"Bad to the Bone"
5-3-19
Alaska ACP

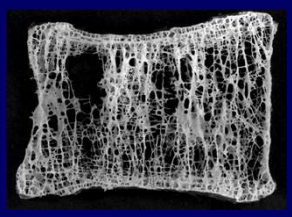
Brad Anawalt, MD
Vice Chair and Professor of Medicine
University of Washington
banawalt@medicine.washington.edu

Disclosures

Author of chapters in UpToDate

Definition of osteoporosis

- NIH Conference
  " A skeletal disorder characterized by compromised bone strength predisposing to an **increased risk of fracture**. Bone strength reflects the integration of two main features: **bone density and bone quality**."



JAMA 2001;285:785

BDA

Case #1

A 55-year old woman is referred to your clinic for possible osteoporosis evaluation after she fell from a 6-foot ladder and broke ribs. She has a history of hypertension but is otherwise healthy. She takes lisinopril/HCTZ. She has never taken hormone therapy. Which of the following historical data would prompt you to order a DXA ?

A. Her history justifies a DXA now
B. She went through menopause at age 42
C. She has a history of kidney stones
D. After 30 pack-years, she quit smoking 4 years ago
E. She is a Native American (Haida)

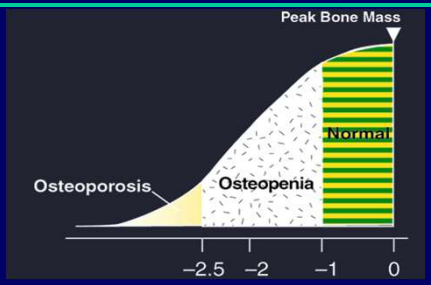
BDA

Screening BMD recommendations

- Women ≥ 65 years
- Postmenopausal women with risk factors
  - Previous fracture*
  - Family history
  - Alcohol, current tobacco use
  - 2° causes of osteoporosis (e.g., GI malabsorption, hyperPTH, early menopause/hypogonadism, liver disease)
- Men
  - > Age 65? >70? > 75? years
  - 2° causes of osteoporosis

BDA

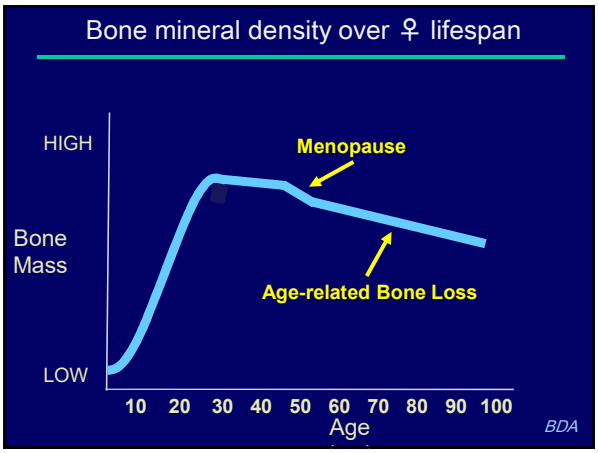
World Health Organization (WHO) Criteria

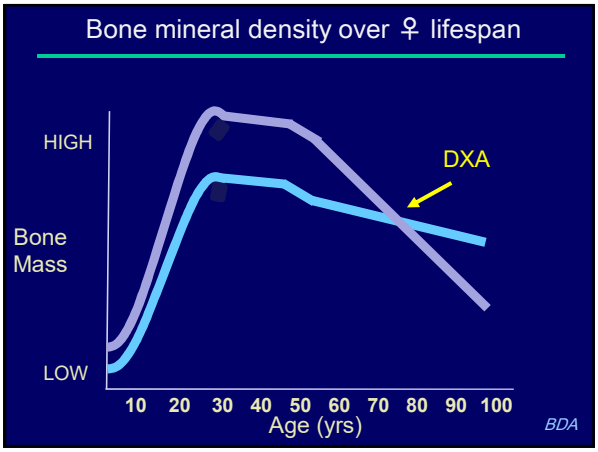


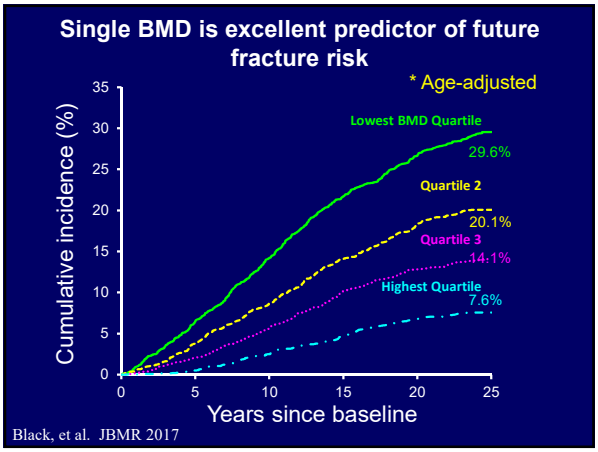
T-Score

IDSA: Diagnosis of Osteoporosis
Postmenopausal ♀ or ♂ >50 years old withT-score<-2.5
Low trauma fragility fracture at any age

BDA


Bone mineral density over ♀ lifespan
HIGH
Bone Mass
LOW
Menopause
Age-related Bone Loss
10 20 30 40 50 60 70 80 90 100
Age
BDA

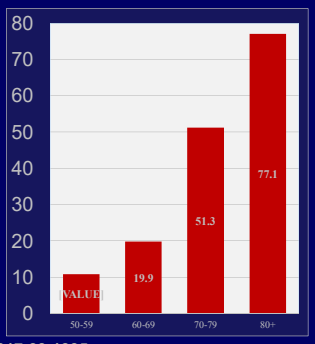

Bone mineral density over ♀ lifespan
HIGH
Bone Mass
LOW
DXA
10 20 30 40 50 60 70 80 90 100
Age (yrs)
BDA


Single BMD is excellent predictor of future fracture risk
* Age-adjusted
Cumulative incidence (%)
0 5 10 15 20 25 30 35
Lowest BMD Quartile
29.6%
Quartile 2
20.1%
Quartile 3
14.1%
Highest Quartile
7.6%
0 5 10 15 20 25
Years since baseline
Black, et al. JBMR 2017

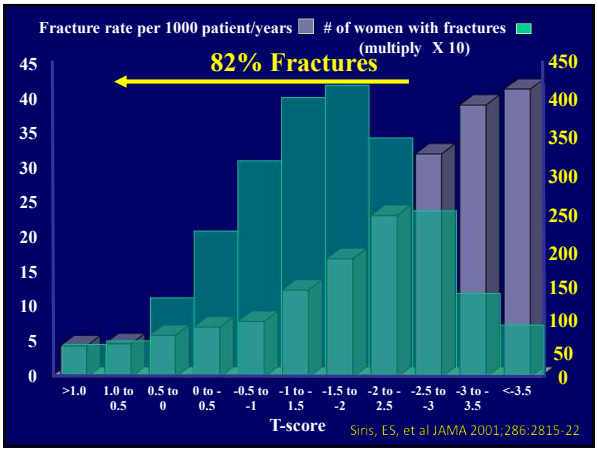
Epidemiology of osteoporosis

% post-menopausal women with osteoporosis

(T score -2.5
Low trauma fx
FRAX criteria)

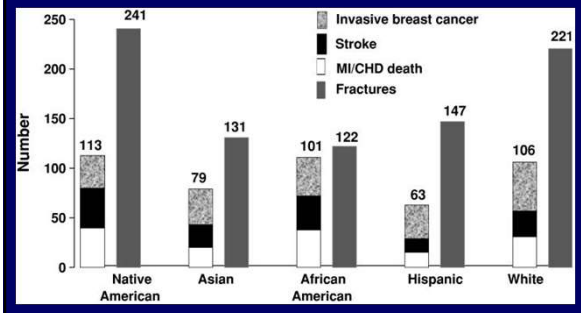


Wright, et al *Osteo Int*, 2017;28:1225 BDA



Siris, ES, et al JAMA 2001;286:2815-22

Epidemiology of osteoporosis



Cauley, et al *Osteo Int* 2008;19:1717-23 BDA

Case #1 answer

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D. After 30 pack-years, she quit smoking 4 years ago
E. She is a Native American (Haida)

BDA

Case #1 (cont'd)

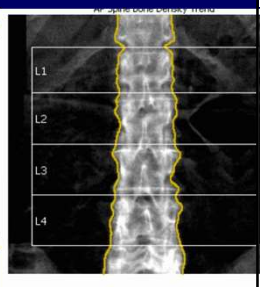
Further history:
PMH:
No low-trauma fractures (fall from standing or less)
No history of liver, kidney or GI disease
FMH: Mother with vertebral fracture at age 63
What bone densitometry study would you order?

A. Heel ultrasound
B. Quantitative CT
C. DXA
D. DXA with trabecular bone score
E. No bone densitometry

BDA

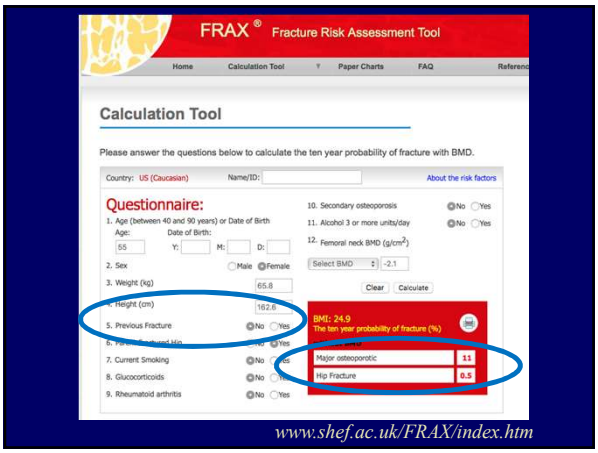
Case #1: 55-year old woman with DXA reasults

Total hip T- score -2.3
Femoral neck T-score -2.1

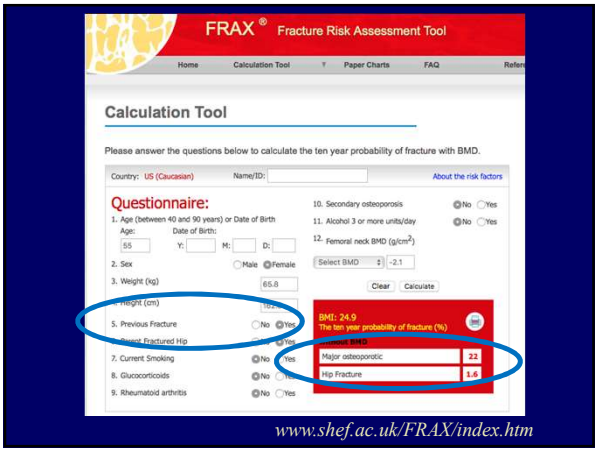


LS BMD T-score -2.7

BDA

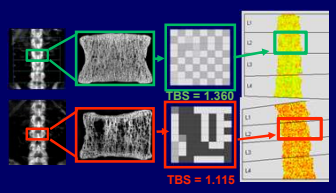


www.shef.ac.uk/FRAX/index.htm



www.shef.ac.uk/FRAX/index.htm

Trabecular Bone Score (TBS)



TBS measures bone heterogeneity

Fracture predictor
>1.35 good quality
1.22-1.35 moderate quality
<1.21- poor quality
Adjust FRAX risk

Pothuaud et al. *Bone* 2008;42:775-87.
Hans et al. *JCD* 2011;14:302-12

Case #1 (cont'd) answer

Further history:

PMH:

No low-trauma fractures (fall from standing or less)

No history of liver, kidney or GI disease

FMH: Mother with vertebral fracture at age 63

What bone densitometry study would you order?

A. Heel ultrasound

B. Quantitative CT

C. DXA

D. DXA with trabecular bone score

E. No bone densitometry

BDA

Case #2

A 71-year old woman is referred to your clinic for management of osteoporosis. She has history of fragility fracture of the left wrist, but a recent DXA demonstrated a T score of -2.9 at the lumbar spine and –2.7 at the hip and femoral neck. Her last menstrual period was at age 51. She has no history suggestive of a secondary cause of osteoporosis. She has hypertension. She takes losartan, aspirin and simvastatin. She walks daily.

Which of the following is the most important next step?

A. Gait assessment

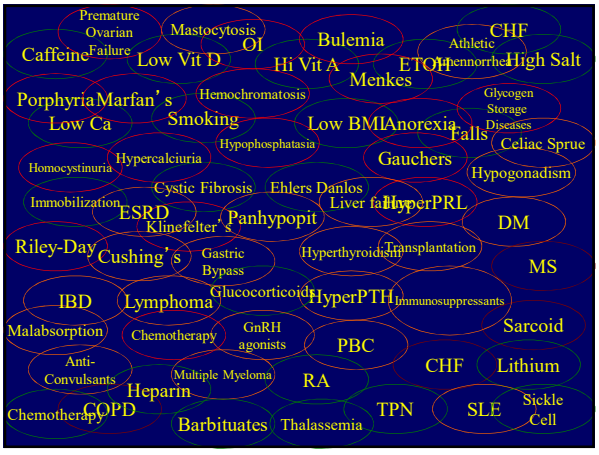
B. Calcium, phosphate

C. Calcium, phosphate, creatinine, SGOT

D. Calcium, phosphate, creatinine, SGOT, 25-OH

E. Calcium, phosphate, creatinine, SGOT, 25-OH D, PTH

BDA

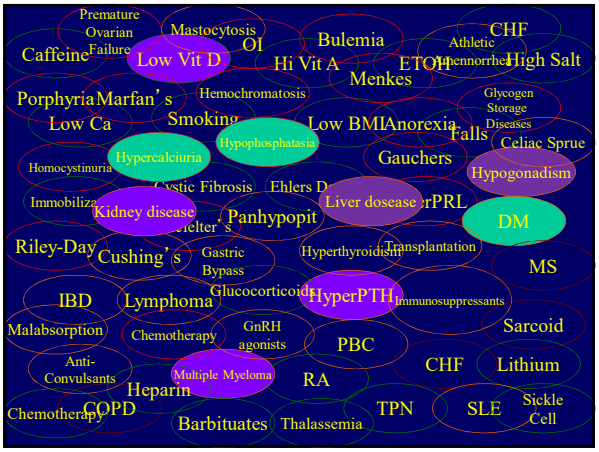


Evaluation of cause of osteoporosis

- Biochemistry Panel with calcium, phosphate, HCO3, creatinine, hematocrit
- Liver function tests (if not previously done)
  - Albumin and SGOT
- 25 OH Vitamin D (Goal 25-40 ng/dl)
- PTH
- Sex hormone evaluation
  - Men- Testosterone
  - Women- menstruation history
- If history or Z score worse than -2, consider more extensive w/u (e.g., 24-hr urine calcium)

Luckey MM, et al. *J Clin Endo Metab.* 2003;88:1405

BDA



Case #2 answer

A 71-year old white woman is referred to your clinic for management of osteoporosis. She has no history of fragility fracture, but a recent DXA demonstrated a T score of -2.9 at the lumbar spine and –2.7 at the hip and femoral neck. Her last menstrual period was at age 51. She has no history suggestive of a secondary cause of osteoporosis. She has hypertension. She takes losartan, aspirin and simvastatin. She walks daily.

Which of the following is the most important next step?

A. Gait assessment
B. Calcium, phosphate
C. Calcium, phosphate, creatinine, SGOT
D. Calcium, phosphate, creatinine, SGOT, 25-OH
E. Calcium, phosphate, creatinine, SGOT, 25-OH D, PTH

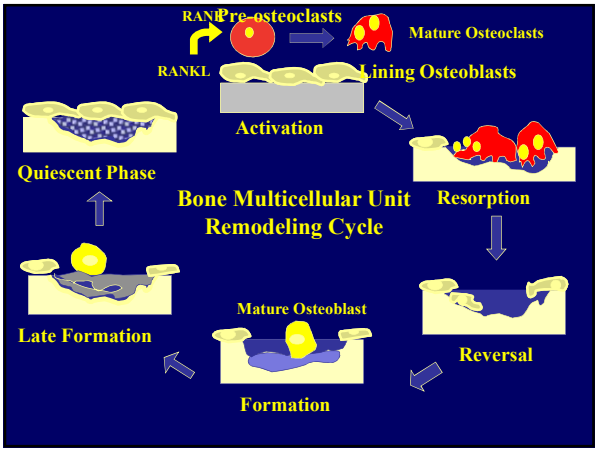
BDA

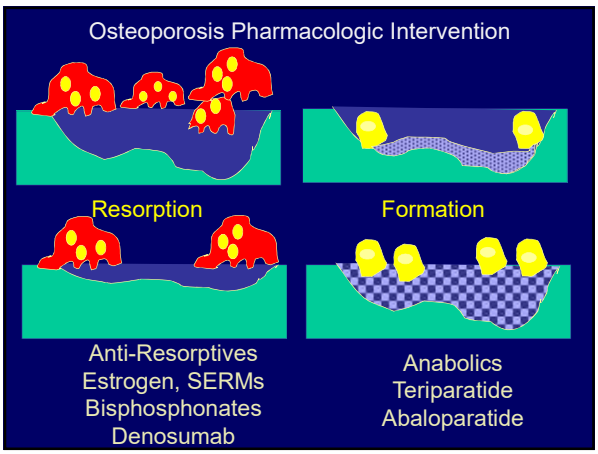
Case #2 (cont'd)

This 71-year old woman has a normal gait. Her laboratory results show no secondary osteoporosis. Her FRAX score is 13% for major osteoporotic fracture and 3.3% for hip fracture. After diagnosing age-related, postmenopausal osteoporosis and recommending adequate calcium and vitamin D intake plus daily weightbearing exercise, which of the following is the most appropriate next step?

A. Zolendronic acid IV every 12-18 months
B. Denosumab IV every 6 months
C. Estrogen patch twice weekly
D. Abaloparatide SC daily

BDA





Primary Prevention Fracture
Minimize risk and maximize benefit

Calcium Vit D Reproductive Health Exercise	Calcium Vit D Estrogen Bisphosphonates Denosumab Anabolics Raloxifene	Calcium Vit D Bisphosphonates Denosumab Anabolics Raloxifene Biomechanical

<45 50 55 60 65 70 75 80 85

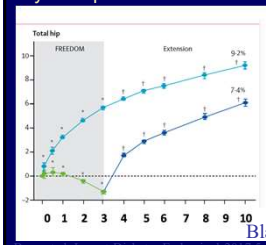
Age yrs)

Bone Loss Prevention Options

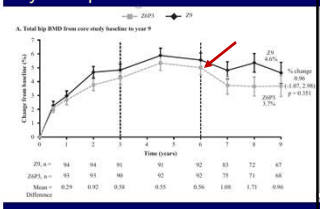
DRUG	BMD LS Increase	BMD TH Increase	Fx	COMMENTS
Estrogen + progestogen	4%- 3 yrs	1.7%- 3 yrs	YES	Treats VMS ↑ Risk of CV in older ♀
Raloxifene	2.4%- 2 yrs	2.4%- 2 yrs	SPINE	Reduction of Breast Ca
Bazedoxifene	2.3%- 1yr	1.4%- 1yr	SPINE	No menstruation
BPN	6.7%- 3yr	4%- 3yr	YES	Long skeletal $T_{1/2}$ BMD plateau
Denosomab	9.2%- 3yr 21%-10y	6%- 3 yr 9.2%-10y	YES	Large gains Rapid BMD loss

BMD effect of denosumab and zoledronic acid

FREEDOM Extension Trial
DMAb
10-year hip BMD increase 9.2%



HORIZON Extension
Zoledronic acid
9-year hip BMD Increase 4.6%



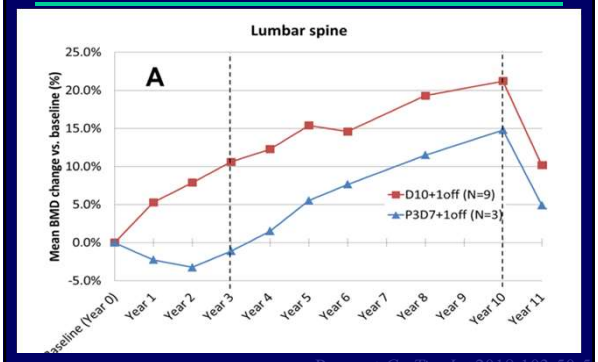
Black, et al *J Bone and Miner Res* 2015;30:

Bone et al. Lancet Diabetes Endocrinol 2017;5:513-23.

Anabolics vs Anti-resorptives

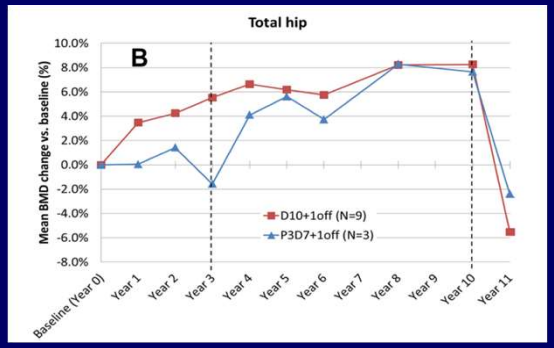
	Teripara-tide	Abalopara-tide	Biphos-phonates	Deno-somab
BMD 2 year	9.7% LS 2.4% Hip	11% LS 4% Hip	5.5% LS 4% Hip	8% LS 4% Hip
Vert Fx	70%	86%	50%	68%
Nonvert Fx	54%	45%	40%	40%
ONSET	6 mos	6 mos	1 year	1 year
COST	+++	+++	+	++
PREFER				

Vertebral BMD ↓↓ 1 year after Denosumab Discontinuation



Popp, et *Ca Tiss Int* 2018;103:50-5

Hip BMD ↓↓ 1 year after Denosumab Discontinuation



Popp, et *Ca Tiss Int* 2018;103:50-54

Case #2 (cont'd) answer

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A. Zolendronic acid IV every 12-18 months
B. Denosumab IV every 6 months
C. Estrogen patch twice weekly
D. Abaloparatide SC daily

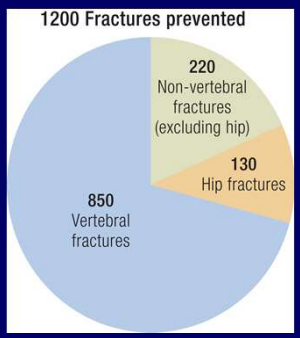
BDA

Concerns about anti-resorption therapy

ONJ

Atypical Femoral Fracture

Benefits > risks: 3-year event rate



1 atypical femoral fracture (1:2000)

Osteonecrosis of jaw even rarer: 1:10,000-100,000

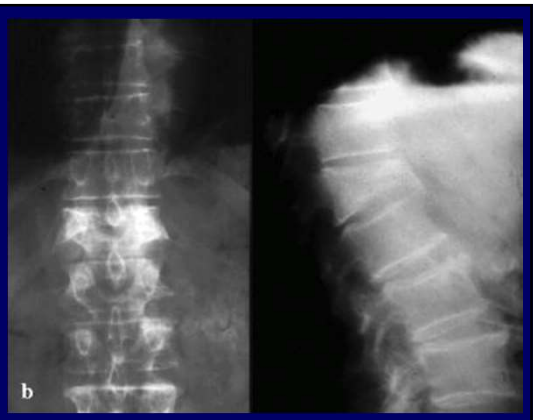
BDA

Case #3

A 72-year old woman has a DXA that demonstrates a lumbar spine T-score of + 0.8 and a T score of femoral neck of -3.5. She is on an aromatase inhibitor for breast cancer and has no other secondary causes osteoporosis.

What is the explanation for her discordant vertebral and femoral neck T-scores?

BDA



Case #3 (cont'd)

A 72-year old woman has a DXA that demonstrates a lumbar spine T-score of + 0.8 and a T score of femoral neck of -3.5. She is on an aromatase inhibitor for breast cancer and has no other secondary causes osteoporosis.

She reports that she had 8 weeks of sharp mid-spine pain last year.

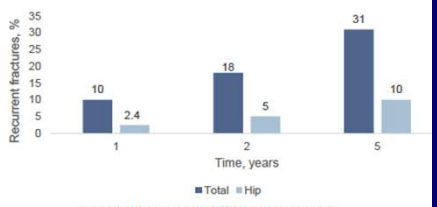
What is her risk of hip fracture in the next 5 years?

A. 2%
B. 5%
C. 10%
D. 20%
E. 30%

BDA

Absolute Risk of Recurrent Fracture after First Fracture

377,561 women with first clinical fracture (excluding fingers/toes/face/skull) identified from Medicare Database



Annualized rates all fx 4.3%/yr during yrs 3-5
Annualized rates hip fx 1.6%/yr during yrs 3-5

Case #3 (cont'd) answer

A 72-year old woman has a DXA that demonstrates a lumbar spine T-score of + 0.8 and a T score of femoral neck of -3.5. She is on an aromatase inhibitor for breast cancer and has no other secondary causes osteoporosis.

She reports that she had 8 weeks of sharp mid-spine pain last year.

What is her risk of hip fracture in the next 5 years?

A. 2%
B. 5%
C. 10%
D. 20%
E. 30%

BDA

Case #4

A 74-year old man has been treated with prednisone (20-40 mg) for polymyalgia rheumatica for 4 months, and his rheumatologist thinks that he might need several more months of therapy. The man has a DXA that demonstrates a lumbar spine T-score of -3.9 and a T score of femoral neck of -3.5. His evaluation for other secondary causes osteoporosis is normal except that his serum testosterone is slightly below normal.

He reports that he had 8 weeks of sharp mid-spine pain 1 months ago.

Of the following, which therapy would you recommend?

A. Denosumab for 2 years followed by teriparatide
B. Teriparatide for 2 years followed by alendronate
C. Romosozumab monotherapy
D. Testosterone plus alendronate

BDA

Osteoporosis Pharmacologic Intervention

Resorption

Formation

Anti-Resorptives
Estrogen, SERMs
Bisphosphonates
Denosumab

Anabolics
Teriparatide
Abaloparatide

Anabolics vs Anti-resorptives

	Teripara-tide	Abalopara-tide	Biphos-phonates	Deno-somab
BMD 2 year	9.7% LS 2.4% Hip	11% LS 4% Hip	5.5% LS 4% Hip	8% LS 4% Hip
Vert Fx	70%	86%	50%	68%
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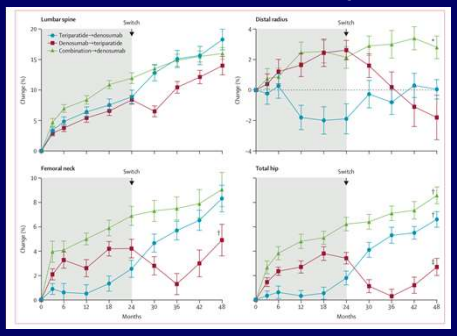
ONSET	6 mos	6 mos	1 year	1 year
COST	+++	+++	+	++
PREFER				

Timing of anabolic and anti-resorptive therapy



Leder, et al *Lancet*, 2015; 386: 1147

Timing of anabolic and anti-resorptive therapy

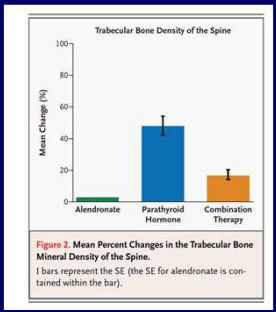


Figure 2. Mean Percent Changes in the Trabecular Bone Mineral Density of the Spine.
I bars represent the SE (the SE for alendronate is contained within the bar).

Finkelstein, et al *NEJM* 2003;349:1216

Case #4 answer

A 72-year old man has been treated with prednisone (20-40 mg) for polymyalgia rheumatica for 4 months, and his rheumatologist thinks that he might need several more months of therapy. The man has a DXA that demonstrates a lumbar spine T-score of – 3.9 and a T score of femoral neck of -3.5. His evaluation for other secondary causes osteoporosis is normal except that his serum testosterone is slightly below normal.

He reports that he had 8 weeks of sharp mid-spine pain 1 months ago.

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B. Teriparatide for 2 years followed by alendronate
C. Romosozumab monotherapy
D. Testosterone plus alendronate

BDA