Bone Health Update

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Rheumatologist

South Carolina
PRISMA HEALTH

Disclosures

None

Goals

1. Improve diagnosis of osteoporosis
2. Understand DXA basics
3. Deepen knowledge of therapeutic options

What is osteoporosis?

"A systemic skeletal disease characterized by low bone mass and microarchitectural deteriorati[illegible] a consequen[illegible]gility and susceptibility to fracture."

There is no cure...

Consensus development conference: diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med. 1993 Jun;94(6):646-50. doi: 10.1016/0002-9343(93)90218-e. PMID: 8506892.

MEDICARE COST OF OSTEOPOROTIC FRACTURES

The National Osteoporosis Foundation (NOF) contracted with the independent actuarial firm, Milliman, to conduct an analysis of the the clinical and cost burden of fractures caused by osteoporosis. The analysis also provides insights on potential economic savings that could be realized if the rate of secondary (repeat) fractures were reduced.

NATIONAL OSTEOPOROSIS FOUNDATION

35 YEARS

In 2015,
2 MILLION
Medicare patients
suffered
2.3 MILLION
fractures

Secondary Osteoporotic Fractures Are Costly.

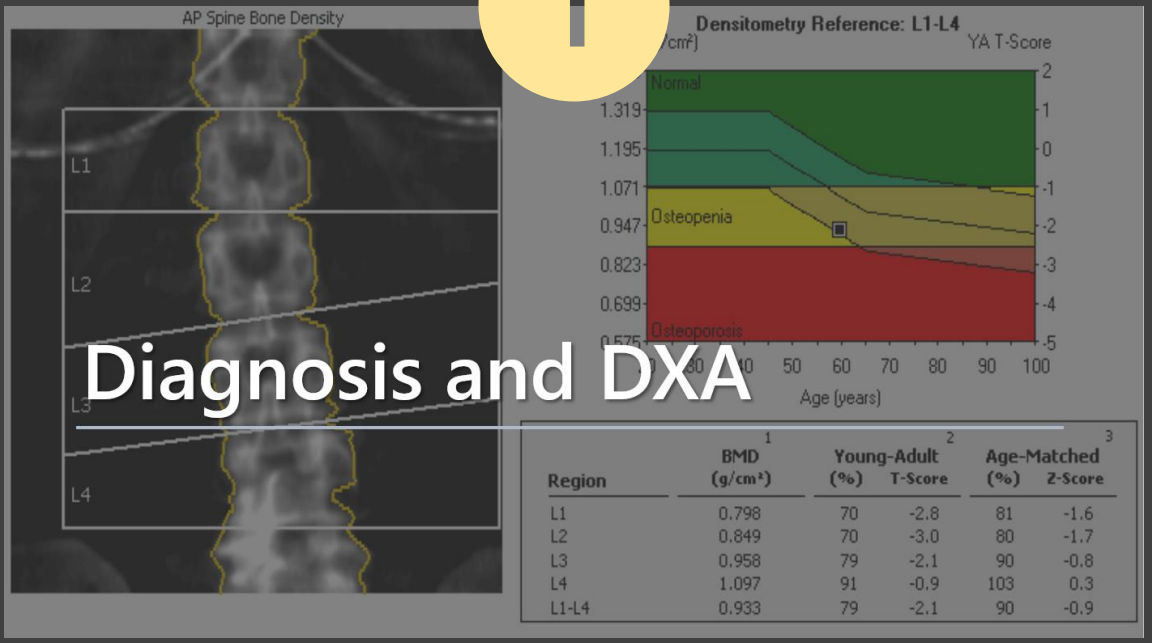
307,000 Medicare patients suffered **1 or MORE** additional fractures at a cost to Medicare of over **$6.3 BILLION**[1]

50%

OF REPEAT FRACTURES COULD BE AVOIDED
with cost-effective and well-tolerated treatments[2]

Framework

1



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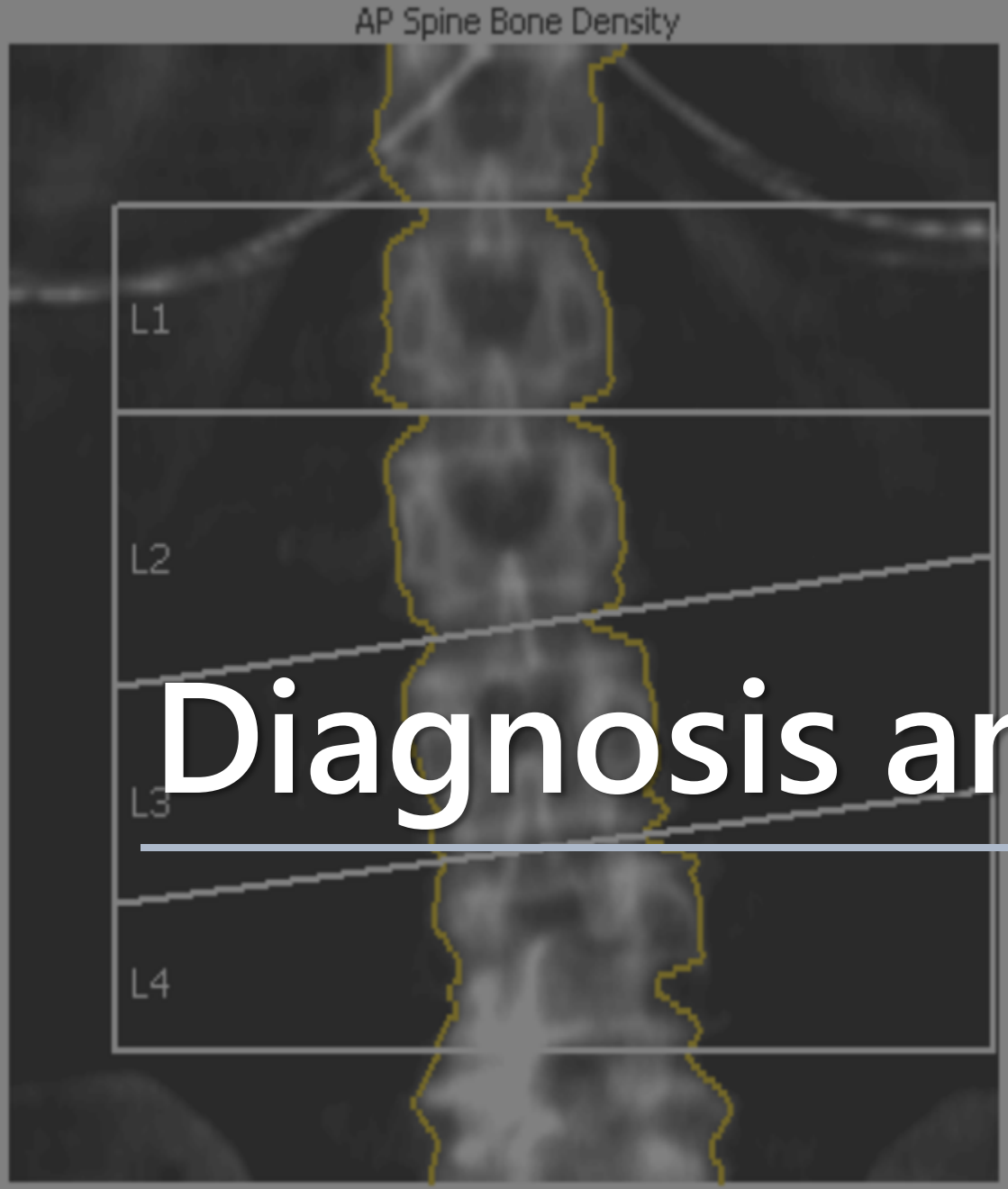
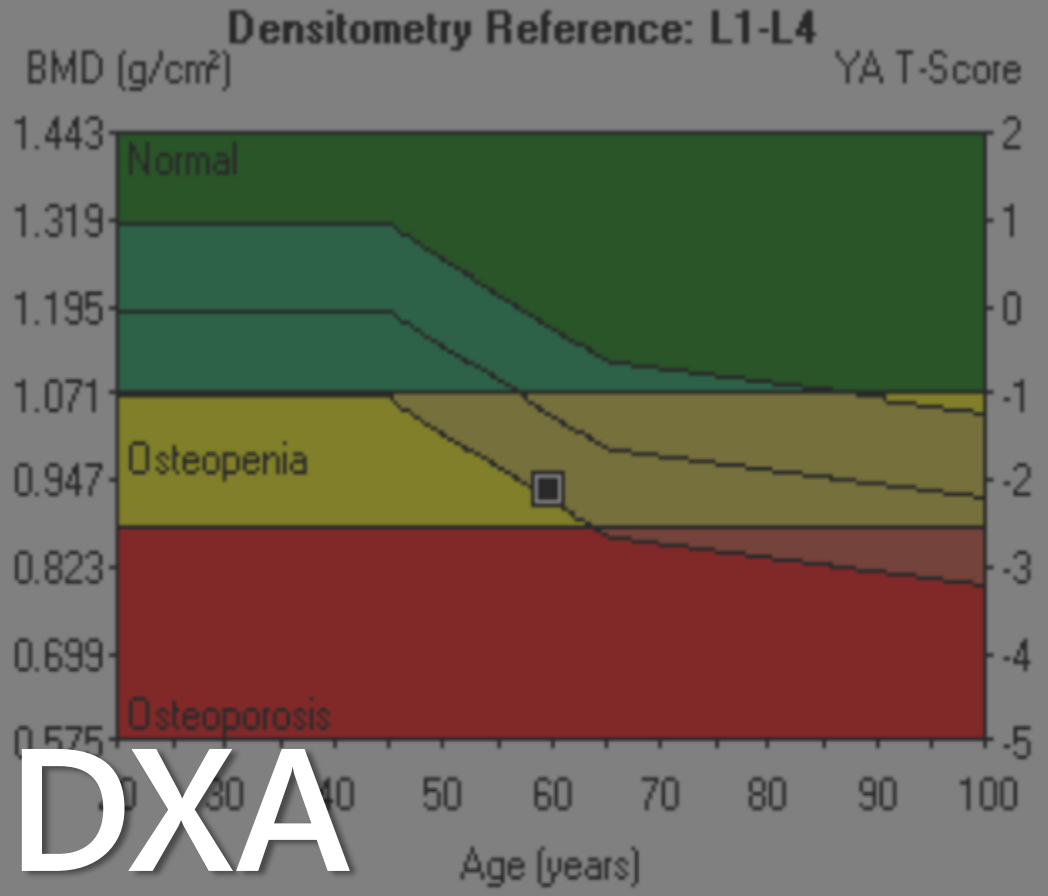
L1-L4	0.933	79	-2.1	90	-0.9

Diagnosis and DXA

2

Treatment





Diagnosis and DXA

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3 ways to diagnose osteoporosis

Diagnosis

1. FRAX
2. Fragility Fractures
3. DXA

Siris, E. S., et al (2014). The clinical diagnosis of osteoporosis: a position statement from the National Bone Health Alliance Working Group. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*, *25*(5), 1439–1443.

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FRAX® Fracture Risk Assessment Tool

Home | Calculation Tool | Paper Charts | FAQ | References | CE Mark | 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 and 90 years) or Date of Birth
   Age: Date of Birth: Y: M: D:
2. Sex ○ Male ○ Female
3. Weight (kg)
4. Height (cm)
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)

Select BMD

Clear Calculate

Weight Conversion

Diagnosis

Major Osteoporotic Fracture: ≥20%

Hip Fracture: ≥3%

Diagnosis

1. FRAX
2. Fragility Fractures
3. DXA

Siris, E. S., et al (2014). The clinical diagnosis of osteoporosis: a position statement from the National Bone Health Alliance Working Group. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*, *25*(5), 1439–1443.

“The definition of an osteoporotic fracture is not straightforward.”

Kanis JA, Oden A, Johnell O et al. (2001) The burden of osteoporotic fractures: a method for setting intervention thresholds. Osteoporosis International 12: 417–27.

Fragility Fracture*

1. Hip +/- DXA = osteoporosis
   - Consider vertebral

2. Vertebral, proximal humerus, pelvic + osteopenia (DXA) = osteoporosis

3. Distal forearm = individualize

Siris, E. S., et al (2014). The clinical diagnosis of osteoporosis: a position statement from the National Bone Health Alliance Working Group. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*, 25(5), 1439–1443.

Diagnosis

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T-scores

1. Postmenopausal Women
2. Men ≥50

T-scores

Diagnosis	T-score
Normal	≥ -1.0

Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. World Health Organ Tech Rep Ser. 1994;843:1-129. PMID: 7941614.

T-scores

Diagnosis	T-score
Normal	≥ -1.0
Osteopenia (Low Bone Mass)	-1.1 to -2.4

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Diagnosis	T-score
Normal	≥ -1.0
Osteopenia (Low Bone Mass)	-1.1 to -2.4
Osteoporosis	≤ -2.5

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T-scores

Diagnosis	T-score
Normal	≥ -1.0
Osteopenia (Low Bone Mass)	-1.1 to -2.4
Osteoporosis	≤ -2.5
Severe Osteoporosis	≤ -2.5 + Fracture

Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. World Health Organ Tech Rep Ser. 1994;843:1-129. PMID: 7941614.

Wait, what is a T-score?

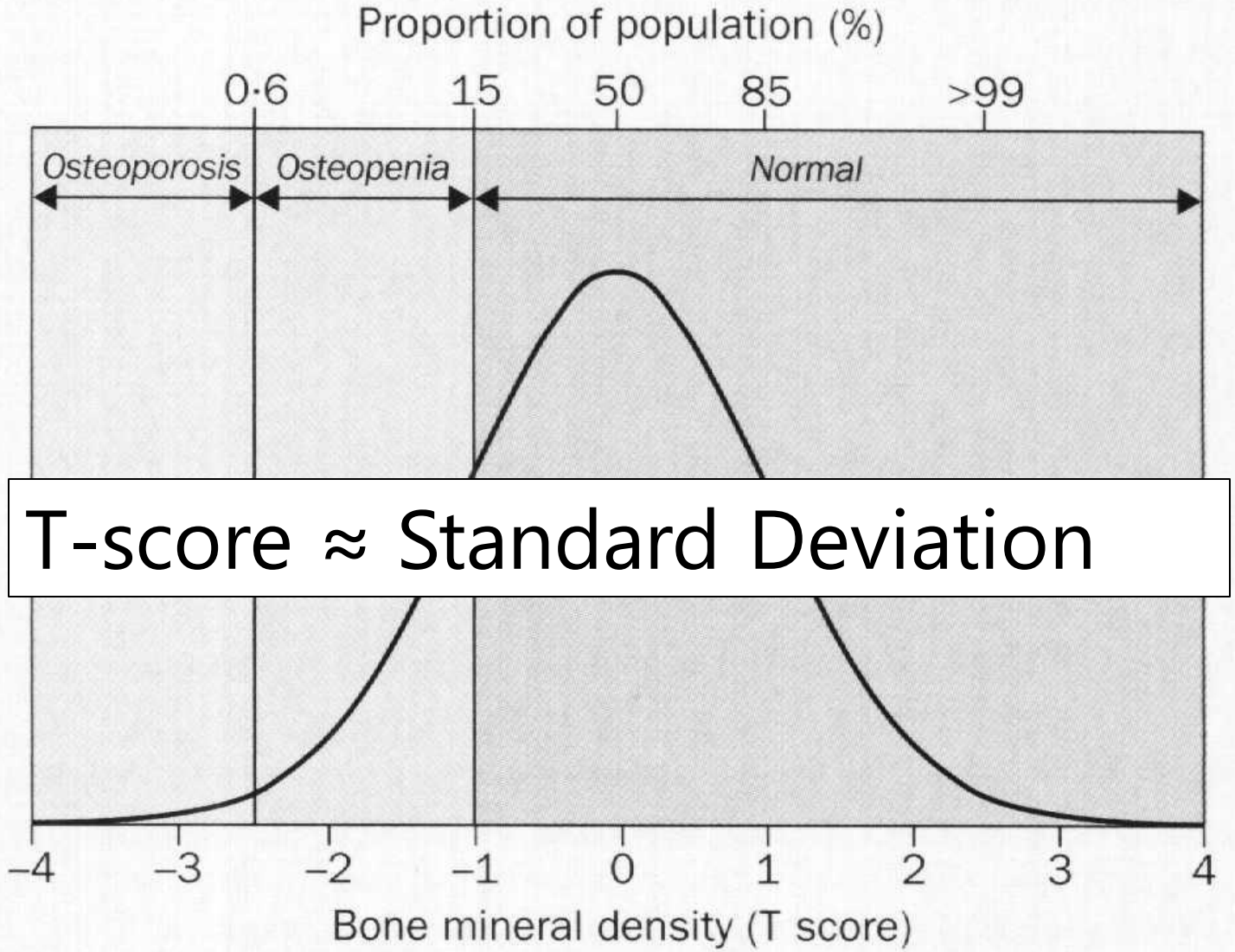


Figure 1: **Distribution of bone mineral density in healthy women aged 30–40 years**

Kanis JA. Diagnosis of osteoporosis and assessment of fracture risk. Lancet. 2002 Jun 1;359(9321):1929-36. doi: 10.1016/S0140-6736(02)08761-5. PMID: 12057569.

T-score Calculation

$$\text{T-score} = \frac{\text{BMD patient} - \text{BMD young-normal mean ref}}{\text{SD young-normal mean ref}}$$

Normative Databases

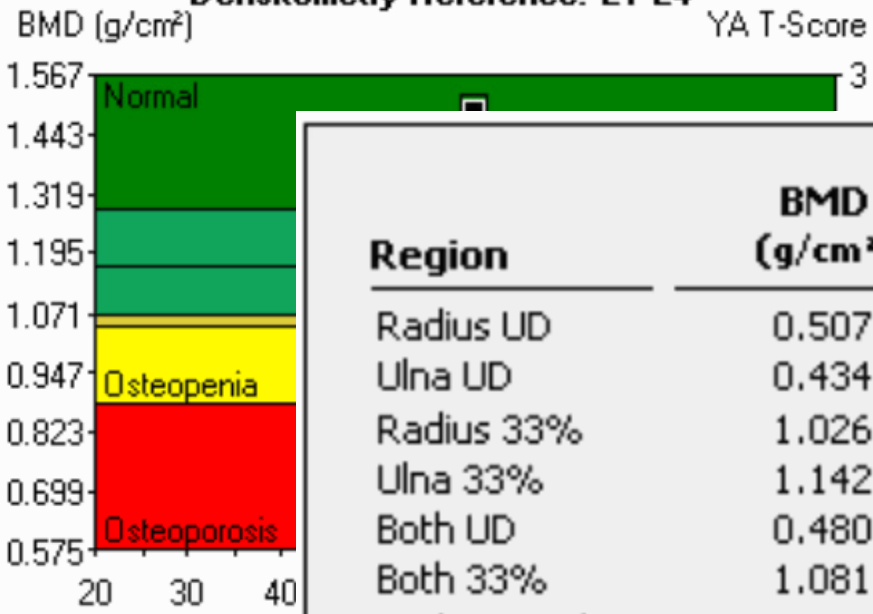
- NHANES III for femoral neck, total hip
- Manufacturer's database for lumbar spine

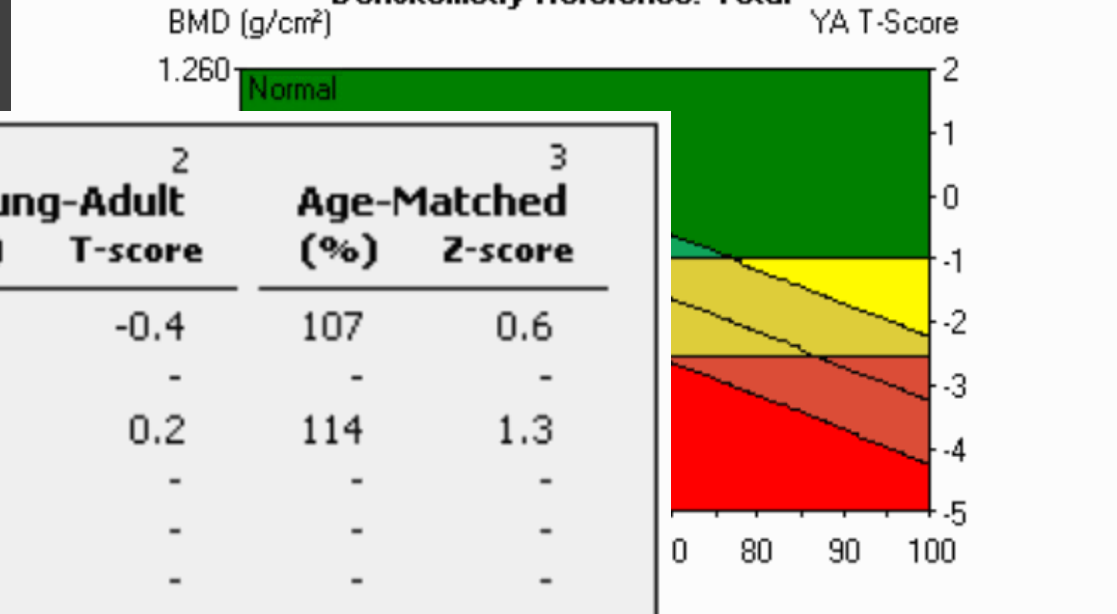
Shuhart CR, Yeap SS, Anderson PA, Jankowski LG, Lewiecki EM, Morse LR, Rosen HN, Weber DR, Zemel BS, Shepherd JA. Executive Summary of the 2019 ISCD Position Development Conference on Monitoring Treatment, DXA Cross-calibration and Least Significant Change, Spinal Cord Injury, Peri-prosthetic and Orthopedic Bone Health, Transgender Medicine, and Pediatrics. J Clin Densitom. 2019 Oct-Dec;22(4):453-471. doi: 10.1016/j.jocd.2019.07.001. Epub 2019 Jul 5. PMID: 31400968.

1 - Statistically 68% of repeat scans fall within 1SD (± 0.010 g/cm² for AP Spine L1-L4)
2 - USA (Combined NHANES (ages 20-30) / Lunar (ages 20-40)) AP Spine Reference Population (v112)
3 - Matched f
11 - World Hea
sian Women:
Normal =
-2.5 SD;
Osteoporo
young
healthy Caucasian Women reference database is used to determine T-scores.)

Different machines can give different T-scores!

But which locations?





Region	1 BMD (g/cm²)	2 Young-Adult (%)	2 Young-Adult T-score	3 Age-Matched (%)	3 Age-Matched Z-score
Radius UD	0.507	96	-0.4	107	0.6
Ulna UD	0.434	-	-	-	-
Radius 33%	1.026	102	0.2	114	1.3
Ulna 33%	1.142	-	-	-	-
Both UD	0.480	-	-	-	-
Both 33%	1.081	-	-	-	-
Radius Total	0.784	103	0.3	113	1.3
Ulna Total	0.794	-	-	-	-
Both Total	0.788	-	-	-	-

Region	BMD (g/cm²)	(%)	T-Score	(%)	Z-Score
L1	1.303	114	1.3	136	2.8
L2	1.424	118	1.8	139	3.3
L3	1.662	136	3.6	160	5.1
L4	1.554	126	2.6	148	4.1
L1-L4	1.495	125	2.4	147	3.9

Region	BMD (g/cm²)	Young-Adult (%)	Young-Adult T-Score	Age-Matched (%)	Age-Matched Z-Score
Neck	0.729	70	-2.2	87	-0.8
Upper Neck	0.610	74	-1.8	93	-0.4
Lower Neck	0.846	-	-	-	-
Wards	0.566	62	-2.6	85	-0.8
Troch	0.651	77	-1.7	91	-0.6
Shaft	0.893	-	-	-	-
Total	0.786	78	-1.8	91	-0.6

Possible Sites

- Individual Vertebra
- 2-4 Vertebra
- Femoral Neck
- Trochanter
- Ward's Area
- Total Hip
- Upper Neck
- Lower Neck
- Dual Femur*
- UD Radius
- UD Ulna
- 33% Radius
- 33% Ulna
- Both UD
- Both 33%
- Radius Total
- Ulna Total
- Both Total

Recommended Sites

Diagnosis from lowest T-score:

- L1-L4 Spine*
- Femoral Neck
- Total Hip
- 33% Nondominant Radius*


You didn’t review the image?
TikTok
@drglaucomflecken

Eur Radiol (2015) 25:1504–1511
DOI 10.1007/s00330-014-3509-y

MUSCULOSKELETAL

Prevalence and type of errors in dual-energy x-ray absorptiometry

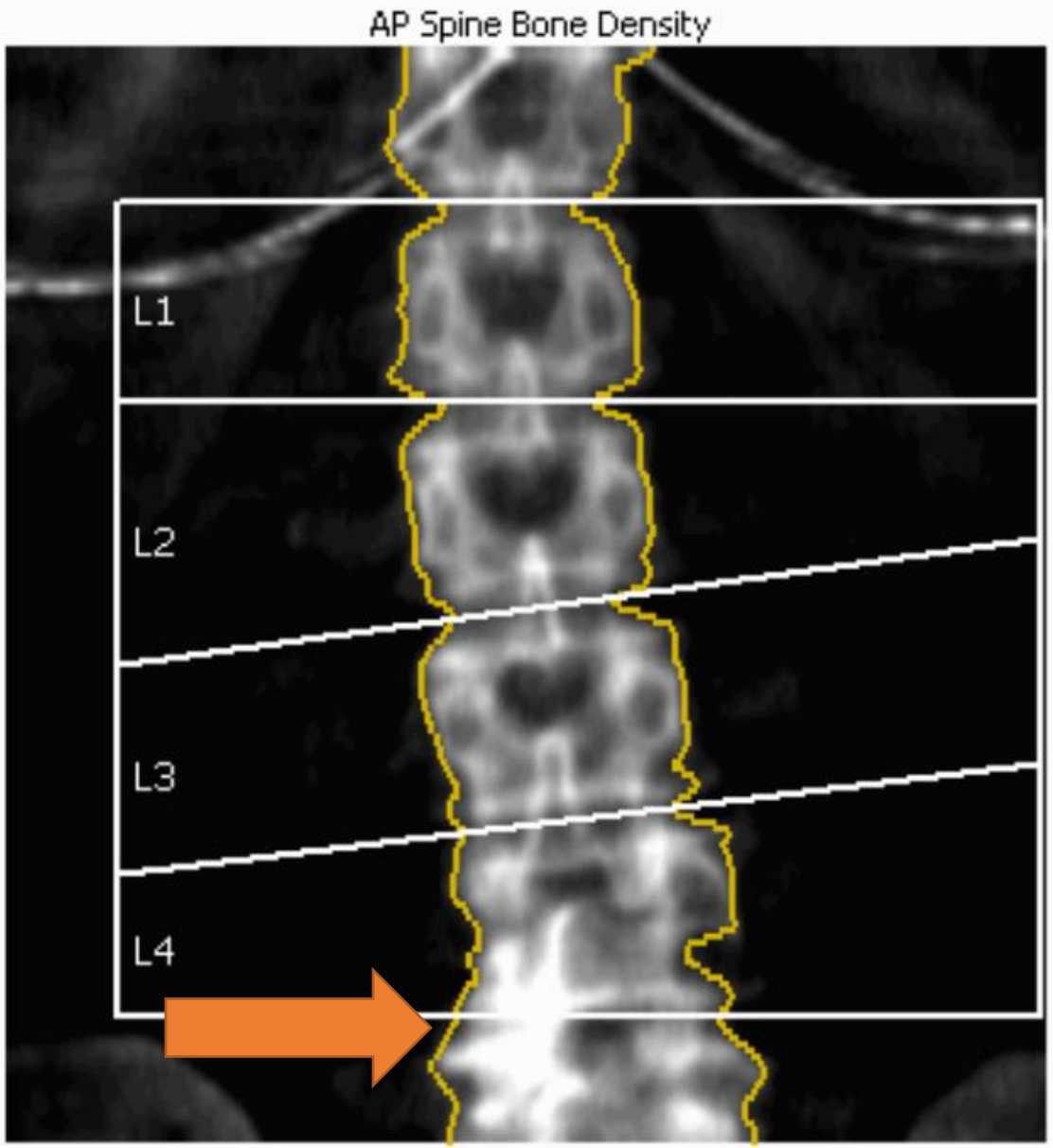
Carmelo Messina · Michele Bandirali · Luca Maria Sconfienza · Nathascja Katia D'Alonzo · Giovanni Di Leo · Giacomo Davide Edoardo Papini · Fabio Massimo Ulivieri · Francesco Sardanelli

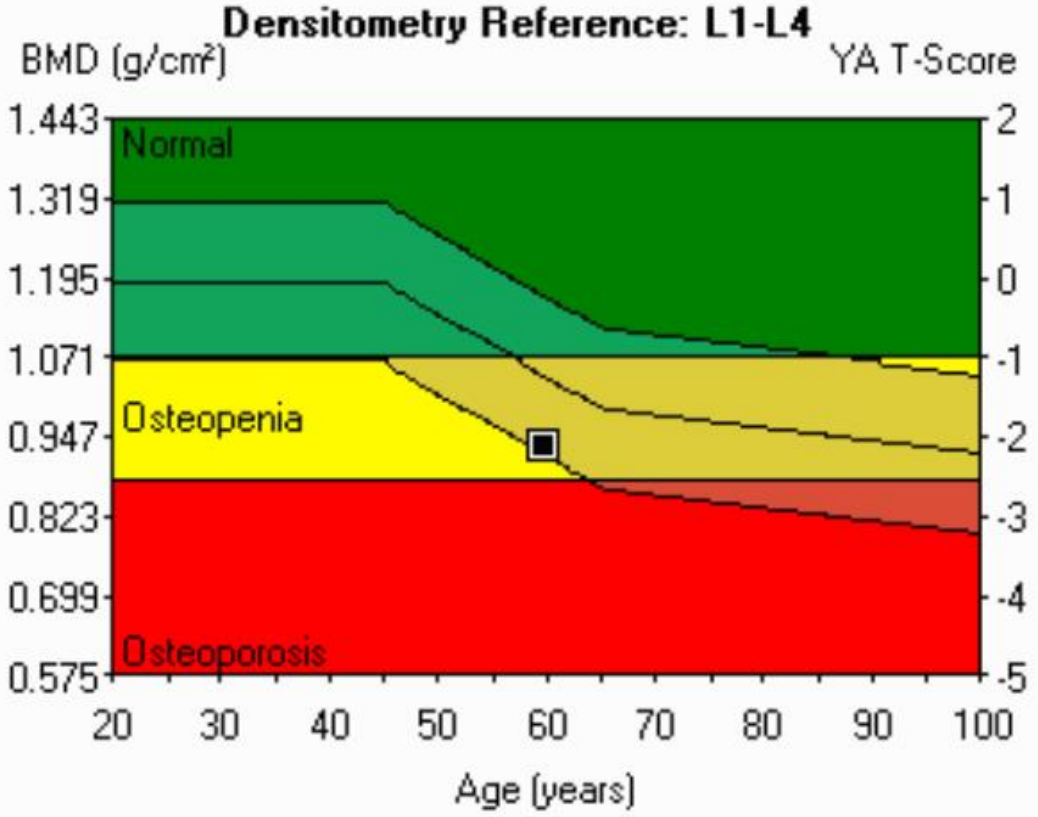
- Retrospective review of f/u DXA images
  - DXA specialist radiologist
- 485 DXA (prior outside)
- Types and quantity of errors

Carmelo et al

- >90% had ≥1 error
- Errors could lead to management implications

Messina C, Bandirali M, Sconfienza LM, D'Alonzo NK, Di Leo G, Papini GD, Ulivieri FM, Sardanelli F. Prevalence and type of errors in dual-energy x-ray absorptiometry. Eur Radiol. 2015 May;25(5):1504-11. doi: 10.1007/s00330-014-3509-y. Epub 2014 Nov 27.





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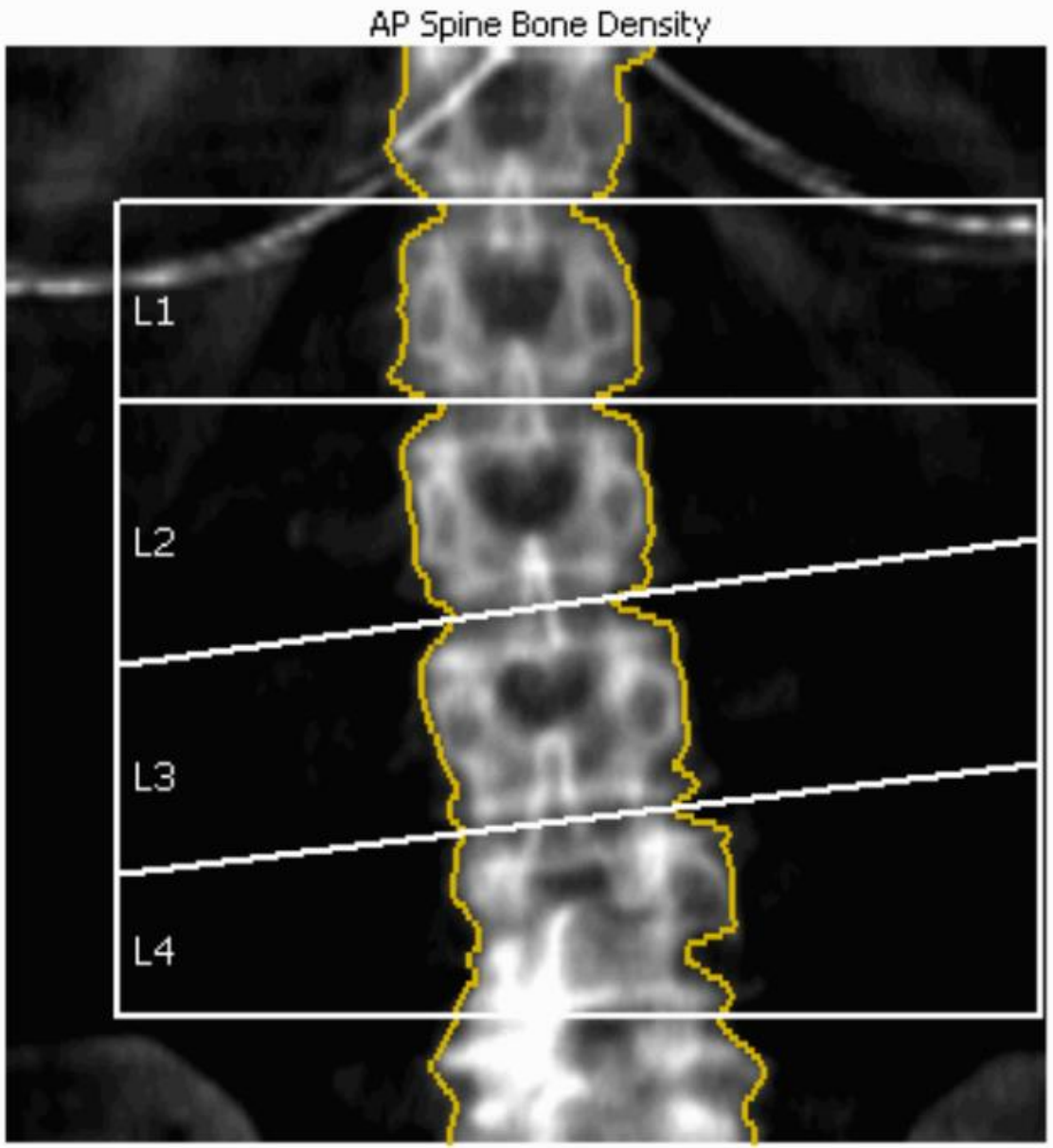

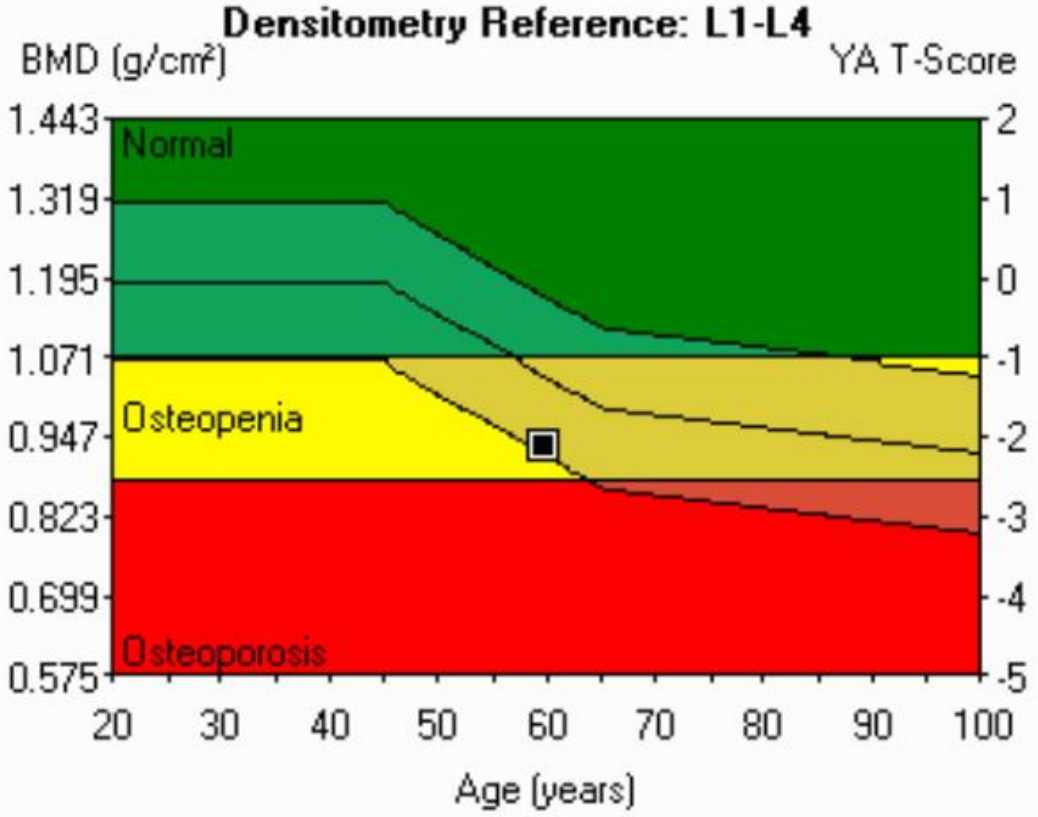

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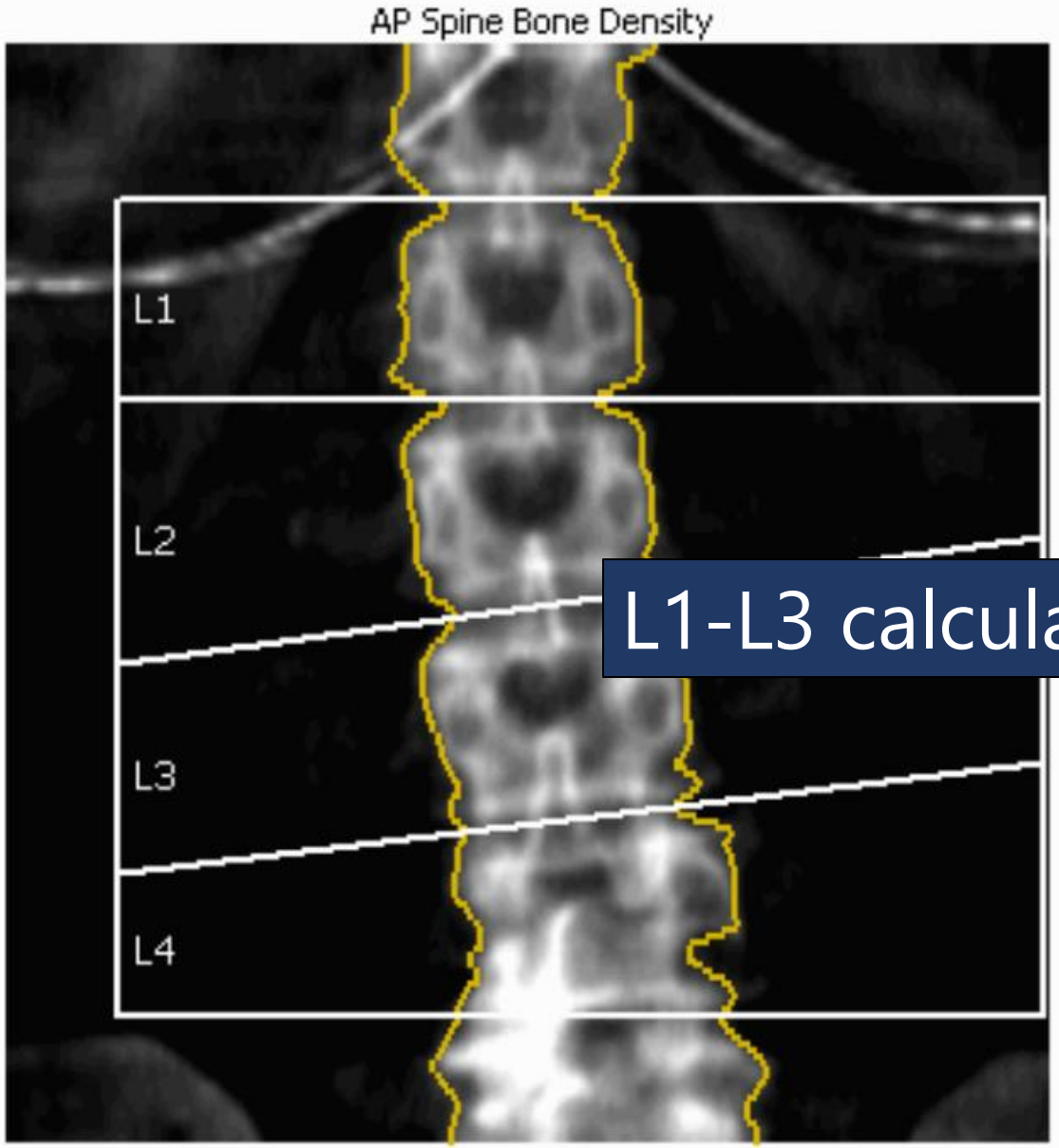

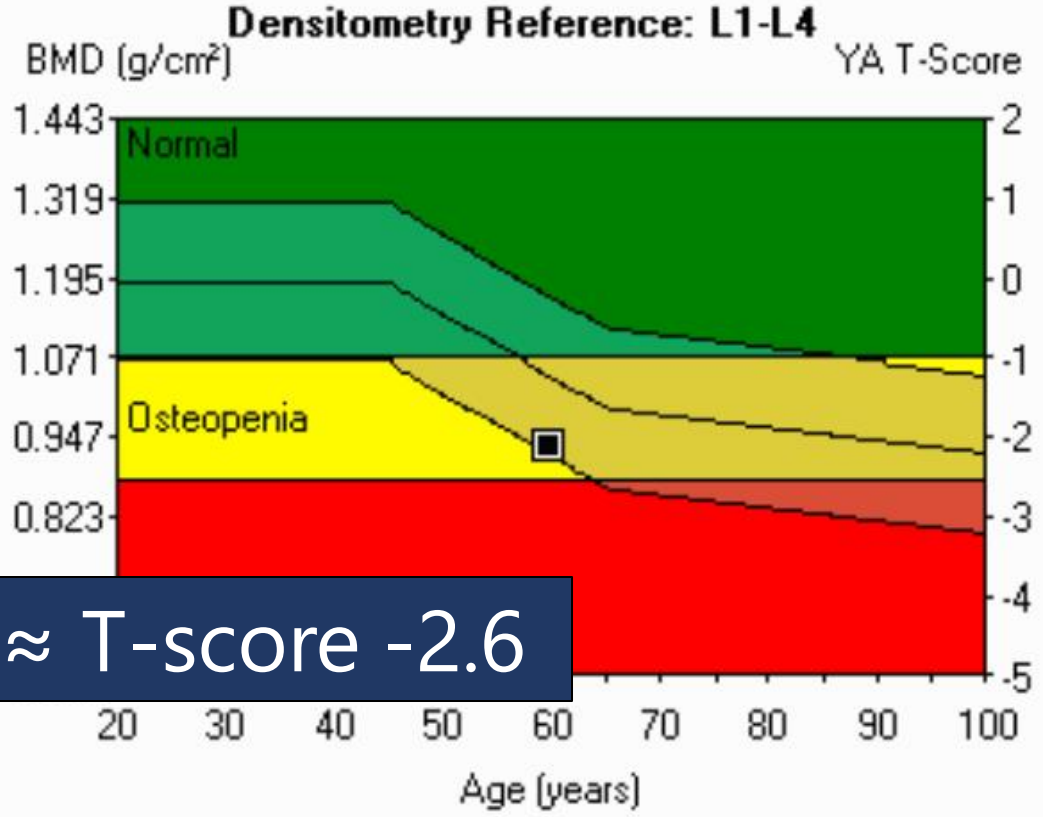

L1-L3 calculation ≈ T-score -2.6

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~~L4~~	~~1.097~~	~~91~~	~~-0.9~~	~~103~~	~~0.3~~
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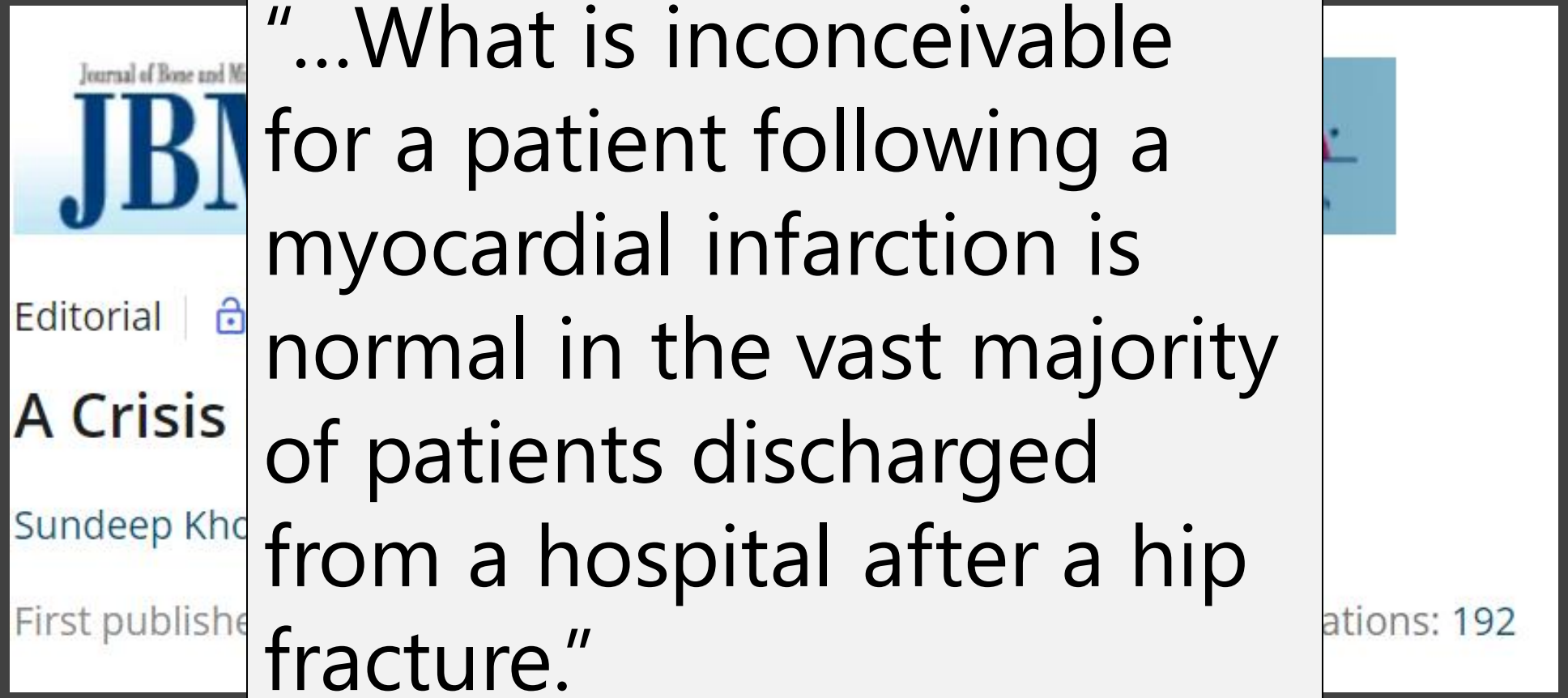
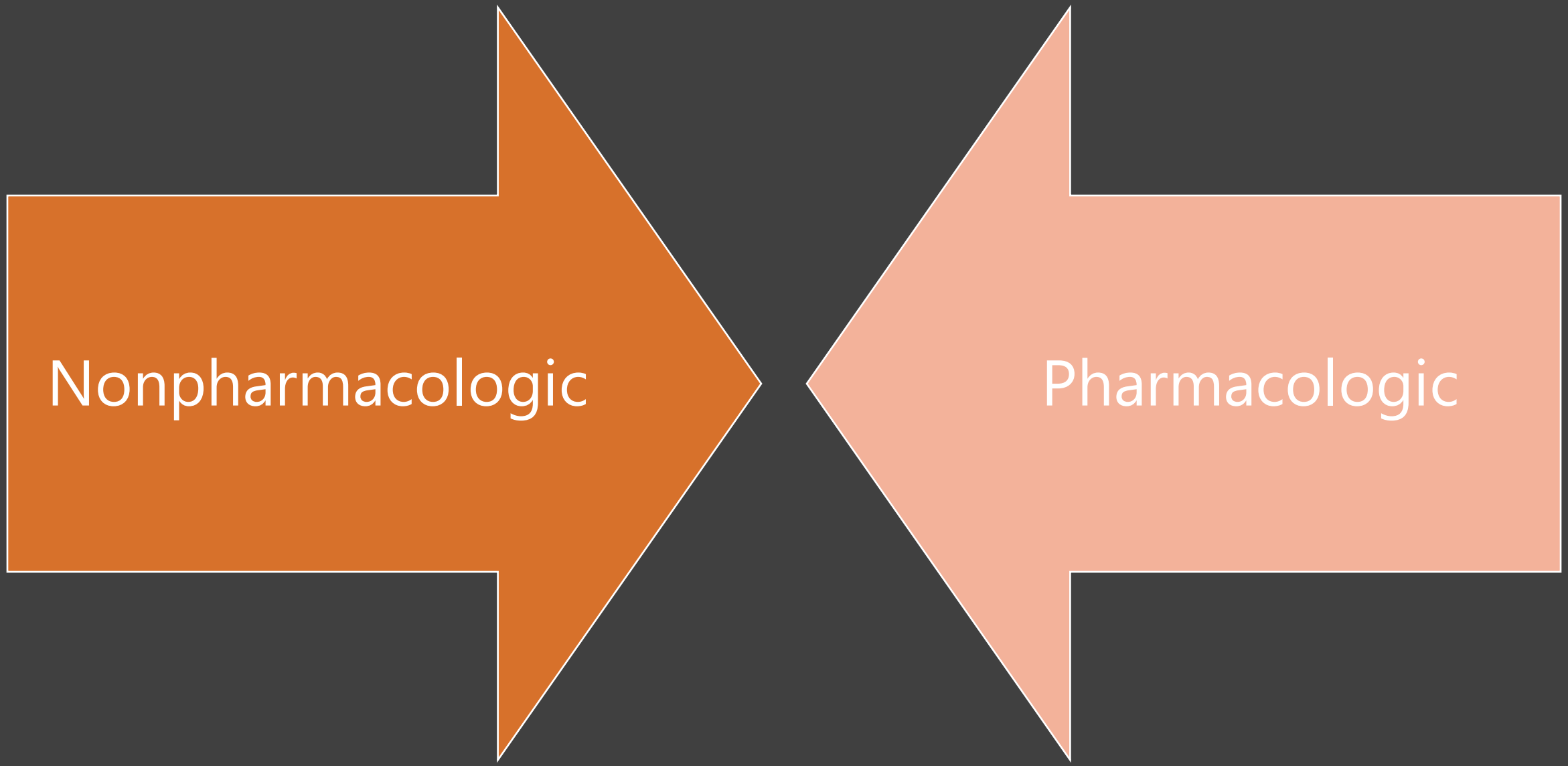
Treatment

- Multinational, Prospective, observational cohort
  - 60,393 postmenopausal women aged 55+
- 1,075 fragility fractures



"…What is inconceivable for a patient following a myocardial infarction is normal in the vast majority of patients discharged from a hospital after a hip fracture."


Nonpharmacologic
Pharmacologic

Nonpharmacologic Therapy

Approach

1. Avoid tobacco and excessive alcohol
2. Weight-bearing exercise
3. Fall prevention
4. Calcium
5. Vitamin D

LeBoff, M., Greenspan, S., Insogna, K. *et al.* The clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int* (2022). https://doi.org/10.1007/s00198-021-05900-y

Approach

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Calcium

Life Stage Group	Calcium mg/day (NAM/BHOF)	Calcium Safe Upper Limit
Women 51-70	1200	2500
Men 51-70	1000	2000
Both 71+	1200	2000

Adapted From: LeBoff, M., Greenspan, S., Insogna, K. *et al.* The clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int* (2022). https://doi.org/10.1007/s00198-021-05900-y

Dietary Calcium

Food	Calcium Content (mg/serving)
Yogurt (8 oz, plain)	415
Sardines (3 oz)	325
Milk (1 cup, nonfat)	299
Soymilk (1 cup)	299

Adapted From: U.S. Department of Agriculture. FoodData Central from NIH Calcium FactSheet. (https://ods.od.nih.gov/factsheets/Calcium-HealthProfessional/#en12)

Dietary Calcium

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Sardines (3 oz)	325
Milk (1 cup, nonfat)	299
Soymilk (1 cup)	299
Breakfast cereals	130
Kale	94
Pinto Beans (1/2 cup)	54
Broccoli (1/2 cup)	21

Adapted From: U.S. Department of Agriculture. FoodData Central from NIH Calcium FactSheet. (https://ods.od.nih.gov/factsheets/Calcium-HealthProfessional/#en12)

HARVARD HEALTH BLOG

Could too much calcium cause heart disease?

February 28, 2020

By Harvard Health Publishing Staff, Harvard Health

Get the calcium you need through dietary sources.

Annals of Internal Medicine

CLINICAL GUIDELINE

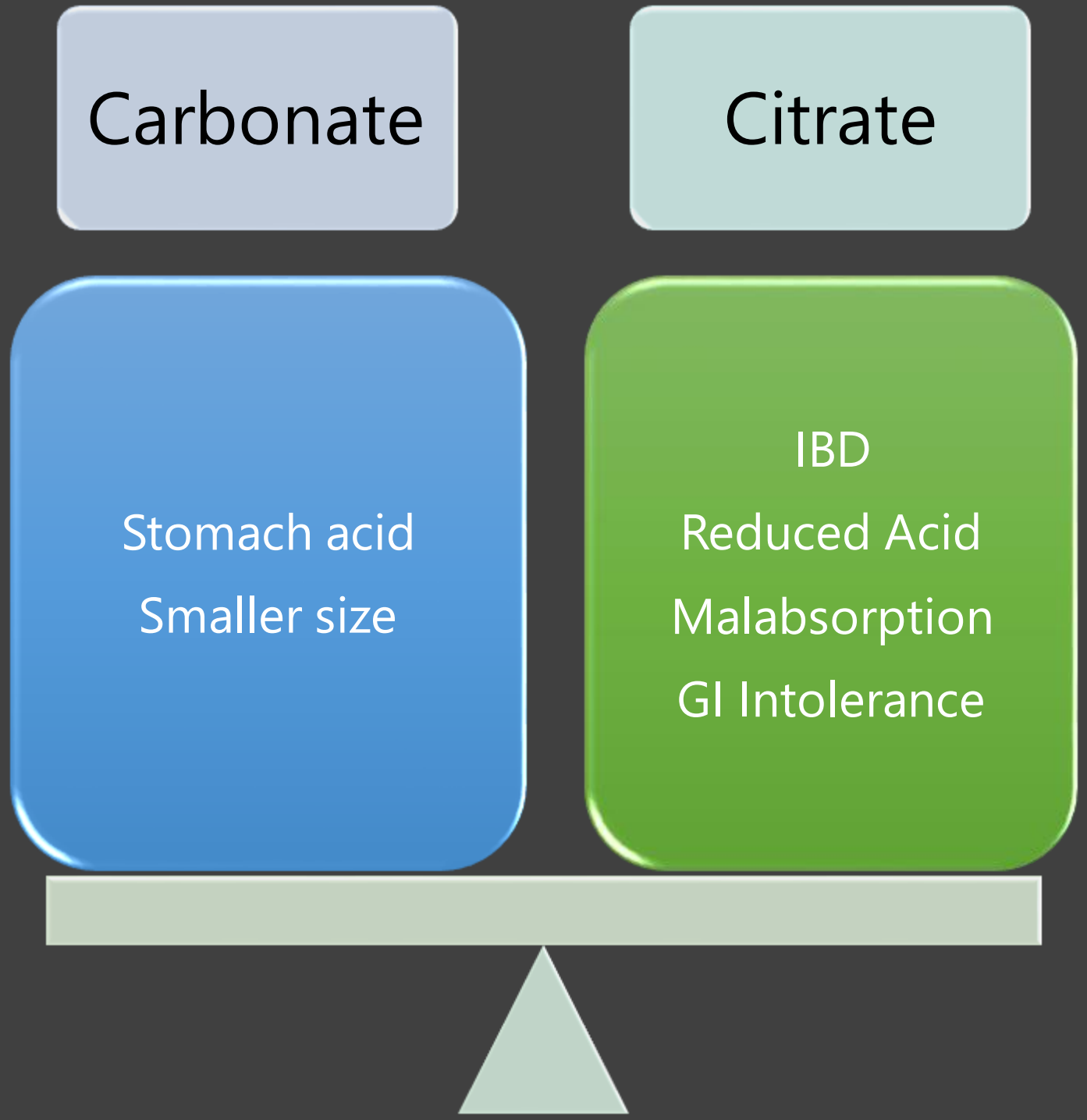
Lack of Ev… Supplem… Adults: A… Foundati…

Stephen L. Kope…
Peter P. Toth, MD…

"…moderate-quality evidence (B level) that calcium with or without vitamin D intake from food or supplements has no relationship (beneficial or harmful) to the risk for cardiovascular and cerebrovascular disease, mortality, or all-cause mortality in generally healthy adults…"

Calcium Recommendations

1. Follow recommended RDA for goal amount
2. Food sources first, supplements to make up difference
3. Choose formulation


Carbonate
Citrate
Stomach acid
Smaller size
IBD
Reduced Acid
Malabsorption
GI Intolerance

Overview

1. Weight-bearing exercise
2. Avoid tobacco and excessive alcohol
3. Fall prevention
4. Calcium
5. Vitamin D

Vitamin D

Vitamin D

Life Stage Group	Vitamin D (units/day) NAM/BHOF
Women 51-70	600/800-1000
Men 51-70	600/800-1000
Both 71+	800/800-1000

Adapted From: LeBoff, M., Greenspan, S., Insogna, K. *et al.* The clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int* (2022). https://doi.org/10.1007/s00198-021-05900-y

Levels

Target: 30-50 ng/mL

LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ, Siris ES. The clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int. 2022 Apr 28. doi: 10.1007/s00198-021-05900-y. Epub ahead of print. PMID: 35478046.

Pharmacologic Therapy

Postmenopausal Women

Abaloparatide (Tymlos)	Alendronate (Fosamax)
Calcitonin	Denosumab (Prolia)
Zolendronate (Reclast)	Ibandronate (Boniva)
Raloxifene (Evista)	Risedronate (Actonel)
Romosozumab (Evenity)	Teriparatide (Forteo)

LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ, Siris ES. The clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int. 2022 Apr 28. doi: 10.1007/s00198-021-05900-y. Epub ahead of print. PMID: 35478046.

Men

	Alendronate (Fosamax)
	Denosumab (Prolia)
Zolendronate (Reclast)	
	Risedronate (Actonel)
	Teriparatide (Forteo)

LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ, Siris ES. The clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int. 2022 Apr 28. doi: 10.1007/s00198-021-05900-y. Epub ahead of print. PMID: 35478046.

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/ AMERICAN COLLEGE OF ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS— 2020 UPDATE

Pauline M. Camacho, MD, FACE[1]; Steven M. Petak, MD, JD, FACP, FCLM, MACE, CCD[2]; Neil Binkley, MD[3]; Dima L. Diab, MD, FACE, FACP, CCD[4]; Leslie S. Eldeiry, MD[5]; Azeez Farooki, MD[6]; Steven T. Harris, MD, FACP, FASBMR[7]; Daniel L. Hurley, MD, FACE[8]; Jennifer Kelly, DO, FACE[9]; E. Michael Lewiecki, MD, FACE, FACP, CCD[10]; Rachel Pessah-Pollack, MD, FACE[11]; Michael McClung, MD, FACP, FACE[12]; Sunil J. Wimalawansa, MD, PhD, MBA, FCCP, FACP, FRCP, DSc, FACE[13]; Nelson B. Watts, MD, FACP, CCD, FASBMR, MACE[14]

AACE

High Risk/No Prior Fractures
Alendronate, denosumab, risedronate, zolendronate
Alternatives: Ibandronate, raloxifene

Very High Risk/Prior Fractures
Abaloparatide, denosumab, romosozumab, teriparatide, zolendronate
Alternatives: Alendronate, risedronate

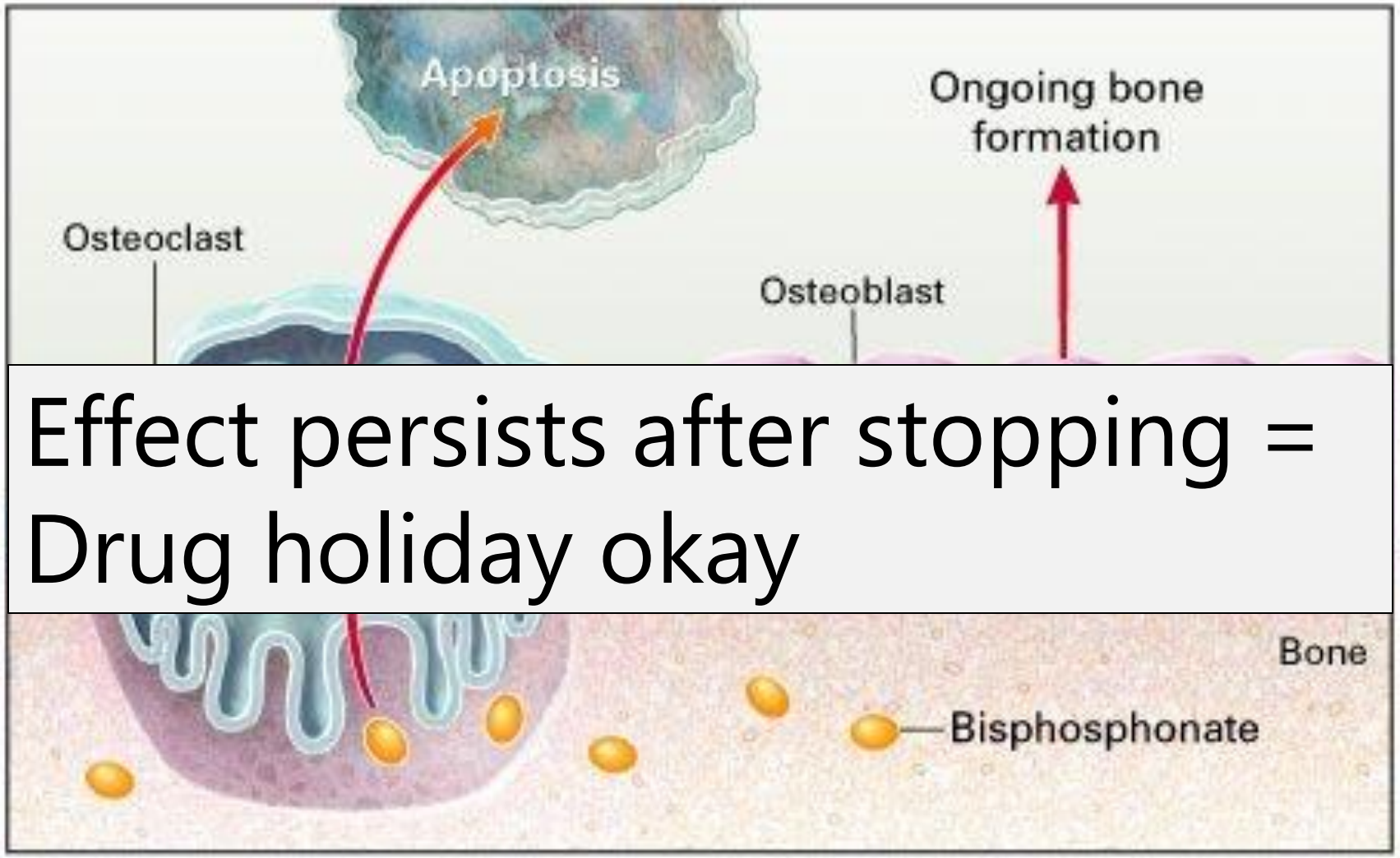
Camacho PM, Petak SM, Binkley N, Diab DL, Eldeiry LS, Farooki A, Harris ST, Hurley DL, Kelly J, Lewiecki EM, Pessah-Pollack R, McClung M, Wimalawansa SJ, Watts NB. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/AMERICAN COLLEGE OF ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS-2020 UPDATE. Endocr Pract. 2020 May;26(Suppl 1):1-46. doi: 10.4158/GL-2020-0524SUPPL. PMID: 32427503.

Overview

- Bisphosphonates
- Denosumab
- Romosozumab
- Parathyroid hormone analogs

Bisphosphonates

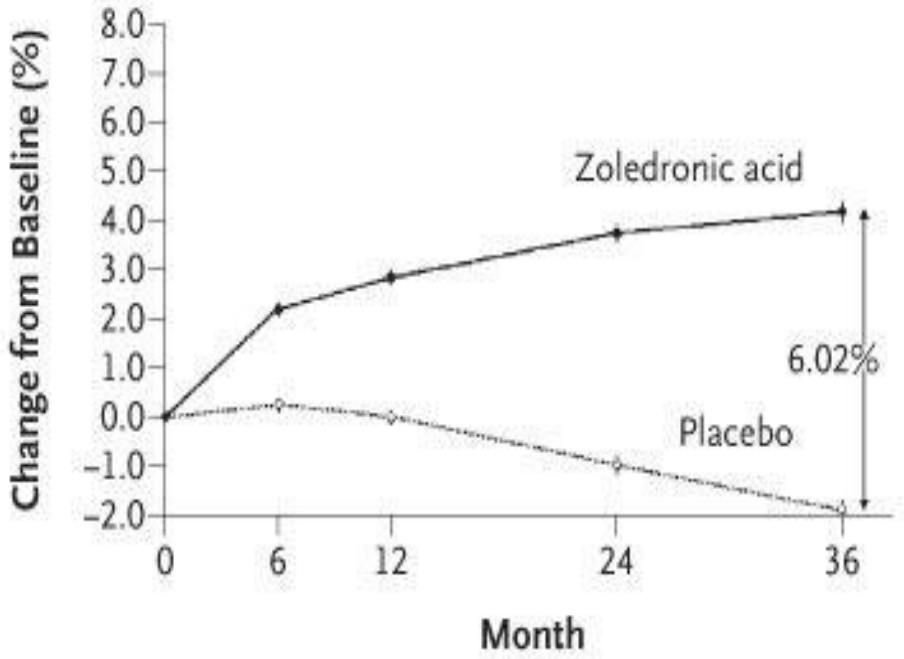
- Antiresorptive
- Oral
  - Alendronate
  - Ibandronate
  - Risedronate
- IV
  - Zolendronate
  - Ibandronate



Effect persists after stopping = Drug holiday okay

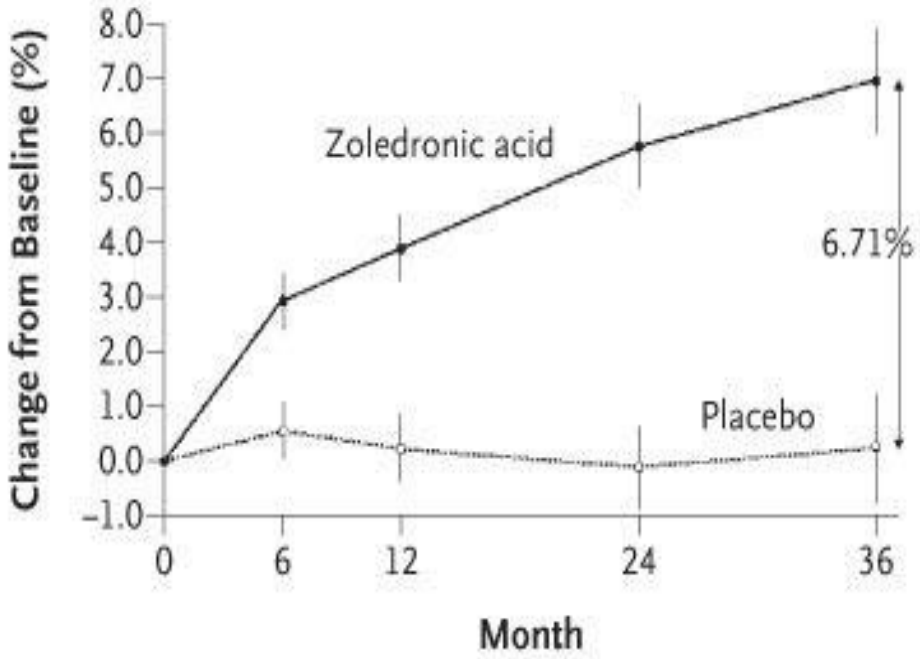
Solomon CG. Bisphosphonates and osteoporosis. N Engl J Med. 2002 Feb 28;346(9):642. doi: 10.1056/NEJM200202283460902. PMID: 11870240.

A Total Hip



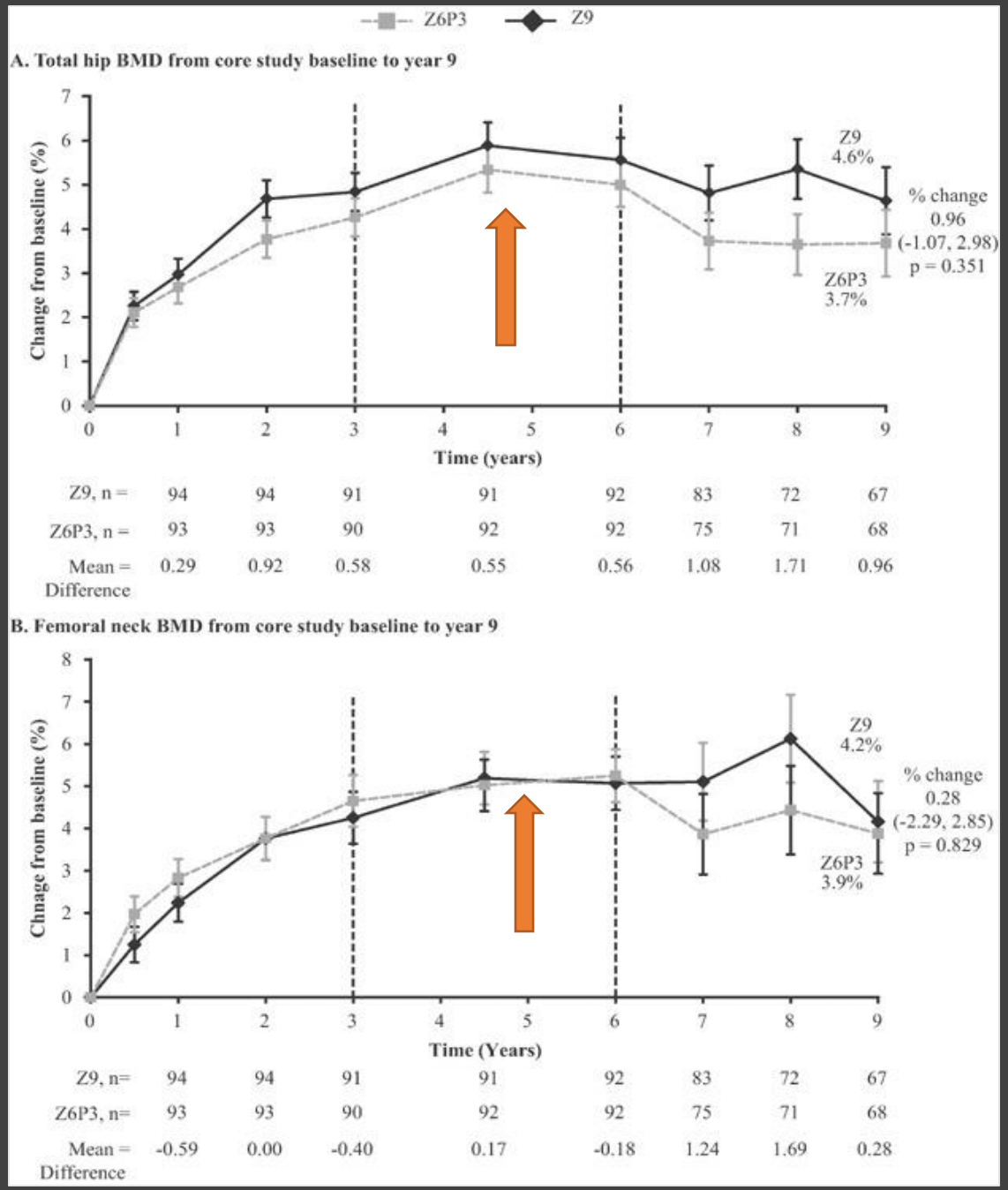
No. at Risk					
Zoledronic acid	3844	3515	3516	3228	3061
Placebo	3839	3543	3542	3248	3077

B Lumbar Spine



No. at Risk					
Zoledronic acid	272	268	262	236	228
Placebo	269	265	258	226	212

Black DM et al. N Engl J Med 2007;356:1809-1822.



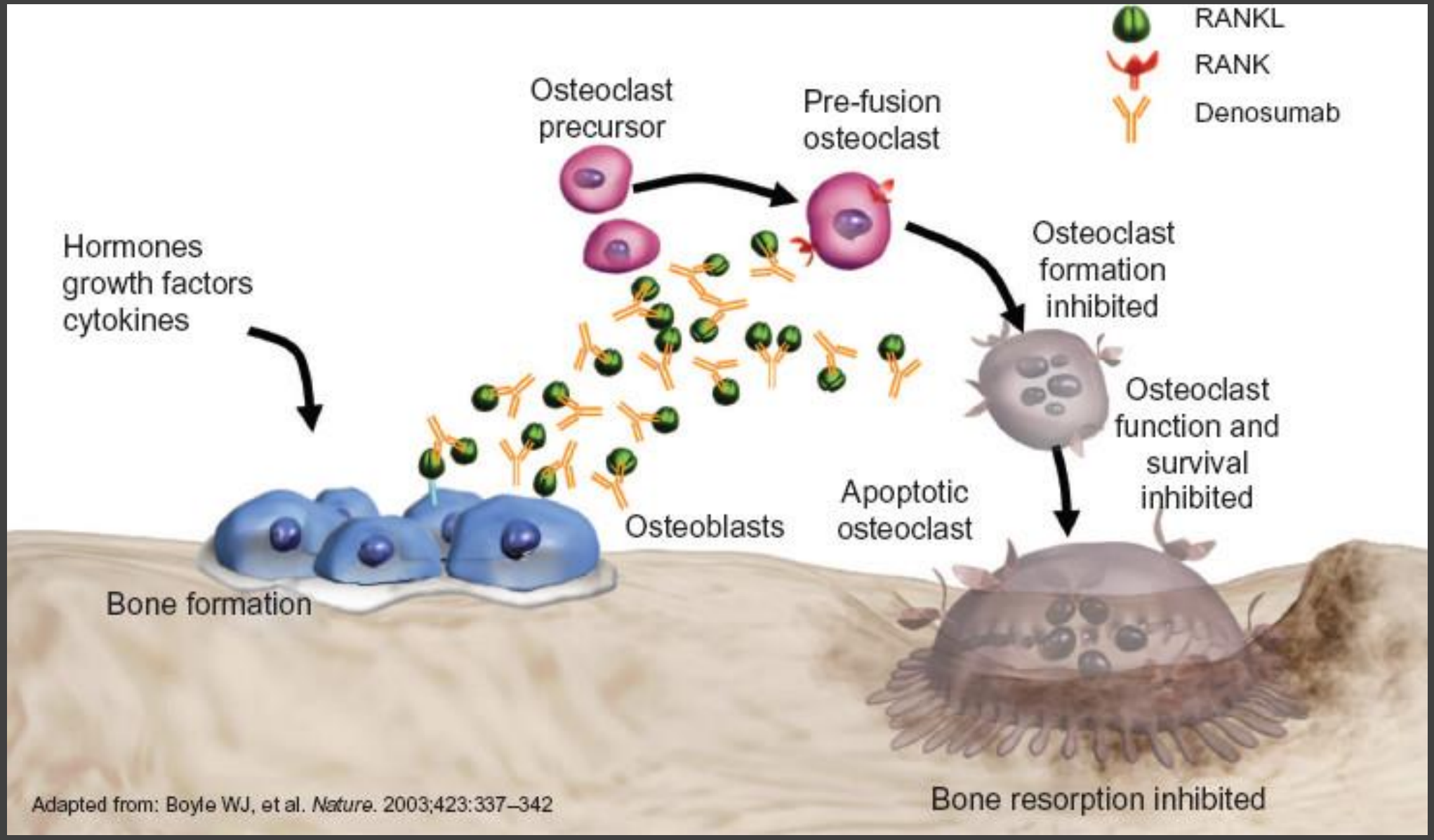
J of Bone & Mineral Res, Volume: 30, Issue: 5, Pages: 934-944, First published: 26 December 2014, DOI: (10.1002/jbmr.2442)

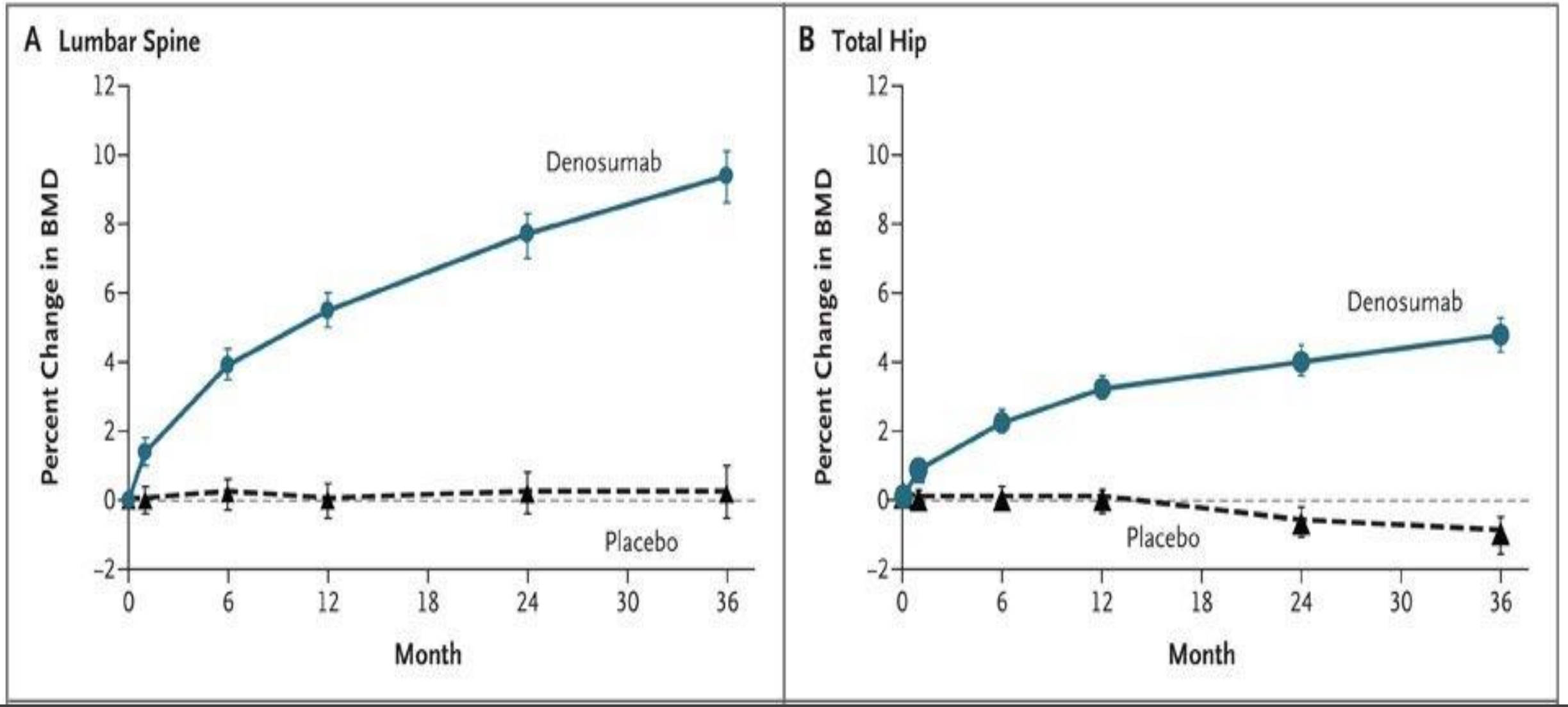
Safety

- Orals: GI Intolerance
- Nephrotoxicity, Hypocalcemia
  - Check vitamin D, calcium, Cr prior to treating
- MSK Pain; Flu-like Symptoms
- Inflammatory Eye Reactions
- Atypical Femur Fractures
- Osteonecrosis of the Jaw

Denosumab

- Antiresorptive (RANKL inhibitor)
- Subcutaneous every 6m


RANKL
RANK
Denosumab
Osteoclast precursor
Pre-fusion osteoclast
Hormones growth factors cytokines
Osteoclast formation inhibited
Osteoclast function and survival inhibited
Apoptotic osteoclast
Osteoblasts
Bone formation
Bone resorption inhibited
Adapted from: Boyle WJ, et al. *Nature*. 2003;423:337–342



Cummings SR et al. N Engl J Med 2009;361:756-765.

Safety

- Possible increased infection risk
- Hypocalcemia; okay in CKD
- Osteonecrosis of the Jaw
- Atypical Femur Fractures
- Rebound Vertebral Fractures

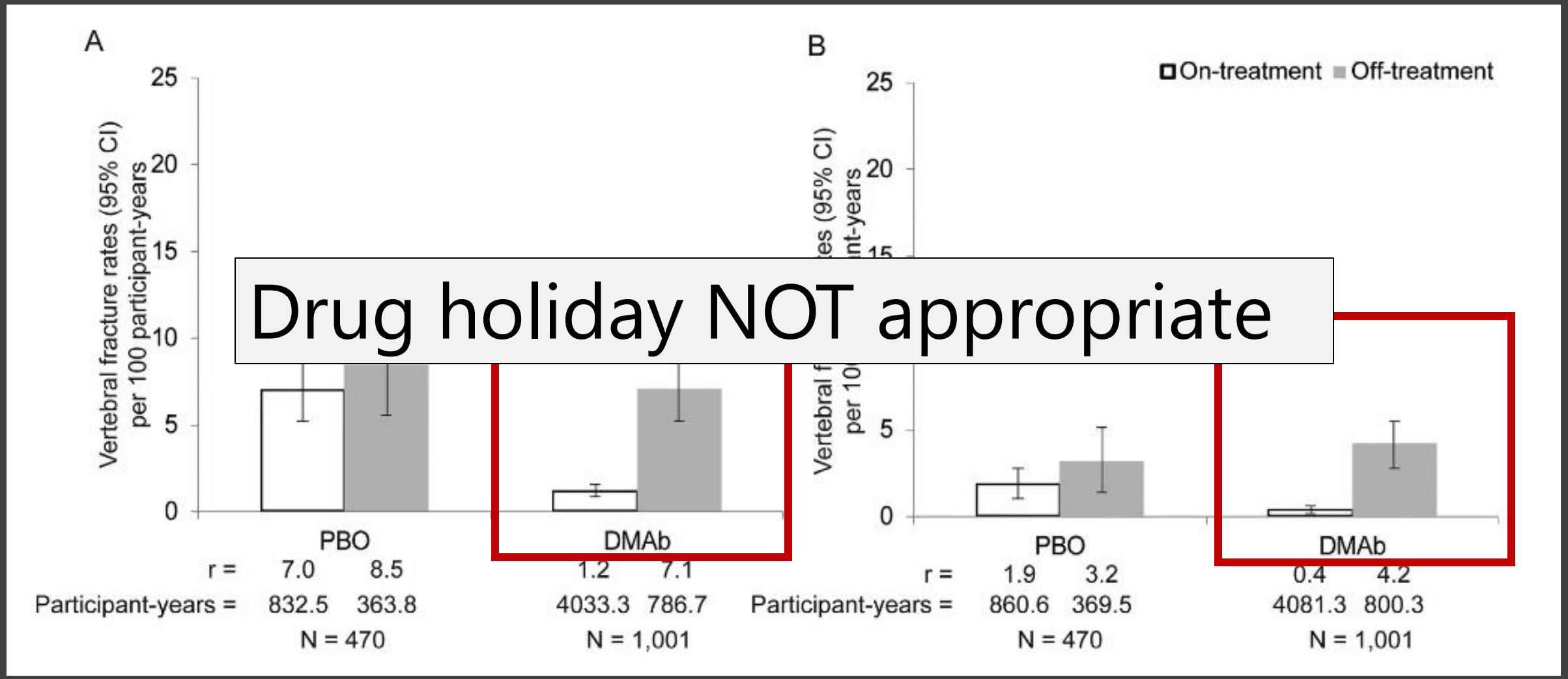
ORIGINAL ARTICLE

JBMR®

Vertebral Fractures After Discontinuation of Denosumab: A Post Hoc Analysis of the Randomized Placebo-Controlled FREEDOM Trial and Its Extension

Steven R Cummings,[1] Serge Ferrari,[2] Richard Eastell,[3] Nigel Gilchrist,[4] Jens-Erik Beck Jensen,[5] Michael McClung,[6] Christian Roux,[7] Ove Törring,[8] Ivo Valter,[9] Andrea T Wang,[10] and Jacques P Brown[11]

- Freedom: 3 year RCT DMAb vs. PBO
- Freedom Extension: 7-year extension
- Discontinuation with >7 months follow up
- Looking for vertebral fractures

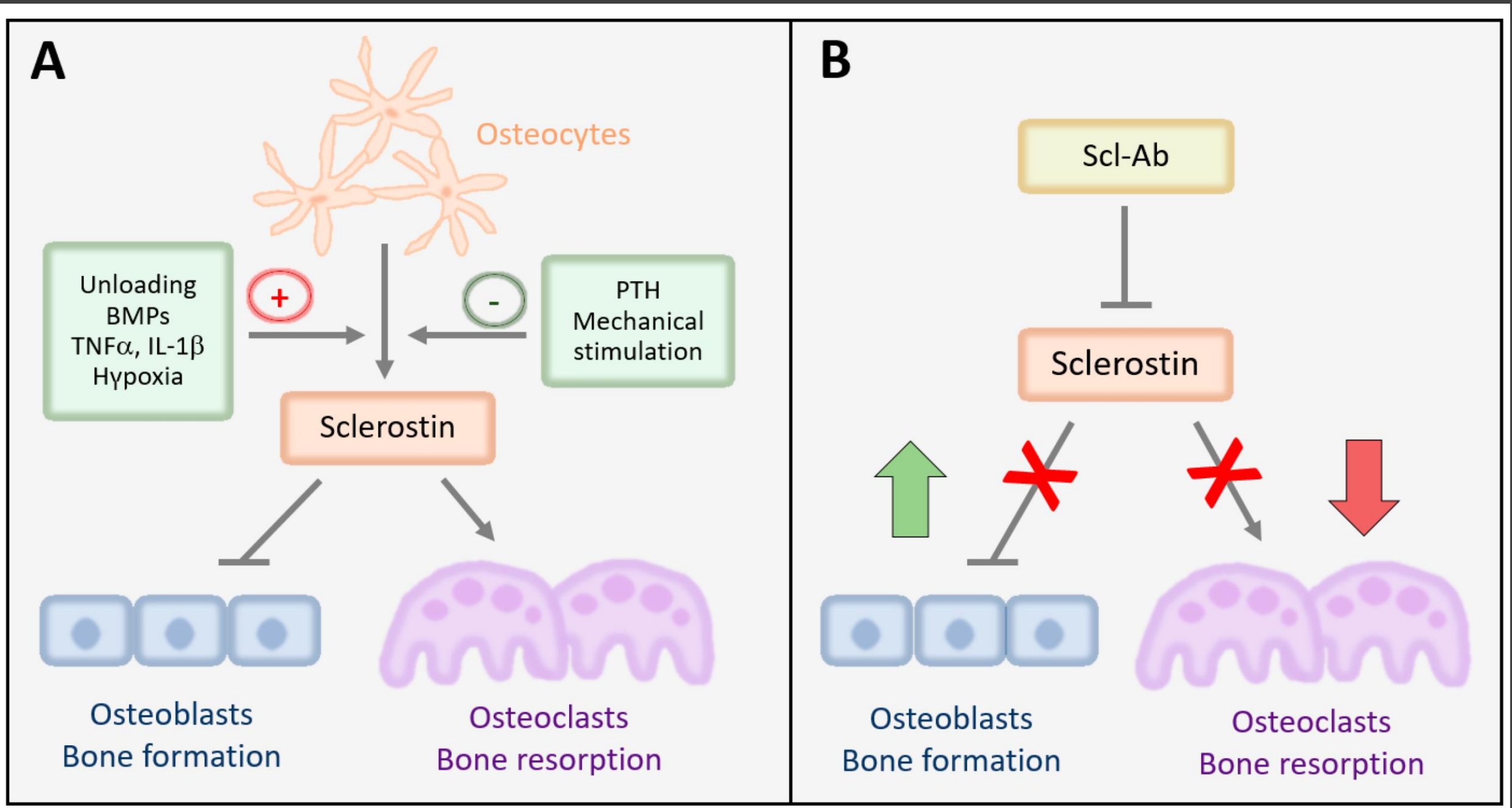


Drug holiday NOT appropriate

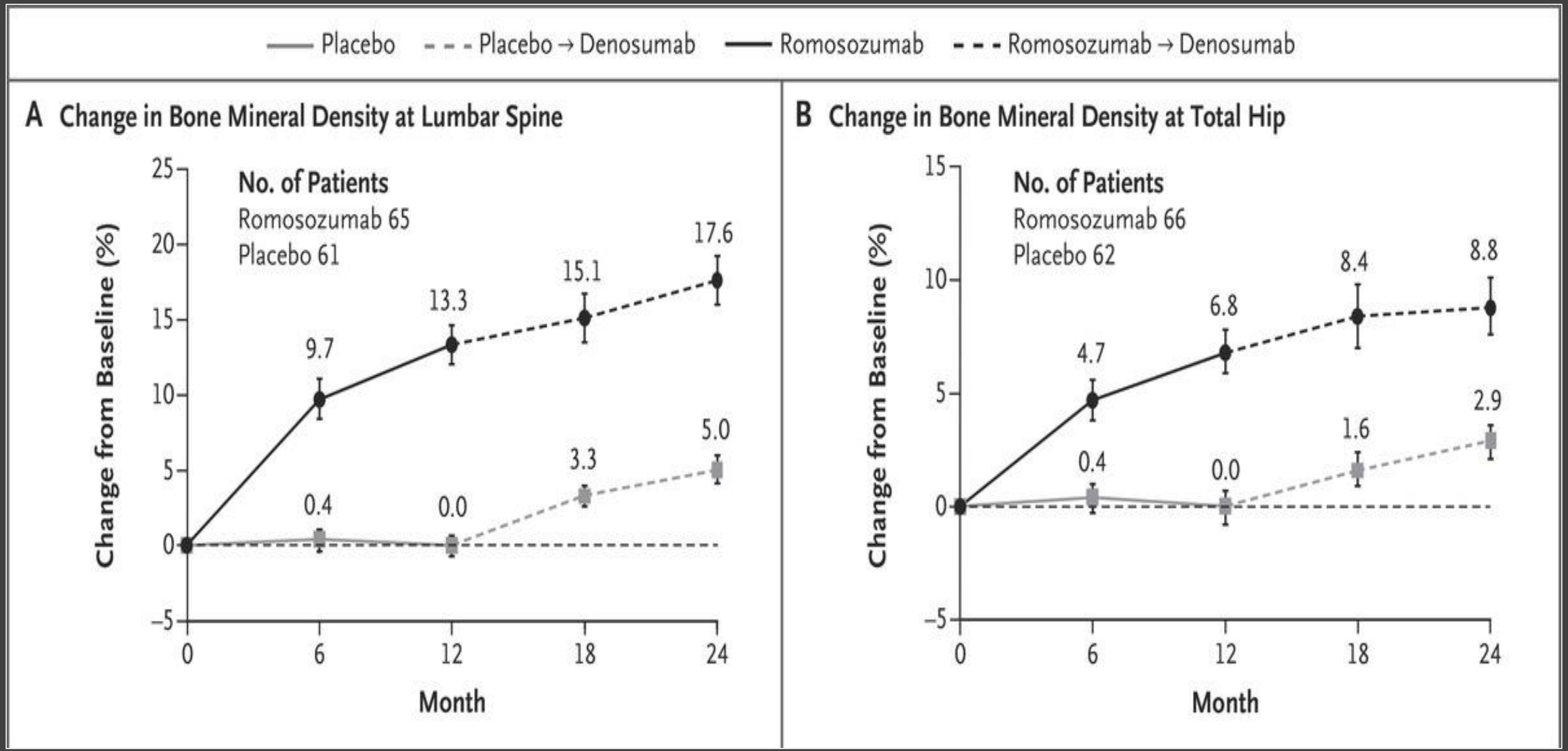
Cummings SR, Ferrari S, Eastell R, Gilchrist N, et al. Vertebral Fractures After Discontinuation of Denosumab: A Post Hoc Analysis of the Randomized Placebo-Controlled FREEDOM Trial and Its Extension. J Bone Miner Res. 2018 Feb;33(2):190-198.

Romosozumab

- Antiresorptive AND anabolic; Sclerostin Inh
- SubQ monthly x 1 year



Rauner M, Taipaleenmäki H, Tsourdi E, Winter EM. Osteoporosis Treatment with Anti-Sclerostin Antibodies—Mechanisms of Action and Clinical Application. *Journal of Clinical Medicine*. 2021; 10(4):787



Cosman F et al. N Engl J Med 2016;375:1532-1543.
Saag KG et al. N Engl J Med 2017;377:1417-1427.

Safety

- Hypocalcemia
- Skin reactions
- Osteonecrosis of the Jaw
- Atypical Femur Fractures (?)
- CV events

Perspective | Pu

Explanat

events in

S.R. Cummings

Osteoporosis Int

3752 Accesses

scular

"Together, these other data indicate that the difference in rates of CVD between alendronate and romosozumab in the ARCH trial is probably due to chance."

ONJ & AFF

ONJ

saving faces | changing lives®

American Association of Oral and Maxillofacial Surgeons

- Case Definition
  - Current or prior treatment with offending drug
  - Exposed bone or bone that can be probed via fistula that has persisted for > 8 weeks
  - No history of jaw radiation or metastatic disease

Mechanisms

- Pathophysiology not well understood
- Most often related to tooth extraction or dentoalveolar surgery; more often in oncology
- No Data: Implants, endodontal or periodontal procedures
- Other Risks: Dentures, periodontal disease, infections, genetics

Khan AA, Morrison A, Hanley DA, Felsenberg D, et al; International Task Force on Osteonecrosis of the Jaw. Diagnosis and management of osteonecrosis of the jaw: a systematic review and international consensus. J Bone Miner Res. 2015 Jan;30(1):3-23.

Incidence

REVIEW

JBMR®

Di… …e Jaw: A S… …s

Aliya… …yan, Ian R… …andi, Edm… Cyru… K. Sh…

Mohamed El Rabbany, Dominique D Pierroz, Riad Sulimani, Deborah P Saunders, Jacques P Brown, and Juliet Compston, on behalf of the International Task Force on Osteonecrosis of the Jaw

"From the currently available data, the incidence of ONJ in the osteoporosis patient population appears to be very low, ranging from 0.15% to less than 0.001% person-years of exposure and may be only slightly higher than the frequency observed in the general population"

Recommendations

saving faces | changing lives®
American Association of Oral and Maxillofacial Surgeons

1. Complete extractions/surgery prior to starting

2. Oral BP <4y without other risk factors
   i. No alteration or delay in oral surgery
   ii. If implants, informed consent

3. Oral BP <4y + risk factors
   i. Consider holding x 2 months prior

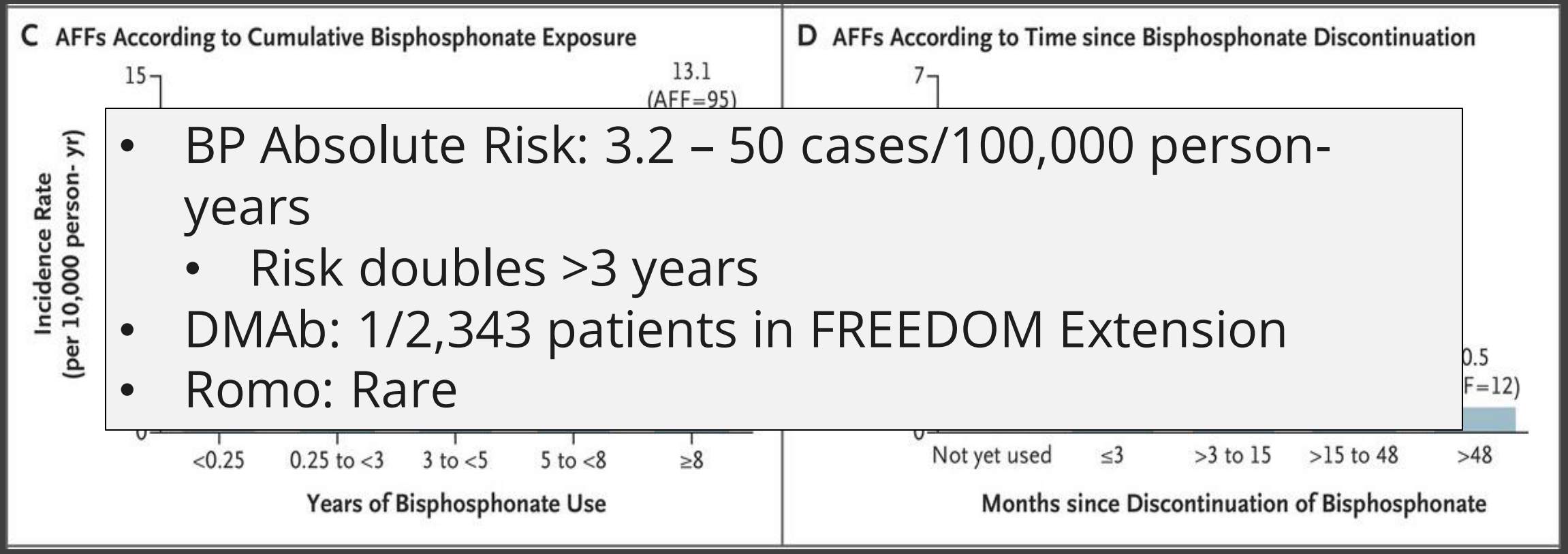
4. Oral BP >4y
   i. Consider holding x 2 months prior

Atypical Femur Fracture

Atypical Femur Fracture

- Prodrome: Pain in the thigh/groin region
- More common in osteoporosis than cancer
  - Likely related to duration
- Other risks: Lateral femoral bowing, autoimmune diseases, GC use

LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ, Siris ES. The clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int. 2022 Apr 28. doi: 10.1007/s00198-021-05900-y. Epub ahead of print. PMID: 35478046.



- BP Absolute Risk: 3.2 – 50 cases/100,000 person-years
  - Risk doubles >3 years
- DMAb: 1/2,343 patients in FREEDOM Extension
- Romo: Rare

DM Black et al. N Engl J Med 2020;383:743-753.
LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ, Siris ES. The clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int. 2022 Apr 28. doi: 10.1007/s00198-021-05900-y. Epub ahead of print. PMID: 35478046.

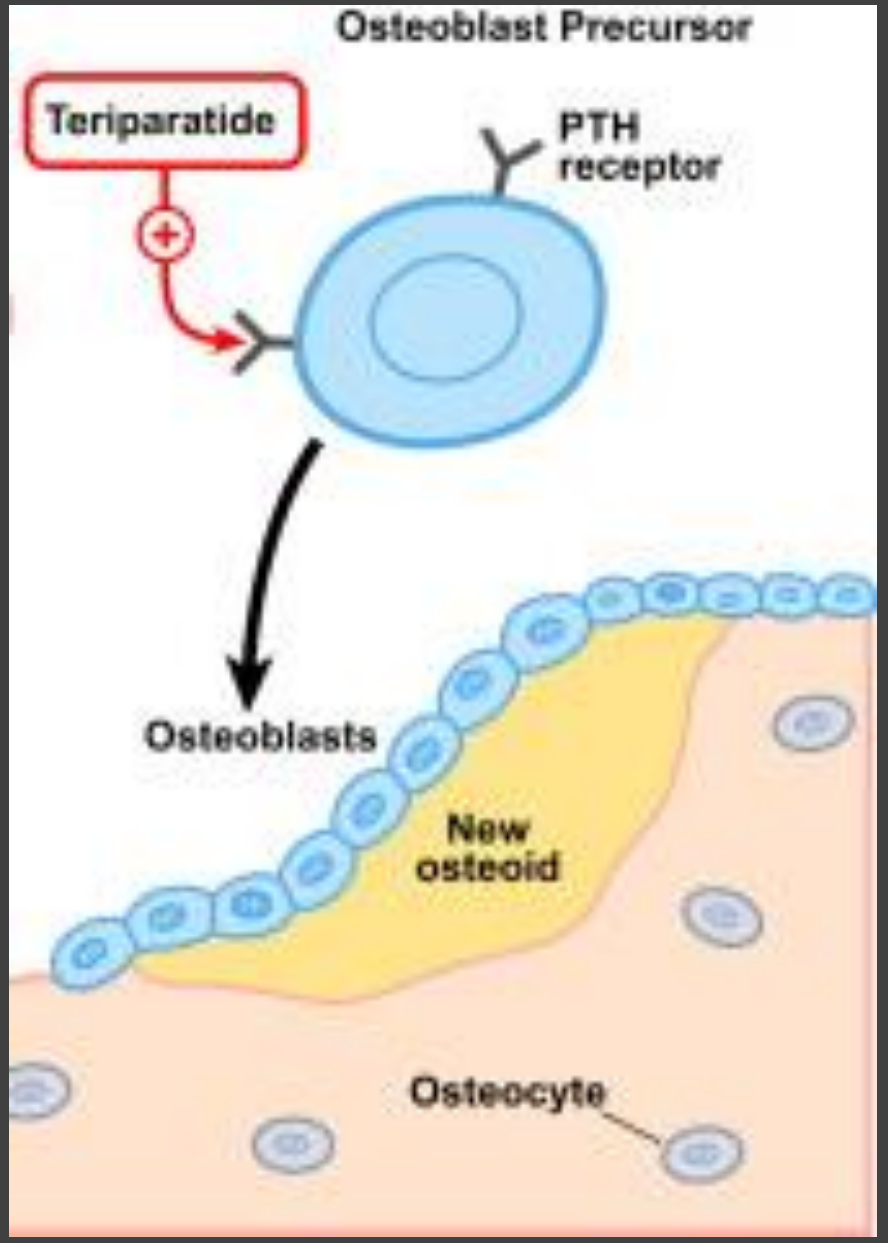
Overview

- Bisphosphonates
- Denosumab
- Romosozumab
- Parathyroid hormone analogs

PTH Analogs

- Teriparatide
  - Anabolic only
  - SubQ (daily) x 2+ years

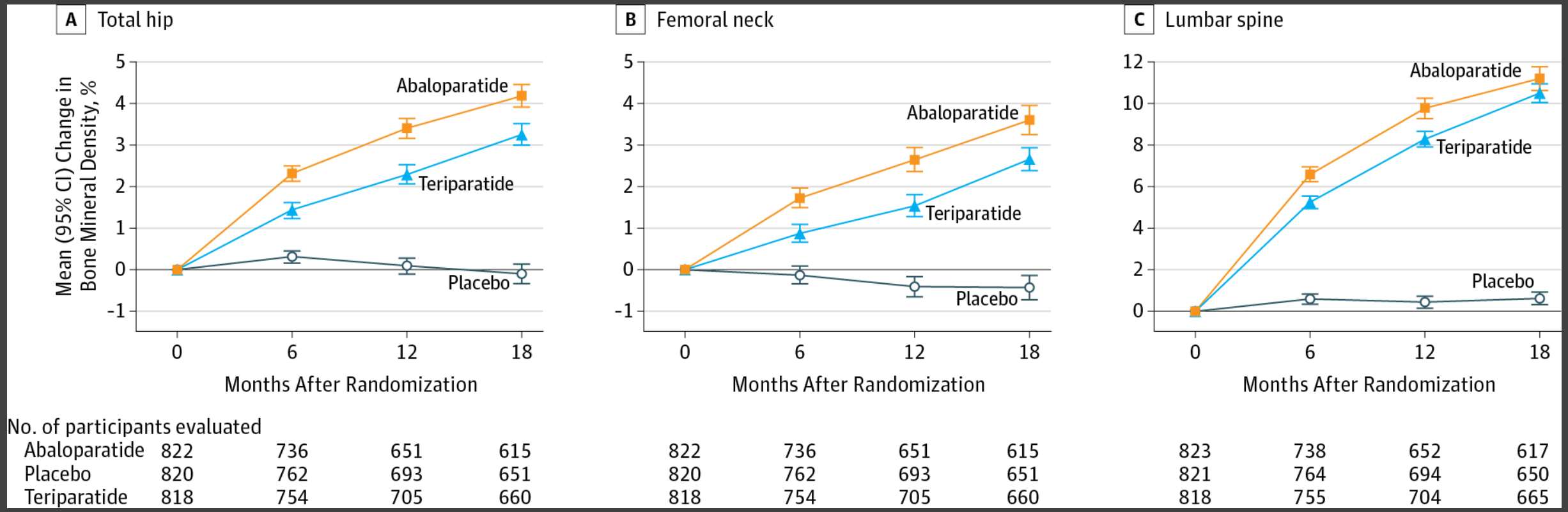
- Abaloparatide
  - Anabolic only
  - SubQ (daily) x 2 years


Osteoblast Precursor
Teriparatide
PTH receptor
Osteoblasts
New osteoid
Osteocyte

Effects of hPTH-(1–34) on osteoblast osteoclast and fibrotic marrow perimeter in male rats

Treatment	n	Osteoblast perimeter (%)	Osteoclast perimeter (%)	Fibrotic marrow perimeter (%)
VEH pump	10	8.8 ± 2.4	2.6 ± 0.8	0
PTH (sc)	7	16.7 ± 2.2[a]	4.8 ± 2.8	0
PTH pump (1 h/day)	4	26.3 ± 4.3[b]	2.8 ± 1.7	0
PTH pump (2 h/day)	6	14.6 ± 2.7	3.6 ± 1.2	0
PTH pump (continuous)	8	9.7 ± 2.6	18.2 ± 4.7[c]	62.9± 14.2[c]

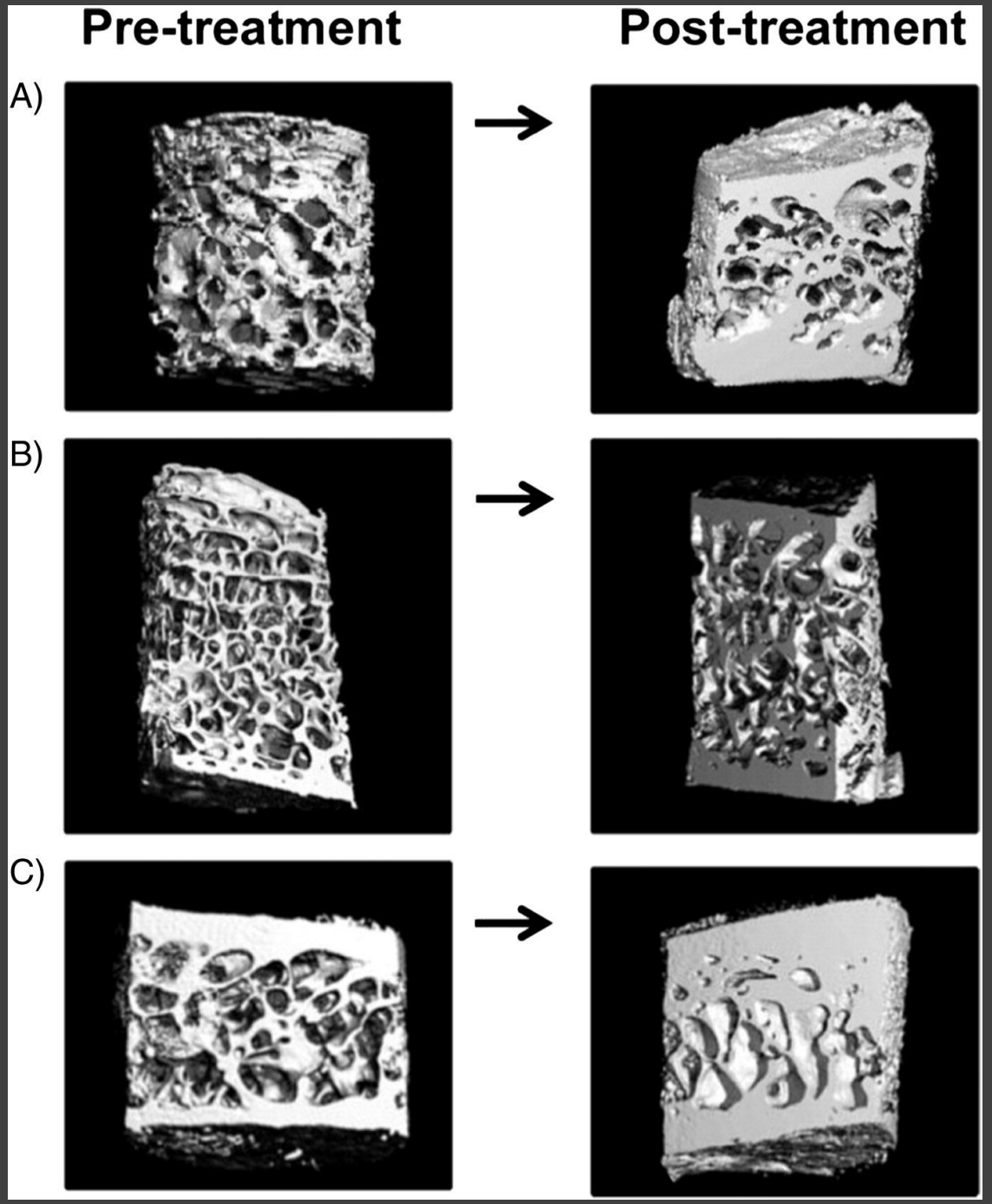
Dobnig H, Turner RT. The effects of programmed administration of human parathyroid hormone fragment (1-34) on bone histomorphometry and serum chemistry in rats. Endocrinology. 1997 Nov;138(11):4607-12. doi: 10.1210/endo.138.11.5505. PMID: 9348185.



No. of participants evaluated

Abaloparatide	822	736	651	615	822	736	651	615	823	738	652	617
Placebo	820	762	693	651	820	762	693	651	821	764	694	650
Teriparatide	818	754	705	660	818	754	705	660	818	755	704	665

JAMA. 2016;316(7):722-733. doi:10.1001/jama.2016.11136



Eriksen EF, Keaveny TM, Gallagher ER, Krege JH. Literature review: The effects of teriparatide therapy at the hip in patients with osteoporosis. Bone. 2014 Oct;67:246-56. doi: 10.1016/j.bone.2014.07.014. Epub 2014 Jul 15.

Safety

- Daily SubQ
- Hypercalcemia, urolithiasis, leg cramps
- Dizziness, palpitations
- Osteosarcoma (rats)

ORIGINAL ARTICLE

JBMR®

Teriparatide Did Not Increase Adult Osteosarcoma Incidence in a 15-Year US Postmarketing Surveillance Study

Alicia Gilsenan,[1] Kirk Midkiff,[1] David Harris,[1] Nicole Kellier-Steele,[2] David McSorley,[1] and Elizabeth B Andrews[1]

[1]RTI Health Solutions, Research Triangle Park, NC, USA
[2]Eli Lilly and Company, Indianapolis, IN, USA

Teriparatide: Label changes and identifying patients for long-term use

CLEVELAND CLINIC JOURNAL OF MEDICINE VOLUME 88 • NUMBER 9 SEPTEMBER 2021

Radius Announces Update on TYMLOS® (abaloparatide) Label

Published: Dec 23, 2021

- FDA approved the removal of the boxed warning from the TYMLOS label, effective December 22, 2021
- The boxed warning had referred to the potential risk of osteosarcoma
- Action follows review of long-term post-marketing data for TYMLOS and PTH class of drugs

What are your goals?

Treat-to-Target

AACE Guideline

High Risk/No Prior Fractures
Alendronate, denosumab, risedronate, zolendronate
Alternatives: Ibandronate, raloxifene

Very High Risk/Prior Fractures
Abaloparatide, denosumab, romosozumab, teriparatide, zoledronate
Alternatives: Alendronate, risedronate

Camacho PM, Petak SM, Binkley N, Diab DL, Eldeiry LS, Farooki A, Harris ST, Hurley DL, Kelly J, Lewiecki EM, Pessah-Pollack R, McClung M, Wimalawansa SJ, Watts NB. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/AMERICAN COLLEGE OF ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS-2020 UPDATE. Endocr Pract. 2020 May;26(Suppl 1):1-46. doi: 10.4158/GL-2020-0524SUPPL. PMID: 32427503.

Bisphosphonates & Drug Holidays

- Only appropriate on bisphosphonates
  - IV: Consider after 3 years
  - Oral: Consider after 5 years
- If T-score is >-2.5; no prior or recent fracture
  - Holiday up to 5 years
  - Reassess risk every 2-3 years
- If T-score is ≤-2.5 +/- recent fracture
  - Consider alternative
  - Oral: Continue up to 10 years
  - IV: Continue up to 6 years
  - Reassess risk every 2-3 years

LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ, Siris ES. The clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int. 2022 Apr 28. doi: 10.1007/s00198-021-05900-y. Epub ahead of print. PMID: 35478046.

Denosumab

Two Options:

1. Denosumab indefinitely

2. Denosumab transition to bisphosphonate (or ? romosozumab and then bisphosphonate)
   - Fractures may happen on PTH analog

Anabolics

Romosozumab x 1 year

-or

Abaloparatide/teriparatide x 2 years

Follow with potent antiresorptive

JOURNAL OF BONE AND MINERAL RESEARCH
Volume 23, Number 10, 2008
Published online on May 19, 2008; doi: 10.1359/JBMR.080506

Effects of Two Years of Daily Teriparatide Treatment on BMD in Postmenopausal Women With Severe Osteoporosis With and Without Prior Antiresorptive Treatment*

Barbara M Obermay
Steven Boonen [6] A

PERSPECTIVE

JBMR®

"When possible, we suggest anabolic therapy first, followed by potent antiresorptive therapy. The common practice of switching to TPTD only after patients have an inadequate response to antiresorptives (intercurrent fracture or inadequate BMD effect) is not the optimal utilization of anabolic treatment."

Department of Epidemiology, Columbia University College of Physicians and Surgeons, New York, NY, USA
[4]Department of Pathology, Columbia University College of Physicians and Surgeons, New York, NY, USA

Effects of Previous Antiresorptive Therapy on the Bone Mineral Density Response to Two Years of Teriparatide Treatment in Postmenopausal Women with Osteoporosis

Steven Boonen, Fernando Marin, Barbara Obermayer-Pietsch, Maria E. Simões, Clare Barker, Emmett V. Glass, Peyman Hadji, George Lyritis, Heide Oertel, Thomas Nickelsen, and Eugene V. McCloskey, for the EUROFORS Investigators

Monitoring Therapy

- Reassess risk every 2-3 years
  - Medication review
  - DXA
  - Interval fractures?

- If treatment stopped:
  - BMD worsen
  - Fracture risk increase
  - Diagnosis never changes

Final Points

- Don’t forget to screen appropriate patients
- 3 ways to diagnose osteoporosis
  - Fragility fractures, FRAX, or DXA
- Treat based on risk

Read This!

BHQF
Bone Health & Osteoporosis FOUNDATION™

Osteoporosis International
https://doi.org/10.1007/s00198-021-05900-y

CONSENSUS STATEMENT

The clinician's guide to prevention and treatment of osteoporosis

M. S. LeBoff[1] · S. L. Greenspan[2] · K. L. Insogna[3] · E. M. Lewiecki[4] · K. G. Saag[5] · A. J. Singer[6] · E. S. Siris[7]

Received: 4 September 2020 / Accepted: 19 February 2021

Thank you!

A. Lee Day, MD, FACP, CCD

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