Understanding Osteoporosis: What’s New? Perspectives from a PCP Bone Head

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  – Eli Lilly
  – Radius Health
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 is a systemic disease characterized by weakened and fragile bone tissue, leading to an increased risk of fracture.
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)

+27% change from 2010 to 2030

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

Wright NC, et al. JBMR doi:10.1002/jbmr2269
The Impact of Osteoporosis and Fractures in the U.S.

EVERY YEAR, THERE ARE 2 MILLION BONE BREAKS THAT ARE NO ACCIDENT, BUT SIGNS OF OSTEOPOROSIS.

“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

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

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

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%

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.\textsuperscript{1,2,4}
- Frequency relative to other diseases, such as cardiovascular disease and breast cancer\textsuperscript{3,4}
- Seriousness of health outcomes\textsuperscript{5,6}

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

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)

- Fall Risk Discussion: 35.00
- COPD Spirometry Testing: 36.30
- Testing/Treatment after Fracture (65-85 year old women): 40.70
- Fall Risk Intervention: 58.60
- Blood Pressure Control in Diabetes: 61.90
- Hemoglobin A1c (HbA1c) Control: 62.70
- Colorectal Cancer Screening: 67.40
- Controlling High Blood Pressure: 67.90
- Eye Exams in Diabetes: 68.80
- Flu Vaccinations (65 and older): 72.40
- Breast Cancer Screening: 72.70
- Disease-Modifying Anti-Rheumatic Drug Therapy: 77.10
- Beta-Blocker Treatment After a Heart Attack: 90.90
- Hemoglobin A1c (HbA1c) Screening: 93.20
- Monitoring Nephropathy in Diabetes: 95.50

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

Reduced Bisphosphonate Prescription Rates Starting in 2008

11,464 additional hip fractures
$469 million additional expenses
2,293 additional deaths

Adapted from Lewiecki EM et al. Osteoporos Int. 2018;29:717-722.
“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.”
Guidelines, Treatments, and Strategies to Reduce Fracture Risk
### Assessing Risk and Diagnosing Osteoporosis: DXA (Bone Mineral Density Testing)

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

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


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\(^2\)

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2. [http://www.shef.ac.uk/FRAX](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.

## Assessing Risk and Diagnosing Osteoporosis: Indications for Vertebral Imaging

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-score $\leq$ -1.5 at spine, total hip or femoral neck</td>
<td>65-69 years</td>
<td>70-79 years</td>
</tr>
<tr>
<td>T-score $\leq$ -1.0 at spine, total hip or femoral neck</td>
<td>70 years and older</td>
<td>80 and older</td>
</tr>
<tr>
<td>• Low trauma fracture (age $\geq$ 50)</td>
<td>Postmenopausal women and men age 50 and older</td>
<td></td>
</tr>
<tr>
<td>• Historical height loss of 1 1/2 inches or more</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Prospective height loss of 0.8 inches or more</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Recent or ongoing long-term glucocorticoid treatment</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*If bone density testing is not available, vertebral imaging may be considered based on age alone.*

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

Pharmacologic therapy for Osteoporosis

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

**Inhibition of resorption**

**Stimulation of formation**

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

**Medications in Development:**
- Sclerostin inhibitor- Romosozumab
## Overview of FDA Approved Medications

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

PMO = Post menopausal; GIOP = Glucocorticoid-induced osteoporosis. Data from prescribing information for individual medications.
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 $37 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 50% could walk independently after 1 year (2). Approximately 34% 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.
<table>
<thead>
<tr>
<th>#</th>
<th>Recommendation</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Offer ALN, RIS, ZOL, or Dmab to reduce risk of hip and vertebral fractures (VFs) in women with osteoporosis</td>
<td>Strong</td>
</tr>
<tr>
<td>2</td>
<td>Treat osteoporotic women for 5 years</td>
<td>Weak</td>
</tr>
<tr>
<td>3</td>
<td>Offer BPs to reduce VF risk in men with osteoporosis</td>
<td>Weak</td>
</tr>
<tr>
<td>4</td>
<td>No BMD monitoring during 5 years of treatment in women</td>
<td>Weak</td>
</tr>
<tr>
<td>5</td>
<td>No E, E+P, or Raloxifene for treatment of PMO</td>
<td>Strong</td>
</tr>
<tr>
<td>6</td>
<td>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</td>
<td>Weak</td>
</tr>
</tbody>
</table>

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

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 osteoporosis.

• 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

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>58</td>
<td>68</td>
<td>78</td>
</tr>
<tr>
<td>Prior fracture</td>
<td>wrist</td>
<td>no</td>
<td>humerus</td>
</tr>
<tr>
<td>Parent fractured hip</td>
<td>no</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Current smoking</td>
<td>yes</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Lumbar spine BMD T-score</td>
<td>-2.8</td>
<td>-2.5</td>
<td>-3.1</td>
</tr>
<tr>
<td>Femoral neck BMD T-score</td>
<td>-2.2</td>
<td>-3.5</td>
<td>-3.3</td>
</tr>
</tbody>
</table>

**BMI: 20.4**

- The ten year probability of fracture (%) with BMD

<table>
<thead>
<tr>
<th>Major osteoporotic</th>
<th>Hip Fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>4.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Major osteoporotic</th>
<th>Hip Fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td>33</td>
<td>14</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Major osteoporotic</th>
<th>Hip Fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td>58</td>
<td>48</td>
</tr>
</tbody>
</table>
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

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 assess 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.
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

Who are the Highest Risk Patients?

• Prior fracture is the most important risk factor for future fracture\textsuperscript{1}
  • Recent Fractures suggest very high risk (Osteoporosis Emergency/Urgency)
    - In over 377,000 women with first fracture\textsuperscript{2}:
      - Absolute Risk of another fracture 10% first year, 18% first 2 years, 31% first 5 years
  • Multiple Fractures also indicate very high risk\textsuperscript{3}
  • Proactive Spine Imaging Required to find Morphometric Vertebral Fractures
    - NHANES VFA Study 2017\textsuperscript{4}
      - Vertebral Fracture Prevalence 5% in the 60s, 10% in the 70s, 20% in the 80s\textsuperscript{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
4. Cosman F et al OI 2017
# Osteoporosis Medication Efficacy

<table>
<thead>
<tr>
<th>Medication</th>
<th>2-year Increase Spine BMD</th>
<th>2-year Increase Total Hip BMD</th>
<th>RRR of Spine Fracture</th>
<th>RRR of Nonvert Fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate¹</td>
<td>5%</td>
<td>3%</td>
<td>53%</td>
<td>20% at 3 years</td>
</tr>
<tr>
<td>Zoledronic acid ²</td>
<td>5-6%</td>
<td>3-4%</td>
<td>70%</td>
<td>25% at 3 years</td>
</tr>
<tr>
<td>Denosumab ³</td>
<td>6-8%</td>
<td>3-4%</td>
<td>68%</td>
<td>20% at 3 years</td>
</tr>
<tr>
<td>Teriparatide⁴</td>
<td>10%</td>
<td>2-3%</td>
<td>65-80%⁴,⁵</td>
<td>53% at 19 months</td>
</tr>
<tr>
<td>Abaloparatide⁵</td>
<td>10%</td>
<td>3-3.5%</td>
<td>86%</td>
<td>43% at 19 months</td>
</tr>
</tbody>
</table>

**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

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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 2 years followed by Teriparatide for 2 years
- **Blue**: Teriparatide for 2 years followed by Denosumab for 2 years

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

<table>
<thead>
<tr>
<th>Pharmacologic agent(s) discussed</th>
<th>ACP</th>
<th>ASBMR Task Force</th>
<th>AACE/ACE</th>
</tr>
</thead>
</table>
| 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 | |

<table>
<thead>
<tr>
<th>Continuation of treatment recommended</th>
<th>“Continuing treatment after 5 years may be beneficial for some patients and may be appropriate after reassessing the risks and benefits of continuing therapy.”</th>
</tr>
</thead>
</table>
| 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.

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

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.
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

- 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

<table>
<thead>
<tr>
<th>Agent</th>
<th>Comments</th>
</tr>
</thead>
</table>
| 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

- Jaw Rot
- Brittle Bones
- Heartburn
- Blood Clots
- Fatal Stroke
- Muscles Ache
- Back Pain
- Atrial Fib
- Femur Snaps
- Brittle Bones
- Joint Pain
Benefits and Risks

Motor Vehicle Accidents

- Wearing seat belts reduces the risk of serious crash-related injuries and deaths by about 50%.

Osteoporosis

- Treatment with bisphosphonates reduces the risk of fractures by about 50%.

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

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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