

Update on the Management of Osteoporosis

44TH ANNUAL WINTER REFRESHER
IN ALBUQUERQUE

February 21, 2026

E. Michael Lewiecki, MD, FACP, FACE

Director, New Mexico Clinical Research & Osteoporosis Center

Director, Bone Health ECHO

University of New Mexico Health Sciences Center

Albuquerque, NM

Disclosure

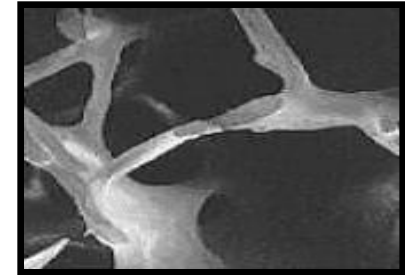
- Amgen - investigator, consultant, speaker
- Radius - investigator, consultant, speaker
- Ultragenyx - investigator
- Kyowa Kirin - consultant, speaker
- Angitia - consultant, investigator
- Ascendis - consultant, speaker

Objectives

- Characterize osteoporosis as a major public health concern
- Describe important clinical advances in the management of osteoporosis
- Identify current concepts in osteoporosis care

Osteoporosis

- 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 (e.g., architecture, turnover, damage accumulation, mineralization)



Burden of Osteoporotic Fractures

- 1 of every 2 women and 1 of every 4 men will have an osteoporotic fracture
- 54 million Americans have osteoporosis or osteopenia that can increase fracture risk
- Over 2 million fractures in the US each year
- Osteoporotic fractures result in more hospitalizations than heart attacks, strokes, and breast cancer combined
- 20% 1-year mortality after hip fracture, with 75% of survivors failing to regain their former functional status



Anyone would have broken a bone if they fell this hard.
No one in my family has osteoporosis.
I only want “natural” treatment.
Why do I need a drug?
What are the side effects?
Don't these drugs cause brittle bones and rotten jaw?
How long do I have to take it?
What is the cost?



Patient with a recent fracture.

Fracture Risk Assessment



Intervention Thresholds



Evaluation / Discussion



Treatment



Follow-up

Concepts

- Diagnosis
- Assessment of fracture risk
- Imminent fracture risk
- Individualizing treatment decisions
- Sequence of therapy
- Technology-enabled collaborative learning

Indications for BMD Testing

- Women age ≥ 65 and men age ≥ 70
- Younger postmenopausal women, perimenopausal women, and men age 50-69 with risk factors for fracture
 - e.g., fracture, smoking, family history, frequent falling
- Adults with a condition or taking a medication associated with low bone mass or bone loss
 - Condition: e.g., rheumatoid arthritis, diabetes, organ transplant
 - Medication: e.g., glucocorticoids, aromatase inhibitors, androgen deprivation therapy

AACE Guidelines

- Three ways to diagnose osteoporosis
 - Fragility fracture, even when BMD is normal
 - T-score ≤ -2.5 at LS, TH, FN, or 1/3 (33%) radius
 - T-score between -1.0 and -2.5 and fracture risk is high with FRAX according to country-specific thresholds
 - USA: MOF $\geq 20\%$, HF $\geq 3\%$
- When the initial diagnosis is by T-score ≤ -2.5 , the diagnosis persists even when T-score is better than -2.5

Diagnosis of Osteoporosis Persists

- 73 year-old woman with LFN T-score = -2.8 and recent Fx T11
 - DXA report: severe osteoporosis, very high fracture risk
- Treatment with denosumab is started
- Two years later T-score = -2.4
 - DXA report: osteopenia, moderate fracture risk
- Consequences
 - Patient is happy
 - Health plan denies coverage
 - Treatment is stopped
 - BMD declines
 - Fracture risk rises

A better DXA report might have been:

“Severe osteoporosis with improvement in BMD representing a good response to therapy. Continuation of treatment is recommended.”

DXA Quality Matters

Best Practices for Dual-energy X-ray Absorptiometry Measurement and Reporting: International Society for Clinical Densitometry

- 1 diagnosis and 1 level of fracture risk per patient
- Precision assessment is required for quantitative BMD comparison
- Incorrect acquisition, analysis, and interpretation can be harmful
- Training and certification is important

Tools for Fracture Risk Assessment

- Dual-energy X-ray Absorptiometry (DXA)
 - Bone Mineral Density (BMD, T-score)
 - Vertebral Fracture Assessment (VFA)
 - Trabecular Bone Score (TBS)
- Clinical Risk Factors
 - Especially age, previous fracture (number, recency)
 - FRAX, FRAX adjustments
 - Other fracture risk algorithms (Garvan, CAROC)

FRAXplus

Calculation Tool

Please answer the questions below to calculate the ten-year probability of fracture with or without BMD.

Continent: Country:

Local Reference:

About the risk factors ⓘ Individuals with fracture risk assessed since 1st June 2011 : 11,455,325

Questionnaire

1. Age (between 40 and 90 years)

2. Sex Female Male

3. Weight Pounds /

4. Height Inches

5. Previous Fracture

6. Parent Fractured Hip

7. Current smoking

8. Glucocorticoids

9. Rheumatoid arthritis

10. Secondary osteoporosis

11. Alcohol 3 or more units/day

12. Femoral neck BMD

Age: 65 BMI: 27.8 with BMD T-score: -2.07

THE TEN-YEAR PROBABILITY OF FRACTURE

Major osteoporotic **34 %**

Hip Fracture **7.4 %**

[What does FRAXplus® do? Click here](#)

- Benefits
 - Quantitative fracture risk
 - Robust supporting data
 - Part of DXA software
 - Included in guidelines
- Limitations
 - Missing risk factors
 - Dichotomous input
 - Variable range of error
 - Only femoral neck BMD
 - Only 4 ethnicities in US
 - Pay for TBS

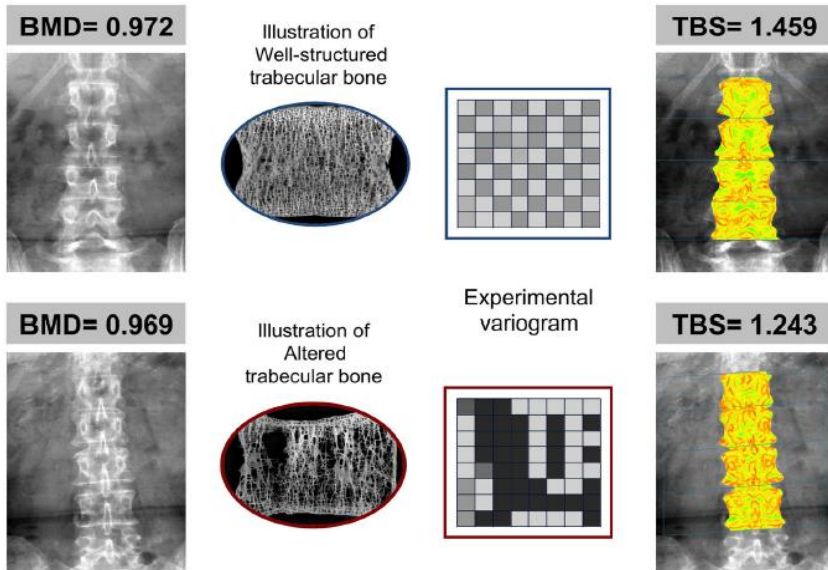
<https://www.fraxplus.org/calculation-tool/>

Vertebral Fracture Assessment (VFA) by DXA

- Recognition of a VF may change diagnostic classification, assessment of fracture risk, and treatment decisions
- VFA is more convenient, less radiation, and less expensive than standard spine X-rays
- Spine imaging (VFA, X-ray) is indicated when T-score is <-1.0 and 1 or more of the following is present:
 - Women \geq age 70 and men \geq age 80
 - HHL \geq 1.5 in.
 - Self-reported but undocumented VF
 - Glucocorticoid therapy \geq 5 mg prednisone per day for \geq 3 mo.

Trabecular Bone Score (TBS) is an Independent Risk Factor for Fracture

Gray-level textural measure derived from LS image by DXA



TBS	Classification	MOF Risk
>1.31	Normal	Low
1.23-1.31	Partially Degraded	Intermediate
<1.23	Degraded	High

Potential clinical applications:

FRAX adjustment.

“Soft bones” or fractures with normal BMD.

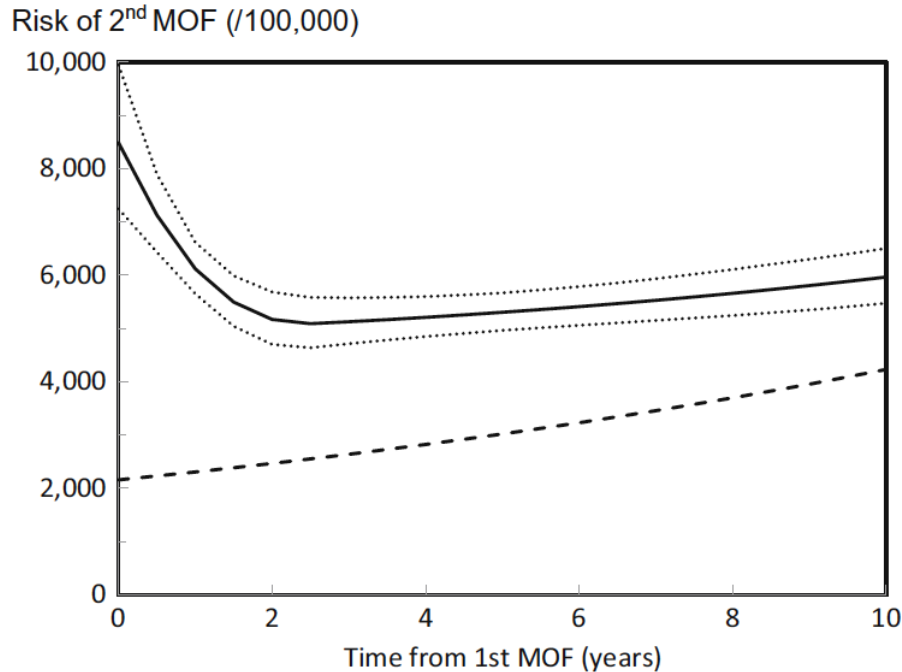
Selection of anabolic therapy.

Monitoring anabolic therapy.

Imminent Fracture Risk

Recent fracture is associated with
higher risk of future fracture
than a remote fracture

Imminent Fracture Risk



- Population-based cohort of 18,872 men and women in the Reykjavik Study
- Risk of a 2nd MOF is very high in the first 2 years after an index fracture and remains higher than those without a previous fracture (dashed line)
- Swiss Association against Osteoporosis (SVGO) defines imminent risk as > 10% risk of fracture in next 2 years

Johansson H et al. *Osteoporos Int.* 2017;28:775-780.
Ferrari S et al. *Swiss Med Wkly.* 2020;150:w20352.

Take Home Message:
Fracture = “Bone Attack”

Evaluation and treatment is urgent

BHOF Treatment Guidelines

Consider pharmacological therapy for postmenopausal women and men aged 50 years and older with the following:

Osteoporosis by T-score

- T-score ≤ -2.5 at FN, TH, LS, or 33%R (uncertainty of data), or . . .

Osteoporosis by Fracture

- Fracture of hip or vertebra regardless of BMD, or . . .
- Fracture of proximal humerus, pelvis, or distal forearm with low BMD and for some patients with normal BMD

Osteoporosis by FRAX

- FRAX 10-year probability of major osteoporotic fracture $\geq 20\%$ or hip fracture $\geq 3\%$, and . . .
- T-score between -1.0 and -2.5 at FN or TH

Evaluate Before Starting Treatment

T-score \leq -2.5 may be something other than osteoporosis
T-score $>$ -2.5 may be osteoporosis
Contributing factors may need correction prior to treatment

Almost everyone

- CBC
- Blood chemistries (CMP+P)
 - Creatinine
 - Calcium
 - Phosphorus (NOT part of CMP)
 - Albumin
 - Alkaline phosphatase
 - Liver enzymes
- 25-OH-vitamin D
- 24-hour urine for Ca, Na

Selected patients

- TSH
- Celiac antibodies
- Bone turnover markers
- Urinalysis
- sIFE, K/L light chain ratio
- Intact PTH
- Overnight dex suppression

Universal Recommendations

- Regular weight-bearing and muscle-strengthening physical activity
- Falls prevention [core strength, balance]
- Avoid tobacco use and excess alcohol
- Identification and treatment of risk factors for fracture
- Calcium 1000-1200 mg/day, ideally from diet
- Vitamin D 800-1000 IU/day, target 30-50 ng/mL

Pharmacological Therapy

Inhibit Bone Resorption (Antiresorptive, Antiremodeling)	Stimulate Bone Formation (Anabolic, Bone Forming)
Alendronate (Fosamax, generic)	Teriparatide (Forteo)
Risedronate (Actonel, Atelvia, generic)	Abaloparatide (Tymlos)
Ibandronate (Boniva, generic)	Romsozumab (Evenity) – “dual-effect”
Zoledronate (Reclast, generic)	
Denosumab (Prolia)	
Raloxifene (Evista, generic)	
Salmon Calcitonin (Miacalcin, generic)	
Estrogen (various)	
CE/Bazedoxifene (Duavee)	

But which one to use?

Risk Stratification and Implications

Level of Risk	Examples	Treatment
Low (ES, AACE)	T-score > -1.0, and no hip or vertebral fracture, and FRAX MOF/HF < 20%/3%	Non-pharmacological
Moderate (ES)	T-score > -2.5, and no hip or vertebral fracture, and FRAX MOF/HF < 20%/3%	Non-pharmacological or bisphosphonate
High (ES, AACE)	T-score ≤ -2.5, or prior hip or vertebral fracture, or FRAX MOF/HF ≥ 20%/3%	Bisphosphonate Denosumab SERM
Very High (ES)	T-score ≤ -2.5 and fractures, or multiple vertebral fractures, or severe vertebral fracture (> 40% vertebral height loss)	Anabolic Bisphosphonate Denosumab
Very High (AACE)	T-score < -3.0, fracture in last 12 months, fracture on treatment, fracture on harmful drugs, multiple fractures, high fall risk, FRAX MOF/HF > 30%/4.5%	Anabolic Bisphosphonate Denosumab

Comparative Effectiveness

Fracture Risk

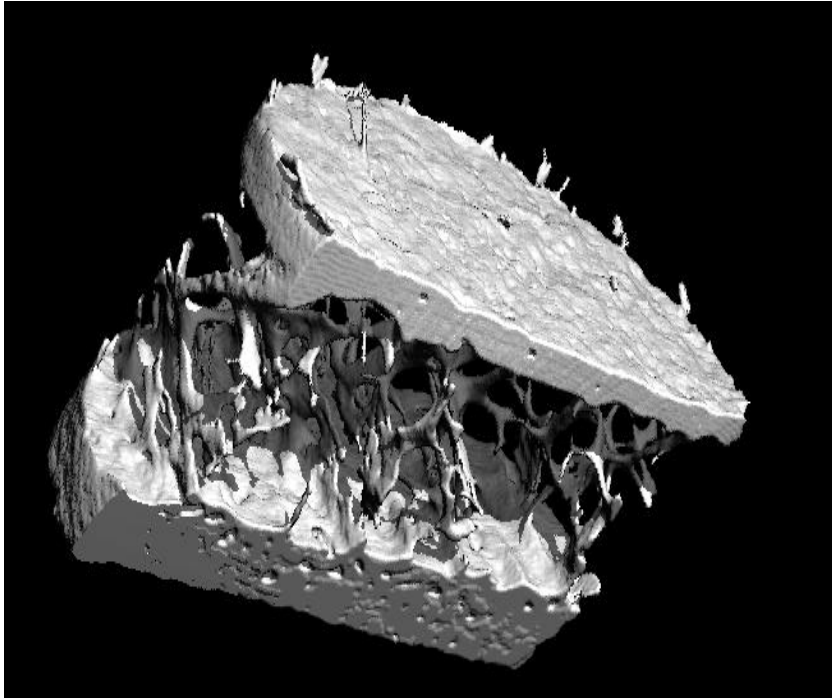
RCTs: Anabolics Reduce Fracture Risk More than BPs

- **GIO:** Teriparatide superior to alendronate
 - Randomized active-controlled trial in 428 men and women with GIO
 - Fewer new radiographic VFs with TPT vs. ALN at 18 months¹
- **Severe PMO:** Teriparatide superior to risedronate
 - Randomized active-controlled trial in 712 women with ≥ 1 painful osteoporotic VF
 - Fewer new radiographic VFs with TPT vs. RIS at 18 months²
- **Severe PMO:** Romosozumab superior to alendronate*
 - Randomized active-controlled trial (ARCH) in 4093 women with ≥ 1 VF or hip fracture
 - Fewer new radiographic VFs and clinical fractures with Romo vs. ALN at 12 months³
- **Severe PMO:** Teriparatide superior to risedronate*
 - Randomized active-controlled trial (VERO) in 1360 women with ≥ 1 VF
 - Fewer new radiographic VFs and clinical fractures with TPT vs. RIS at 12 months⁴

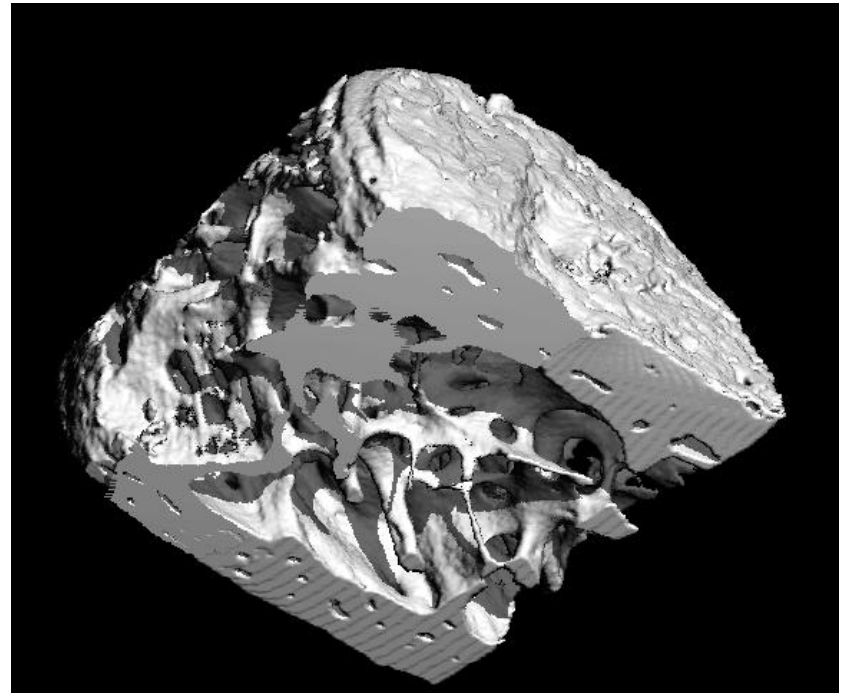
*Fractures = Primary Endpoint

1. Saag KG et al. N Engl J Med. 2007;357:2028-2039. 2. Hadji P et al. Osteoporos Int. 2012;23:2141-50.
3. Saag KG et al. N Engl J Med. 2017;377:1417-1427. 4. Kendler DL et al. Lancet. 2018;391:230-240.

What I show patients

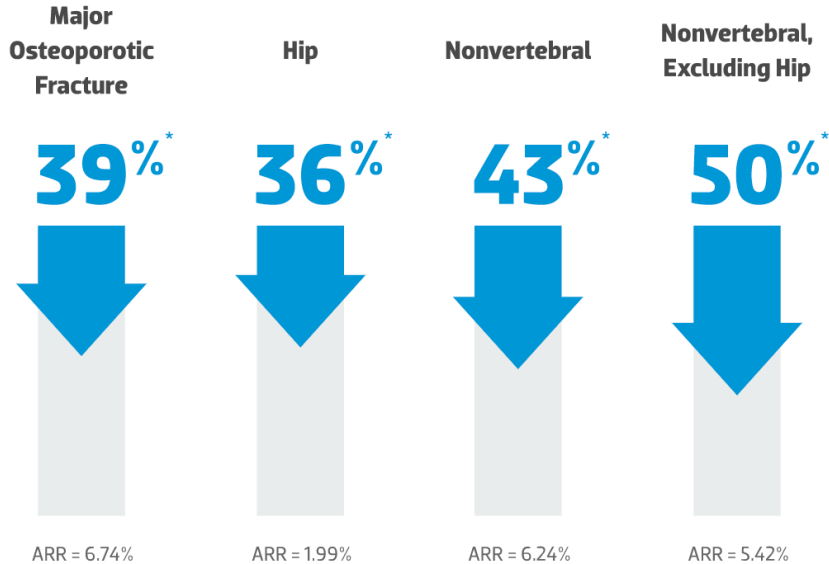


Baseline



After 21 Months of Teriparatide

RWE: Dmab Reduces Fracture Risk More than ALN



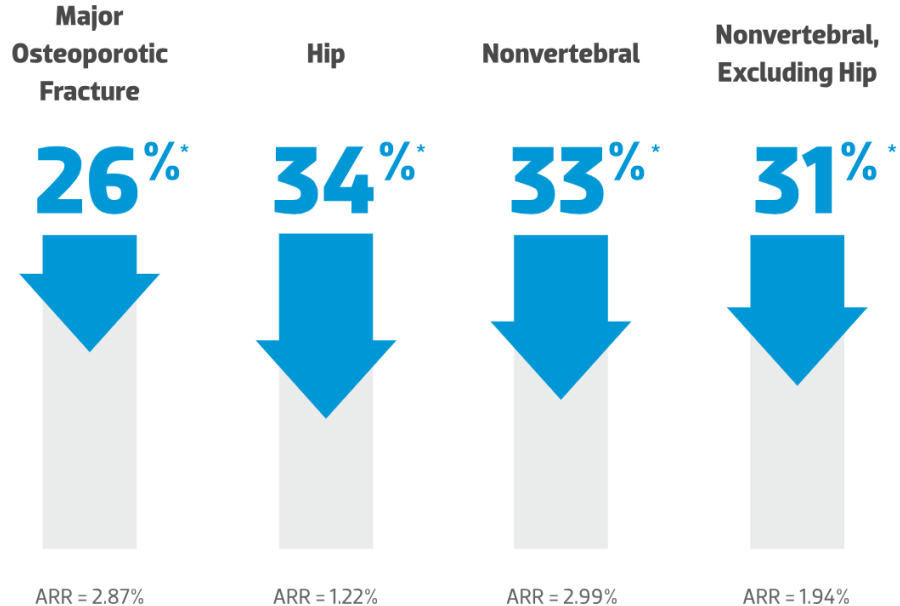
- Retrospective observational cohort study using USA Medicare claims data
- 478,651 women age > 65 with osteoporosis started on treatment with Dmab or ALN from 2012 to 2018
- Fracture risk reduction was greater with Dmab and ALN with greater risk reduction of MOF with longer duration of treatment with Dmab

Presented at WCO-IOF-ESCEO Congress in Barcelona; May 2023.

Image from www.evenityproliahcp.com

Curtis JR et al. J Bone Miner Res. 2024. Accepted.

RWE: Dmab Reduces Fracture Risk More than ZOL



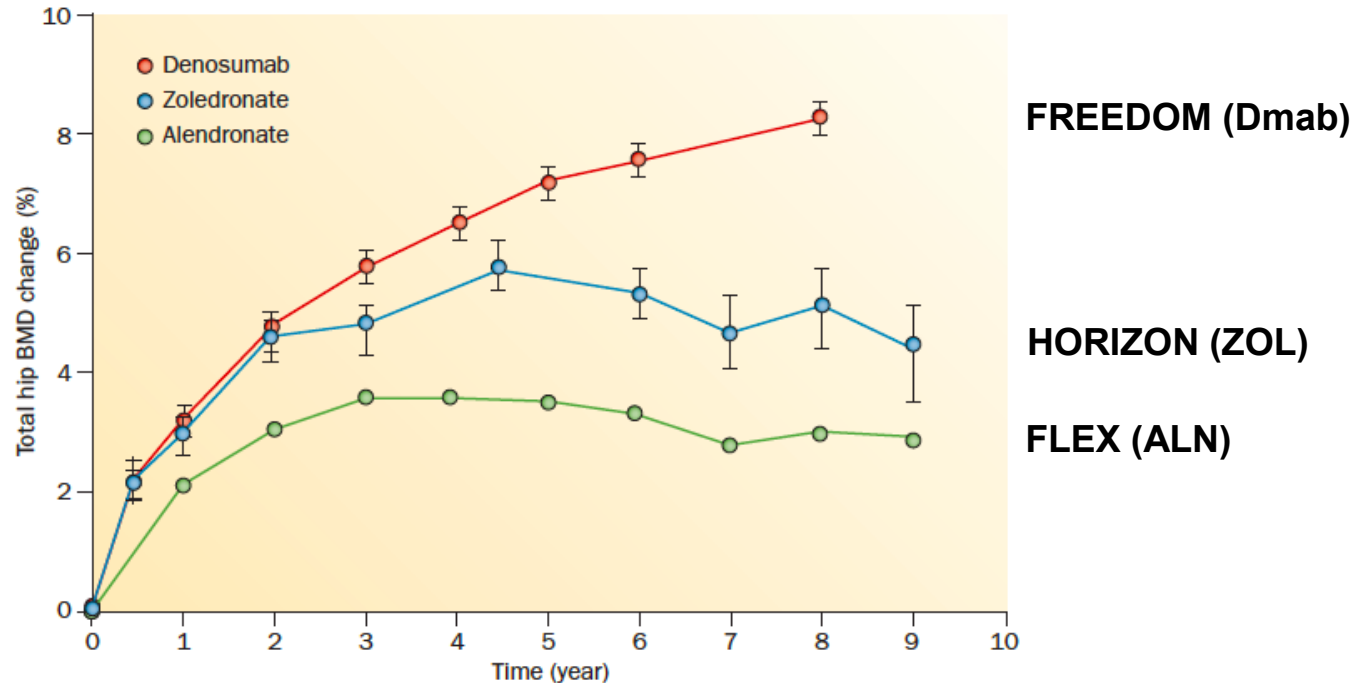
- Retrospective observational cohort study using USA Medicare claims data
- 478,651 women taking Dmab vs. 37,328 on ZOL
- Fracture risk reduction was greater with Dmab than ZOL

Comparative Effectiveness

BMD and Bone Strength

Antiresorptive Drugs are Not All the Same:

TH BMD - Dmab > ZOL > ALN

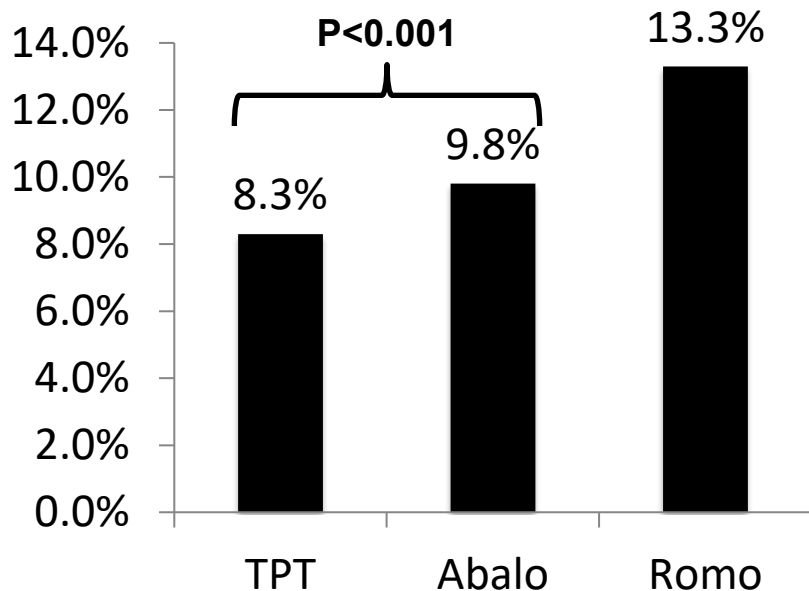


Anabolic Drugs are Not all the Same

LS and TH BMD - Romo > Abalo > TPT

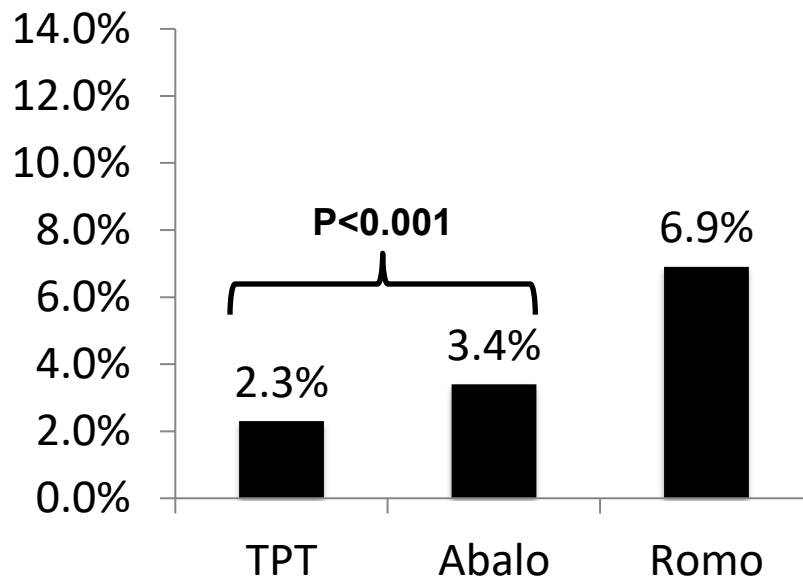
(1-Year BMD Changes in ACTIVE and FRAME)

Lumbar Spine BMD



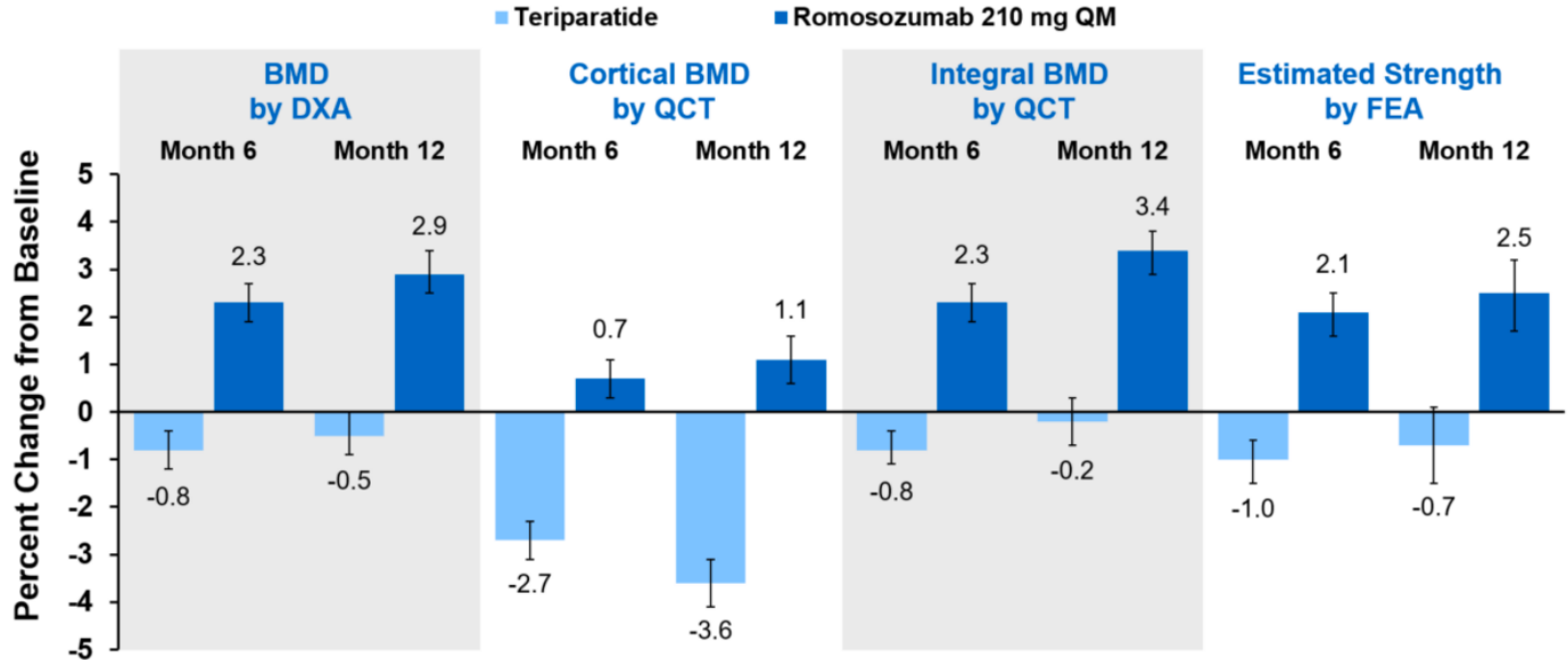
Consistent with 1-year phase 2 study data with Romo vs. open label TPT

Total Hip BMD



ACTIVE. Miller PD et al. JAMA. 2016;316:722-733.
FRAME. Cosman F et al. N Engl J Med. 2016;375:1532-1543.

STRUCTURE: After ALN, Romo Increases BMD and Bone Strength at TH More than TPT at 12 Months



All P-values < 0.001

Langdahl BL et al. Lancet. 2017;390:1585-1594.

Sequence of Therapy Matters

Consider anabolic before antiresorptive therapy for very high risk patients

BMD Decrease with Anabolic (TPT) after Antiresorptive (ALN, RIS, Dmab)

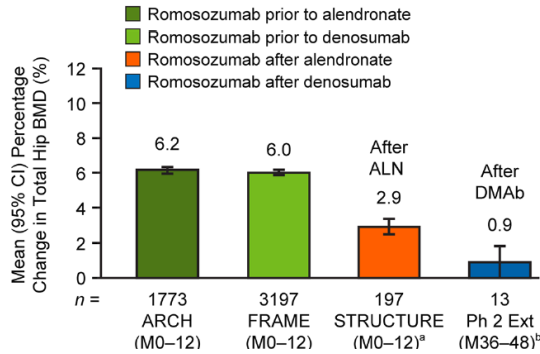
Study	Sample size	Treatment paradigm	% Change in total hip BMD during TPTD/PTH treatment			
			6 mo	12 mo	18 mo	24 mo
Ettinger et al. ⁽²⁷⁾	33	Alendronate (mean 29.3 mo) → TPTD (18 mo)	-1.8%	-1.0%	+0.3%	-
Boonen et al. ⁽²⁴⁾	107	Alendronate (median 29.2 mo) → TPTD (24 mo)	-1.2%	-0.6%	+0.6%	+2.1%
Boonen et al. ⁽²⁴⁾	59	Risedronate (median 23.4 mo) → TPTD (24 mo)	-1.6%	-0.4%	+0.9%	+2.9%
Miller et al. ⁽³⁰⁾	158	Risedronate (mean 37.2 mo) → TPTD (12 mo)	-1.2%	-0.3%	-	-
Miller et al. ⁽³⁰⁾	166	Alendronate (mean 38.0 mo) → TPTD (12 mo)	-1.9%	-1.7%	-	-
Cosman et al. ⁽²⁶⁾	50	Alendronate (mean 45.7 mo) → TPTD (18 mo)	-0.8%	-	+0.9%	-
Leder et al. ⁽²⁸⁾	27	Denosumab (24 mo) → TPTD (24 mo)	-1.7%	-2.7%	-1.7%	-0.7%

Transient or sustained bone loss at the hip
with antiresorptive followed by teriparatide

BMD Gains > with Anabolic Before Antiresorptive

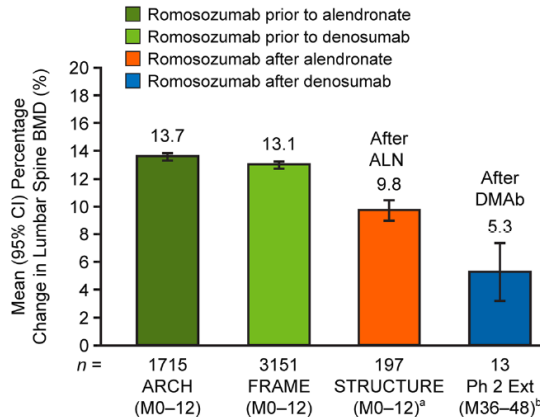
TH

a. 1 Year Gains With Romosozumab



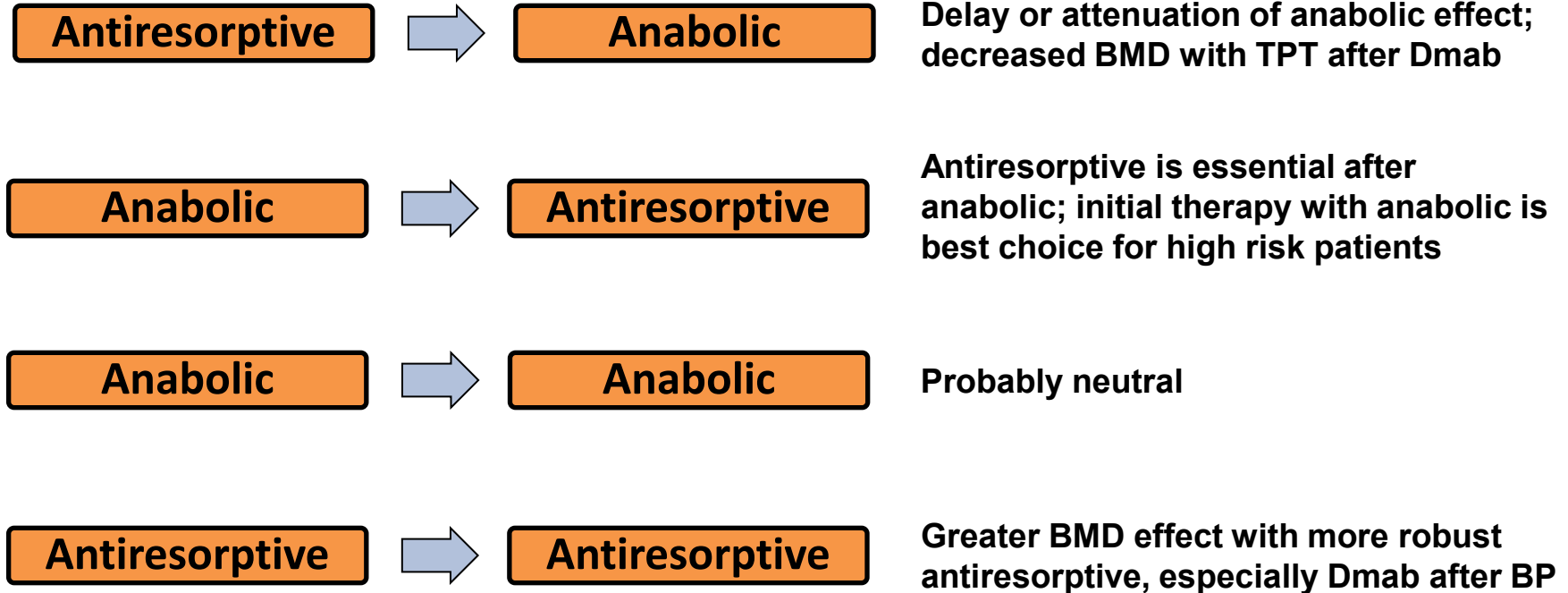
LS

c. 1 Year Gains With Romosozumab



- Review of data in 4 RCTs with Romo before antiresorptive (ARCH, FRAME) or after (STRUCTURE, phase 2 extension)
- Larger mean BMD increases and greater BMD responder rates with Romo before ALN or Dmab compared to after

Sequence of Osteoporosis Therapy



Treat-to-Target

Goal of treatment is to achieve an acceptable level of fracture risk

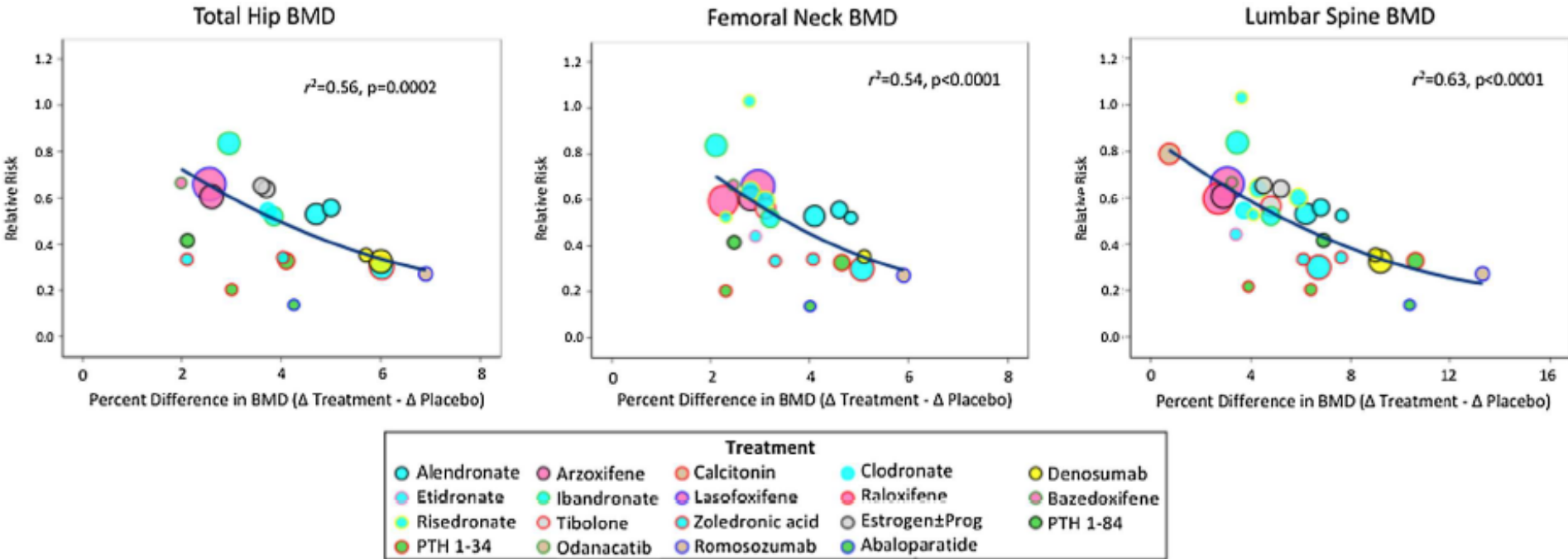
Major Principles

- Treatment targets should be individualized with consideration of the indication for treatment, recency of fracture, number and site of prior fractures, severity of VFs, BMD, and other risk factors
- TH BMD has emerged as the most useful treatment target because it consistently predicts vertebral and non-vertebral fracture risk reduction

Selecting Initial Treatment

- Consider treatment with at least 50% probability of attaining a treatment target can be attained over a reasonable period of time (about 3 years), with greater urgency for patients at imminent risk of fracture
- For patients at very high fracture risk, consider anabolic therapy first, followed by an antiresorptive agent

VFs and BMD Response to Therapy



Lowest Baseline T-score Allowing > 50% of Women to Achieve T-score > -2.5 Over Approximately 3 Years

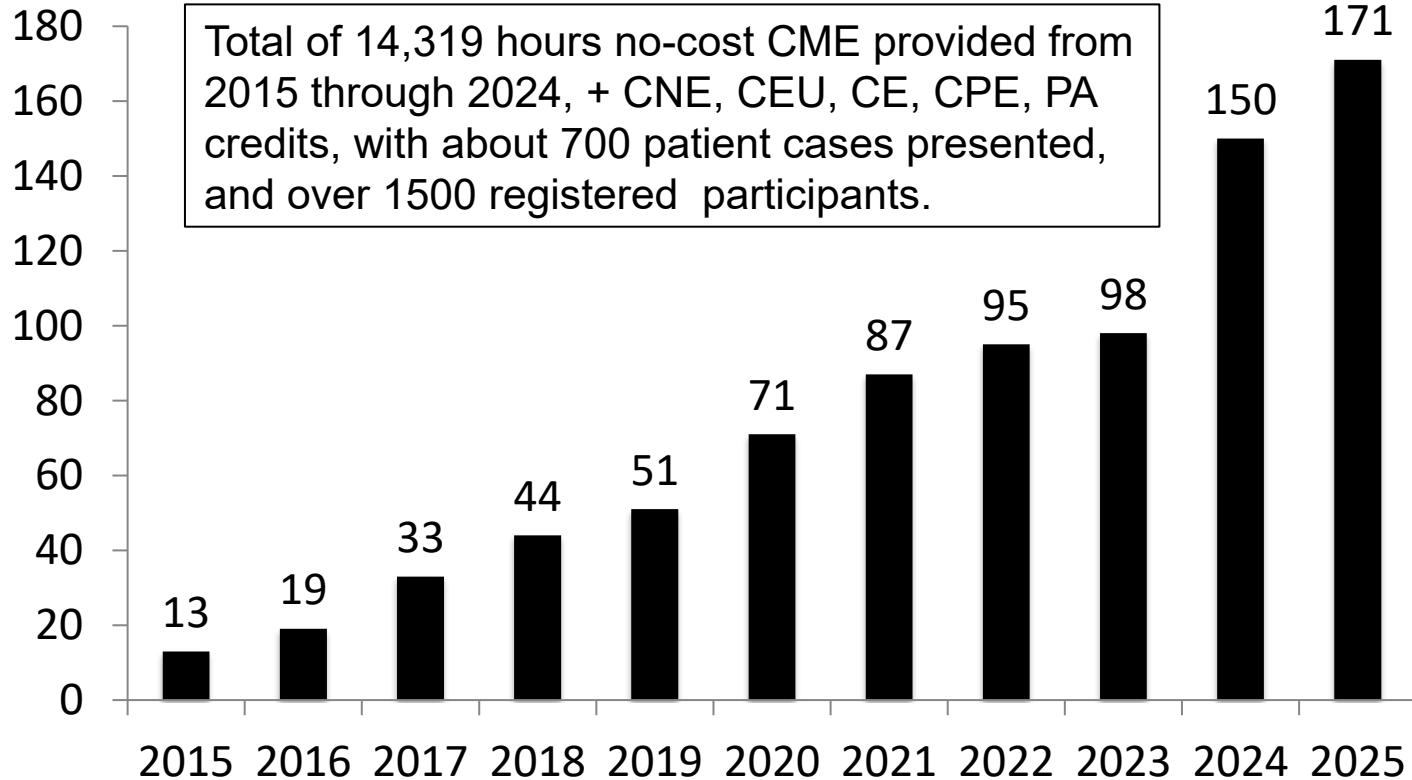
Treatment	Total Hip	Lumbar Spine
Alendronate	-2.7	-3.0
Denosumab*	-2.8	-3.1
Romozosumab/Alendronate	-2.9	-3.5
Abaloparatide/Alendronate	-2.9	-3.5
Romozosumab/ Denosumab	-3.1	-3.7

*Dmab for more than 3 years will continue to improve BMD, while BMD typically remains stable with BP after 3 years



Technology-enabled Collaborative Case-based Learning

UNM Bone Health ECHO Average Attendance



Data compiled by Project ECHO.

Summary

- Osteoporosis is a lifelong disease that warrants lifelong attention
- We can treat it, but we can't cure it
- Any treatment is better than none, but some are better than others
- Fracture risk stratification can guide selection of initial therapy
- To participate in Bone Health ECHO and discuss challenging cases . . .
 - Register at www.ofnm.org, or
 - Contact me at mlewiecki@gmail.com, or
 - Google “bone” and “ECHO”