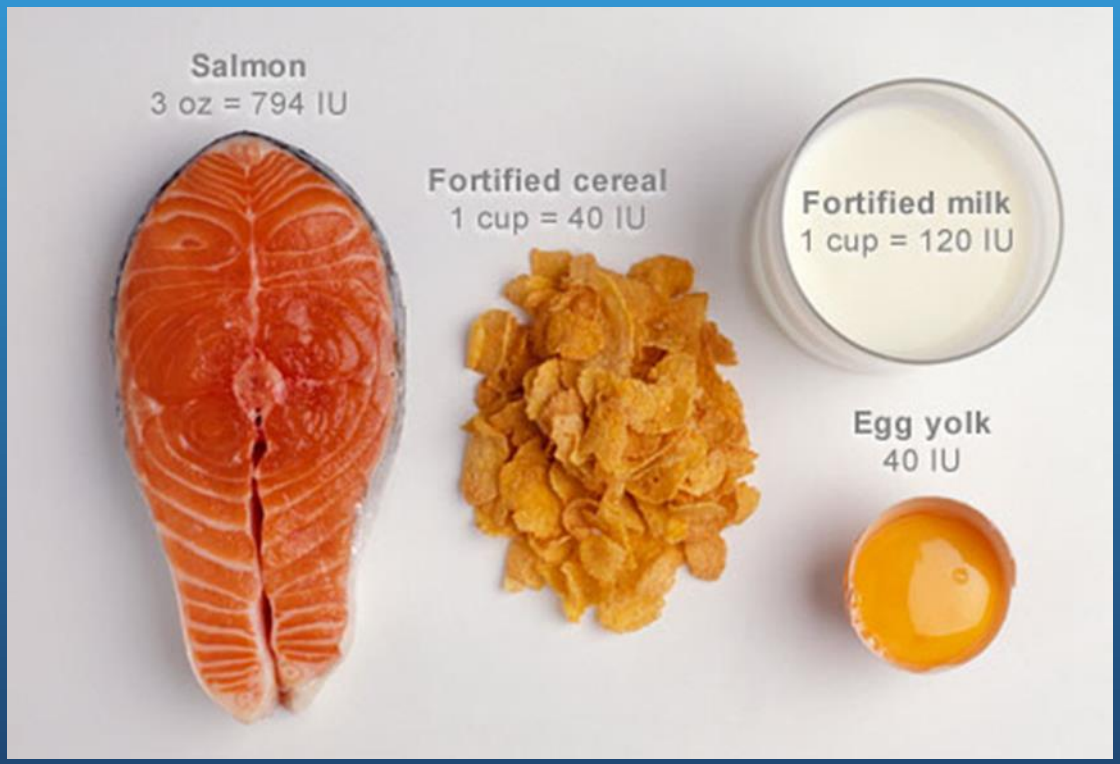
Vogiatzi MG, JBMR, 2009

Bisphosphonates

- Improves bone mineral density (~15% in 2 yrs)
- Can be given as a daily pill or intravenous every 3-6 months
  - Pills usually avoided in kids (significant GI side effects)
- Give if there is ongoing bone loss or fractures

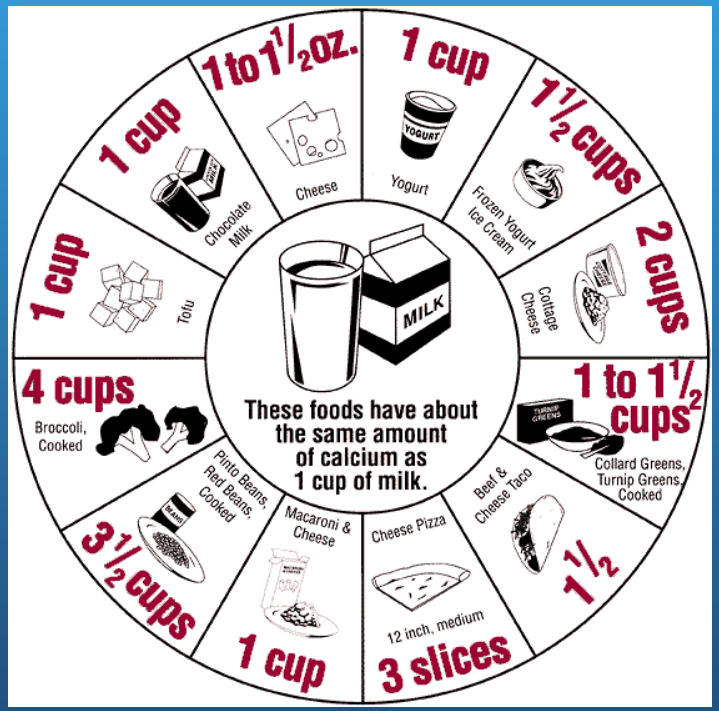
Vitamin D3 intake ~ 1,000 units daily

- Aim for around Vitamin D3 1,000 units daily



Calcium Intake ~1,000 mg daily

- 1 cup of milk ~ 300 mg



Zinc Supplementation Study: RCT Trial Baseline Characteristics

Group	Zinc (24)	Placebo (18)
Age, y	17.5±5.6	17.4±4.7
B-Thal	62%	77%
% Asian	75%	61%
% Female	50%	50%
Ht Z-score	-1.8±1.1	-1.6±1.3
Ferritin, ng/dL	1994	2033
Chelation	Desferal (7)	Desferal (3)
	Exjade (10)	Exjade (12)
	Combo (1)	Combo (1)
25OHD <30 ng/mL	71%	67%
Dietary Zn, %RDA	133%	137%
Plasma Zn,	82±14	82±16
≤70 , ug/dL	23%	28%

Intervention: 25 mg Zn/d or placebo

18 months

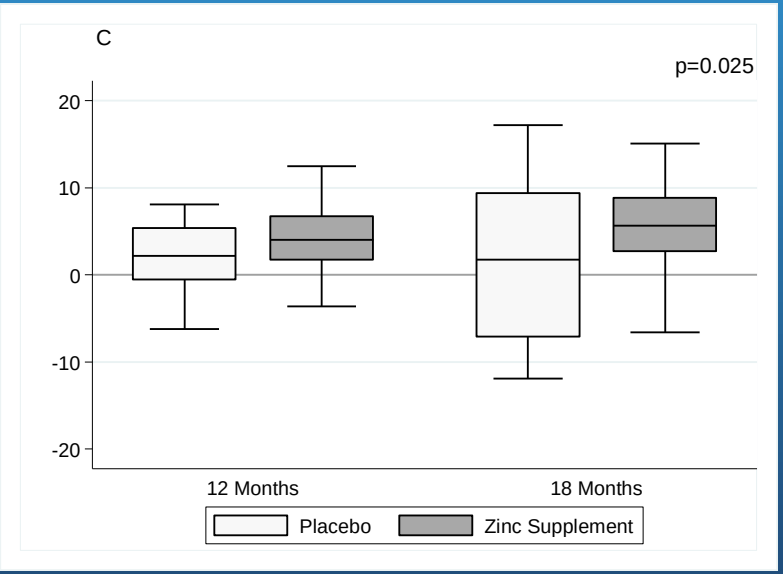
Fung EB et al AJCN 2013

% Change in Whole Body BMC & BMD

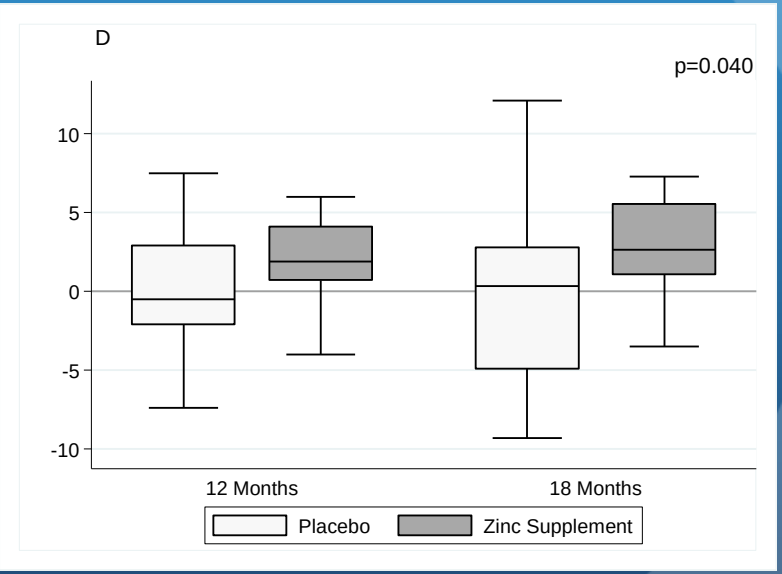
compared to baseline value in Placebo vs. Zinc Groups*

**Data controlled for puberty and baseline value*

Absolute Difference 4.3%



Absolute Difference 3.0%



Adherence to supplements overall: placebo 78% / zinc 82%

Others

- **Zinc:** Meat, chicken, nuts and lentils and fortified cereal
- **Vitamin K:** Dried plums (prunes) and certain dark green leafy vegetables like kale, collard greens, spinach, mustard greens, turnip greens and Brussels sprouts
- Strontium: data is still early. Mainly in seafood, small amounts in whole milk, wheat bran, poultry and root vegetables
- Try to eat 1.5 cups of fruit and 2 cups of vegetables every day

Modifiable Contributors to Suboptimal Bone Health

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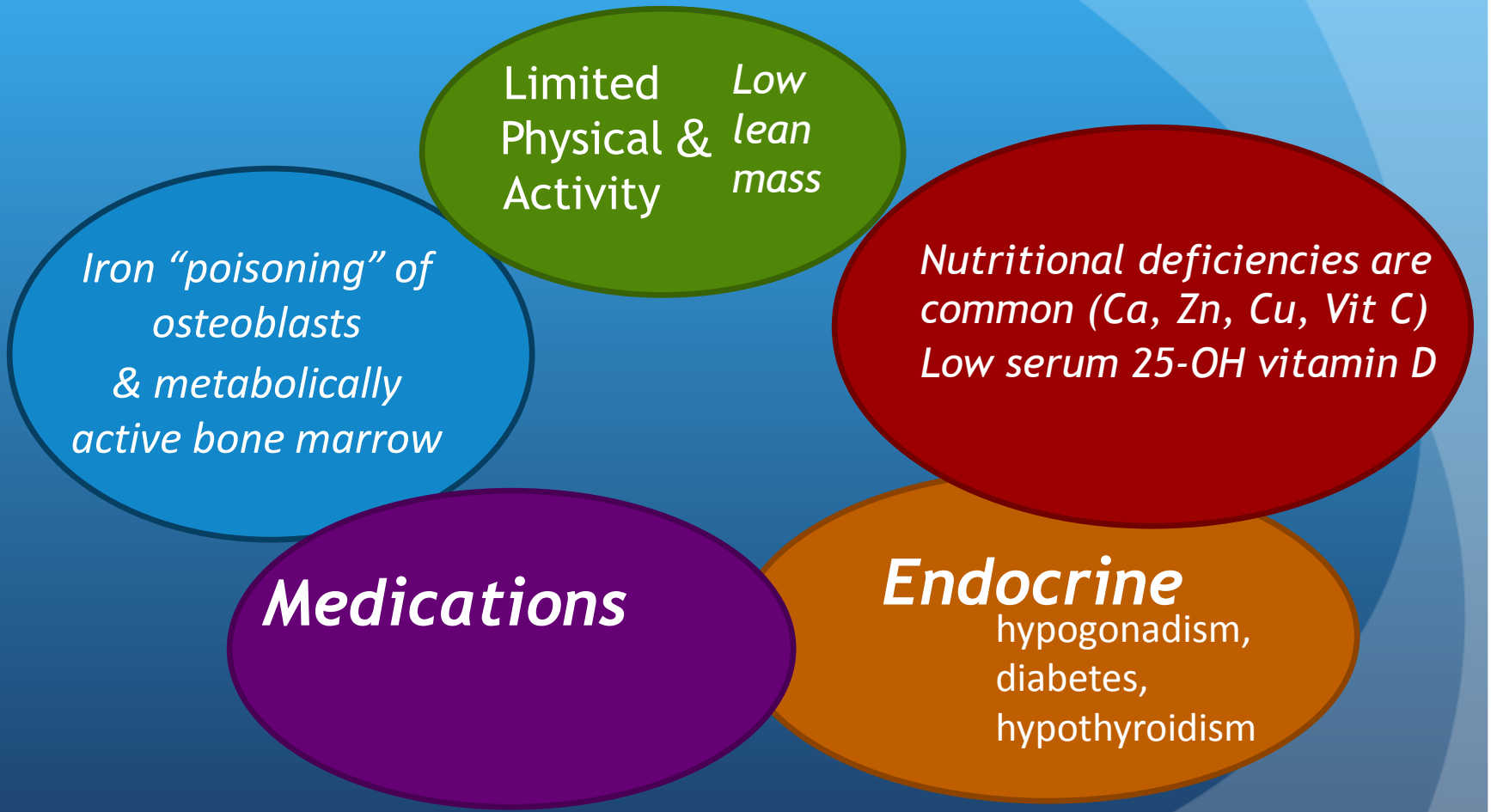

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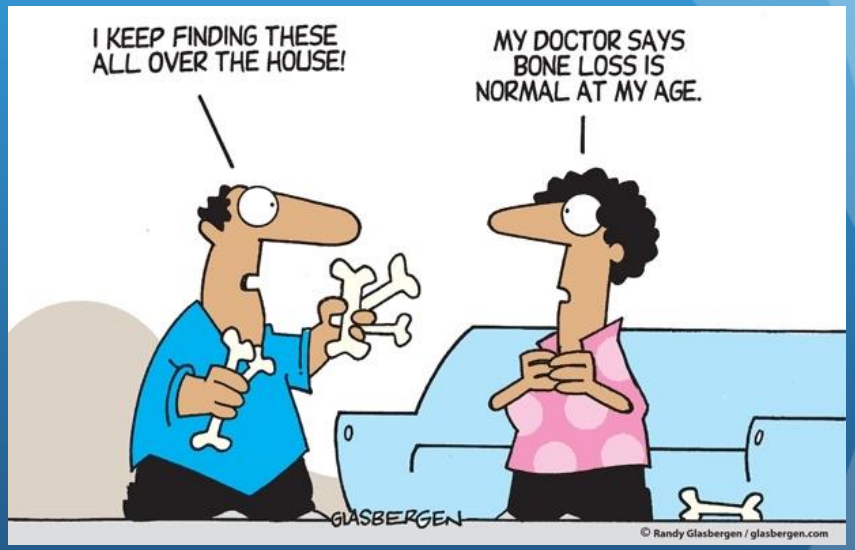
Medications associated with bone loss

- Chelators
  - desferal
- Glucocorticoids
- Proton Pump Inhibitors
- Anti-Seizure medications
  - Carbamazepine
  - Phenytoin
- Excess thyroid hormone
- Diuretics



Modifiable Contributors to Suboptimal Bone Health

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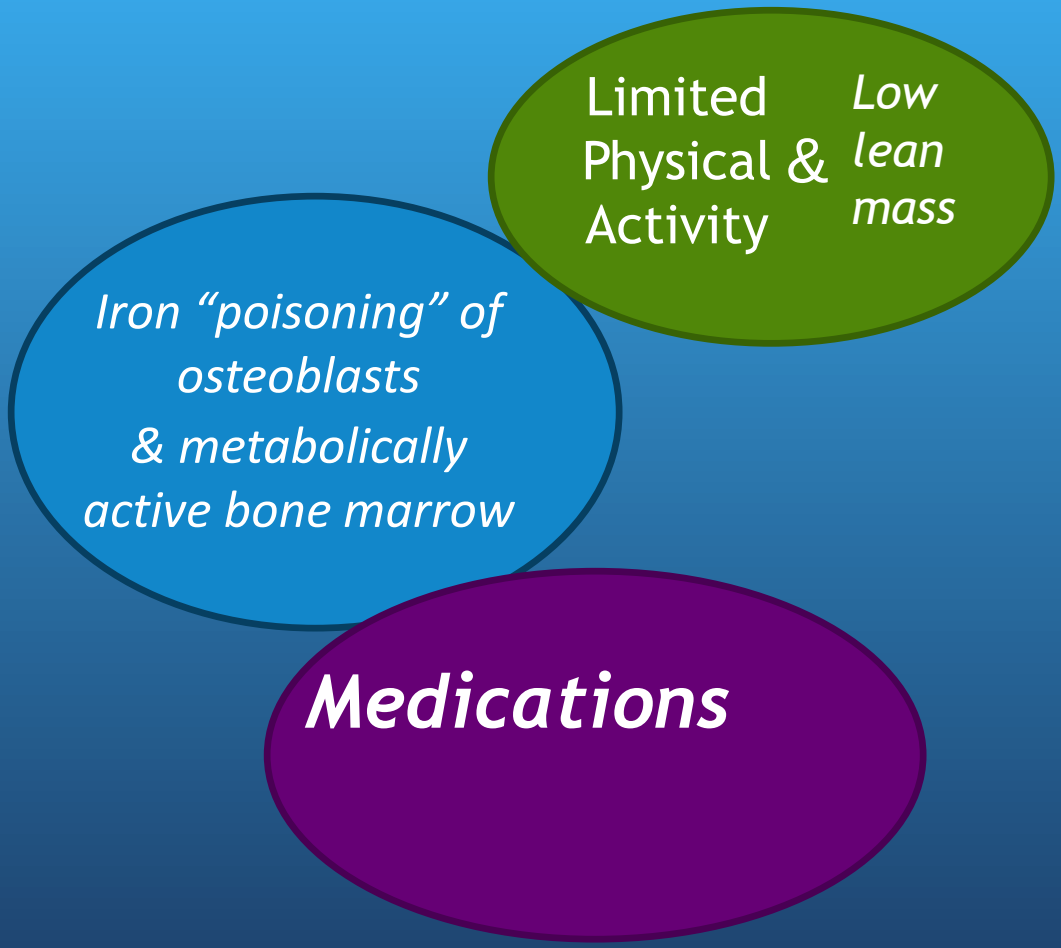

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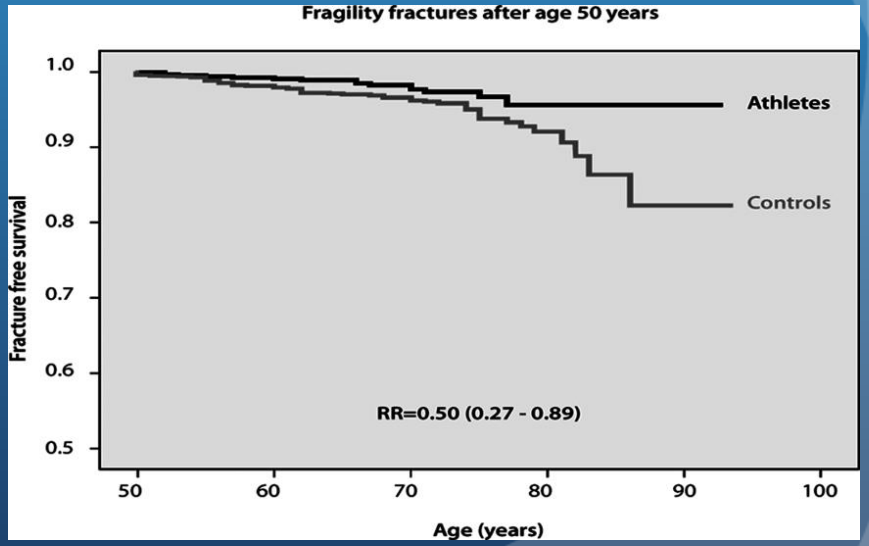
Physical Activity

- Improve balance, bone mass and muscle mass
- Immobility associated with rapid bone loss
- Weight-bearing and muscle strengthening exercise:
  - Walking
  - Jogging
  - Dancing
  - Tennis

Athletes were 50% less likely to break a bone



To Sum Up…

- Peak bone accrual occurs during rapid growth
  - Stops around 25-30 years old
- Practice what can be modified
  - Optimize nutrients
  - Monitor and treat endocrinopathies or other systemic issues
  - Be judicious with medications
  - Keep Hb levels optimals
  - Weight bearing exercise
- As adults, we no longer build bone but can slow down resorption

Thank you for your attention

Special Bill Murray Thanks

- Dr. Mona Al Mukaddam
- Dr. Ellen Fung
- Dr. Ashatosh Lal
- Dr. Elliott Vichinsky
- Shannon Gaine, P.N.P.
- Wendy Murphy, LCSW

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