ACP Colorado-Evidence Based Management of Osteoporosis

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Disclosures

- None

Learning Objectives

- At the end of the session participants will know how to:
  - Use bone density screening appropriately in various patient populations
  - Optimize individualized treatment for patients at low risk and high risk for fracture using non-pharmacologic as well as pharmacologic therapy
  - Be familiar with some recent controversies and unknowns regarding length of treatment and tools for monitoring

Question #1

A 66 year old woman ask you about osteoporosis screening. According to guidelines she should be screened if:

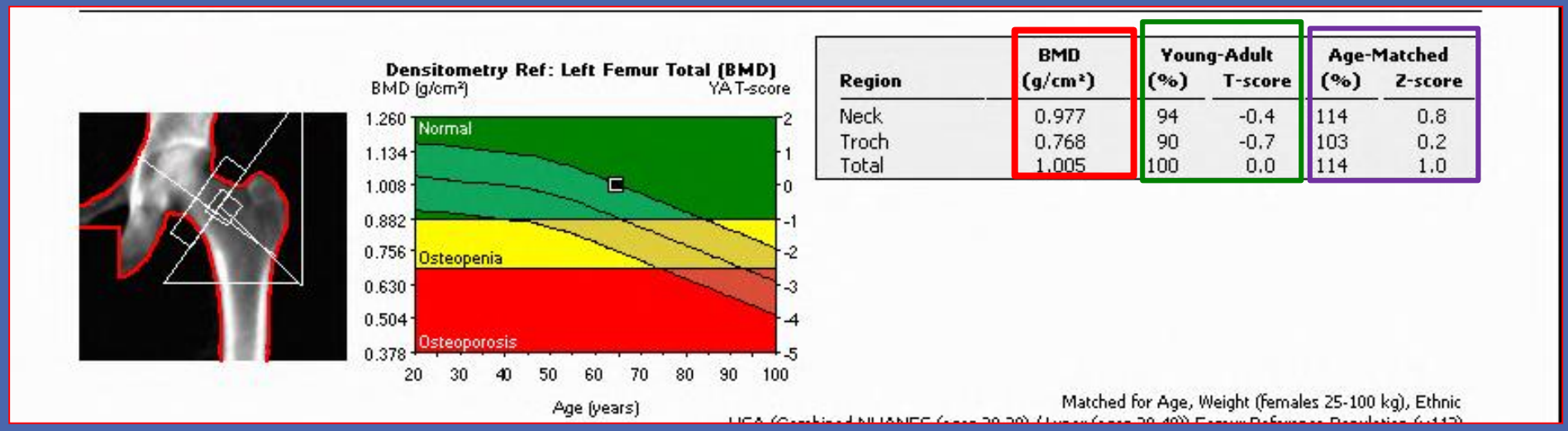
A) She has sustained a fracture as an adult

B) She is on glucocorticoids at a dose of more than 7.5mg daily

C) Her mother has a history of hip fracture

D) All of the above—all women over 65 should be screened regardless of additional risk factors

BMD= Bone mineral content in g/2D projected area of bone being measured



Region	BMD (g/cm²)	Young-Adult (%)	Young-Adult T-score	Age-Matched (%)	Age-Matched Z-score
Neck	0.977	94	-0.4	114	0.8
Troch	0.768	90	-0.7	103	0.2
Total	1.005	100	0.0	114	1.0

T-score=(patient's BMD-young normal mean)/SD of young normal

Z-score is an age matched comparison
Z-scores include race and (sometimes) weight as well.

Definitions by T-score in postmenopausal women

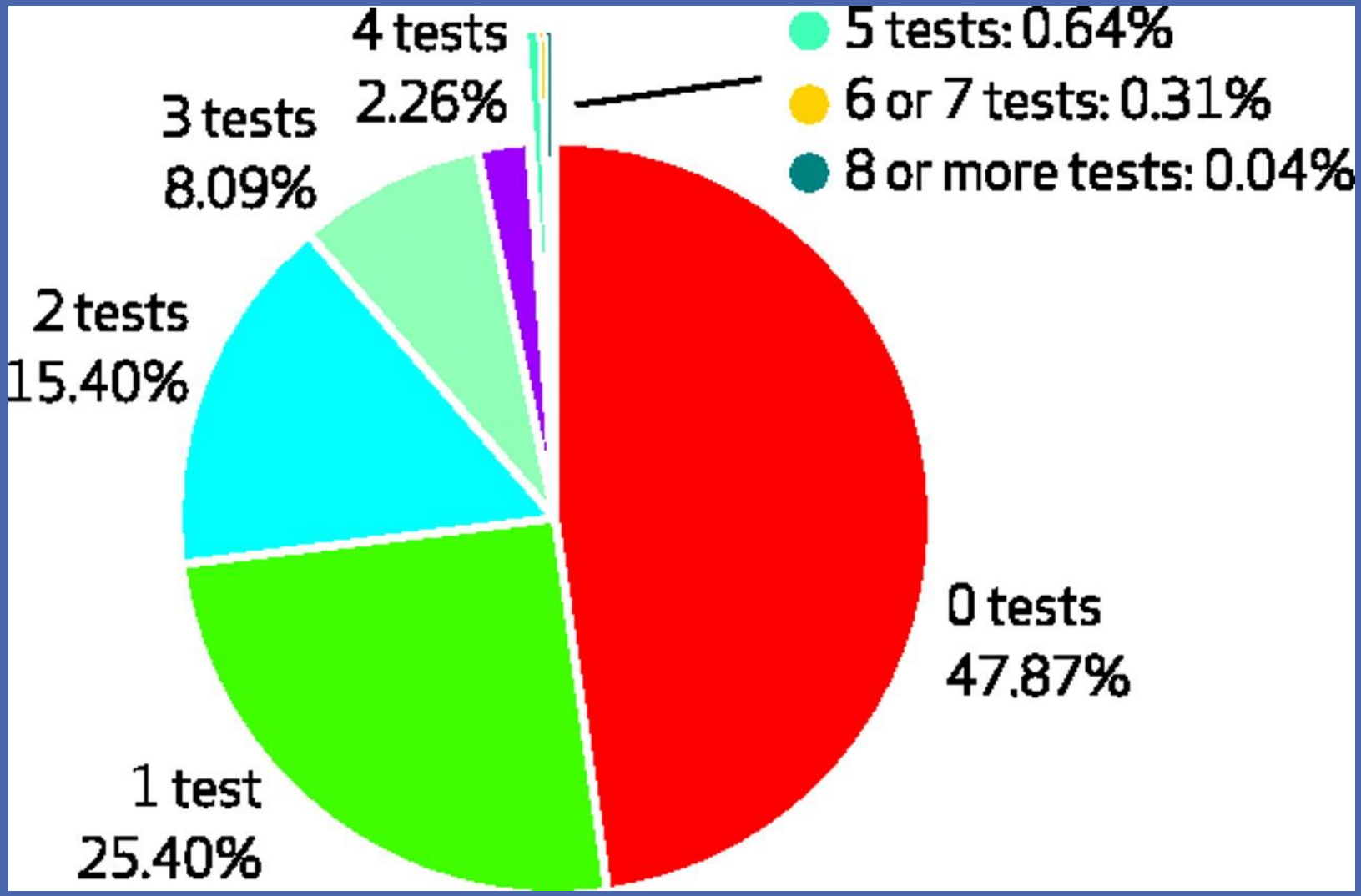
	T score
Normal	-1.0 or higher
Osteopenia (low bone mass)	-1.1 to –2.4
Osteoporosis	-2.5 and below
Severe osteoporosis	-2.5 and below, with a low trauma fracture

- Put in picutres of guidelines

POPULATION	RECOMMENDATION
Postmenopausal women over 65	Screen regardless of risk factors
Postmenopausal women between 50-64	Screen if 1 or more risk factor present • NOF • Endocrine Society • Canadian Osteoporosis Society Screen if FRAX 10 y risk> or = 9.3% • USPTF Additional screening calculators • ORAI/OST/OSIRIS/SCORE
Men > 70	Insufficient evidence • USPTF Screen regardless of risk factors • NOF • Endocrine Society • ISCD
Men 50-70	Insufficient evidence • USPTF Screen if 1 or more risk factors • NOF • Endocrine Society • ISCD

Oconnor Med Clin N Am 2016

Many women are NOT screened

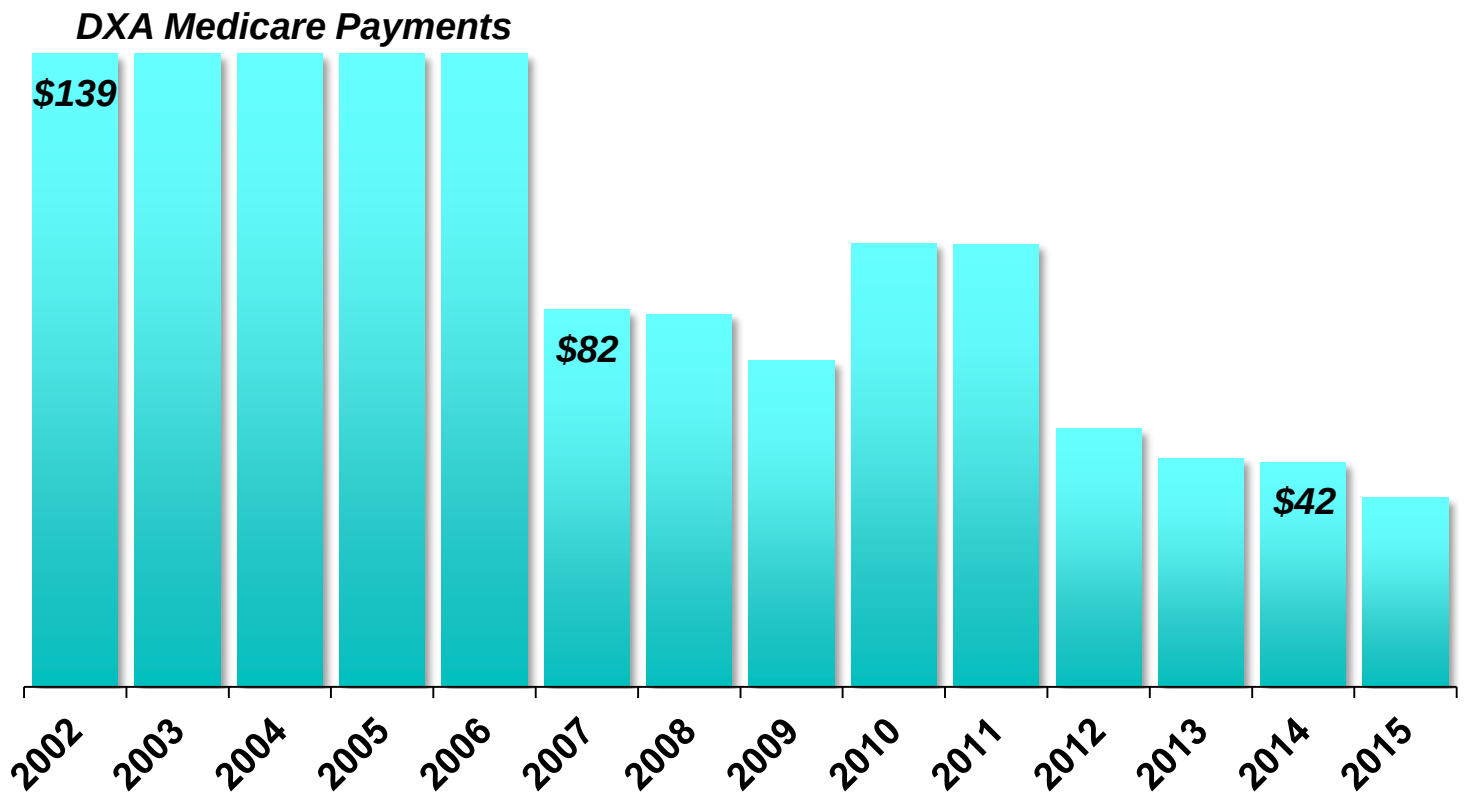


Distribution Of Elderly Female Fee-for-Service Medicare Beneficiaries By Cumulative Number Of DXA Tests, 2002–08.

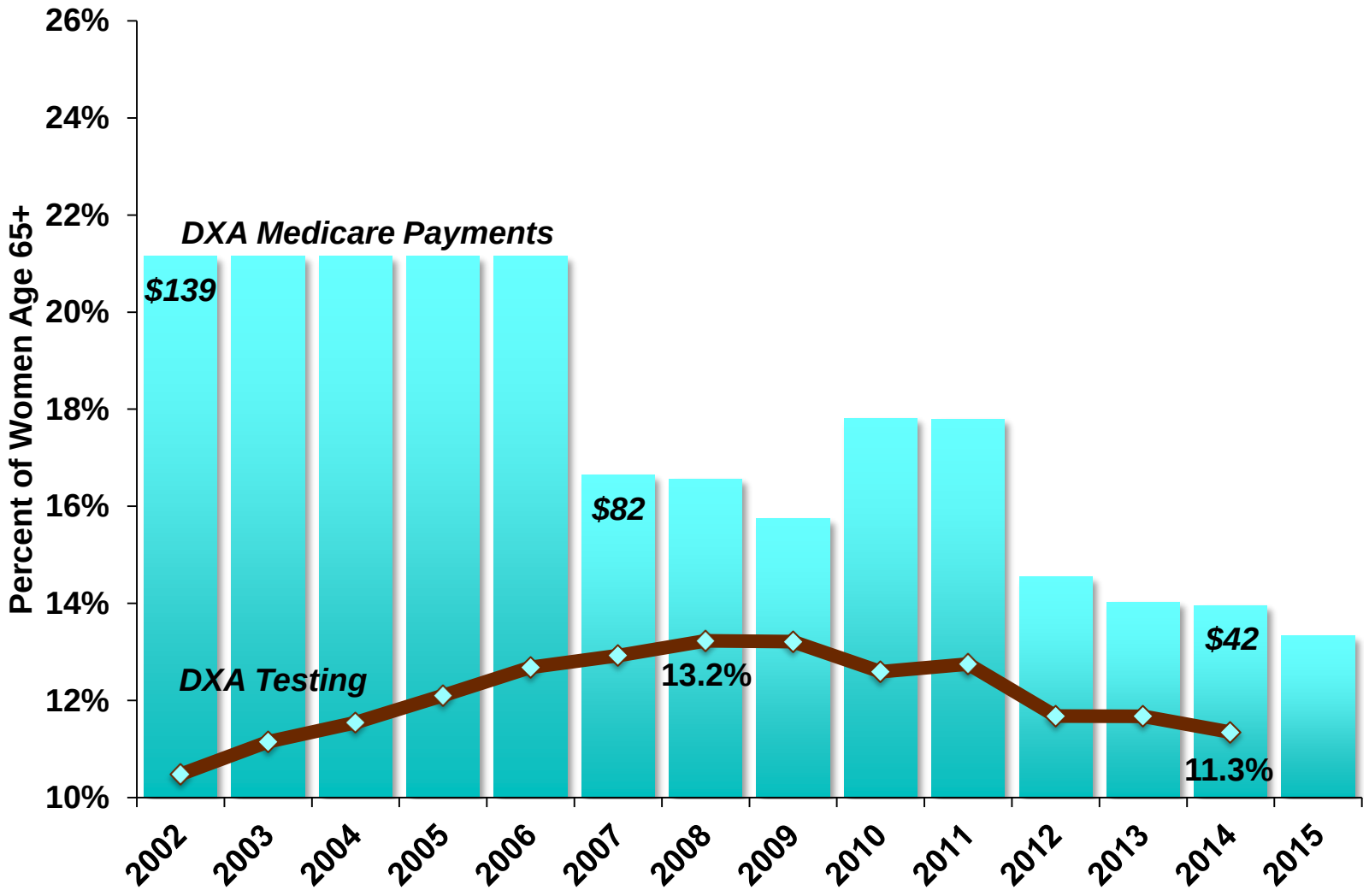
King A B , and Fiorentino D M Health Aff 2011;30:2362-2370

HealthAffairs

Are we at the breaking point?



Lewiecki EM et al. ASBMR Oral Presentation #1077. 2016.



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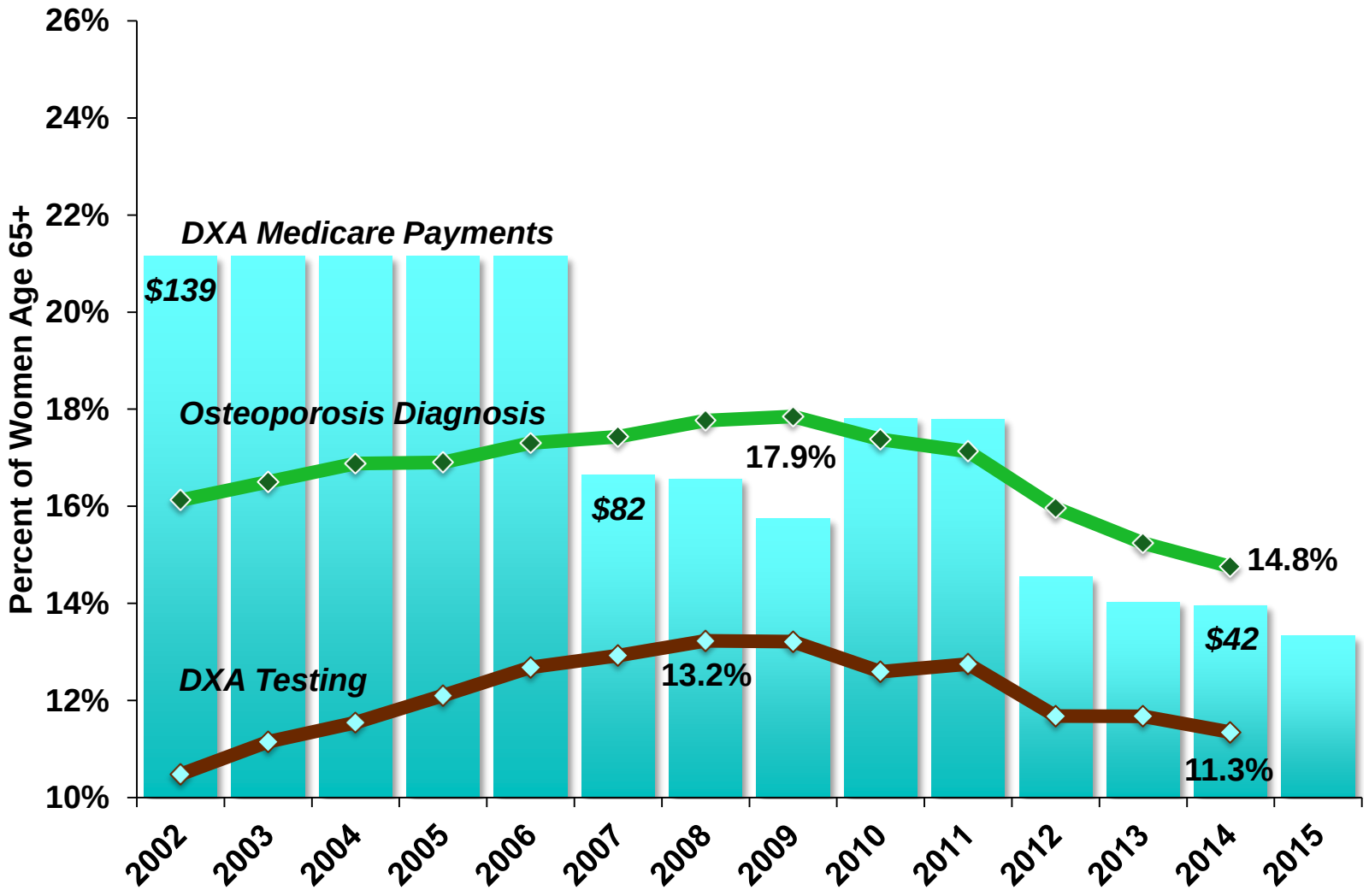

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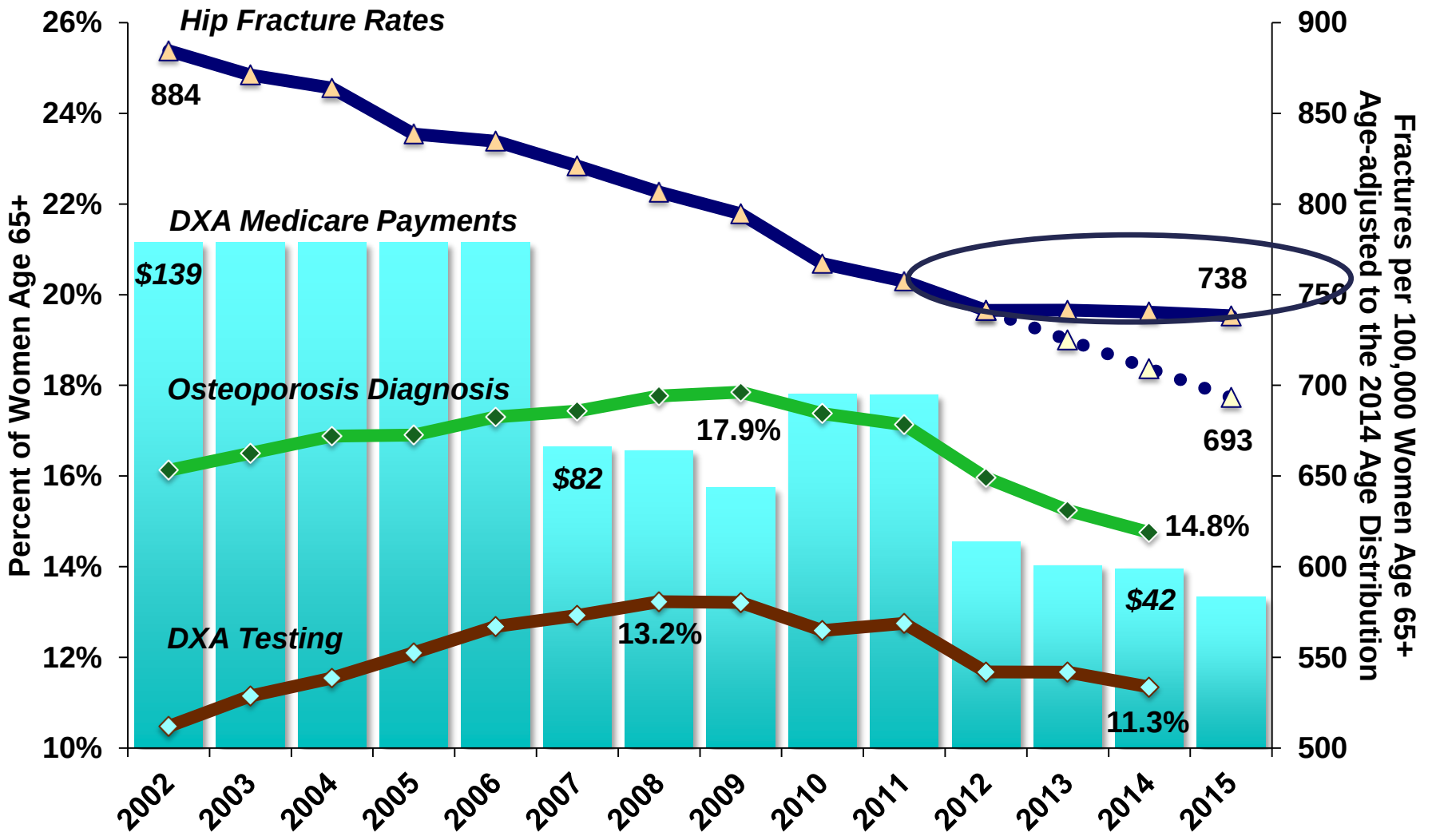
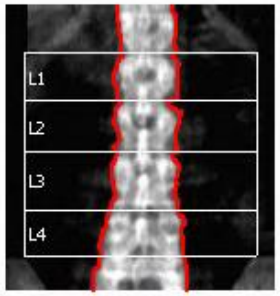
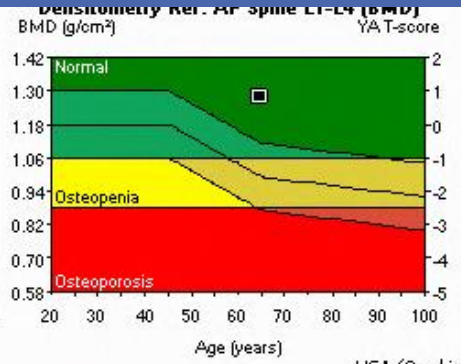


Lewiecki EM et al. ASBMR Oral Presentation #1077. 2016.

65 year old woman: screening study



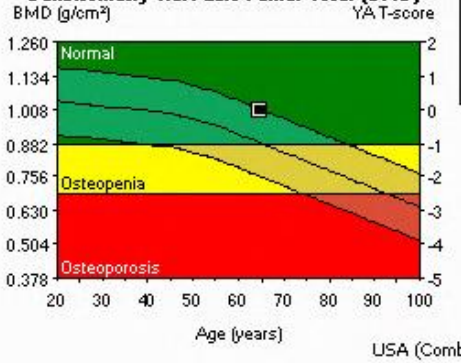


Region	(g/cm²)	(%)	T-score	(%)	Z-score
L1	1.246	110	1.0	132	2.5
L2	1.261	105	0.5	124	2.1
L3	1.346	112	1.2	133	2.8
L4	1.241	103	0.3	122	1.9
L1-L2	1.254	108	0.7	128	2.3
L1-L3	1.289	110	1.0	131	2.5
L1-L4	1.276	108	0.8	128	2.4
L2-L3	1.307	109	0.9	129	2.4
L2-L4	1.284	107	0.7	127	2.3
L3-L4	1.293	108	0.8	128	2.3

Matched for Age, Ethnic
USA (Combined NHANES (ages 20-30) / Lunar (ages 20-40)) AP Spine Reference Population (v112)
Statistically 68% of repeat scans fall within 1SD (± 0.021 g/cm² for AP Spine L1-L4)

Image not for diagnosis

Densitometry Ref: Left Femur Total (BMD)

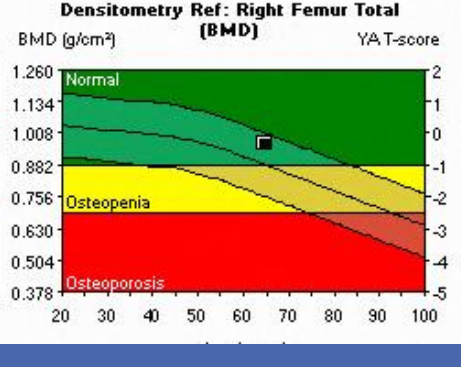


Region	BMD (g/cm²)	Young-Adult (%)	Young-Adult T-score	Age-Matched (%)	Age-Matched Z-score
Neck	0.977	94	-0.4	114	0.8
Troch	0.768	90	-0.7	103	0.2
Total	1.005	100	0.0	114	1.0

Matched for Age, Weight (females 25-100 kg), Ethnic
USA (Combined NHANES (ages 20-30) / Lunar (ages 20-40)) Femur Reference Population (v112)
Statistically 68% of repeat scans fall within 1SD (± 0.019 g/cm² for Left Femur Total)

Image not for diagnosis

Densitometry Ref: Right Femur Total (BMD)



Region	BMD (g/cm²)	Young-Adult (%)	Young-Adult T-score	Age-Matched (%)	Age-Matched Z-score
Neck	0.871	84	-1.2	101	0.1
Troch	0.729	85	-1.1	97	0.2
Total	0.965	96	-0.3	109	0.6

Matched for Age, Weight (females 25-100 kg), Ethnic

How should we decide whether to treat?

- Fracture risk is more than bone mineral density
  - FRAX
  - http://www.shef.ac.uk/FRAX/
  - Developed to integrate risks factors to predict fracture with or without access to DXA machine.

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: 65 Date of Birth: Y: M: D:
2. Sex ○ Male ◉ Female
3. Weight (kg) 59
4. Height (cm) 162.6
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)

GE-Lunar .871 T-score: -1.2

Clear Calculate

BMI: 22.3
The ten year probability of fracture (%)
with BMD

Major osteoporotic	7.7
Hip Fracture	0.7

If you have a TBS value, click here: Adjust with TBS

Print tool and information

Weight Conversion

Pounds → kg

130 Convert

Height Conversion

Inches → cm

64 Convert

04980365
Individuals with fracture risk assessed since 1st June 2011

How should we decide whether to treat?

NOF Guidelines

Treat postmenopausal women or men >50 with:

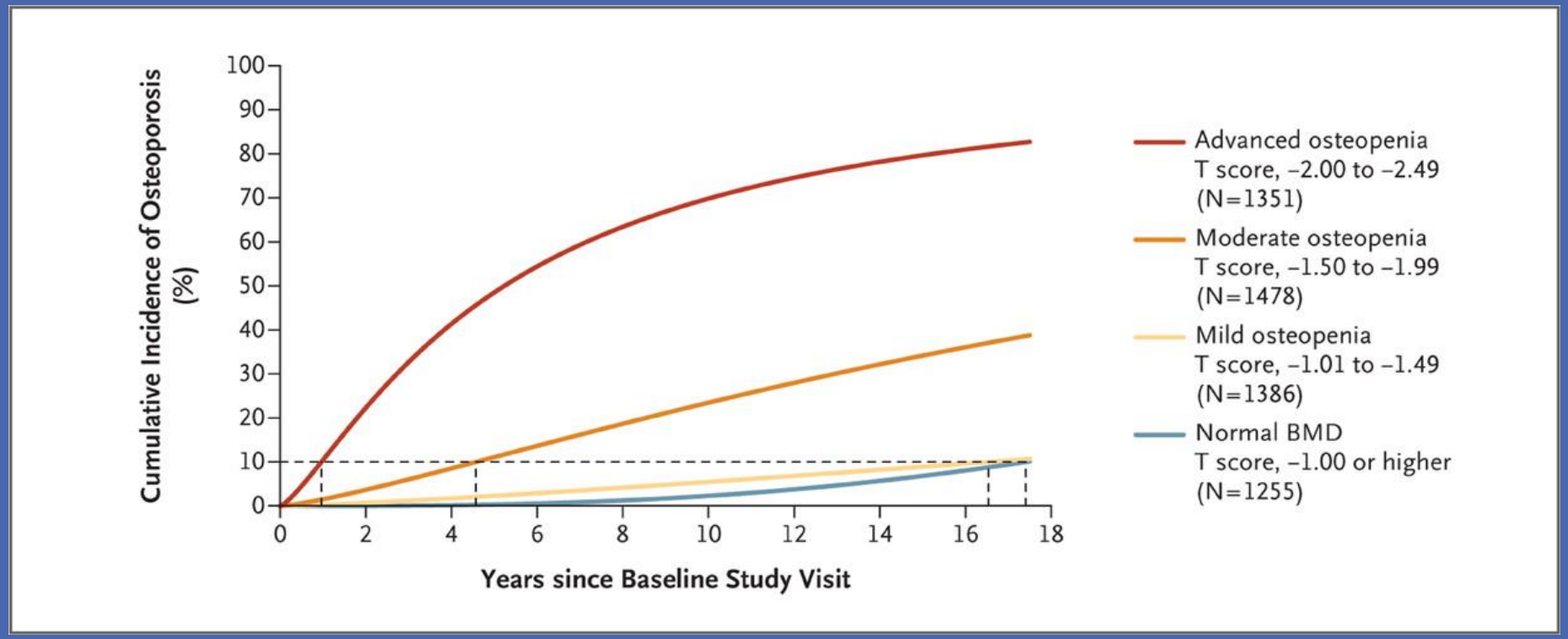
- Hip or vertebral fracture
- T-score of <-2.5 with no other risk factors
- T-score of -1.0 to -2.5 with any of the following:
  - (a) other prior fractures, or
  - (b) secondary cause associated with high risk of fracture, or
  - (c) 10-year fracture risk as assessed by FRAX™ of 3% or more at the hip, 20% or more for major osteoporosis-related fracture (humerus, forearm, hip or clinical vertebral fracture)

Issues with FRAX

- ?Consistency
  - 50 year old woman with low T-score
- Data for treating patients with higher BMD is lacking.
- Weighing of factors (i.e long term glucocorticoids, dose)
- Not all risk factors included: diabetes, other medications
- Hip vs spine

Watts et al. J Clin Densitometry
Watts et al JBMR 2009
Collins G Current Osteoporosis Reports

If we decide not to treat her, when should she be screened again?



Women in this study were older, 67+
Applies to repeat studies, not screening
Everyone who had osteoporosis at baseline was not included

Gourlay ML et al. N Engl J Med 2012;366:225-233.

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Should we treat her with calcium and Vitamin D?

- Mixed data on fracture prevention
- Calcium and Vitamin D are given in all the trials
- Threshold Vitamins
- Too much is not better!

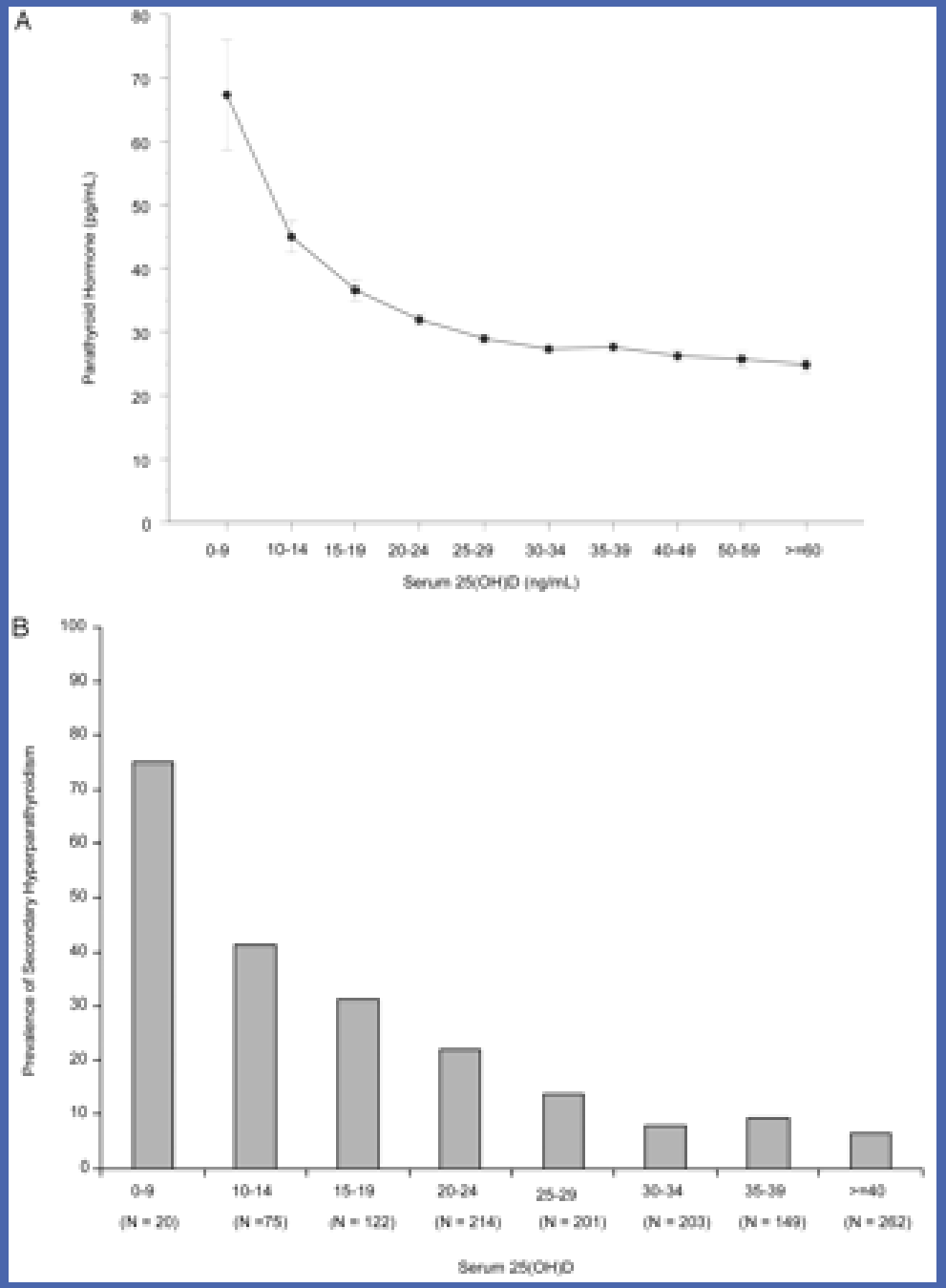
IOM: Calcium and Vitamin D

AGE	Calcium intake	MAX
19-50 M/F	1000	2500
51-70 M	1000	2000
51-70 F	1200	2000
71+	1200	2000

AGE	RDA Vitamin D	Max
19-70 male and female	600 IU	4000 IU
70 +	800 IU	4000 IU

Raised concern for risk for harm at: >2000 mg Ca per day

Endocrine Society guidelines similar but note it may take 1500-2000 to reach a level of 30ng/ml



Where did the target of 30 ng/ml come from?

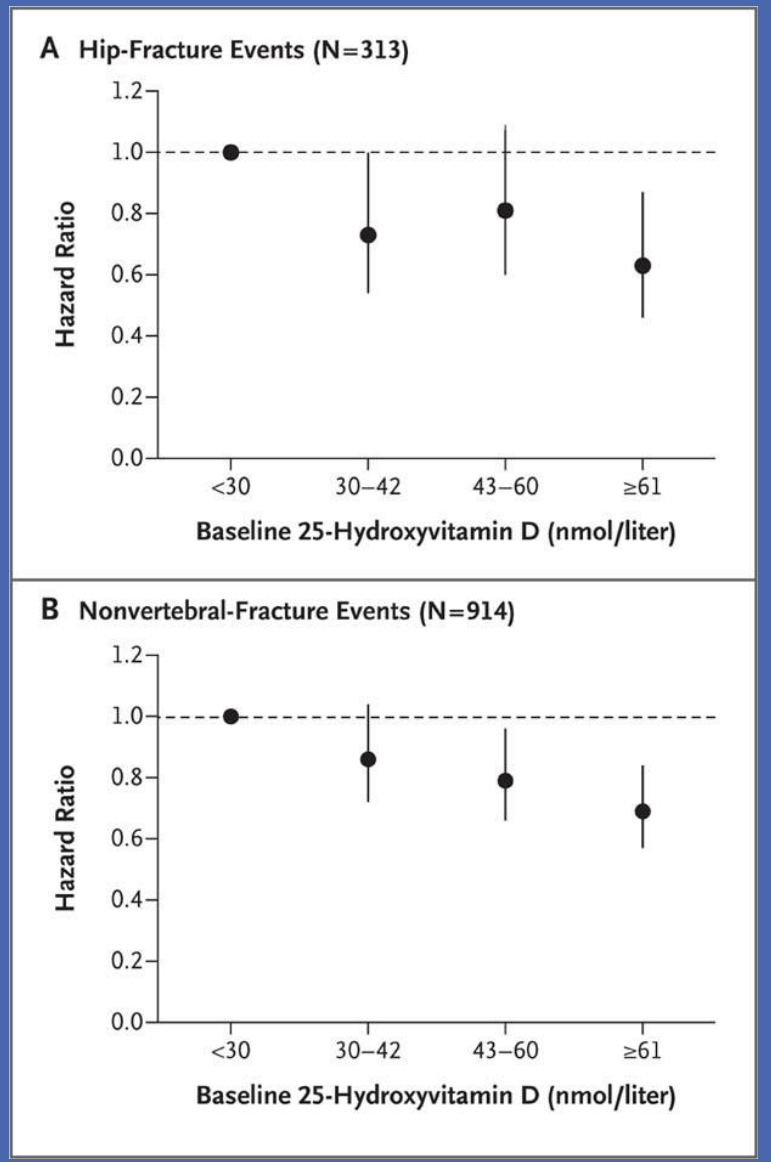
Holick, M. F. et al. J Clin Endocrinol Metab 2005;90:3215-3224

Are there groups that may benefit from D?

Table 2. Incidence of Fracture among 31,022 Participants, According to Vitamin D Treatment Dose and Actual Intake.*

Analysis	No. of Participants	Hip Fracture			Any Nonvertebral Fracture		
		No. of Fractures	Relative Risk (95% CI)	P Value	No. of Fractures	Relative Risk (95% CI)	P Value
Intention-to-treat analysis							
Control	15,495	586	1.00		1948	1.00	
Treatment	15,527	525	0.90 (0.80–1.01)	0.07	1822	0.93 (0.87–0.99)	0.03
Treatment-dose analysis							
Control	15,495	586	1.00		1948	1.00	
≤400 IU/day	10,111	255	0.89 (0.74–1.07)	0.20	1225	0.96 (0.89–1.05)	0.40
>400 IU/day†	5,416	270	0.91 (0.78–1.06)	0.22	597	0.89 (0.80–0.98)	0.02
Actual-intake analysis‡							
Control	15,495	586	1.00		1948	1.00	
0–360 IU/day	3,935	100	1.00 (0.79–1.26)	0.99	425	0.96 (0.86–1.07)	0.44
361–637 IU/day	3,836	110	1.03 (0.83–1.29)	0.78	520	1.01 (0.91–1.12)	0.85
638–791 IU/day	3,790	164	1.01 (0.83–1.23)	0.92	419	0.90 (0.80–1.01)	0.08
792–2000 IU/day	3,966	151	0.70 (0.58–0.86)	<0.001	458	0.86 (0.76–0.96)	0.007
Sensitivity analysis							
Control	15,495	586	1.00		1948	1.00	
0–337 IU/day	3,353	84	1.01 (0.79–1.30)	0.91	465	1.06 (0.95–1.17)	0.32
338–360 IU/day	5,652	114	0.83 (0.66–1.05)	0.11	619	0.89 (0.80–0.98)§	0.02
361–699 IU/day	2,640	180	1.14 (0.93–1.41)	0.21	326	1.05 (0.91–1.22)	0.52
700–2000 IU/day	3,882	147	0.71 (0.58–0.87)	0.001	412	0.81 (0.72–0.91)	<0.001
Internal validation							
0–360 IU/day	18,153	639	1.00		2193	1.00	
361–637 IU/day	4,976	150	1.03 (0.84–1.26)	0.80	681	1.04 (0.95–1.15)	0.37
638–791 IU/day	3,865	168	1.02 (0.84–1.24)	0.83	431	0.92 (0.82–1.03)	0.16
792–2000 IU/day	4,028	154	0.70 (0.58–0.86)	<0.001	465	0.86 (0.77–0.97)	0.01

* All analyses were adjusted for study, age group, sex, and type of dwelling. To limit false positive results and correct for multiplicity, we used a P value of 0.0125 to indicate significance.
† All trials included doses between 700 and 2000 IU per day.
‡ Among 21,241 participants from the eight trials that used vitamin D combined with any dose of calcium supplementation, a benefit was present only at the highest actual-intake level of vitamin D.
§ In the sensitivity analysis for adherence-adjusted dose without supplements outside the study protocol, 511 participants in the Women's Health Initiative trial[17] shifted from the highest actual-intake level (792 to 2000 IU per day) and 1356 shifted from the second-highest actual-intake level (638 to 791 IU per day) to the second-lowest adherence-adjusted intake level (338 to 360 IU per day). See the Supplementary Appendix for additional information.



Bischoff-Ferrari HA et al. N Engl J Med 2012;367:40-49

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Table 3. Subgroup Benefits at the Highest Actual-Intake Level of Vitamin D (792–2000 IU per Day), as Compared with Control Group.*

Subgroup	Treatment Group	Control Group	Hip Fracture				Any Nonvertebral Fracture			
			Treatment Group	Control Group	Relative Risk (95% CI)	P Value	Treatment Group	Control Group	Relative Risk (95% CI)	P Value
	no. of participants		*no. of fractures*				*no. of fractures*			
Age										
All	3966	15,495	151	586	0.70 (0.58–0.86)	<0.001	458	1948	0.86 (0.76–0.96)	0.007
65–74 yr	1018	7,521	13	128	0.72 (0.39–1.31)	0.27	122	900	1.09 (0.90–1.33)	0.39
75–84 yr	2603	5,989	130	332	0.72 (0.58–0.89)	0.003	299	791	0.76 (0.66–0.88)	<0.001
≥85 yr	345	1,985	8	126	0.54 (0.25–1.20)	0.13	37	257	0.87 (0.59–1.30)	0.50
Type of dwelling										
All	3966	15,495	151	586	0.70 (0.58–0.86)	<0.001	458	1948	0.86 (0.76–0.96)	0.007
Community dwelling	2103	10,735	42	253	0.68 (0.48–0.96)	0.03	238	1314	0.95 (0.82–1.10)	0.52
Institution	1863	4,760	109	333	0.70 (0.55–0.89)	0.004	220	634	0.74 (0.62–0.87)	<0.001
Baseline 25-hydroxyvitamin D										
All†	412	2,220	11	177	0.55 (0.29–1.05)	0.07	51	484	0.80 (0.59–1.10)	0.18
<30 nmol/liter	106	517	2	42	0.40 (0.08–1.91)	0.25	7	106	0.56 (0.24–1.34)	0.19
≥30 nmol/liter	306	1,703	9	135	0.60 (0.29–1.22)	0.17	44	378	0.87 (0.62–1.23)	0.43
Additional calcium intake										
All	2580	10,615	123	368	0.71 (0.56–0.88)	0.002	315	1414	0.87 (0.76–1.00)	0.05
<1000 mg	294	10,145	6	359	0.65 (0.25–1.68)	0.38	25	1372	0.62 (0.39–0.97)	0.04
≥1000 mg	2286	470	117	9	0.77 (0.30–1.96)	0.59	290	42	1.19 (0.82–1.74)	0.36

* All analyses were adjusted for study, age group, sex, and type of dwelling. After Bonferroni adjustment, with a P value of less than 0.00625 considered to indicate statistical significance, there were no significant interactions between the highest actual-intake level of vitamin D and the four subgroups.
† Data on baseline 25-hydroxyvitamin D levels were available for a total of 4383 participants in nine trials.

Bischoff-Ferrari HA et al. N Engl J Med 2012;367:40-49

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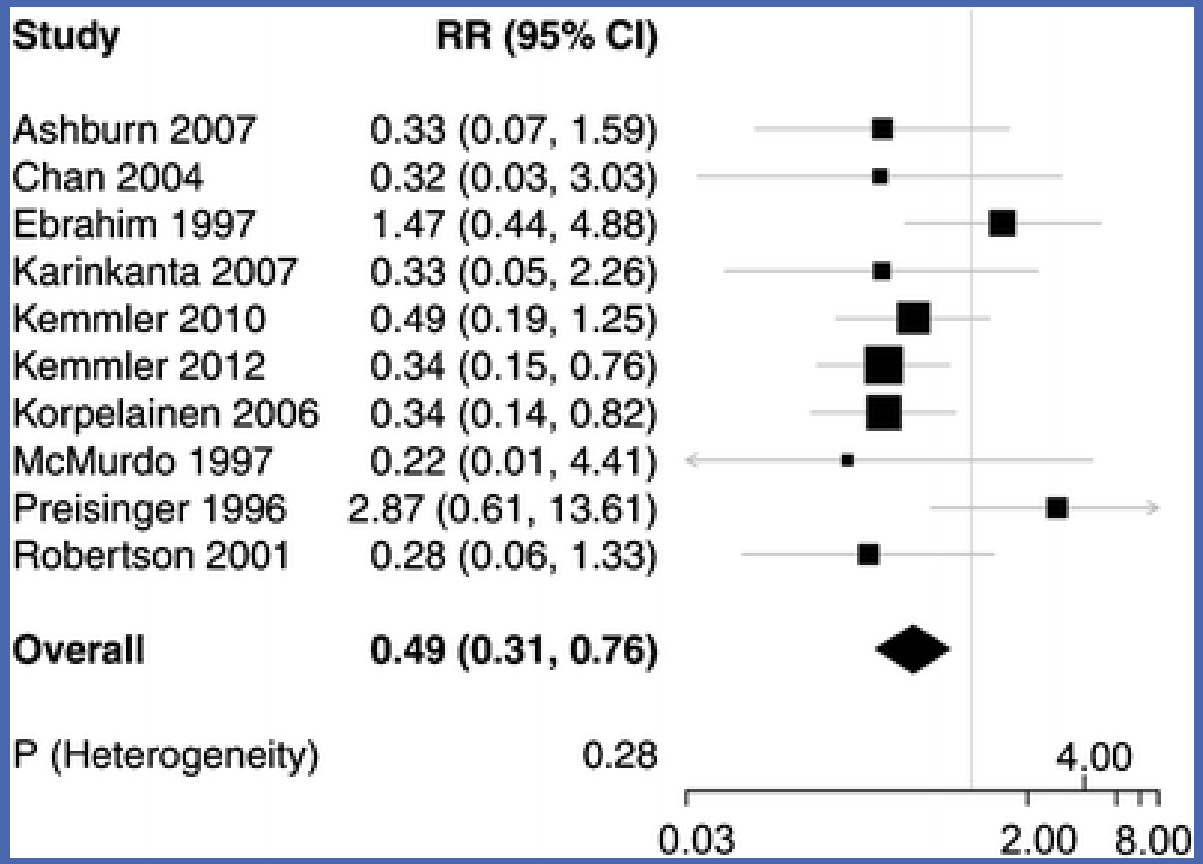
EXERCISE FOR OSTEOPOROSIS

- Weight bearing exercise
  - High impact (running, jumping rope, stairs)
  - Low impact (elliptical, stair stepper, fast walking)
- Muscle strengthening
- Balance exercises
- Posture exercises
- www.nof.org

META-AnALYSIS: FRACTURE REDUCTION WITH EXERCISE



10 controlled exercise trials reported fractures
3 controlled exercise trails reported vertebral fractures

Exercise group 36/754 fractures
Control Group 73/670
Vertebral 19/103 vs 31/102

Kemmler Osteoporosis International 2013

Conclusion from Case 1

- All women ages 65 and up should be screened for osteoporosis with bone density
- Patients within other groups should be reviewed for risk factors
- FRAX can be a useful tool to help risk stratify patients whose bone density is in the osteopenia/low bone mass category
- Calcium, Vitamin D and weight bearing exercise should be a part of bone health, but their role in fracture prevention remains unclear, particularly in the younger, community dwelling population.

Question #2

A 74 year old man falls on ice and breaks his hip. Which of the following is true:

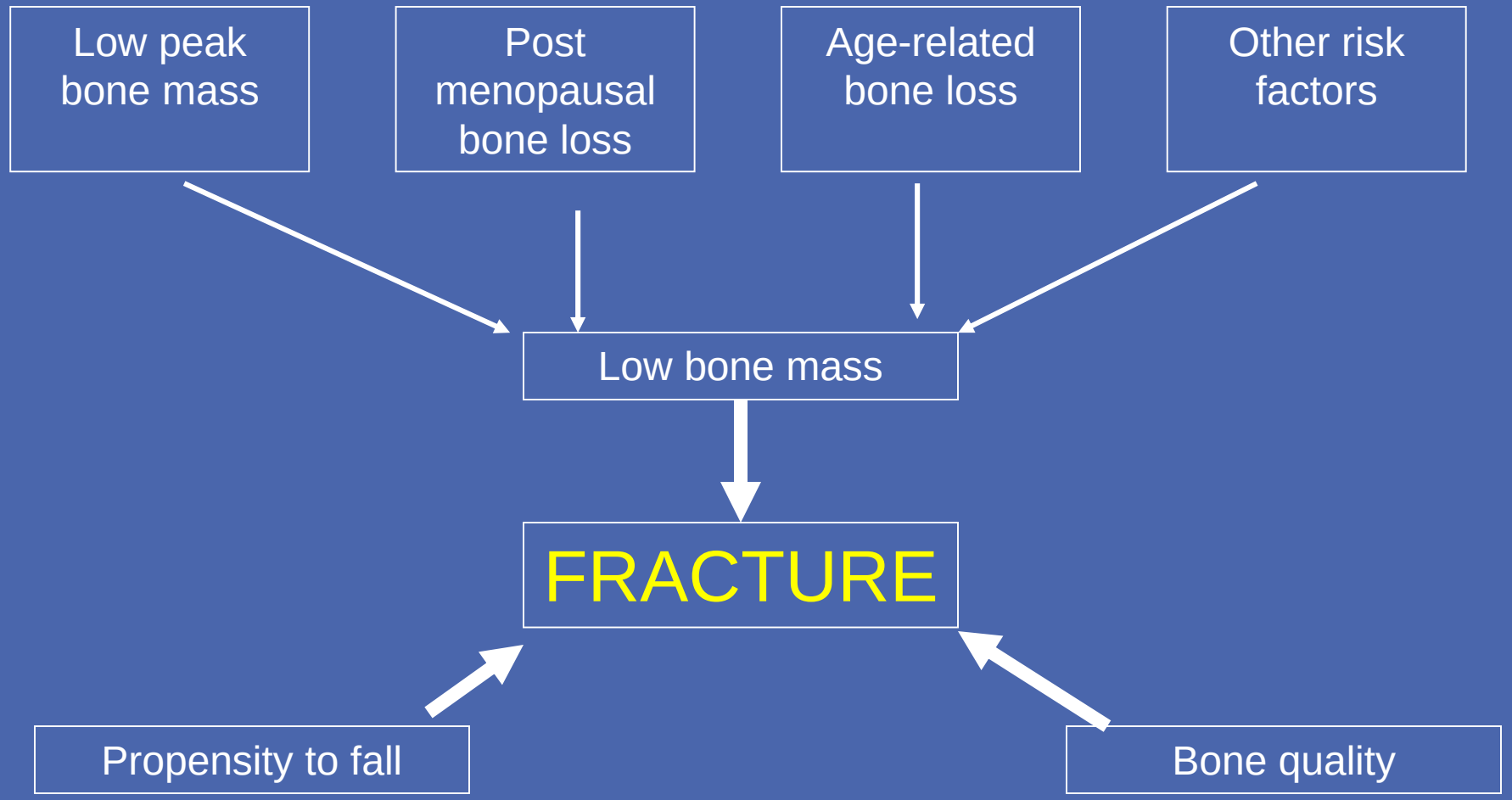
A) His chance of dying in the next year is about 10%

B) The likelihood of finding a secondary cause of osteoporosis is lower than if he were female

C) This is an osteoporotic fracture

D) Bisphosphonate therapy is unlikely to help prevent future fracture

Pathogenesis of Fracture



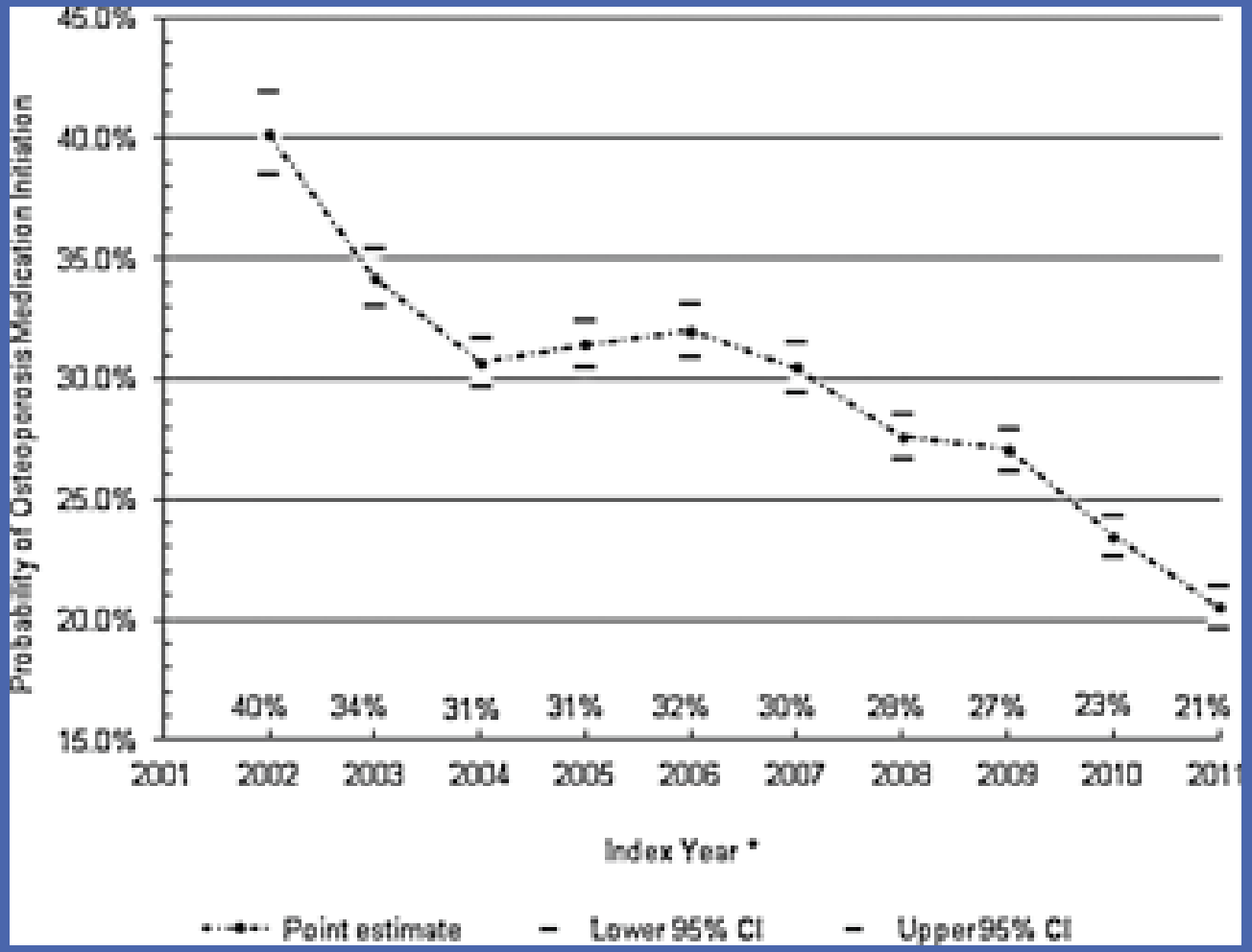
Adapted from Melton LJ and Riggs BL. Osteoporosis: Etiology, Diagnosis and Management, Raven Press 1988, pp155-179.

Osteoporotic Fractures: Why Worry?

- 2 million fractures occur in the US each year.
- Approximately 50% of women over 50 will experience an osteoporotic fracture.
- The lifetime risk of hip fracture is 1 in 6 for women.
- The mortality after hip fracture is 20%
- Only 40 % of patients with hip fracture fully regain their pre-fracture level of independence .
- Vertebral fractures predict future fractures (5 fold vertebral and 2-3 fold hip)

Adapted from IOF Slide, www.nof.org

Medication use is trending DOWN (2002-2011)



Journal of Bone and Mineral Research
Volume 29, Issue 9, pages 1929-1937, 20 AUG 2014 DOI: 10.1002/jbmr.2202
http://onlinelibrary.wiley.com/doi/10.1002/jbmr.2202/full#jbmr2202-fig-0002

The JAMA Network

Undertreatment of Osteoporosis in Men With Hip Fracture

Arch Intern Med. 2002;162(19):2217-2222. doi:10.1001/archinte.162.19.2217

Table 2. Mortality With Time After Fracture*

Years Since Fracture	Men	Women
1	7/17 (41.2)	13/53 (24.5)
2	13/26 (50.0)	11/47 (23.4)
3	15/28 (53.6)	28/66 (42.4)
4	12/17 (70.6)	18/33 (54.5)
5	17/22 (77.3)	35/54 (64.8)

*Data are given as number of deceased divided by total number of fracture events (percentage). Calculated by chronologic year of study. Overall mortality was 58% for men and 42% for women ($P = .004$).

Question #3

A 73 year old woman is found to have osteoporosis on a screening DXA. She is worried about treatments due to what she has read on line. Help characterize her risks and benefits

A) Her risk of atypical femoral fracture is 1% over 5 years of bisphosphonate therapy

B) Flu like reactions can be seen with IV bisphosphonate therapy

C) If she needs a tooth extracted, markers of bone turnover can help gauge her risk for ONJ

D) She can reduce her risk of hip fracture by about 10% with oral bisphosphonate therapy

FDA Approved Osteoporosis Therapies

Drug	Class	Vertebral fracture	Hip fracture	Non vertebral	Cost
Raloxifene	antiresorptive	+			$
Alendronate	antiresorptive	+	+	+	generic
Risedronate	antiresorptive	+	+	+	$
Ibandronate	antiresorptive	+			$
Zoledronate	antiresorptive	+	+	+	$$$
Denosumab	antiresorptive	+	+	+	$$$$
Teriparatide	anabolic	+		+	$$$$$
Abaloparatide	anabolic	+		+	$$$$$

" I have heard there those medications actually cause MORE fractures…"

"Those just make you keep old brittle bone"

"Oh no, I am not taking that stuff—it rots your teeth"

Bisphosphonates: Remember the good!

	Alendronate	Risedronate	Ibandronate
Vertebral Fractures Reduction vs placebo	45%	39%	48%
Non Vertebral Fractures	23%	20%	25%
Hip Fractures	53%	26%	None published

- ? Decrease breast cancer risk (observational)
- Skeletal metastases
- Decreased mortality?

Silverman Osteoporosis International 2012, Center JCEM 2011

Hip Fracture Treatment with IV Zoledronic Acid

Table 2. Rates of Fracture and Death in the Study Groups.*

Variable	Placebo	Zoledronic Acid	Hazard Ratio (95% CI)	P Value
Fracture — no. (cumulative %)				
Any	139 (13.9)	92 (8.6)	0.65 (0.50–0.84)	0.001
Nonvertebral	107 (10.7)	79 (7.6)	0.73 (0.55–0.98)	0.03
Hip	33 (3.5)	23 (2.0)	0.70 (0.41–1.19)	0.18
Vertebral	39 (3.8)	21 (1.7)	0.54 (0.32–0.92)	0.02
Death — no. (%)	141 (13.3)	101 (9.6)	0.72 (0.56–0.93)	0.01

* Rates of clinical fracture were calculated by Kaplan–Meier methods at 24 months and therefore are not simple percentages. There were 1062 patients in the placebo group, and 1065 in the zoledronic acid group. Because of variable follow-up, the number and percentage of patients who died are provided on the basis of 1057 patients in the placebo group and 1054 patients in the zoledronic acid group in the safety population.

included men

Lyles K et al. N Engl J Med 2007;357:1799-1809

The NEW ENGLAND JOURNAL of MEDICINE

Side effect concerns: Osteonecrosis of the Jaw

- Exposed necrotic bone in maxillofacial region that fails to heal in 6-8 weeks
- Usually follows an extraction or other invasive procedure
- Events are rare:
  - Incidence/100,000 patient years (ASBMR Task Force)
    - Oral bisphosphonates: 1.04-69
    - IV bisphosphonates: 0-90
    - Denosumab: 0-30.2
    - Oncology: 0-12,200

Shannon et al J American Geriatrics Society 2011, Zhang et al Rheum Dis Clin N Am 2011, ASBMR Task Force Khan et al JBMR 2015.

Side effect concerns: Osteonecrosis of the Jaw

- Other risk factors:
  - Glucocorticoids, poor oral hygiene, ill fitting dentures, diabetes
- Serum CTX and other bone turnover markers do not predict ONJ
- Dental exam and other work prior to treatment initiation when possible
- Communications with dental colleagues is key

American Dental Association Guidelines November 2011, ASBMR Task Force Khan et al JBMR 2015

Concerns for side effects: atypical fractures

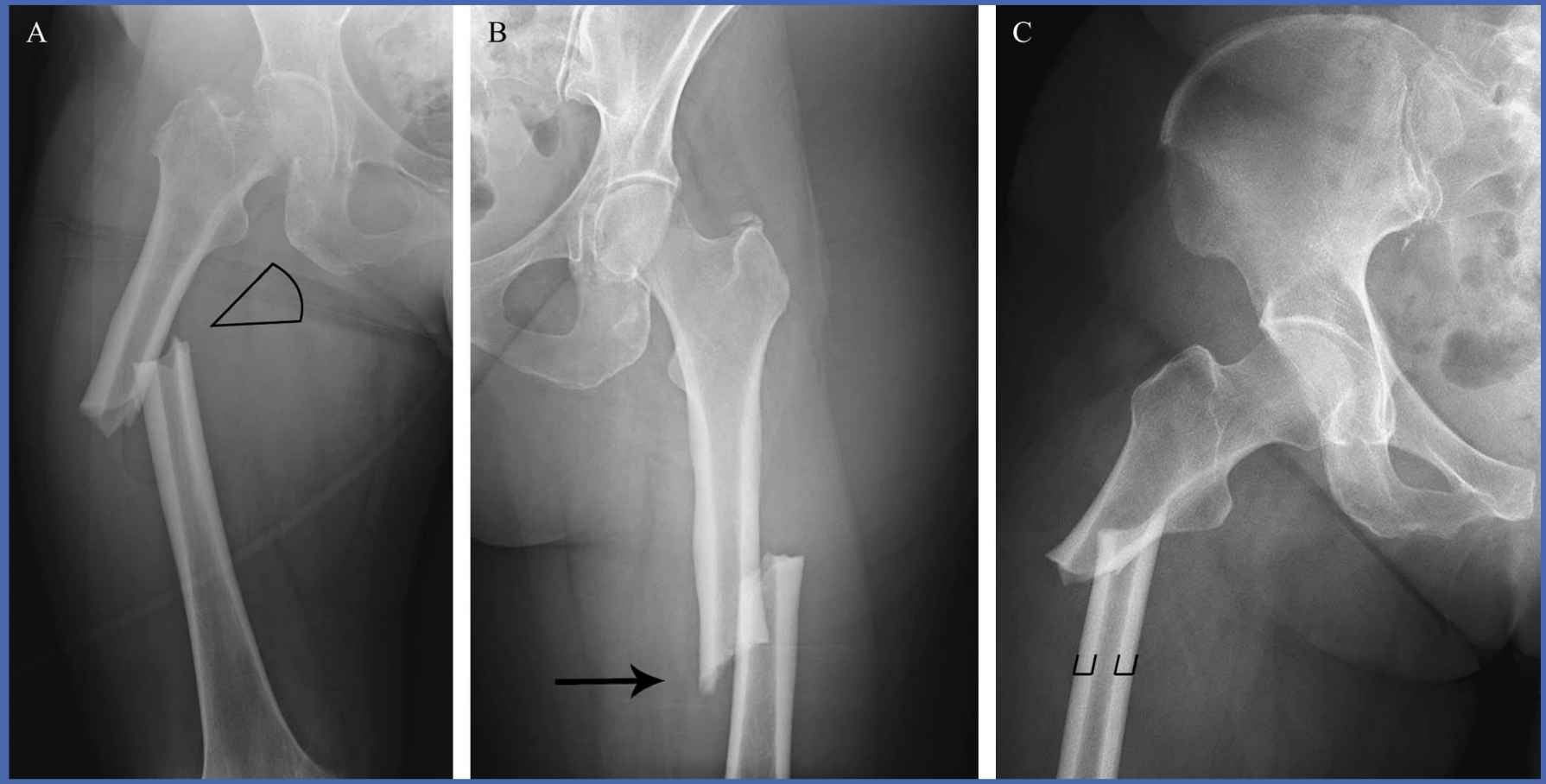


FIGURE 1. Representative radiographs of femoral shaft fractures sustained from minimal trauma in patients taking alendronate. Although each radiograph demonstrates the pattern in its entirety, we have highlighted the following features. A, Fracture pattern pictured with an arch measuring 30 degrees to highlight transverse nature. B, The arrow pointing out the unicortical beak C, Hypertrophied cortices outlined.

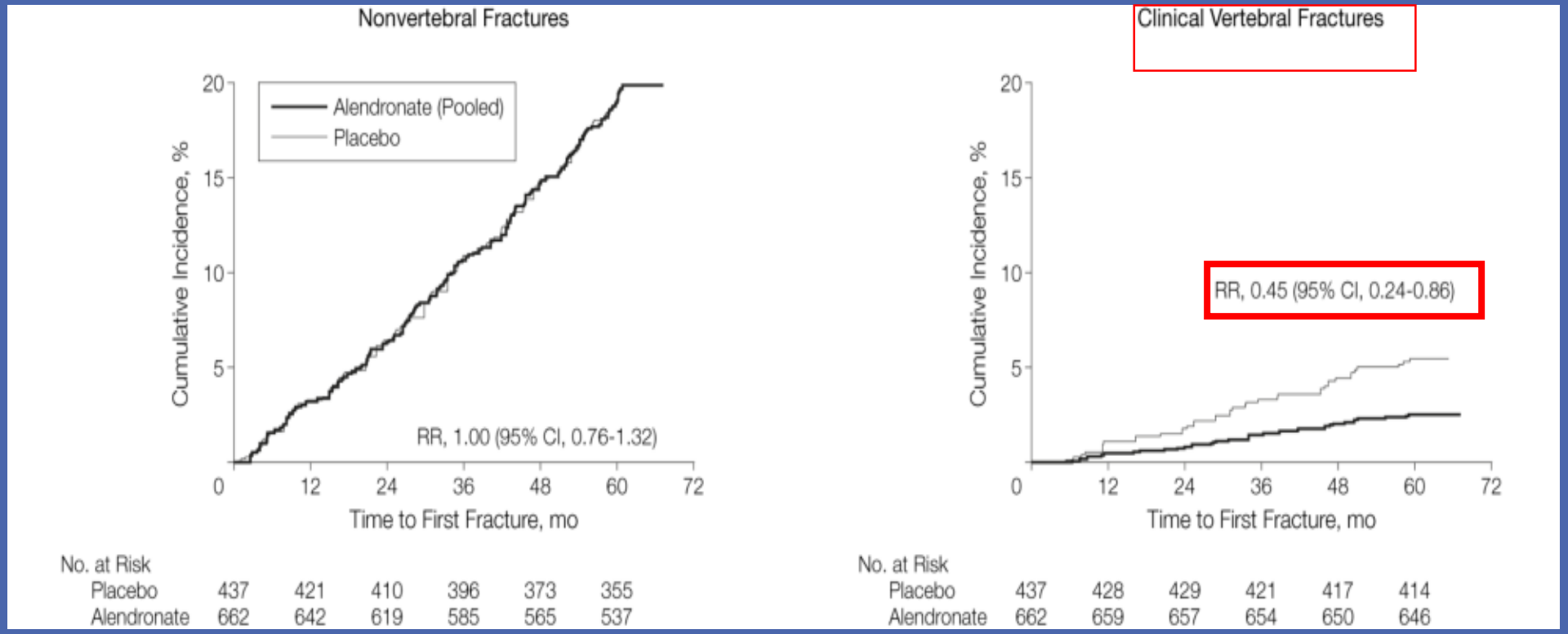
Neviaser et al. J Orthop Trauma 2008

Side effect concerns: atypical femoral fractures

- Prevalence remains unclear
- 3.2-50 cases/100,000 patient years
- Risks goes up with longer use and declines when stopped
- 1.8/100,000/year with 2 year exposure
- 113/100,000/year with 8 to 9.9 year exposure
- Weigh patients individual risk of typical fracture vs risk of side effects.
- Investigate complaints of thigh pain in patients on bisphosphonates.
- Consider risks and benefits of long term treatment

Abrahamsen Bone 2012, ASBMR Task Force JBMR 2010, JBMR January 2016

How long should we treat with bisphosphonates?



Black, D. M. et al. JAMA 2006;296:2927-2938.

JAMA

Who gets a drug holiday: look at risks

Risk of Clinical Vertebral Fracture and Number Needed to Treat for 5 Years to Prevent One Clinical Vertebral Fracture in the Fracture Intervention Trial Long-Term Extension (FLEX) Study.*

Femoral Neck BMD T Score at Start of Extension†	5-Yr Risk of Clinical Vertebral Fracture		Risk Difference (95% CI)	Number Needed to Treat
	Placebo Group	Alendronate Group‡		
	no./total no. (%)			
All women in study				
All BMD T scores	23/437 (5.5)	16/662 (2.5)	2.9 (0.3–5.4)	34
Less than or equal to –2.5	11/132 (9.3)	9/190 (4.5)	4.8 (0.8–9.2)	21
Greater than –2.5 and less than or equal to –2.0	9/126 (5.8)	3/185 (2.8)	3.0 (0.3–6.7)	33
Greater than –2.0	3/179 (2.3)	4/282 (1.1)	1.2 (0.2–2.8)	81
Women with no prevalent vertebral fracture at start of FLEX study				
Less than or equal to –2.5	6/75 (8.0)	4/109 (3.8)	4.2 (0.6–9.1)	24
Greater than –2.5 and less than or equal to –2.0	3/82 (3.0)	1/121 (1.4)	1.6 (0.2–5.0)	63
Greater than –2.0	2/130 (1.8)	2/203 (0.9)	1.0 (0.1–2.6)	102
Women with prevalent vertebral fracture at start of FLEX study				
Less than or equal to –2.5	5/57 (11.1)	5/81 (5.3)	5.8 (0.8–12.1)	17
Greater than –2.5 and less than or equal to –2.0	6/44 (11.1)	2/64 (5.3)	5.8 (0.8–13.6)	17
Greater than –2.0	1/49 (3.7)	2/79 (1.7)	2.0 (0.3–5.6)	51

Black DM et al. N Engl J Med 2012.

How long to continue treatment?

- Editorial in same issue (NEJM 2012) suggests
  - Patients with femoral neck T-score < -2.5 and vertebral fractures and <-2.0"may benefit from more than 3-5 years of treatment"
  - Those with T score above –2.0 are "unlikely to benefit from continued treatment."
- This cannot be extrapolated to other medications.
- Osteoporosis is a chronic long term disease, like diabetes or hypertension.
- The reason some medications can be stopped is that they are still releasing into the bone, not because the patient is cured.

Conclusions from Cases 2 and 3

- There are rare but serious side effects of therapy that need to be discussed, but the benefits of treatment in high risk patients generally outweigh the risks
- Communication with patients and colleagues is key
- The concept of a "drug holiday" only applies to bisphosphonates

Question #4

- A 68 year old man is putting a pan away in the cupboard and notes a sharp pain. He goes to the emergency room and is found to have a T12 compression fracture. Which of the following therapies has NOT been shown to prevent future spine fracture?

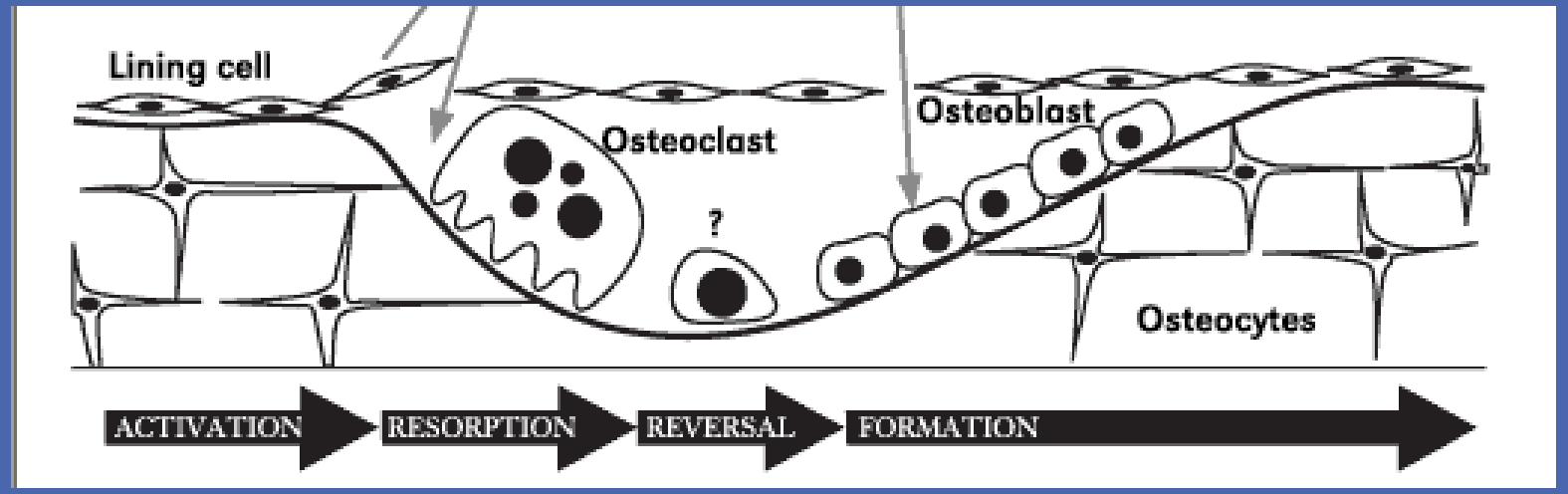
A) Denosumab

B) IV zoledronic acid

C) Testosterone

D) Teriparatide

What are the other options?



Bone resorption | **Bone formation**

Antiresorptive therapy
Bisphosphonates
RANK-L inhibitor
(SERMs/Estrogen)

Anabolic therapy
Teriparatide
Abaloparatide

www.surgeongeneral.gov

Currently FDA Approved therapies

Drug	Class	Vertebral fracture	Hip fracture	Non vertebral	Cost
Raloxifene	antiresorptive	+			$
Alendronate	antiresorptive	+	+	+	generic
Risedronate	antiresorptive	+	+	+	$
Ibandronate	antiresorptive	+			$
Zoledronate	antiresorptive	+	+	+	$$$
Denosumab	antiresorptive	+	+	+	$$$$
Teriparatide	anabolic	+		+	$$$$$
Abaloparatide	anabolic	+		+	$$$$$

	Given how	Advantages	Disadvantages	Cautions
Oral bisphosphonates	Oral daily, weekly or monthly	Widely available, low cost	Side effects: esophagitis, MSK sx	Rare: ONJ, atypical fractures CrCl
IV bisphosphonates	IV once every 3 months or once every 12	Once yearly Avoids oral side effects	Side effects: acute phase rxn MSK sx	Rare: ONJ, atypical fractures Cr Cl
Denosumab	Subcut q6 months	No renal adjustment	Side effects: skin reaction, hypocalcemia	Rare: ONJ, atypical fx
Teriparatide	Subcut daily	Anabolic action, in GIO advantages for vs spine vs alendronate	Nausea, leg cramps, increased calcium	Avoid if RF for osteosarcoma: XRT, unfused epiphyses
Abaloparatide	Subcut daily	Anabolic action ? Less hypercalcemia	Nausea, leg cramps, increased calcium	Avoid with RF for osteosarcoma:

Guidelines create confusion

ENDOCRINE SOCIETY

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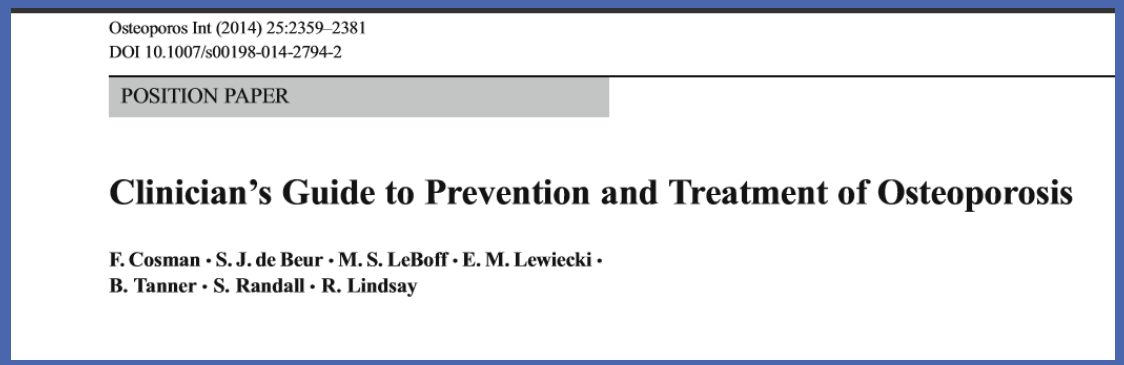

Osteoporos Int (2014) 25:2359–2381
DOI 10.1007/s00198-014-2794-2

POSITION PAPER

Clinician's Guide to Prevention and Treatment of Osteoporosis

F. Cosman · S. J. de Beur · M. S. LeBoff · E. M. Lewiecki ·
B. Tanner · S. Randall · R. Lindsay

NATIONAL OSTEOPOROSIS FOUNDATION

AACE

The American Association of Clinical Endocrinologists
The Voice of Clinical Endocrinology ® Founded in 1991

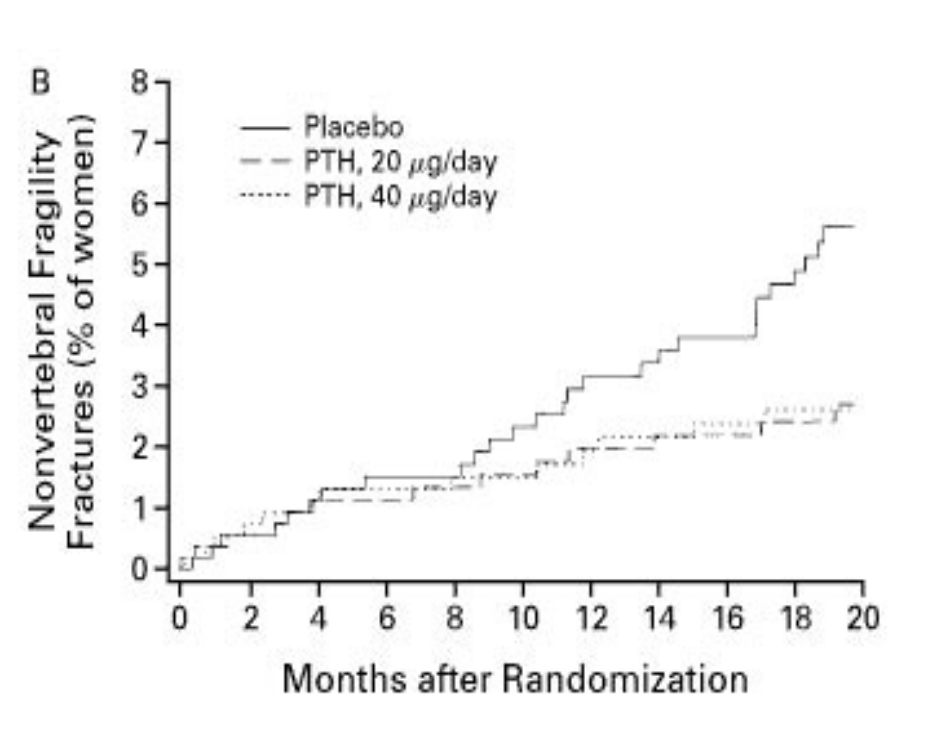
GUIDELINES CAN CREATE CONFUSION

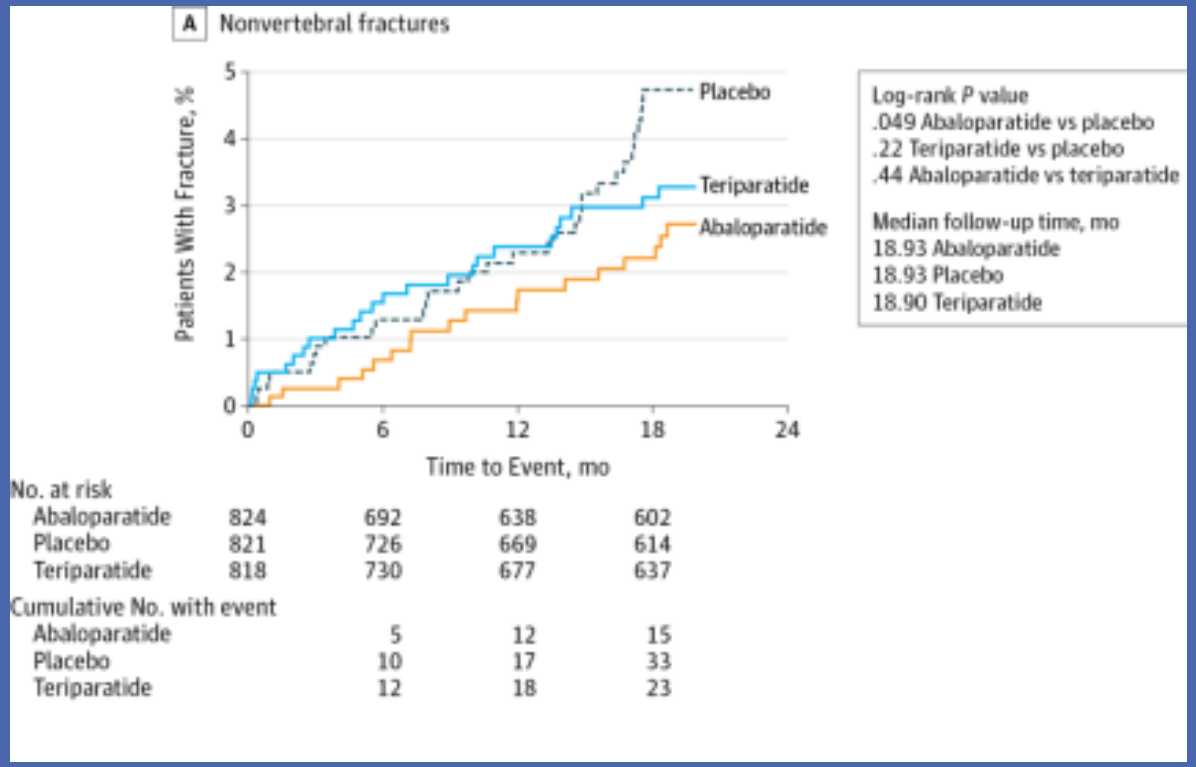
Recommendation 1: *ACP recommends that clinicians offer pharmacologic treatment with alendronate, risedronate, zoledronic acid, or denosumab to reduce the risk for hip and vertebral fractures in women who have known osteoporosis. (Grade: strong recommendation; high-quality evidence)*

Recommendation 2: *ACP recommends that clinicians treat osteoporotic women with pharmacologic therapy for 5 years. (Grade: weak recommendation; low-quality evidence)*

ACP Guidelines 2017

Abaloparatide and teripratide fracture data

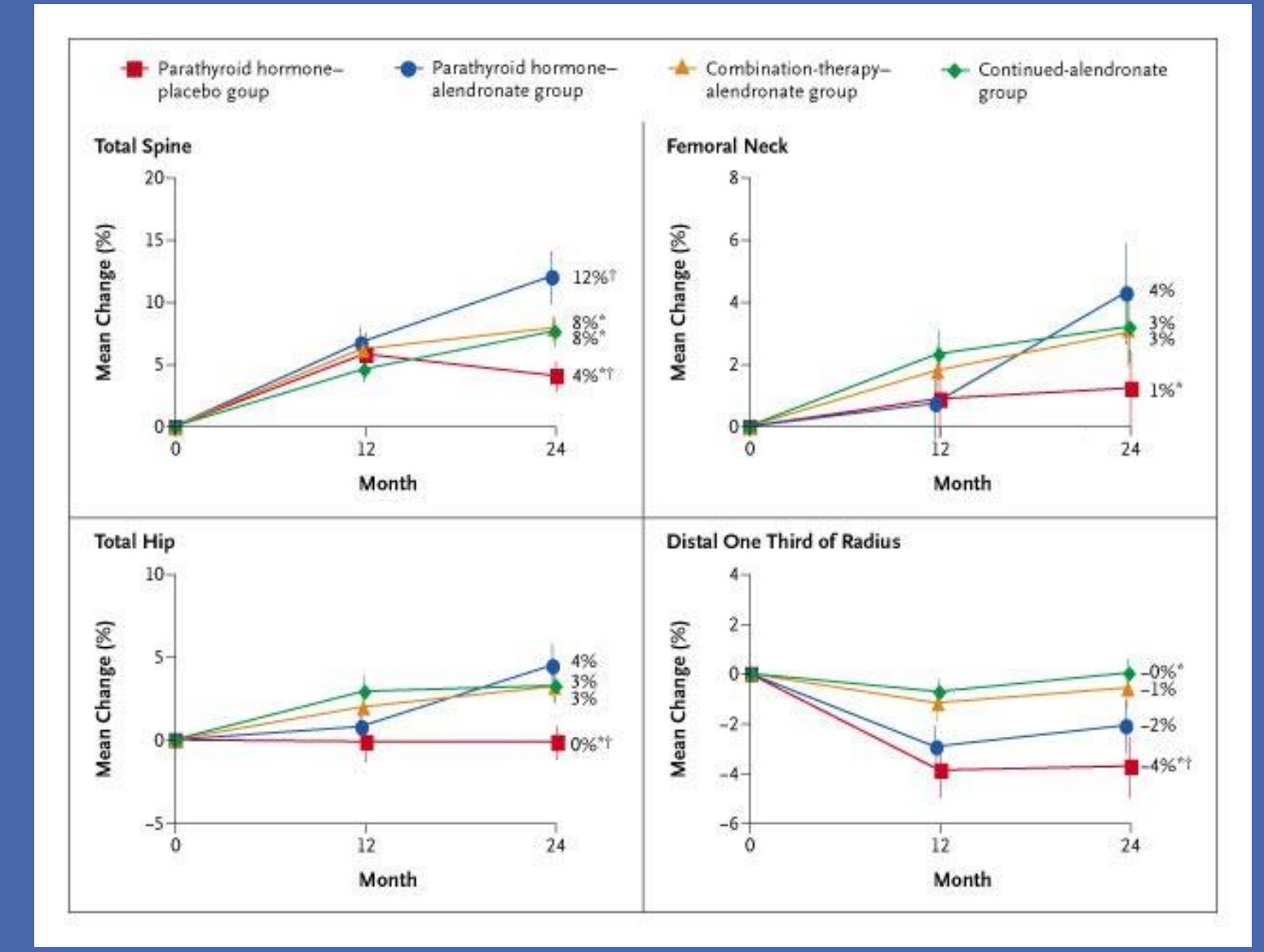




Neer RM et al. N Engl J Med 2001;344:1434-1441.

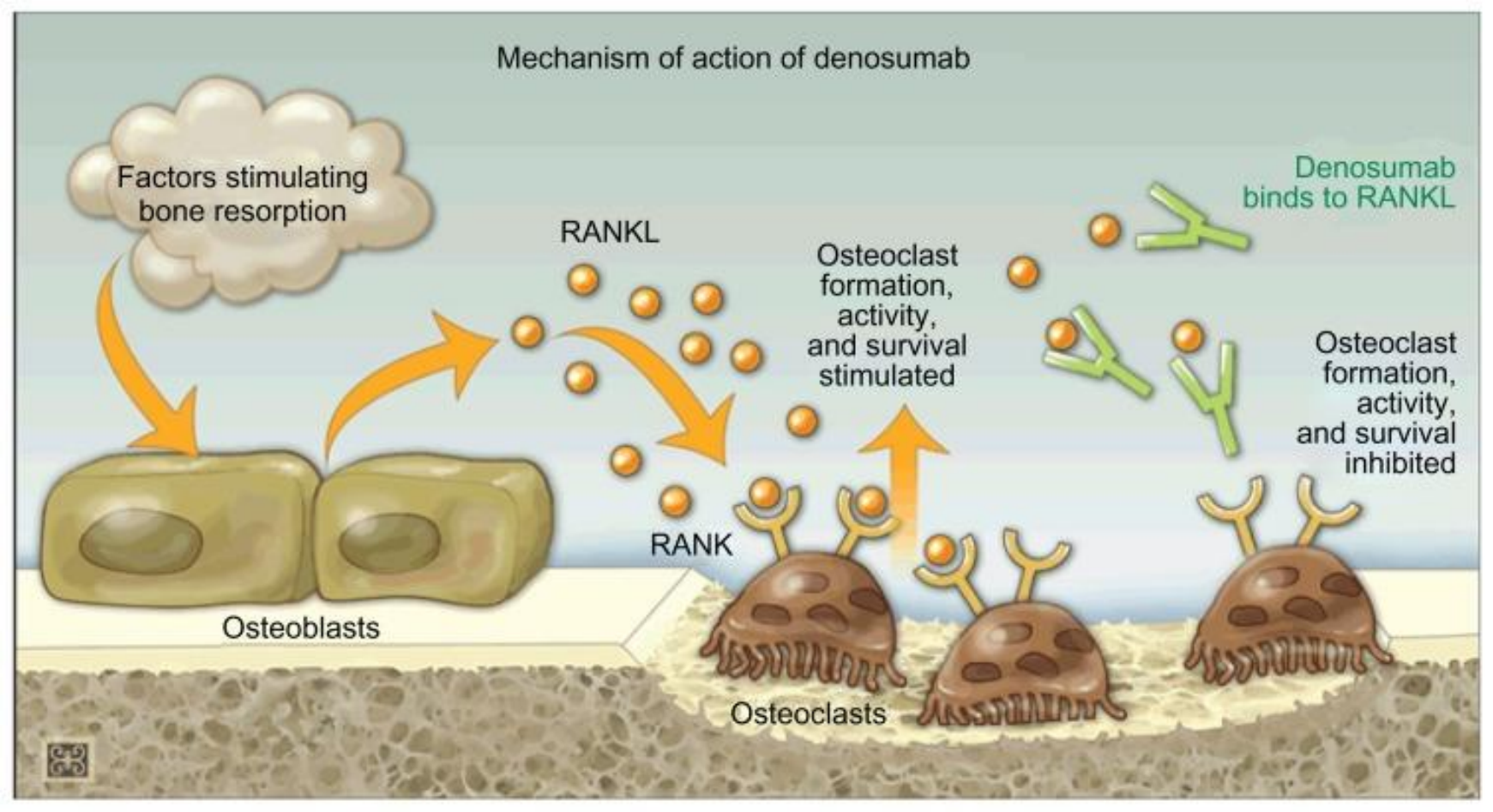
Miller et al JAMA 2016

After 2 years of PTH, then what?



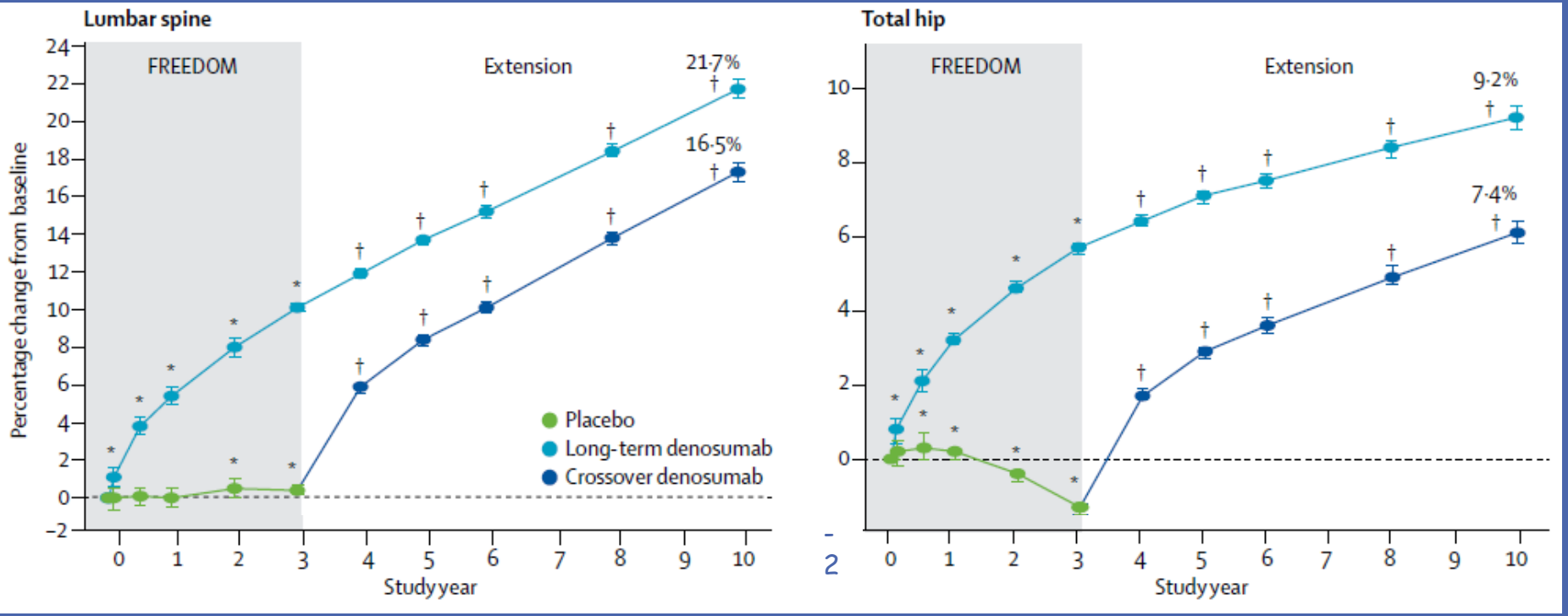
Black et al. NEJM 2005

Denosumab



Paller, CJ et al Clinical Interventions in Aging

Denosumab - FREEDOM Trial (extension)

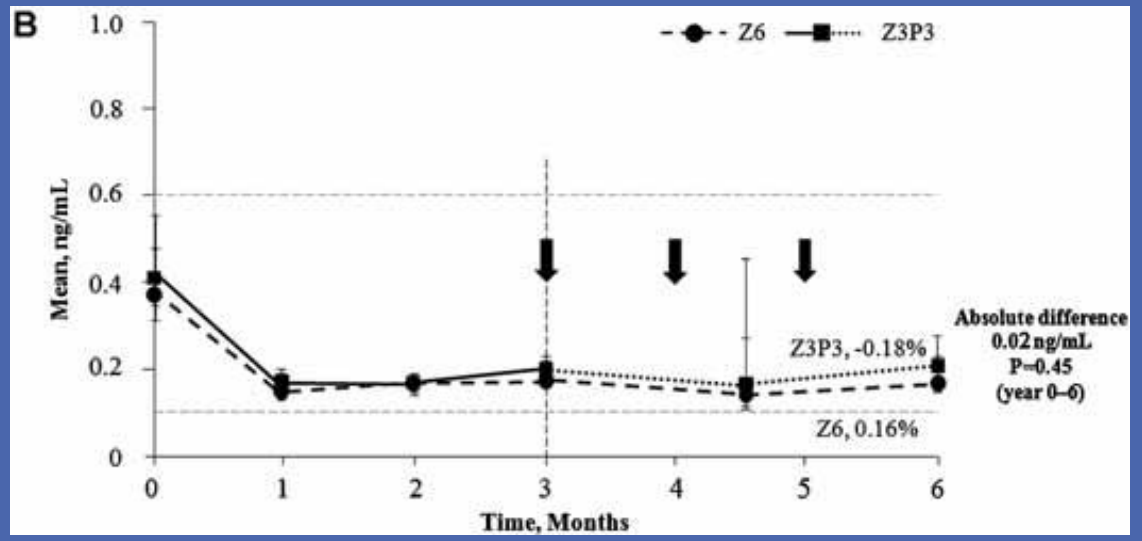


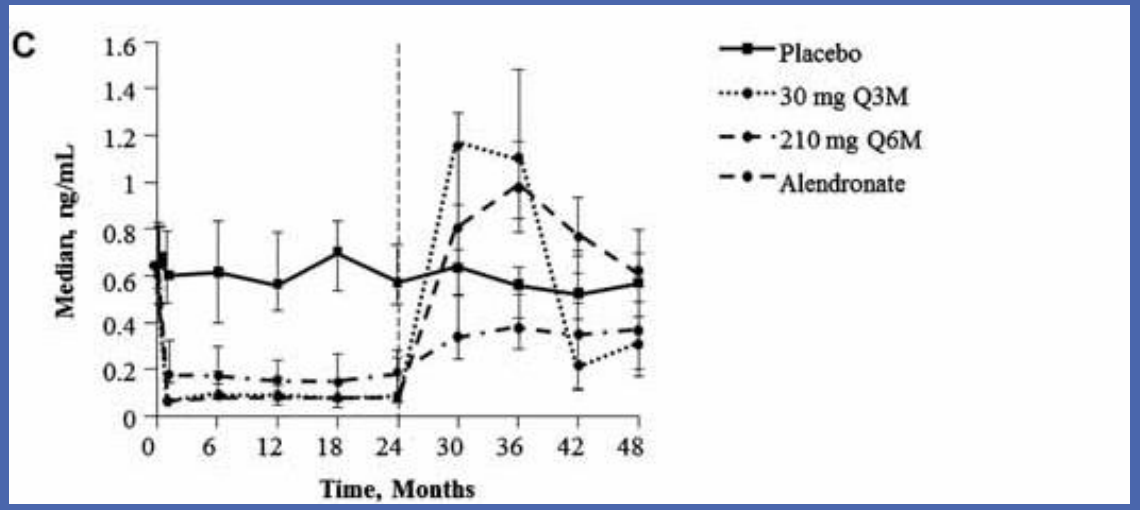
Bone, HG et al Lancet 2017.

Osteoporosis medications: not all the same

How long to treat depends on:

- Patient risk
- Medication type





Conclusions

- There are many options for osteoporosis treatment
- Often the highest risk patients are not being treated
- There are a variety of agents to treat osteoporosis—we must understand their pharmacology and the pros and cons of each

Thank you for your attention