Understanding Osteoporosis: What's New?

Perspectives from a PCP Bone Head

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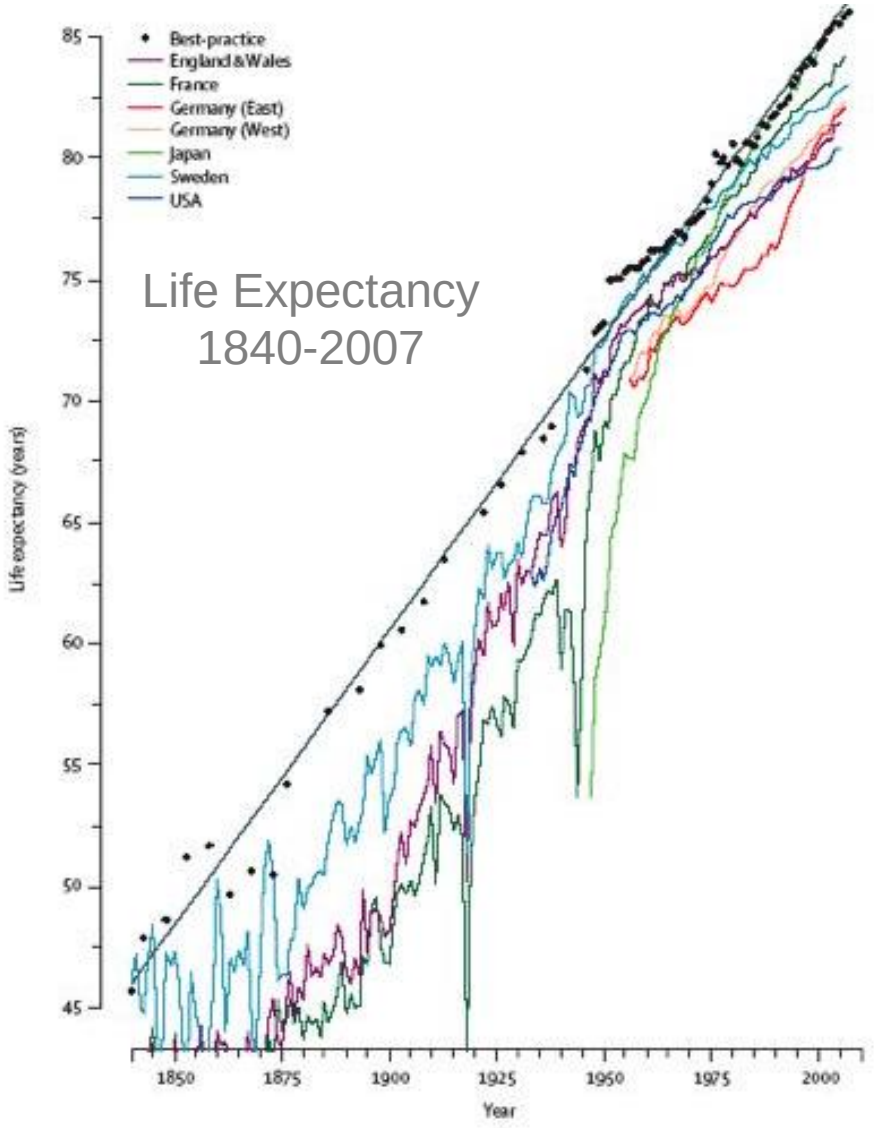
Life Expectancy Has Increased Virtually Linearly



If the increase in life expectancy continues through the 21st century, most babies born since 2000 in countries with long life expectancies will celebrate their 100th birthdays.

Christensen, Lancet, 2009; 374, 1196-1208

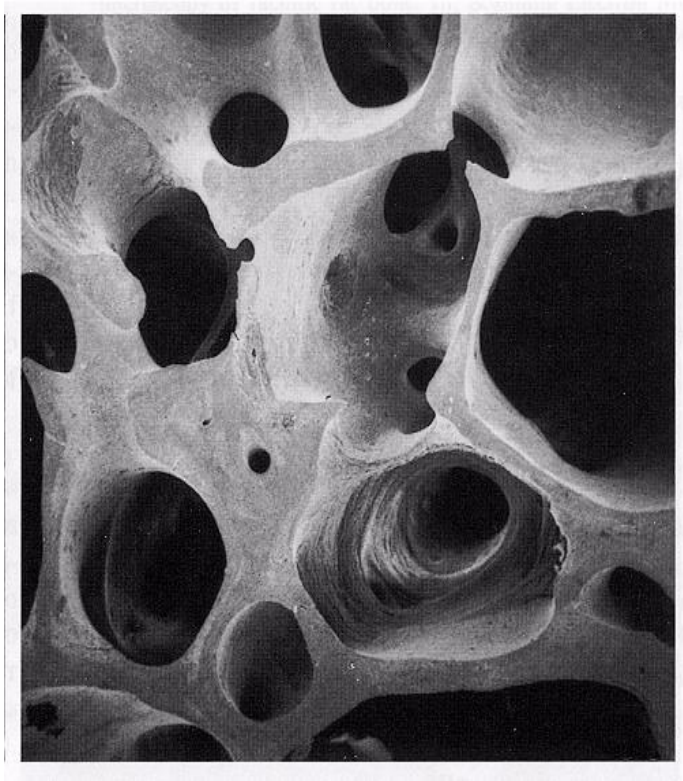
"You can't help getting older, but you don't have to get old."

George Burns

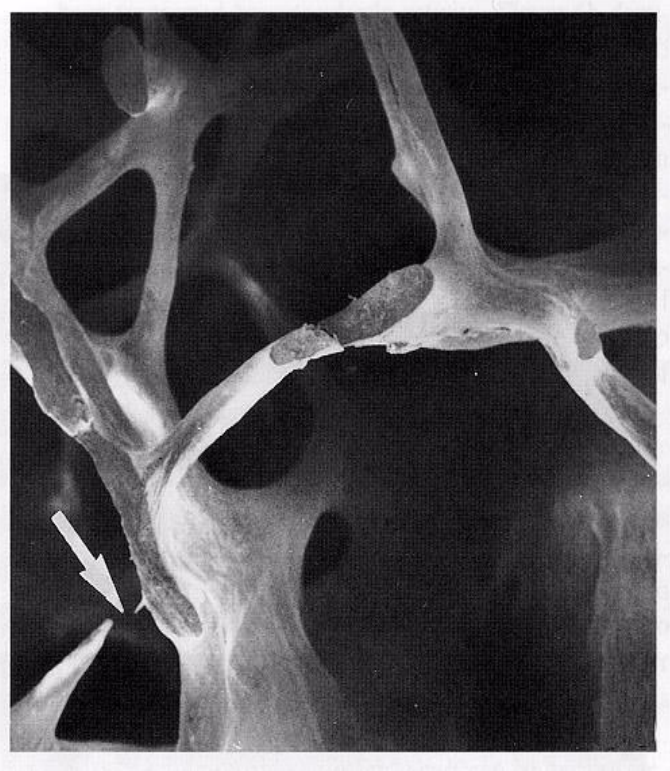
Osteoporosis and Fractures Make Us Old…..

Osteoporosis: Definition

Osteoporosis is a systemic disease characterized by weakened and fragile bone tissue, leading to an increased risk of fracture



Normal

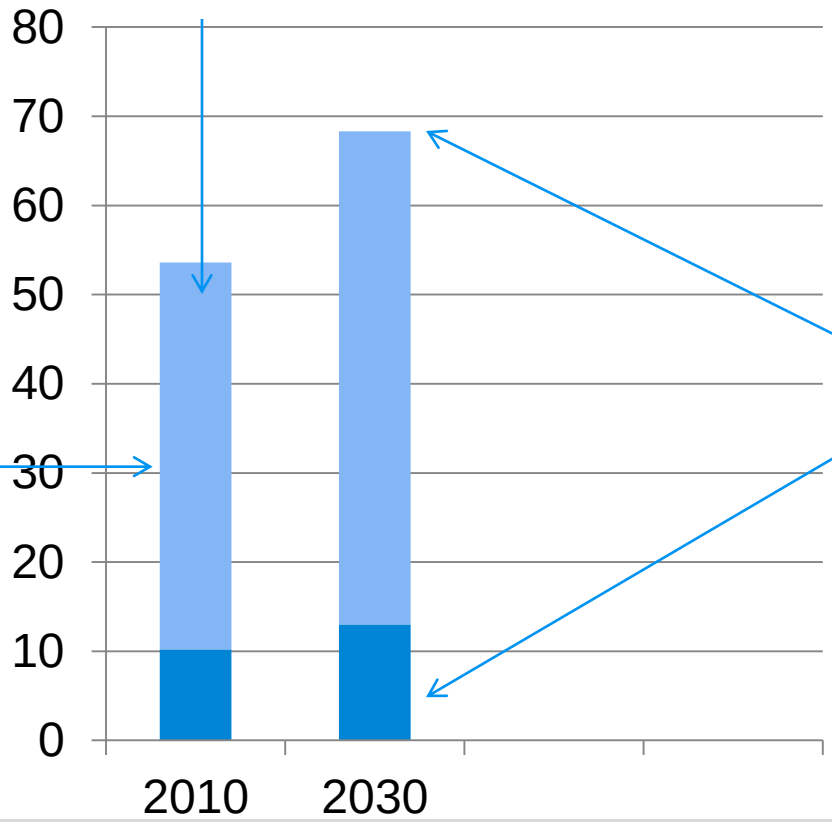


Osteoporosis

Prevalence of Osteoporosis and Low Bone Mass

Americans Age 50 and Above Affected by Osteoporosis/Low Bone Mass, 2010 to 2030 (projected)

54 million of 99 million
Americans age 50+ (2010)



17% of the ENTIRE U.S. POPULATION (2010)

+27% change from 2010 to 2030

The Impact of Osteoporosis and Fractures in the U.S.

"Cast Mountain" represents just 1 DAY of fractures caused by osteoporosis in the US

- 1 fracture every 16 seconds
- ½ of women and ¼ of men over age 50 will break a bone due to osteoporosis
- 26% of women refracture within 1 year after a vertebral fracture
- Every year of the 300,000 hip fractures, ~1/4 die within one year**, 1/4 end up in nursing homes,** and **1/4 never regain previous function**

By 2025, the number of fractures is estimated to rise to 3 million per year

Lindsay et al. Osteoporos Int. 2005;16:78-85. Wright et al. J Bone Miner Res. 2014;29(11):2520-6.
Burge et al. J Bone Miner Res. 2007;22(3):465-75.

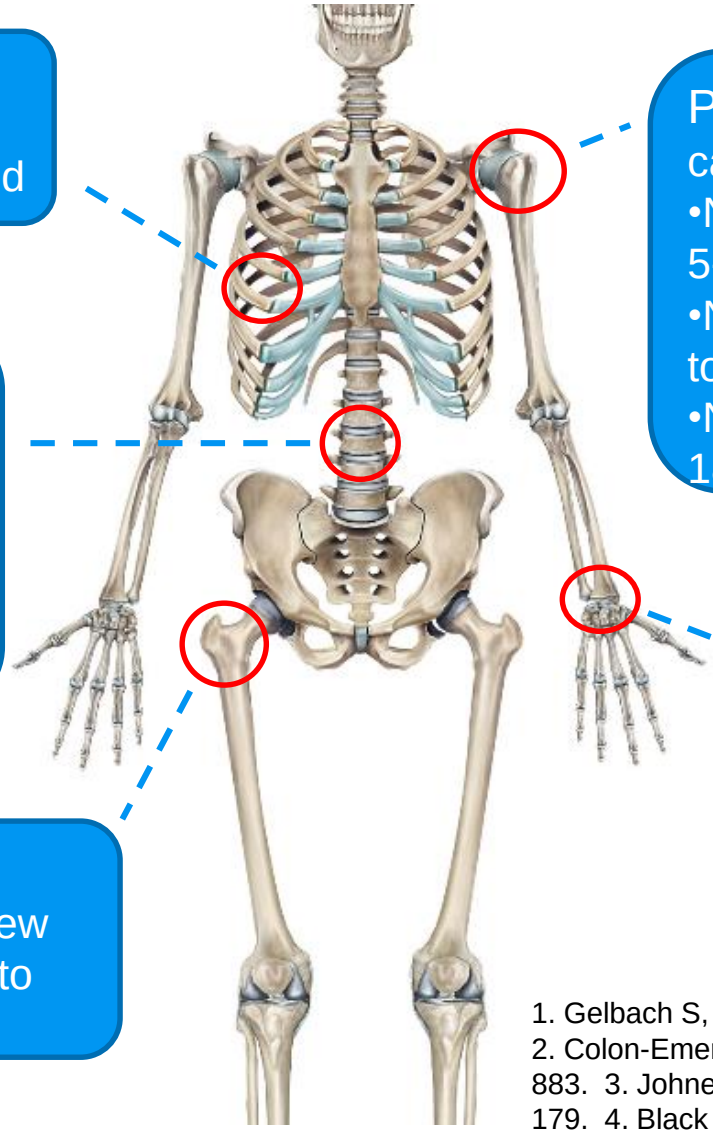
Half of Patients Presenting with Hip Fractures Have Suffered a Prior Fracture

Prior Fracture Increases the Risk of Subsequent Fracture

Prior rib fracture
can increase risk of new vertebral fracture by 2.3-fold

Prior vertebral fracture
can increase risk of
- New vertebral fracture 9.1-fold
- New hip fracture 7.1-fold
- New wrist fracture 2.3-fold

Prior hip fracture
can increase risk of new vertebral fracture 1.6 to 5.9-fold



Prior shoulder fracture
can increase risk of
- New wrist fracture by up to 5-fold
- New vertebral fracture by up to 10-fold
- New hip fracture by up to 18-fold

Prior wrist fracture
can increase risk of new vertebral fracture by 37%

1. Gelbach S, et al. J Bone Min Res. 2012;27(3):645-653. 2. Colon-Emeric C, et al. Osteoporos Int.2003;14(11):879-883. 3. Johnell O, et al. Osteoporos Int. 2004;15(3):175-179. 4. Black DM, et al. J Bone Min Res. 1999;14:821-828

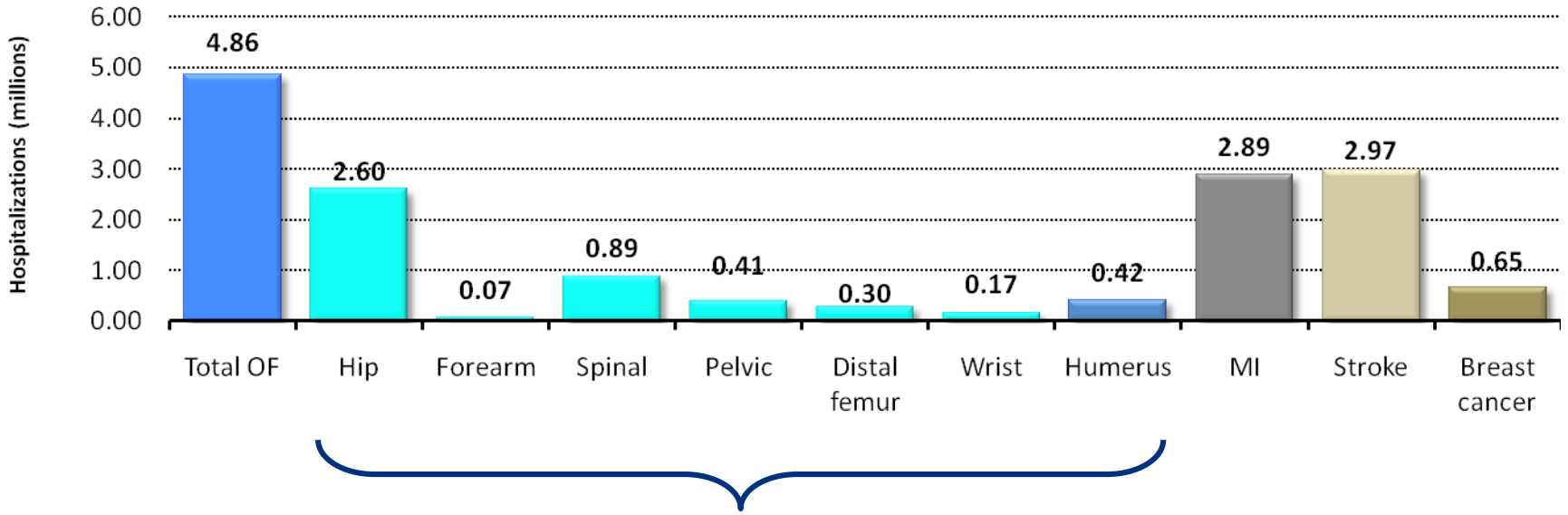
Osteoporosis and Osteoporotic Fractures are Not Perceived as Important Health Risks

- Studies conducted in the US, Canada, and Europe have consistently found that women tend to underestimate the risk of osteoporosis with respect to:
  - Risk factors contributing to increased susceptibility to osteoporotic fractures.[1,2,4]
  - Frequency relative to other diseases, such as cardiovascular disease and breast cancer[3,4]
  - Seriousness of health outcomes,[5,6]

1. Giangregorio L, et al. *BMC Musculoskelet Discord.* 2008;9(38).
2. Gregson CL, et al. *Osteoporos Int.* Jul 25 2013.
3. Gerend MA, et al. *Health Psychology.* May 2004;23(3):247-258.
4. Siris ES, et al. *Osteoporos Int.* Jan 2011;22(1):27-35.
5. Rozenberg S, et al. *Osteoporos Int.* 1999;10(4):312-315.
6. Sale JE, et al. *Journal of Clinical Densitometry.* Oct-Dec 2010;13(4):370-378.

Osteoporotic Fractures Account for More Hospitalizations than do Cardiovascular Disease, Stroke, and Breast Cancer

Hospitalizations for Osteoporotic Fractures and Other Serious Conditions From 2000 to 2011 in women ≥55 years



~4.9 Million Hospitalizations for Osteoporotic Fractures during a 12-year Study Period

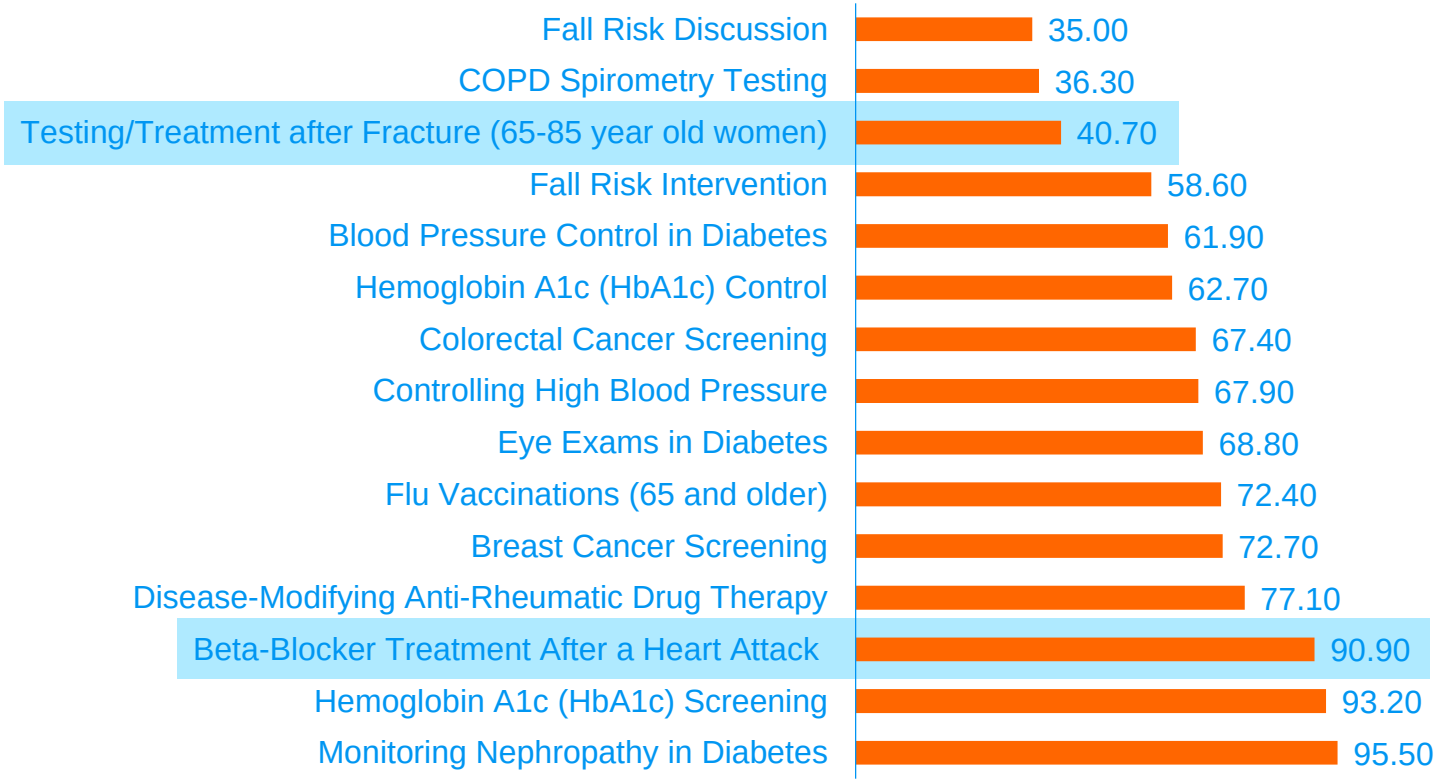
Singer A, et al. *Mayo Clin Proc*. 2015;90:53-62

Why Do We Treat “Osteoporosis?”

Fracture is What’s Important and We Are Failing to Prevent Them…..

Osteoporosis Care Lags Far Behind Other Major Diseases/Conditions

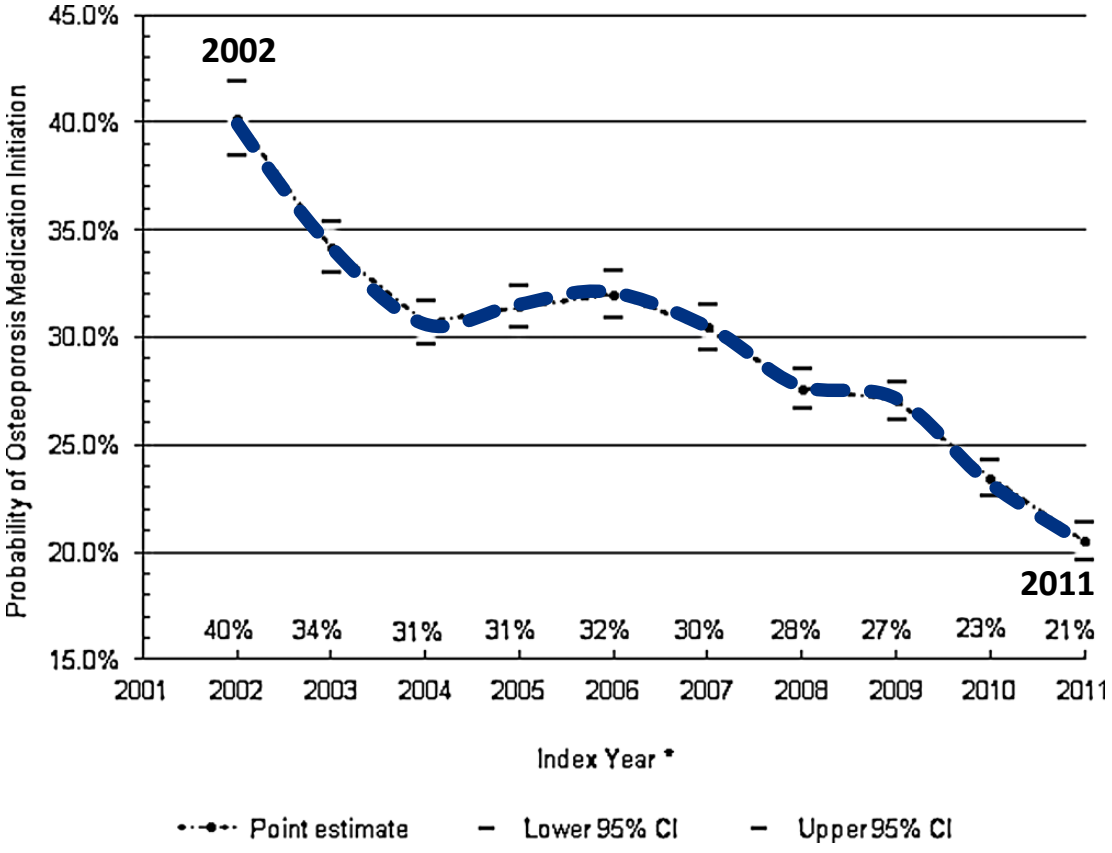
2016 State of Health Care Quality (2015 HEDIS Medicare HMO data)



National Committee on Quality Assurance. 2016 state of health care quality. 2016. Available at: http://www.ncqa.org/report-cards/health-plans/state-of-health-care-quality/2016-table-of-contents. Accessed April 12, 2017.

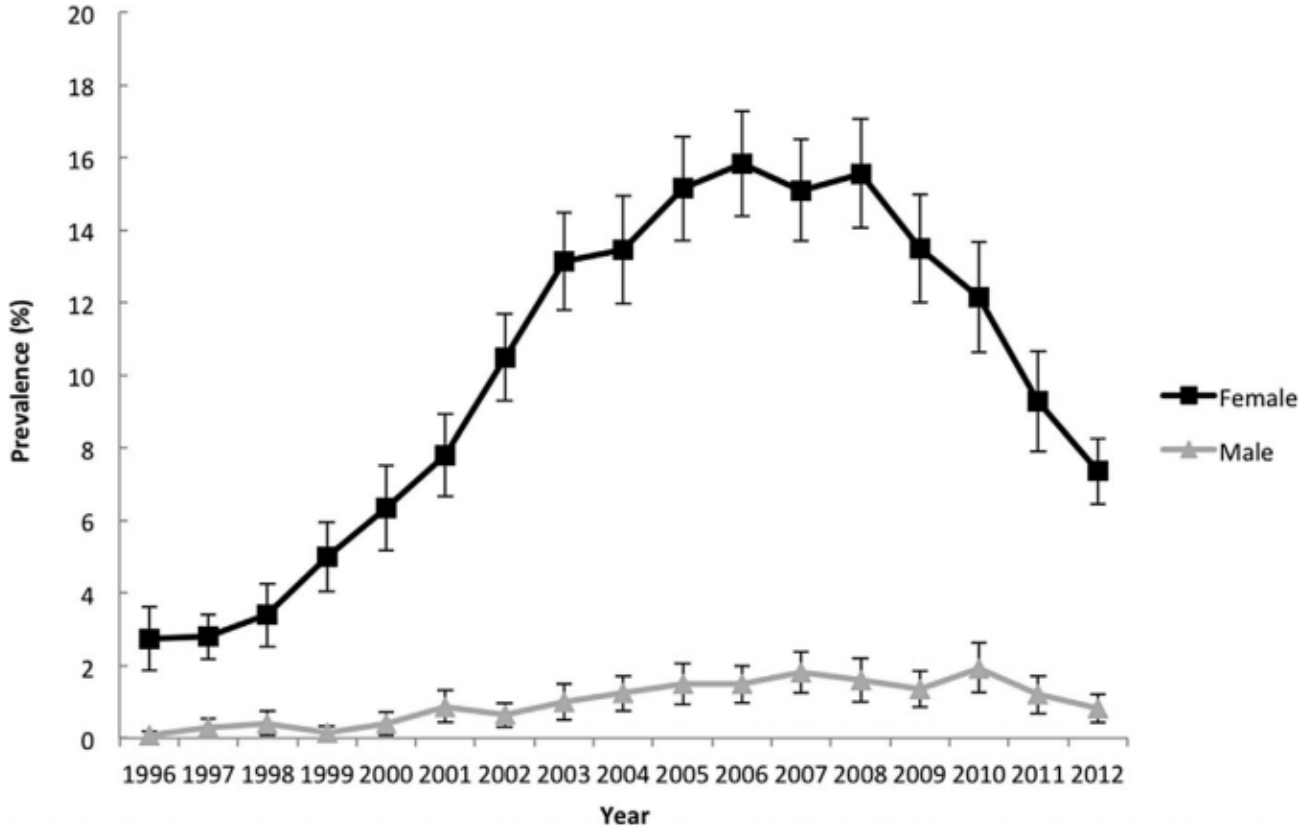
Osteoporosis Care Gap: Treatment After Hip Fracture

Review of US insurance claims data (commercial + Medicare) in 96,887 patients hospitalized with hip fracture, 2002-2011



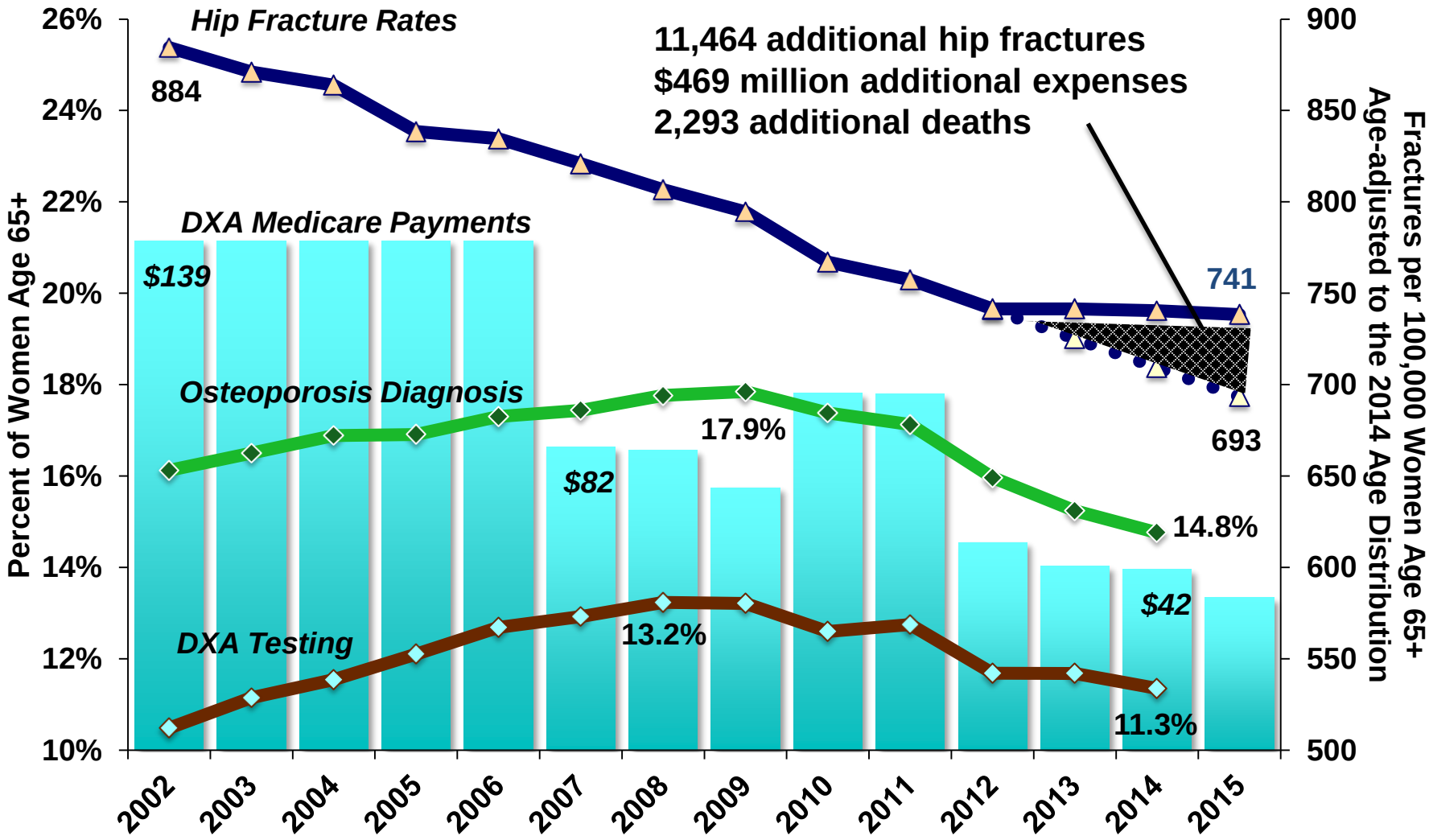
Solomon DH et al. J Bone Miner Res. 2014;29:1929–1937

Reduced Bisphosphonate Prescription Rates Starting in 2008



Jha S et al. J Bone Miner Res. 2015;30:2179-2187.

US Hip Fracture Trends 2002-2015



Adapted from Lewiecki EM et al. Osteoporos Int. 2018;29:717-722.

A Crisis in the Treatment of Osteoporosis

"To draw an analogy from another field, in 2016 it is virtually inconceivable that a patient discharged from the hospital following a myocardial infarction would not be prescribed a full armamentarium of drugs for secondary cardiovascular prevention (eg, a statin, antihypertensive, and others). ***Yet what is inconceivable for a patient following a myocardial infarction is the norm in the vast majority of patients discharged from hospital after a hip fracture.***"

Khosla and Shane, J Bone Min Res, 2016 DOI: 10.1002/jbmr.2888

Guidelines, Treatments, and Strategies to Reduce Fracture Risk

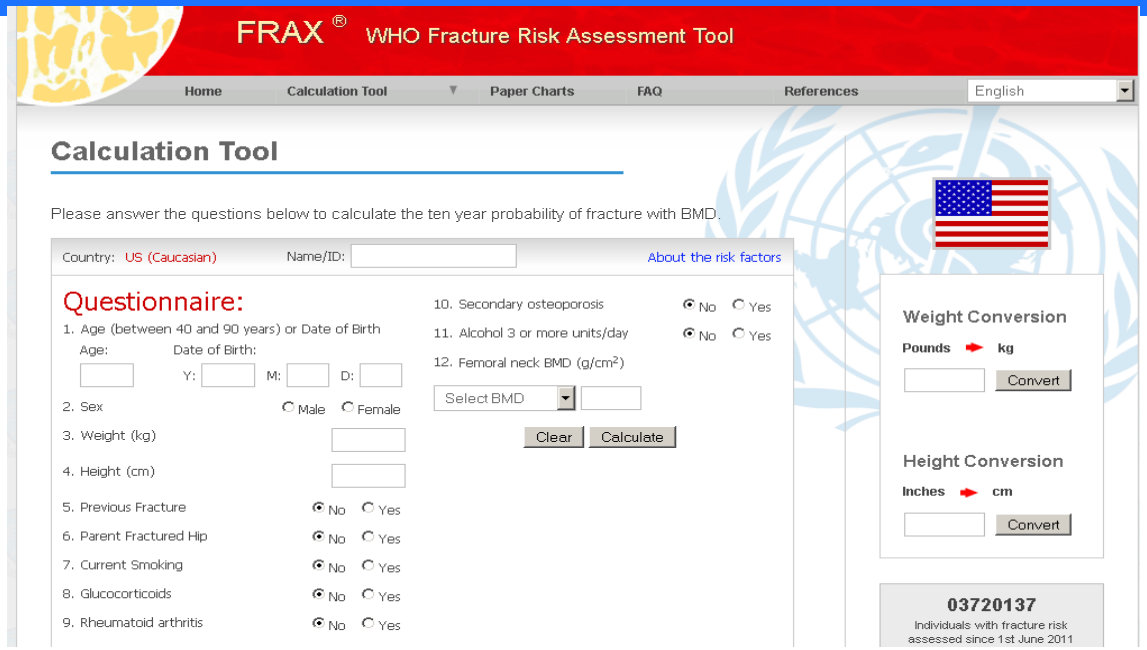
Assessing Risk and Diagnosing Osteoporosis: DXA (Bone Mineral Density Testing)

Criterion	Women	Men
Age-Based	65 years and older	70 years and older
Based on Risk Factors	Postmenopausal, <65 with 1+ risk factor(s) Perimenopausal with specific risk factor* associated with increased fracture risk Postmenopausal, discontinuing estrogen	50-70 years with 1+ risk factor(s)
Regardless of Gender	Fragility fracture (adulthood/ after age 50) Comorbid high-risk condition or exposure to high-risk medication associated with low bone mass or bone loss Anyone being considered for pharmacologic therapy	

***Low body weight, prior low-trauma fracture or high risk medication**

NOF Clinician's Guide to Prevention and Treatment of Osteoporosis. Cosman F, et al. *Osteoporosis International*. 25(10):2359-2381,2014.
Baim, et al. *J Clin Densitometry.* 11(1):75-91,2008.

Fracture Risk Calculators: FRAX® Tool



Rationale

- >50% of fractures occur in non-osteoporotic women (NORA data)[1]
- Assessment of risk factors are important

- FRAX provides a quantitative risk estimate based on BMD and other key factors in **treatment-naïve patients** 40-90 years of age
- **General parameters for use of FRAX: patients with low bone mass (osteopenia)**
- Provides 10-year probability of major osteoporotic fracture (hip, spine, proximal humerus, distal forearm) and 10-year probability of hip fracture[2]

1. Siris E, et al. Arch Intern Med. 2004;164(10):1108
2. http://www.shef.ac.uk/FRAX

Vertebral Fractures

- Vertebral fracture is the most common osteoporotic fracture and indicates a high risk for future fractures
- Most vertebral fractures are not clinically apparent when they first occur and often are undiagnosed for many years.
- Proactive vertebral imaging (lateral spine film or VFA) is the only way to diagnose these fractures
- Finding a previously unrecognized vertebral fracture may change the diagnostic classification, alter future fracture risk, and influence treatment decisions.
- Red flags for vertebral fractures include height loss, postural changes (kyphosis), and worsening back pain
- Height should be measured at regular intervals with a wall-mounted system or stadiometer

Lindsay R, et al. *Osteoporos Int.* 16:78-85,2005.
NOF Clinician's Guide to Prevention and Treatment of Osteoporosis. Cosman F, et al. *Osteoporosis International*. 25(10):2359-2381,2014.

Assessing Risk and Diagnosing Osteoporosis: Indications for Vertebral Imaging

Criterion	Women	Men
T-score ≤-1.5 at spine, total hip or femoral neck	65-69 years	70-79 years
T-score ≤-1.0 at spine, total hip or femoral neck	70 years and older	80 and older
• Low trauma fracture (age ≥50) • Historical height loss of 1 1/2 inches or more • Prospective height loss of 0.8 inches or more • Recent or ongoing long-term glucocorticoid treatment	Postmenopausal women and men age 50 and older • *If bone density testing is not available, vertebral imaging may be considered based on age alone.*	

NOF. Clinician's Guide to Prevention and Treatment of Osteoporosis. Cosman F, et al. *Osteoporosis International*. 25(10):2359-2381,2014.

3 Ways to Diagnose Osteoporosis

- Bone mineral density (BMD) testing (WHO, ISCD)
  - T-score ≤ -2.5 at Lumbar spine (LS), Total hip (TH), Femoral neck (FN), (or 33% Radius)
- Fragility fracture (NBHA)
  - Low trauma hip fracture regardless of BMD
  - Low trauma vertebral, proximal humerus, pelvis and some distal radius fractures with T-score between -1.0 and -2.5
- FRAX (NBHA, USA only) 10-year risks
  - Major osteoporotic fracture (MOF) risk ≥ 20% OR
  - Hip fracture risk ≥ 3%

WHO Technical Report. 1994; ISCD Official Positions. 2015.
Siris ES et al. Osteoporos Int. 2014;25:1439-1443.

WHO – World Health Organization; ISCD – International Society of Clinical Densitometry; NBHA – National Bone Health Alliance

NOF Treatment Guidelines

Consider pharmacological therapy, after appropriate evaluation for secondary causes, for postmenopausal women and men age 50 and older, when:

Osteoporosis by T-score

- T-score ≤ -2.5 at FN, TH, or LS, or . . .

Clinical Osteoporosis

- Hip or vertebral (clinical or morphometric) fracture, or . . .

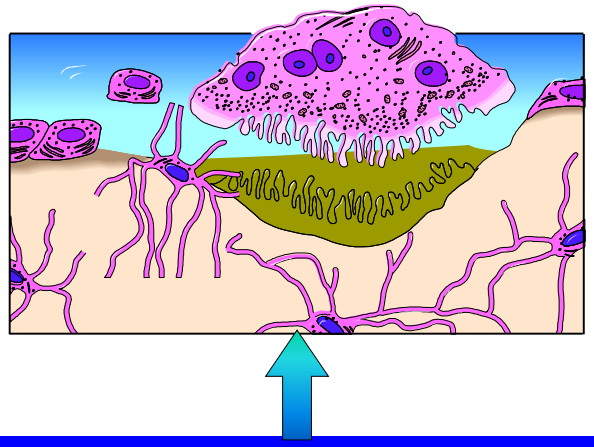
Low BMD + High Fracture Risk

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

Clinician's judgment and/or patient preferences may indicate treatment for people with 10-year fracture probabilities above or below these levels

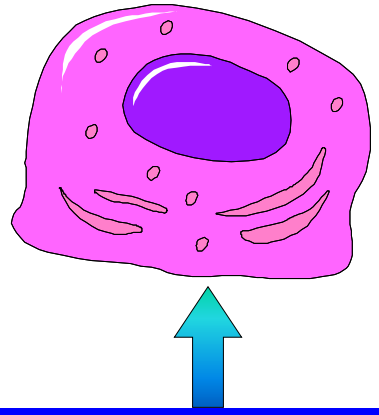
National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. 2014.

Pharmacologic therapy for Osteoporosis



Inhibition of resorption

- **Hormone Therapy**
- **EAA – Raloxifene**
- **TSEC – estrogen/bazedoxifene**
- **Calcitonin**
- **Bisphosphonates**
- **RANK Ligand Inhibitor – Denosumab**



Stimulation of formation

- **Parathyroid hormone (PTH) analog – Teriparatide**
- **PTHrP analog - Abaloparatide**

Medications in Development:

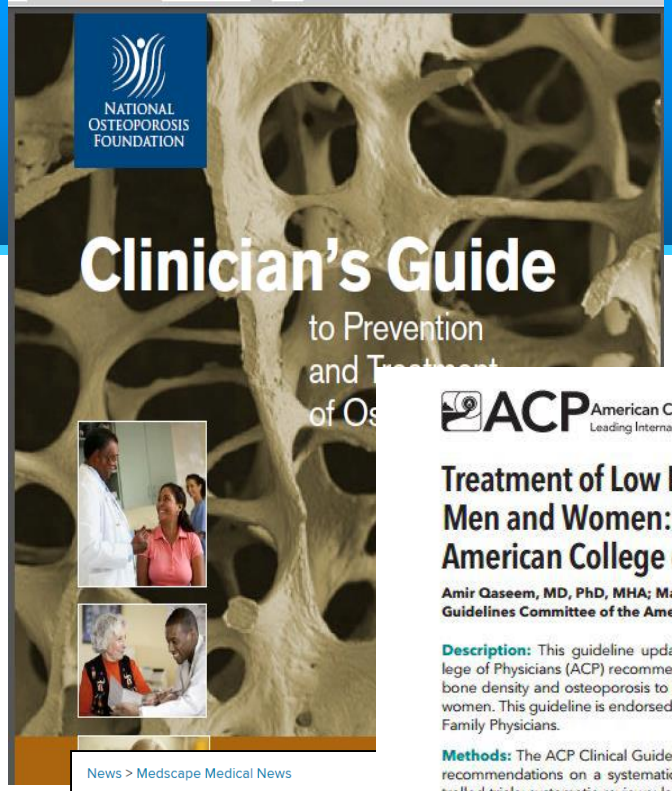
- Sclerostin inhibitor- Romosozumab

25

Overview of FDA Approved Medications

Drug	FDA Indication	Dose and Regimen
Estrogen	PMO prevention	Multiple formulations and regimens; oral, topical; cyclic, continuous
Estrogen/ bazedoxifene	PMO prevention	0.45mg/20mg PO daily
Raloxifene	PMO prevention and treatment	60 mg PO daily
Calcitonin	PMO treatment in women ≥5 years post-menopause	200 IU intranasally once daily (alternate nostrils) 100 IU SQ every other day
Alendronate	PMO prevention PMO, male, GIOP treatment	Prevention: 5 mg PO daily or 35 mg PO weekly Treatment 10 mg PO daily or 70 mg PO weekly
Risedronate	PMO, GIOP prevention PMO, male, GIOP treatment	5 mg PO daily; 35 mg PO weekly; 150 mg PO monthly; Delayed release/Enteric Coated form – 35 mg PO weekly after breakfast
Ibandronate	PMO prevention and treatment	150 mg PO monthly 3 mg IV every 3 months
Zoledronic acid	PMO, GIOP prevention PMO, male, GIOP treatment	Prevention: 5 mg IV every 2nd year Treatment: 5 mg IV once yearly
Denosumab	PMO, male treatment, GIOP treatment, CTIBL/HALT	60 mg SQ every 6 months
Teriparatide	PMO, male, GIOP treatment	20 mcg SQ daily (for maximum 2 years lifetime)
Abaloparatide	PMO treatment	80 mcg SQ daily (for maximum 2 years lifetime)

PMO = Post menopausal; GIOP – Glucocorticoid-induced osteoporosis Data from prescribing information for individual medications



News > Medscape Medical News

New USPSTF D
Osteoporosis Sc

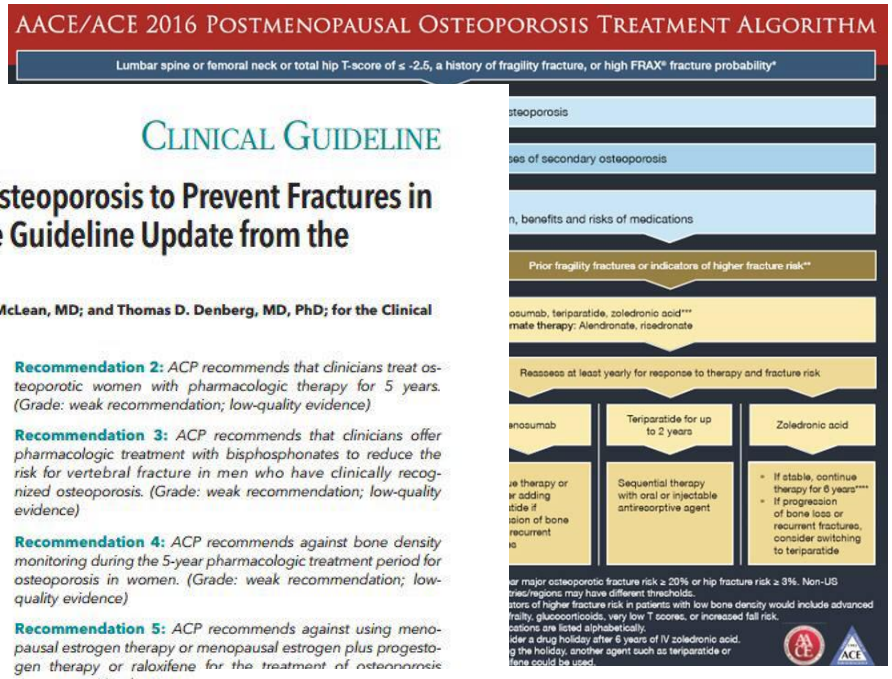
Nancy A. Melville
November 07, 2017

SPECIAL FEATURE

Clinical Practice Guideline

Osteoporosis in Men: An Endocrine Society Clinical Practice Guideline

Nelson B. Watts, Robert A. Adler, John P. Bilezikian, Matthew T. Drake, Richard Eastell, Eric S. Orwoll, and Joel S. Finkelstein



ACP American College of Physicians
Leading Internal Medicine, Improving Lives

CLINICAL GUIDELINE

Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update from the American College of Physicians

Amir Qaseem, MD, PhD, MHA; Mary Ann Forciea, MD; Robert M. McLean, MD; and Thomas D. Denberg, MD, PhD; for the Clinical Guidelines Committee of the American College of Physicians*

Description: This guideline updates the 2008 American College of Physicians (ACP) recommendations on treatment of low bone density and osteoporosis to prevent fractures in men and women. This guideline is endorsed by the American Academy of Family Physicians.

Methods: The ACP Clinical Guidelines Committee based these recommendations on a systematic review of randomized controlled trials; systematic reviews; large observational studies (for adverse events); and case reports (for rare events) that were published between 2 January 2005 and 3 June 2011. The review was updated to July 2016 by using a machine-learning method, and a limited update to October 2016 was done. Clinical outcomes evaluated were fractures and adverse events. This guideline focuses on the comparative benefits and risks of short- and long-term pharmacologic treatments for low bone density, including pharmaceutical prescriptions, calcium, vitamin D, and estrogen. Evidence was graded according to the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system.

Target Audience and Patient Population: The target audience for this guideline includes all clinicians. The target patient population includes men and women with low bone density and

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

Recommendation 3: *ACP recommends that clinicians offer pharmacologic treatment with bisphosphonates to reduce the risk for vertebral fracture in men who have clinically recognized osteoporosis. (Grade: weak recommendation; low-quality evidence)*

Recommendation 4: *ACP recommends against bone density monitoring during the 5-year pharmacologic treatment period for osteoporosis in women. (Grade: weak recommendation; low-quality evidence)*

Recommendation 5: *ACP recommends against using menopausal estrogen therapy or menopausal estrogen plus progestogen therapy or raloxifene for the treatment of osteoporosis in women. (Grade: strong evidence)*

Recommendation 6: *ACP make the decision whether of age or older who are at discussion of patient prefere*

Menopause: The Journal of The North Americ
Vol. 17, No. 1, pp. 23-24
DOI: 10.1097/gme.0b013e3181cdd4a7
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♾ Text printed on acid-free paper

NAMS continuing medical education activity

Management of osteoporosis in postmenopausal women:

2010 position statement of The North American Menopause Soci

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

PRACTICE BULLETIN

CLINICAL MANAGEMENT GUIDELINES FOR OBSTETRICIAN–GYNECOLOGISTS

NUMBER 129, SEPTEMBER 2012
(Reaffirmed 2016)

(Replaces Practice Bulletin No. 50, January 2004)

Osteoporosis

Osteoporosis has a fivefold greater prevalence in women than in men. In the United States, although women only have twice the fracture rate of men, they sustain 80% of hip fractures because older women far outnumber older men. In 2005, the cost for direct care of the estimated 2 million osteoporosis-related fractures was projected to be $17 billion, with hip fractures accounting for approximately 72% of the cost (1). Morbidity and loss of function can occur with all fractures and consequently present a significant burden to the patient, the family, and society. Morbidity and mortality are especially high with hip fractures. Of women older than 80 years who have had a hip fracture, only 56% could walk independently after 1 year (2). Approximately 3–6% of women die of complications while hospitalized for hip fracture, an outcome often correlated with comorbidity and age (2, 3). Many aspects of gynecology and obstetrics can affect bone health. Obstetrician–gynecologists have the opportunity to play a key role in the prevention of osteoporosis and osteoporotic fractures. The purpose of this practice bulletin is to review the diagnosis, evaluation, and treatment of osteoporosis.

ACP Clinical Practice Guideline 2017

#	Recommendation	Strength
1	Offer ALN, RIS, ZOL, or Dmab to reduce risk of hip and vertebral fractures (VFs) in women with osteoporosis	Strong
2	Treat osteoporotic women for 5 years	Weak
3	Offer BPs to reduce VF risk in men with osteoporosis	Weak
4	No BMD monitoring during 5 years of treatment in women	Weak
5	No E, E+P, or Raloxifene for treatment of PMO	Strong
6	Decision to treat women age ≥ 65 with osteopenia and high fracture risk should be based on discussion of patient preferences, fracture risk profile, benefits, harms, and cost of medication	Weak

Commentaries from ASBMR, AACE, ISCD, NOF, NBHA, and many letters to the editor

Qaseem A et al. Ann Intern Med. 2017;166:818-839.

ACP Guideline Considerations and Challenges in Treating Patients: Target Patient Population

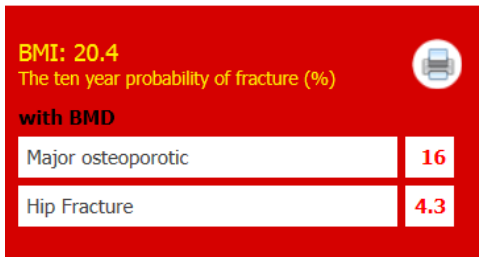
- Osteoporosis encompasses men and women with fragile bones, but very different levels of fracture risk.
- Consideration of patient diversity is critical for effective treatment of osteoporossi.
- Patient diversity, particularly with respect to level of fracture risk, is important in determining initial osteoporosis therapy as well as duration of therapy.

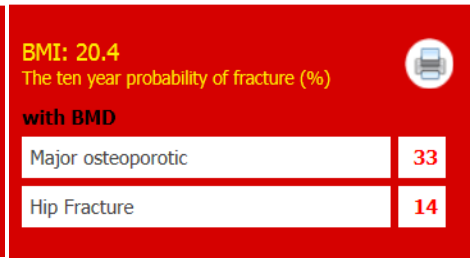
Challenges in Treating Patients: Target Patient Population

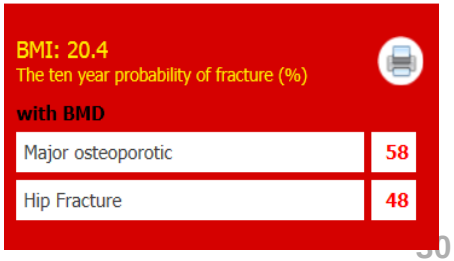
Fracture risk among “unequivocally” osteoporotic patients

Caucasian female, height 63”, weight 115 lbs, + family h/o osteoporosis

Patient	1	2	3
Age	58	68	78
Prior fracture	wrist	no	humerus
Parent fractured hip	no	yes	yes
Current smoking	yes	no	no
Lumbar spine BMD T-score	-2.8	-2.5	-3.1
Femoral neck BMD T-score	-2.2	-3.5	-3.3







AACE Treatment Algorithm

Treat when LS, TH, or FN T-score ≤ -2.5, fragility fracture, or high FRAX (MOF ≥ 20% or HP ≥ 3%) after evaluation for secondary causes

No prior fracture or moderate fracture risk

- Alendronate, denosumab, risedronate, zoledronic acid
- Alternate: ibandronate, raloxifene

Prior fragility fracture or indicators of higher fracture risk*

- Denosumab, teriparatide,* zoledronic acid
- Alternate: alendronate, risedronate

*Higher fracture risk indicators include advanced age, frailty, glucocorticoids, very low T-score, increased fall risk

*Abaloparatide had not yet been approved when the guidelines were written

AACE Guidelines. Endocrine Practice. 2016;22(Suppl 4).

Limitations of AACE Algorithm

- Does not clearly distinguish the advantages and disadvantages of treatment options
- Does not address sequence of therapy
- Does not provide sufficient detail in defining levels of risk
  - How old is “advanced age”?
  - How much glucocorticoids and for how long?
  - How low is “very low” T-score?
  - How to asses fall risk?

Guidelines were intentionally slightly vague to allow informed clinicians to individualize treatment decisions, but too vague to provide guidance for non-experts and for health plans and agencies hoping to set policies for drug coverage

Treat-to-Target: Report of ASBMR-NOF Working Group

- Stratify patients according to level of fracture risk
- Identify a treatment target that represents an acceptable level of risk
- Initiate treatment with an agent most likely to reach the target
- Monitor for response to treatment and to track progress in reaching the target
- If patient is not responding or not on track to reach the target, then consider altering treatment plan

Cummings SR et al. J Bone Miner Res. 2017;32:3–10.

Who are the Highest Risk Patients?

- Prior fracture is the most important risk factor for future fracture[1]
  - Recent Fractures suggest very high risk (Osteoporosis Emergency/Urgency)
    - In over 377,000 women with first fracture[2]:
      - Absolute Risk of another fracture 10% first year , 18% first 2 years, 31% first 5 years
  - Multiple Fractures also indicate very high risk[3]
  - Proactive Spine Imaging Required to find Morphometric Vertebral Fractures
    - NHANES VFA Study 2017[4]
      - Vertebral Fracture Prevalence 5% in the 60s, 10% in the 70s, 20% in the 80s[3]
- Other considerations
  - Very low BMD: T-score <-3.5 (?)
  - Very high Fracture risk: FRAX MOF >30% or hip fracture >4.5% (?)

1. Kanis J Bone 2004
2. Balasubramanian A et al OI 2018
3. Gehlbach et al OI 20007
4. Cosman F et al OI 2017

Osteoporosis Medication Efficacy

	2-year increase spine BMD	2-year increase total hip BMD	RRR of spine fracture	RRR of nonvert fracture
Alendronate[1]	**5%**	**3%**	**53%**	**20% at 3 years**
Zoledronic acid [2]	**5-6%**	**3-4%**	**70%**	**25% at 3 years**
Denosumab [3]	**6-8%**	**3-4%**	**68%**	**20% at 3 years**
Teriparatide[4]	10%	2-3%	65-80%[4,5]	53% at 19 months
Abaloparatide[5]	10%	3-3.5%	86%	43% at 19 months

Benefits of Treatment

Bisphosphonates, denosumab, teriparatide, raloxifene: reduction in vertebral fracture

Alendronate, risedronate, zoledronic acid, denosumab, teriparatide: reduction in nonvertebral fracture

Alendronate, risedronate, zoledronic acid, denosumab: reduction in hip fracture [6]

Teriparatide

High-quality evidence showed that treatment with teriparatide reduces radiographic vertebral and non-vertebral fractures compared with placebo in post-menopausal osteoporotic women (34, 110–120).

[6]

1.Black et al. Lancet. 1996
2.Black et al. N Engl J Med. 2007
3.Cummings et al. N Engl J Med. 2009
4.Neer et al. N Engl J Med. 2001
5.Miller et al. JAMA.2016
6.Qaseem et al. Ann Int Med, 2017

Osteoporosis Treatment Sequence

PERSPECTIVE

JBMR®

Treatment Sequence Matters: Anabolic and Antiresorptive Therapy for Osteoporosis

Felicia Cosman,[1,2] Jeri W Nieves,[1,3] and David W Dempster[1,4]

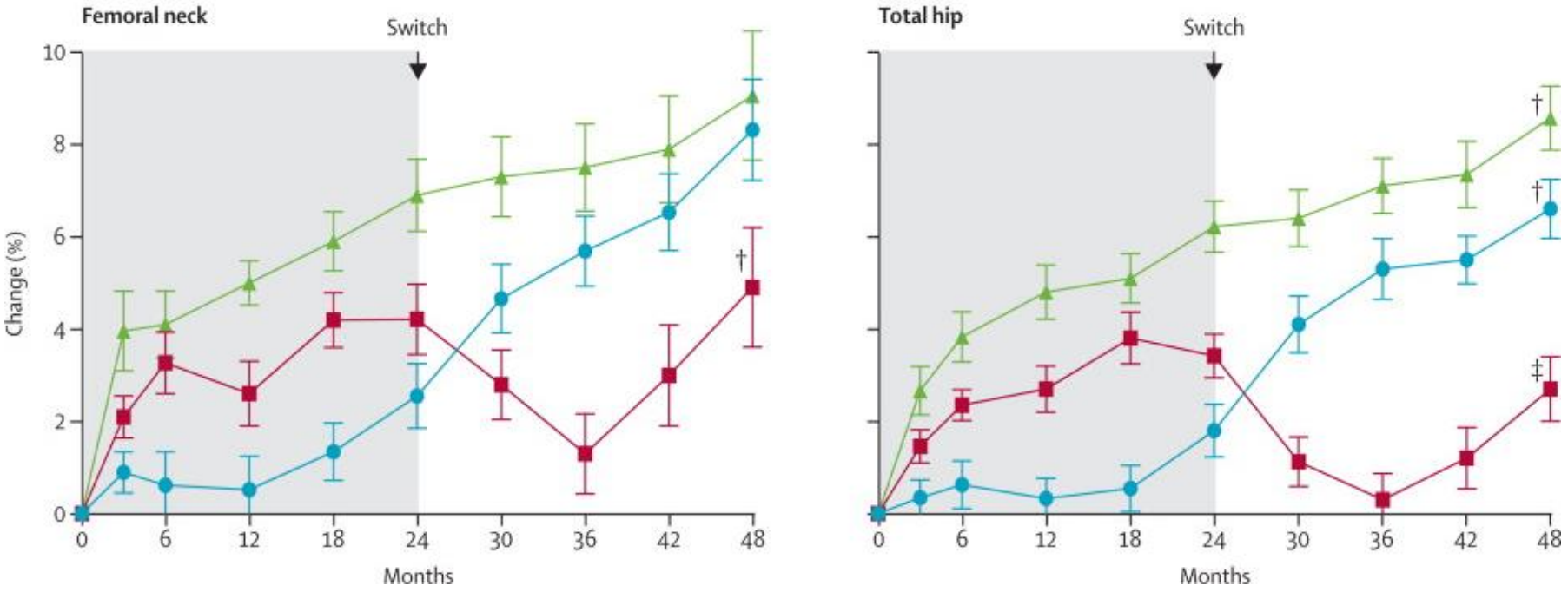
Table 1. Hip BMD Effect of Switching From Potent Antiresorptive Therapy to TPTD

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%

- Suggest anabolic therapy first, followed by antiresorptive therapy.
- Practice of switching to TPTD only after an inadequate response to antiresorptives (fracture or inadequate BMD effect) is not optimal utilization of anabolic treatment.
  - When switching from BP to TPTD, BMD increases are blunted compared to *de novo TPTD.*
  - This may also result in transient loss of hip BMD and strength.
- Continuing a potent antiresorptive while starting TPTD might improve hip outcomes.

Osteoporosis Treatment Sequence:
4 Year Sequential Treatment with Teriparatide and Denosumab (DATA-Switch)

Greater BMD gains when an anabolic agent is used first followed by a potent antiresorptive agent, as compared to when an anabolic is used second line after therapy with an antiresorptive



Green Combination Teriparatide +Denosumab for 2 years followed by Denosumab for 2 years
Red: Denosumab for 2years followed by Teriparatide for 2 years
Blue Teriparatide for 2 years followed by Denosumab for 2 years

Leder BZ et al. Lancet 2015, 386:1147–55

ACP Guideline Considerations: Duration of Treatment

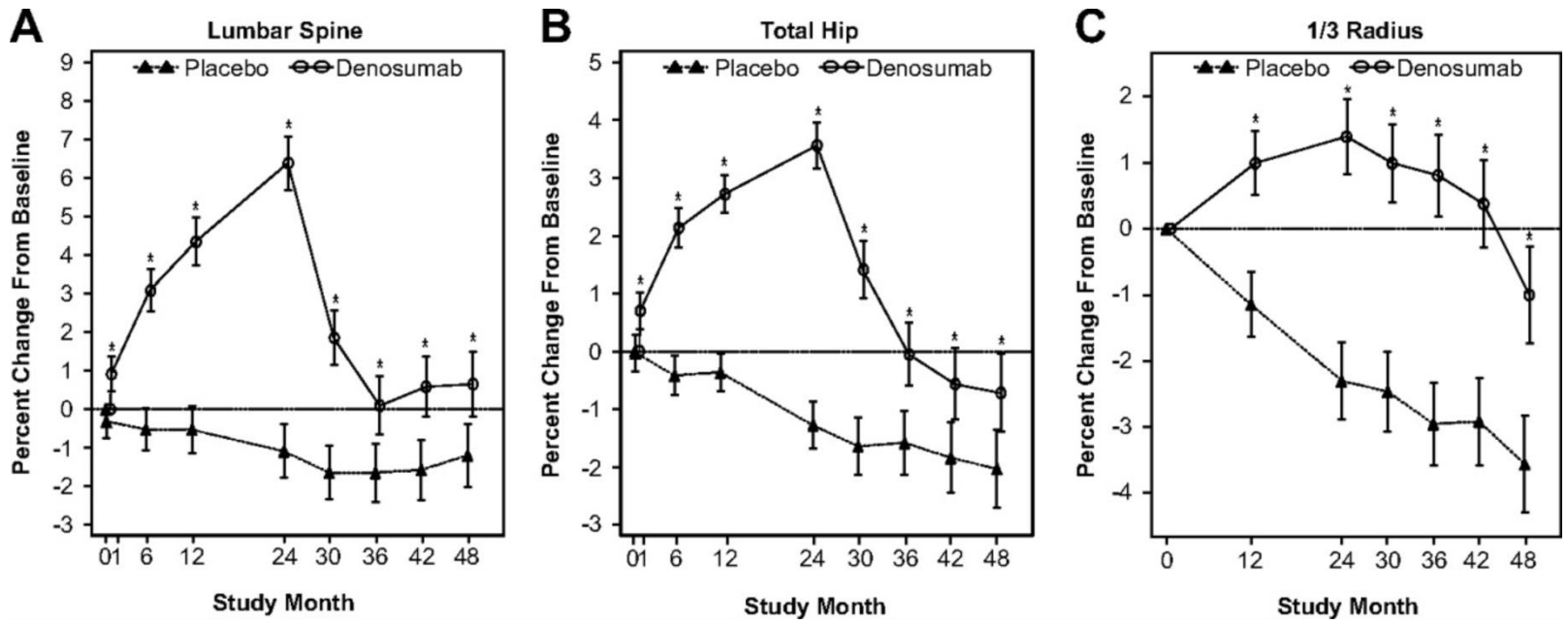
- Suggesting an optimal treatment duration of 5 years does not fully reflect the great variability in disease severity among patients treated with osteoporosis medications.
- Discontinuation of therapy or a **“drug holiday”** is a **bisphosphonate specific concept**
- Drug holidays may be appropriate for some patients taking bisphosphonates, but not all, and abrupt cessation of other medications, particularly denosumab, is not appropriate.
- **Osteoporosis is a chronic disease and as such, requires lifelong *management***
- Monitoring after discontinuation of bisphosphonate treatment and re-initiation of anti-fracture therapy need to be addressed and individualized to provide the best patient outcomes.

Duration of Therapy: A Comparison of Guidelines/Recommendations

	ACP	ASBMR Task Force	AACE/ACE
Pharmacologic agent(s) discussed	Treat osteoporotic women with "pharmacologic therapy" for 5 years	Bisphosphonates (BPs): Advise 5 years of oral BP and 3 years of IV BP	•Oral BPs: consider a holiday after 5 years of stability in moderate-risk patients and 6-10 years in higher-risk patients •IV ZA: consider a holiday after 3 annual doses in moderate-risk patients and 6 annual doses in higher-risk patients. •A drug holiday is not recommended with denosumab
Continuation of treatment recommended	"Continuing treatment after 5 years may be beneficial for some patients and may be appropriate after reassessing the risks and benefits of continuing therapy." In text only	Consider up to 10 years of BP (or alternative) treatment for: •Hip, spine or multiple other OP fractures before/during treatment •Hip BMD T-score ≤-2.5 •High fracture risk defined by older age (70–75 years), other strong risk factors for fracture, •FRAX fracture risk score that is above country specific thresholds	Agree with ASBMR Task Force: patients initially at high risk/remain at high risk receive 10 years for oral BP or 6 years for IV ZA. Teriparatide or raloxifene may be used during BP holiday for higher-risk patients Other agents should be continued for as long as clinically appropriate
Assessment of fracture risk after discontinuation of treatment		Every 2-3 years, including DXA	Ending of BP "holiday" based on individual patient – fracture occurrence or fracture risk or change in BMD (DXA) or BTMs

ASBMR – American Society for Bone and Mineral Research; AACE/ACE – American Association of Clinical Endocrinologists/American College of Endocrinology; DXA – dual-energy X-ray absorptiometry; ZA – zoledronic acid

Effects of Denosumab Discontinuation



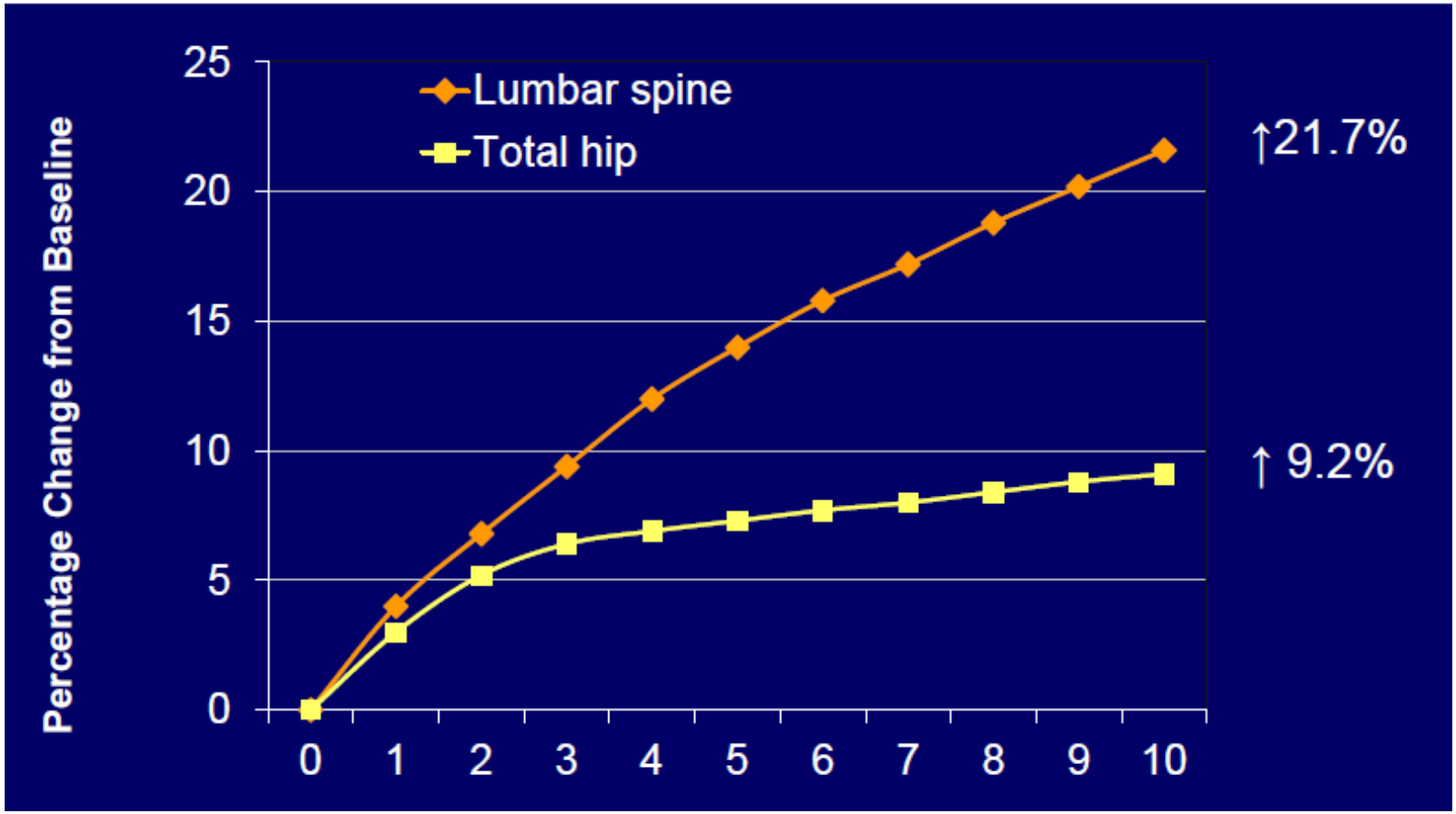
- Effects of denosumab on BMD are reversible upon treatment discontinuation, reflecting the biological mechanism of action of denosumab.
- Continued therapy is required to maintain treatment effects.
- Multiple vertebral fractures have been seen after abrupt discontinuation of denosumab
- If treatment is to be stopped, follow-on therapy with another antiresorptive is recommended

Bone HG, et al. J Clin Endocrinol Metab. 2011;96(4):972-980.

Long-term Treatment Efficacy: Denosumab

Change in lumbar spine and total hip bone mineral density through 10 years with denosumab treatment

FREEDOM and the Open-Label FREEDOM Extension

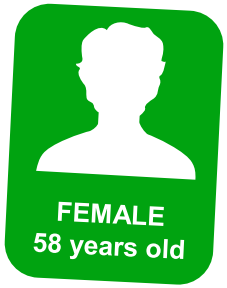


Bone HG, et al. Lancet Diabet Endocrinol 2017;5:513-523

Duration of Therapy: What Does This Mean in Clinical Practice?

- The duration of therapy needs to be individualized
- In patients with osteoporosis at moderate fracture risk, consider treatment with bisphosphonates for 3-5 years.
- In patients who remain at high risk after 3-5 years, consider continuing therapy, adding or switching to an anabolic agent.
- Denosumab cannot be stopped (or switched to teriparatide) without a prior transition to a bisphosphonate.
- Continue to evaluate for re-initiation of therapy; A drug holiday does **not** equal drug retirement

Hormonal Therapies



54-year-old woman:

Family history

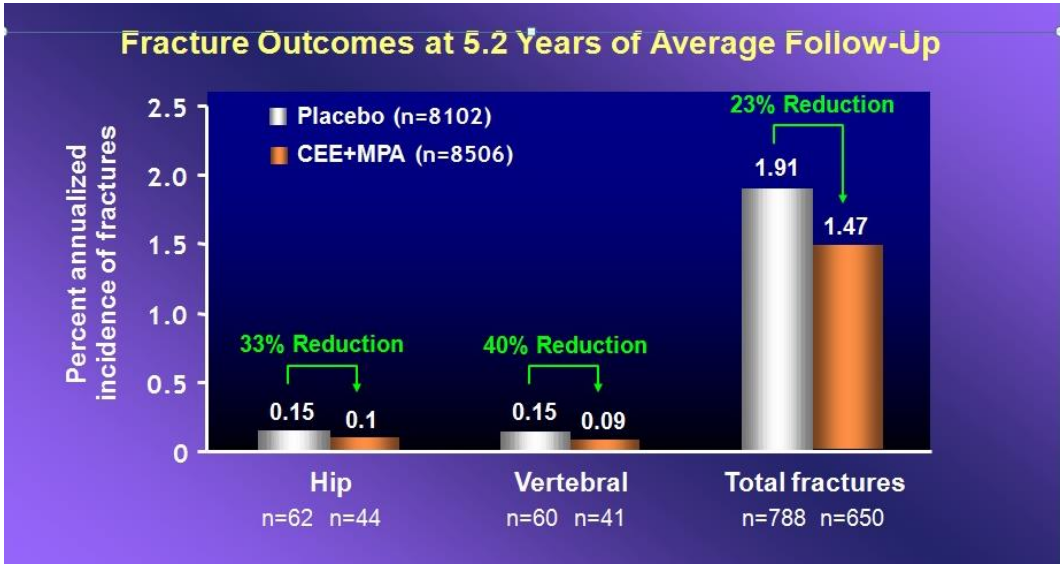
Mother – osteoporosis
+breast cancer in family

History

67 inches
130 pounds
No prior fracture

Evaluation:
Lumbar spine T-score –2.7
Left total hip -2.2; femoral neck -2.1

Women's Health Initiative



Rossouw JE, et al. JAMA 2002;288:321-33

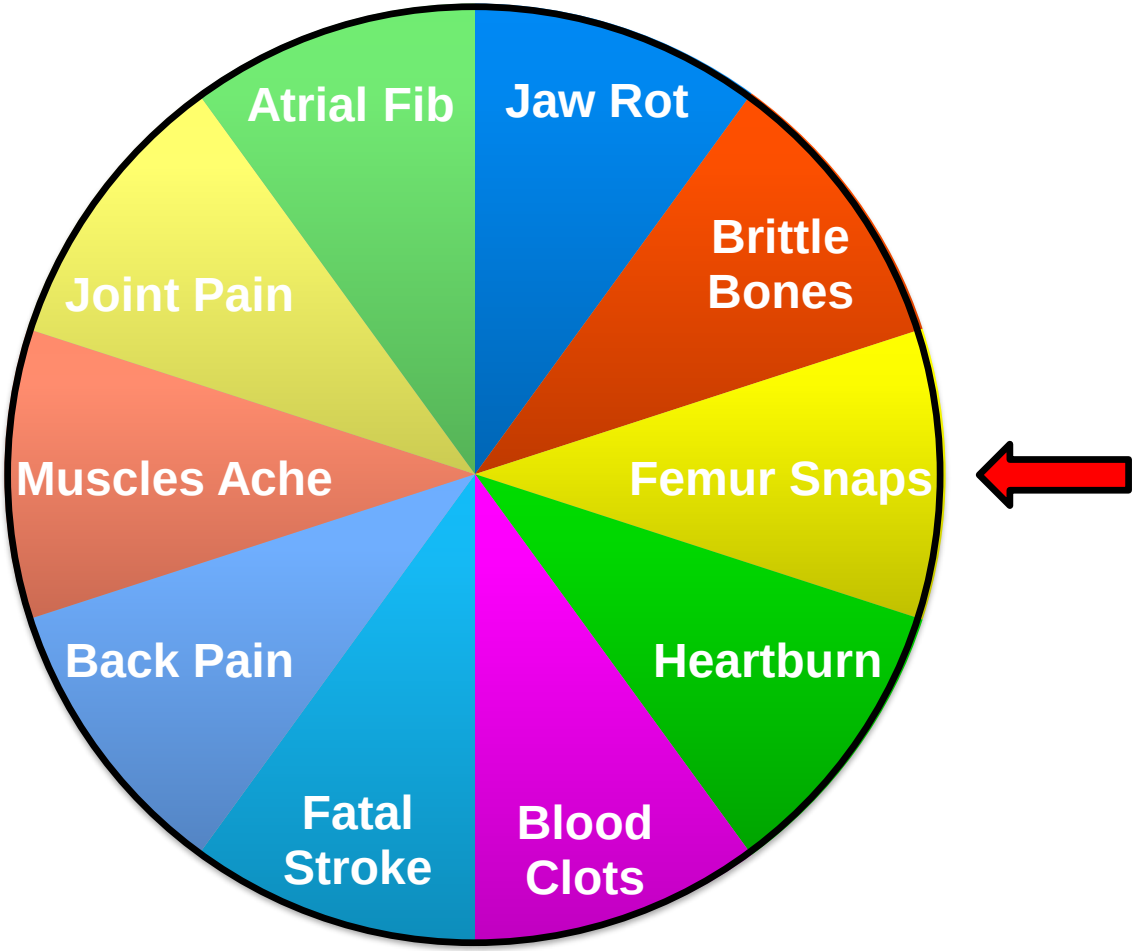
- Raloxifene does not reduce hip and non-spine fracture incidence but does reduce spine fracture incidence and increases BMD modestly.
- Raloxifene reduces breast cancer risk

Individualizing Treatment

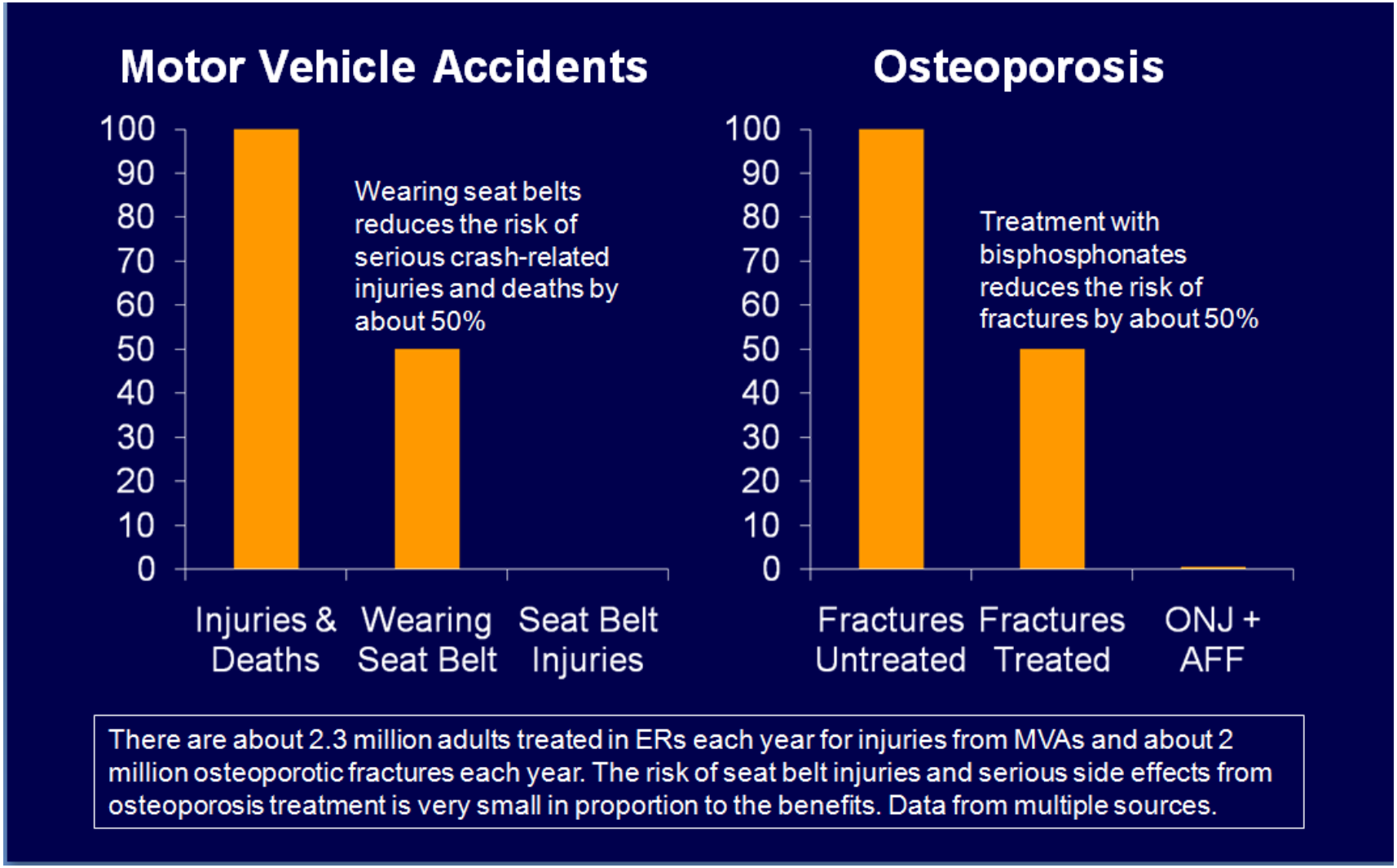
Agent	Comments
Oral BPs	Pro: inexpensive, work well in many patients Con: GI distress, avoid with low GFR, bad rep in lay press
ZOL	Pro: very long dosing interval, post-hip fracture data (decreased mortality) Con: acute phase reaction, avoid with low GFR, IV
Dmab	Pro: long dosing interval, greatest BMD increase of anti-resorptives, SC, 10-year safety and tolerability data Con: FDA list of “side effects” (back pain, high cholesterol, etc.)
RLX	Pro: not a BP, decreases invasive breast cancer risk Con: VTE, hot flashes, no proven hip/nonvertebral fracture decrease
TPTD	Pro: anabolic, long term experience [SEQUENCE MATTERS] Con: high cost, daily injection, refrigeration, rat osteosarcoma
Abalo	Pro: anabolic, no refrigeration [SEQUENCE MATTERS] Con: high cost, daily injection, rat osteosarcoma

Personal opinion.

Osteoporosis Wheel of Fear



Benefits and Risks



There are about 2.3 million adults treated in ERs each year for injuries from MVAs and about 2 million osteoporotic fractures each year. The risk of seat belt injuries and serious side effects from osteoporosis treatment is very small in proportion to the benefits. Data from multiple sources.

Shared Decision Making

Shared (participatory) Decision Making:

- HCPs and patient share information, discuss options, and reach collaborative decision
- HCP may offer recommendation that patient chooses to accept or reject

- Components:
  - Understanding the risks associated with the condition
  - Understanding the options, including the risks, benefits, alternatives, and uncertainties
  - Weighing personal values regarding potential benefits and harms
  - Participating in decision making at the desired level

Sheridan SL, et al. *Am J Prev Med*. 2004;26:56-66

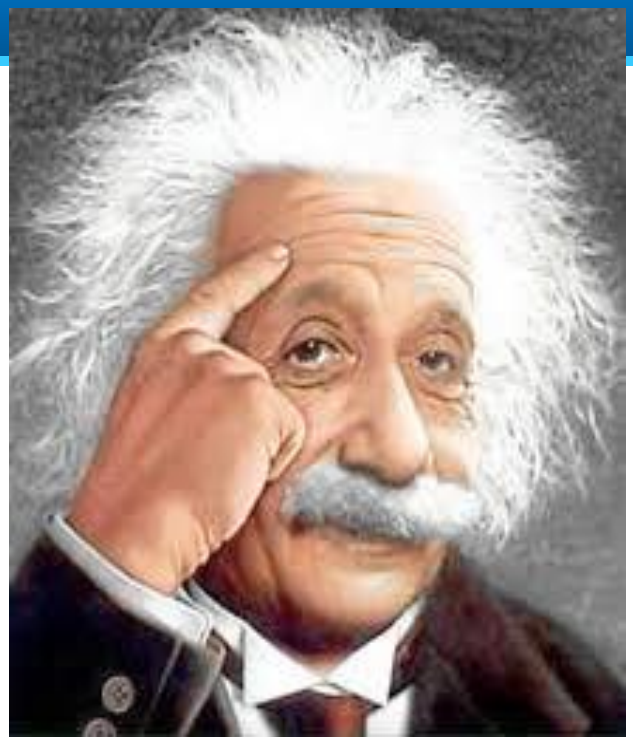
Strategies to Improve Osteoporosis Care: Effective Risk Communication

- General
  - Listen to patient attentively: goals, fears, experiences
  - Develop relationship of trust and teamwork
  - Use decision aids when appropriate
- **Fracture risk**
  - **Be sure patient understands the risk and the consequences of a fracture**
- Treatment risk and benefits
  - Explain goals of therapy
  - Personalize drug selection
  - Describe risks that are common, including feared risks
  - Monitor for tolerance, compliance, persistence and effectiveness

How We Improve the Osteoporosis Care Gap: Fracture Liaison Service (FLS)

- Systematic identification of fracture patients, entering them in a registry, and coordinating post-fracture care to assure that they receive appropriate evaluation and treatment to reduce the risk of more fractures
    - Recognize that in addition to fixing the fracture, osteoporosis needs to be evaluated and treated
    - Capitalize on the teachable moment
- FLS programs have greatly reduced the number of fractures and achieved cost savings
- Identification of “fragility” or “low trauma” fracture
    - Falls from standing height or less resulting in fracture
    - Majority of fragility fractures happen from a fall
    - Does not matter how “hard” the surface or how “bad” the fall
        - It is about energy transfer and bone strength

Maintaining Independence is THE Reason to Treat Osteoporosis and Fractures



“Insanity: doing the same thing over and over again and expecting different results.”

Albert Einstein

A Different Approach to Osteoporosis and Fracture Management is Needed

Understanding Osteoporosis: What's New?

Perspectives from a PCP Bone Head

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