# Building Strong Bones: What CV Nurses Need to Know about Fracture Prevention and Osteoporosis

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# Disclosures

Advisory Board:

- LabCorp
- AMAG
- Radius Health

Speaker:

- TherapeuticsMD

# Objectives

1. Describe risk factors for bone fracture and the use of bone densitometry and the FRAX calculation to determine 10-year fracture risk
2. List strategies for the prevention of low bone density and fracture
3. Discuss evidence-based pharmacologic therapy for the management of osteopenia and osteoporosis including long-term use of drugs and drug holidays
4. Apply shared decision-making strategies (risk vs benefit analysis ) within clinical cases to optimize treatment plans incorporating current evidence in the management of bone health

# The Link Between Osteoporosis and Cardiovascular Disease (CVD)

# The Link Between Osteoporosis and Cardiovascular Disease (CVD)

Seemingly unrelated conditions:

- Risk of CVD and stroke are higher in patients with a history of osteoporotic fracture or low bone mass
- Patients with cardiovascular disease are at higher risk for bone loss and osteoporotic fracture

Laroche M, Percourneau V, Bain H, Osteoporosis and ischemic cardiovascular disease, Joint, Bone, Spine, Vol 84. 4:July 2017. 427-432.

# The Link Between Osteoporosis and Cardiovascular Disease (CVD)

- Hypotheses:
  - Shared risk factors
  - Common pathophysiological mechanisms
  - Common genetic factors
  - Causal association
- Low bone mineral density (BMD) has been related to increased:
  - Cardiovascular mortality
  - Cardiovascular morbidity
  - Subclinical measures of atherosclerosis

Farhat G, Cauley J, The link between osteoporosis and cardiovascular disease, Clin Cases Miner Bone Metab. 2008Jan-Apr; 5(1):19-34

# The Link Between Osteoporosis and Cardiovascular Disease (CVD)

- CVD and osteoporosis are common age-related conditions associated with significant morbidity, mortality and disability
- Increasing body of biologic and epidemiologic evidence:
  - Support for a link between the two conditions that cannot be explained by age alone
- Pathophysiology common pathogenetic mechanisms:
  - Proteins, parathyroid hormone, phosphate, oxidized lipids and vitamins D and K are implicated in both bone and vascular metabolism
  - This indicates a possible common pathophysiologic mechanism

Lello s, Capozzi A, Osteoporosis and cardiovascular diseae: an update. Gynecol Endocrinol 2015;31(8):590-4

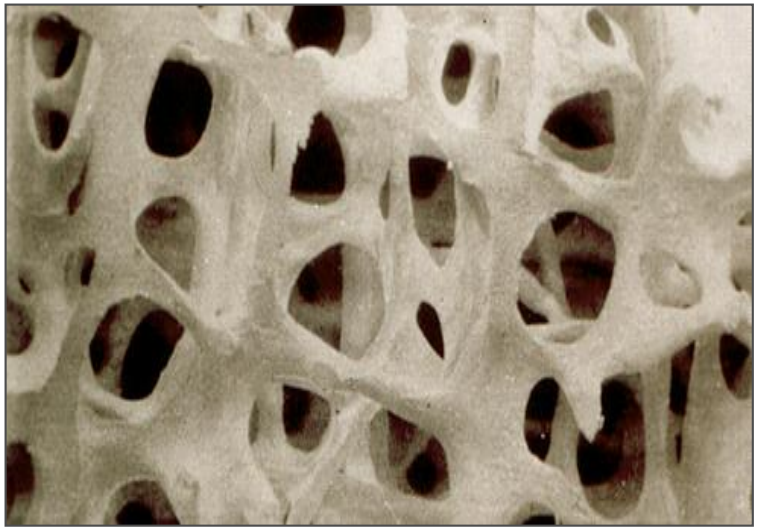
# The Link Between Osteoporosis and Cardiovascular Disease (CVD)

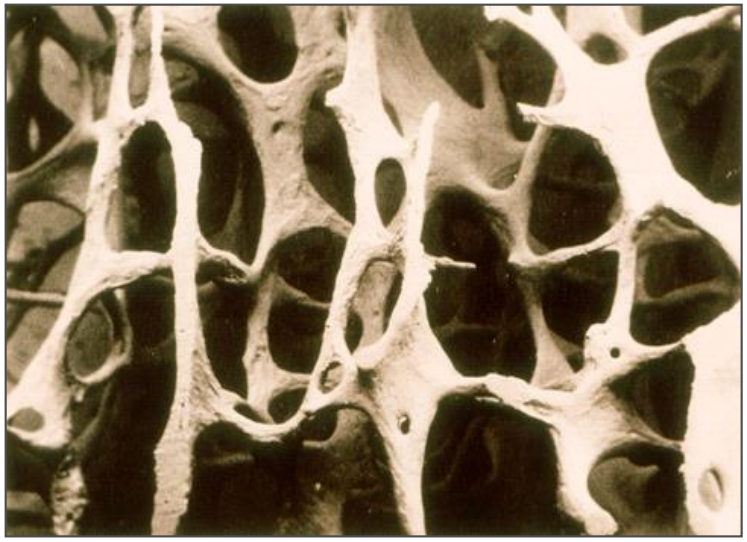
- Atherosclerotic calcification and bone mineralization share common features
  - Mechanisms similar to those in bone mineralization
  - Mineral in calcium deposits of plaques similar chemical composition to hydroxyapatite crystals which form the inorganic bone matrix
- The Multiple Outcomes of Raloxifene Evaluation (MORE) trial:
  - Indicates that osteoporosis was a strong predictor of incident cardiovascular events in postmenopausal women independent of age and other traditional cardiovascular risk factors

Tanko L, Christiansen C, Cox DA, Geiger MJ, McNabb MA, Cummings SR. Relationship between osteoporosis and cardiovascular disease in postmenopausal women. J Bone Miner Res. 2005;20:1912-1920.

# Osteoporosis Overview

# Osteoporosis: Definition





A disease characterized by low bone mass and microarchitectural deterioration of bone tissue leading to enhanced bone fragility and a consequent increase in fracture risk

Pentice A *Public Health Nutr* 2004;7:227-43; WHO Study Group In *Assessment of Facture Risk and Its Application to Screening for Postmenopausal Osteoporosis*. Geneva: WHO, 1994
Photos courtesy of NAMS slide set for clinicians

# A Gender Related Condition

- Osteoporosis is the most common bone disorder affecting humans
- The risk of hip fracture doubles for every 5- to 6-year increase in age from ages 65-85
- Of the 10 million Americans estimated to have osteoporosis, 8 million are women (80%)

# Vertebral Fractures

Significant consequences for patients

- Acute and chronic pain
- Kyphosis and height loss
- Impaired function
- Increased morbidity and mortality
- Increased fracture risk

Delmas PD, et al. J Bone Miner Res. 2005;20:557-563

# Hip and Other Non-Vertebral Fractures Have Significant Consequences

- Hip fracture associated with
  - Loss of ambulatory status in 30% of patients
  - Increased morbidity and mortality
  - Increased fracture risk
  - Major reason for admission to chronic care facilities
- Non-vertebral fractures
  - Pain
  - Increased risk of future fractures

# Fewer Than 35% of Hip Fracture Patients Receive Pharmacologic Treatment Within 6 Months

Fracture Liason Service (FLS)

- To identify and treat patients with a recent fragility fracture
- Has been show to be effective and save money
- Multidisciplinary system approach
- Identifies patients at or proximate, to the time they are treated at the hospital for fracture
- Provides easy access to osteoporosis care.

Mitchell PJ. Best practices in secondary fracture prevention: fracture liaison services. Current Osteopor Reports. 2013;11:52–60

# Who Should Be Screened?

National Osteoporosis Foundation (NOF) recommends screening for:

- Women aged ≥65 years and men aged ≥70 years, regardless of risk factors
- Postmenopausal and menopausal transitioning women and men aged 50 to 69 years with clinical risk factors for fracture
- Postmenopausal women and men aged >50 years who have had an adult-age fracture
- Adults with a condition or taking a medication associated with low bone mass or bone loss

Dual-energy x-ray absorptiometry (DXA) is the current standard for measuring bone mineral density (BMD)

Cosman F, et al. *Osteoporos Int*. 2014;25(10):2359-2381.

# Who Should Be Screened?

North American Menopause Society (NAMS)[1]:

- All women ≥65 years, regardless of clinical risk factors
- Postmenopausal women with medical causes of bone loss
- Postmenopausal women ≥50 years with additional risk factors
- Postmenopausal women with a fragility fracture

US Preventive Services Task Force (USPSTF):

- Recommendations currently under review

1. North American Menopause Society. *Menopause*. 2010;17(1):23-54.

# What Are the Risk Factors?

Most common risk factors:[1,2,3]

- Postmenopausal
- Female
- Low body mass index (BMI)
- Caucasian
- Poor calcium intake
- Lifestyle (eg, smoking, caffeine consumption >300 mg/d)


1. Watts N, et al. *Endo Pract*. 2010; 16(Suppl 3):1-37.
2. Li S, et al. *Nutr J*. 2015 Apr 18; 14:38.
3. Cosman F, et al. *Osteoporosis Int. 2014; 25(10): 2359-2381.*

# Other Risk Factors

Chronic medical conditions also increase risk and include:[1,2,3]

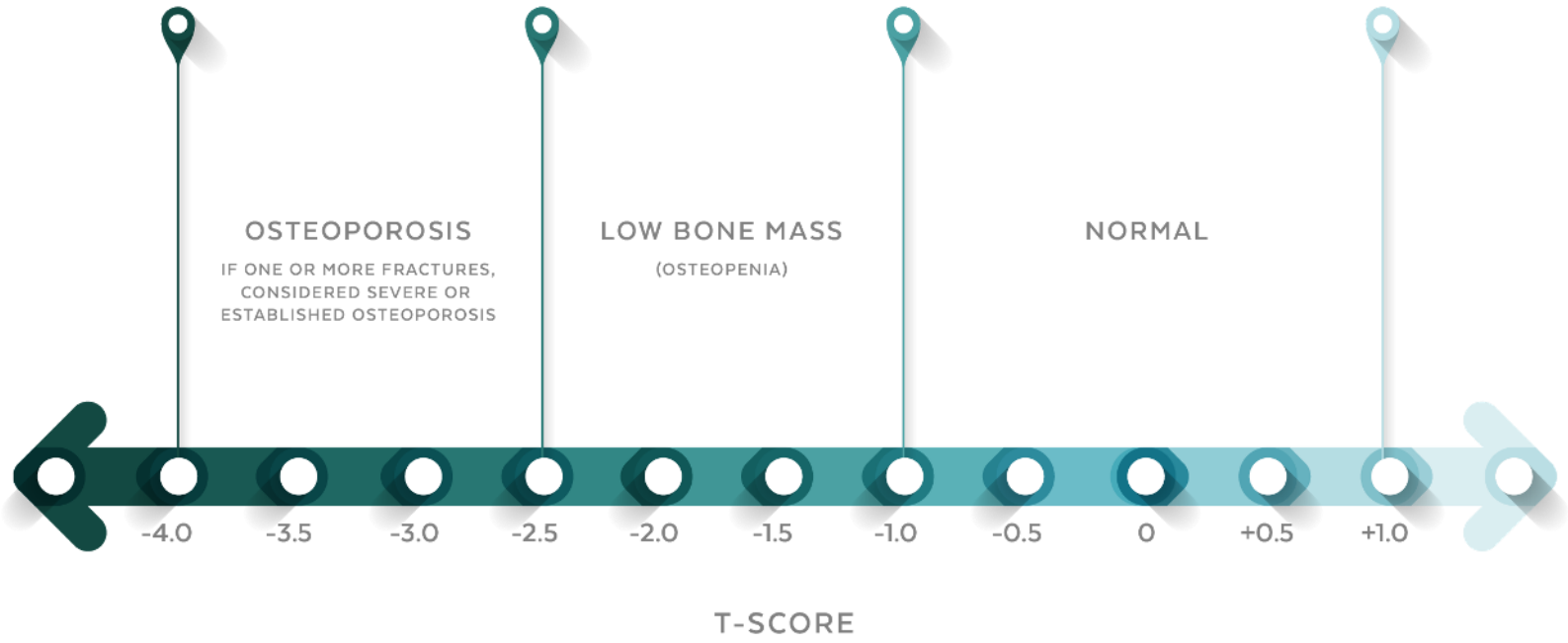
- Chronic kidney disease
- Oral glucocorticoids (≥5 mg/d of prednisone for >3 months)
- Estrogen deficiency
- Hyperparathyroidism
- Systemic lupus erythematosus
- Conditions associated with malabsorption (eg, celiac disease, inflammatory bowel disease)
- Chronic obstructive pulmonary disorder


1. Watts N, et al. *Endo Pract*. 2010; 16(Suppl 3):1-37.
2. Li S, et al. *Nutr J*. 2015 Apr 18; 14:38.
3. Cosman F, et al. *Osteoporosis Int. 2014; 25(10): 2359-2381.*

# Interpreting Bone Densitometry Results

Bone Density
FRAX: 10-Year Fracture Risk Calculation

# T-Score Classifications




Cosman F, et al. *Osteoporos Int*. 2014;25(10):2359-2381.

# Using FRAX

**To find those individuals at high risk for fracture, who are not yet osteoporotic!**

If your patient has osteoporosis by T-score, you do not have to look at FRAX. BUT, you may look at FRAX!

More fractures occur in men and women with T-scores from -1.0 to -2.5!

# FRAX: Gauging 10 Year Fracture Probability


https://www.shef.ac.uk/**FRAX**/tool.jsp

Country : US (Caucasian) Name / ID : About the risk factors

# Questionnaire:

1. Age (between 40-90 years) or Date of birth

Age: 52 Date of birth: Y: 1956 M: D:

2. Sex ○ Male ◉ Female

3. Weight (kg) 58.97

4. Height (cm) 167.64

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 per day ◉ No ○ Yes

12. Femoral neck BMD (g/cm²)

Hologic 0.610 **T-score: -2.1**

Clear Calculate

BMI 21.0

The ten year probability of fracture (%)

| | |
|---|---|
| Major osteoporotic | 7.5 |
| Hip fracture | 1.5 |

# Application of FRAX™ In the US

- Intended for post-menopausal women and men age 50 and older
- Has not been validated in patients currently or previously treated with pharmacotherapy for osteoporosis. In such patients, clinical judgment must be exercised in interpreting FRAX scores.
  - Patients who have been off osteoporosis medication for 1 to 2 years or more might be considered untreated.

# Application of FRAX™ In the US

- Frax can be calculated with either femoral neck BMD or total hip BMD, but, when available, femoral neck BMD is preferred.  Use of BMD from non hip sites is not recommended.
- T scores must be converted to a reference standard to be used. The FRAX patch is available at www.NOF.org to make the calculation
- FRAX may be calculated by going to the FRAX calculator at the University of Sheffield website

# Application of FRAX™ In the US

The use of FRAX™ is for clinical guidance only and is not a rule.

Consider intervention strategies for those:

- Who do not have osteoporosis by BMD
- Do not meet the cut points after FRAX
- Are not high enough risk of fracture despite low BMD

Conversely, the recommendations do not mandate treatment

Make decisions to treat on a case- by- case basis.

# Who Should Be Treated?

NOF recommends treating the following:

- Patients with osteopenia or low bone mass with a history of fragility fracture of the hip or spine
- Patients with a T-score of –2.5 or lower in the spine, femoral neck, total hip, or 1/3 of radius
- Patients with a T-score between –1.0 and –2.5 if the FRAX 10-year risk for major osteoporotic fracture is ≥20% or if the 10-year risk of hip fracture is ≥3%

Camacho PM, et al. *Endo Prac.* 2016;22(suppl 4):1-42.

# Clinical Case

A 79-year-old Caucasian female presents for an osteoporosis risk evaluation. She has no medical problems, no history of fracture, and no family history of fracture. Her history is negative for smoking, glucocorticoid use, and excessive alcohol consumption.

**Exam:** weight, 154 lb; height, 64 in

**DXA results:**

Femoral neck BMD ($g/cm^2$), 0.730

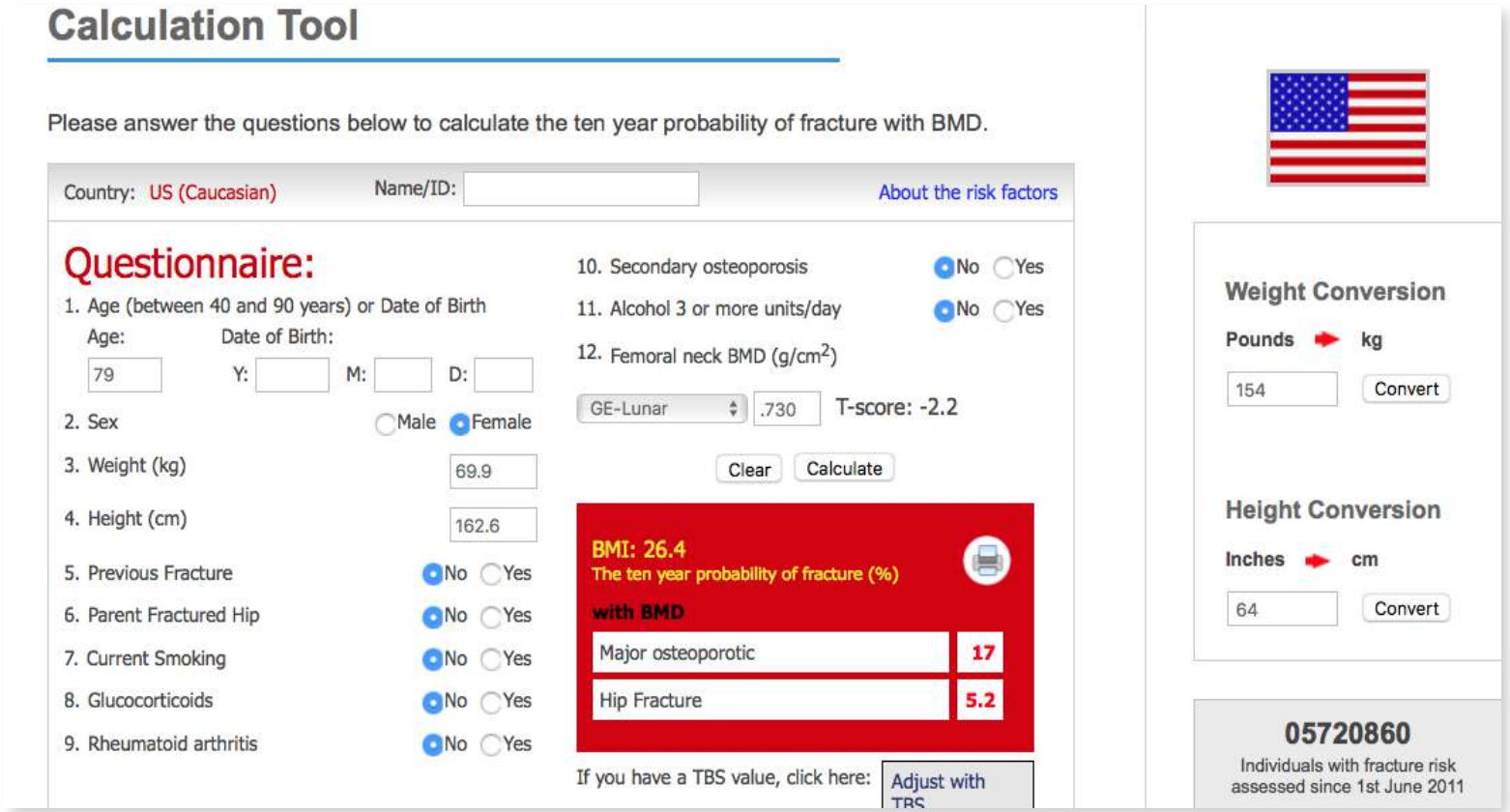
GE Lunar T-score: spine, –1.5; hip, –2.2

FRAX 10-year risk of fracture: Major osteoporotic, 17%; hip, 5.2%

**Based on this information:**

- Does she require treatment due to osteoporosis?
- Is she at risk for a major fracture in the next 10 years?
- Is a discussion of preventive treatment indicated?

# Clinical Case #1 (Cont)




www.sheffield.ac.uk/FRAX/

# Treatment

## When and How

# Non-Pharmacologic Interventions

- Goal of non-pharmacologic intervention is to prevent future fractures through lifestyle change
- The role of Vitamin D in osteoporosis
  - May be important as both adjuvant and treatment
  - Might be important in the response to therapy
  - The effect on muscle strength, balance and risk of falls is important
- Exercise
- Fall Prevention

# NOF Guidelines: When to Treat

## Pharmacologic Treatment

- Postmenopausal women or men over age 50 with a prior hip or spine fracture
- Postmenopausal women or men over 50 with a BMD T-score of -2.5 or lower at the hip or spine
- Postmenopausal women or men over 50 with T-score between -1 and -2.5 at the femoral neck, total hip, or spine if:
  - 10 year probability (from FRAX) of hip fracture is ≥ 3%
  - 10 year probability of a major osteoporosis-related fracture is ≥ 20%

National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. National Osteoporosis foundation; Washington, DC. 2014

# Treatment Recommendations

- No pharmacologic therapy should be considered indefinite in duration
- After the initial three to five year treatment period, a comprehensive risk assessment should be performed
- There is no uniform recommendation that applies to all patients and duration decisions need to be individualized

National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. National Osteoporosis foundation; Washington, DC. 2014

# Current Pharmacologic Agents Approved for the Treatment of Osteoporosis

- Anti-resorptive agents
  - Bisphosphonates
    - Weekly oral alendronate (Fosamax)
    - Weekly or monthly risedronate (Actonel)
    - Monthly oral or quarterly IV ibandronate (Boniva)
    - Once yearly infusion Zoledronic Acid (Reclast)
  - Rank Ligand Inhibitor
    - Denosumab (Prolia)

National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. National Osteoporosis foundation; Washington, DC. 2014

# Current Pharmacologic Agents Approved for the Treatment of Osteoporosis

- Calcitonin
- Selective estrogen receptor modulators (SERMS)
  - Raloxifene (Evista)

> Anabolic agents

- Parathyroid hormone (Forteo)
- Abaloparatide (Tymlos)

# Anti-resorptive Therapy

Bisphosphonates
Rank Ligand Inhibitors
SERMS
Calcitonin

# Osteoporosis Treatment

## Bisphosphonates

# Effects of Bisphosphonates

- Decreased bone turnover
- Increased BMD at spine and hip
- Decreased risk of vertebral and hip fractures
- Sustained effects with continued treatment
- Best studied class of agents used in treating osteoporosis
- Long term safety record

Black DM, et al. *Lancet*. 1996;348:1535-1541, Body J, et al. J Clin *Endocrinol Metab*. 2002;87:4528-4535

# Bisphosphonates

| Drug | Mechanism of action | Prevention dose | Treatment dose | Fracture risk reduction |
|---|---|---|---|---|
| Alendronate | Antiresorptive agents that inhibit osteoclast function | 5 mg/d[a] or 35 mg/wk[a] | 10 mg/d[a] or 70 mg/wk[a] | Spine, hip, nonvertebral |
| Ibandronate | | 2.5 mg/d[a] or 150 mg/mo[a] | 2.5 mg/d[a], 150 mg/mo[a], or 3 mg[b] every 3 mo | Vertebral |
| Risedronate | | 5 mg/d[a], 35 mg/wk[a], or 150 mg/mo[a] | 5 mg/d[a], 35 mg/wk[a], or 150 mg/mo[a] | Spine, hip, nonvertebral |
| Zoledronic acid | | 5 mg[b] every second year | 5 mg/y[b] | Spine, hip, nonvertebral |

[a]By mouth.
[b]Intravenously.

Camacho PM, et al. *Endo Prac.* 2016;22(suppl 4):1-42.
McClung M, et al. *Am J Med.* 2013;126(1):13-20.

# ORAL BISPHOSPHONATES

## > Pros

- Osteoporosis prevention and treatment
- Reduction in risk of vertebral fractures (w/ and w/o pre-existing fx)

## > Cons

- Require lifestyle change
  - empty stomach
  - water only
  - may lead to non-compliance
- GI adverse effects
- Marginal efficacy in non-vertebral fractures (e.g. hip)
- Long-term safety is unconfirmed

# IV Bisphosphonate

# Zoledronic Acid

HORIZON Fracture Trials: Efficacy Conclusions

- Reduces incidence of vertebral fractures by 70% (with significant reduction at 1 year)
- Reduces hip fractures by 41%
- Reduces nonvertebral fractures by 25%, over 3 years in patients with osteoporosis, defined by prevalent vertebral fractures and osteoporosis by BMD of the hip

Black DM, etal. N Engl J Med. 2007;356:1809-1822

# Bioavailability and High Binding Affinity Allow Zoledronic Acid to be Dosed Once Yearly

- Zoledronic acid bypasses the GI tract, eliminating absorption limitations
- Year long efficacy of zoledronic acid is attributable to the high binding affinity of zoledronic acid to bone
- Bioavailability:
  - approximately 61% directly to bone
  - Approximately 39% eliminated from circulation within 24 hours

Zoledronic acid (prescribing information) East Hanover, NJ: Novartis Pharmaceuticals Corp; June 2008

# Antiresorptive Agents Beyond Bisphosphonates

# Denosumab

## RANK Ligand Inhibitor

- Fully human monoclonal antibody
- Specifically targets a ligand called RANKL (that binds to a receptor called RANK) which is a key mediator of:
  - Osteoclast formation
  - Function
  - Survival
- Improves cortical and trabecular bone density, volume and strength
- Currently being studied across a range of conditions including osteoporosis, treatment induced bone loss, bone metastases, multiple myeloma and rheumatoid arthritis

# Expanded Indications For Denosumab

- Treatment of postmenopausal women with osteoporosis at high risk for fracture
- Treatment to increase bone mass in men with osteoporosis at high risk for fracture
- **Treatment of glucocorticoid-induced osteoporosis in men and women at high risk for fracture**
- **Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer**
- **Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer**

# Discontinuation of Denosumab Therapy

- Denosumab discontinuation may lead to an increased risk of multiple vertebral fractures.
- Re-evaluation should be performed after 5 years of denosumab treatment.
- Patients considered at high fracture risk should either:
  - Continue denosumab therapy for up to 10 years
  - Or be switched to an alternative treatment.

**Discontinuation of Denosumab therapy for osteoporosis: A systematic review and position statement by ECTS.**
Tsourdi E[1], Langdahl B[2], Bone. 2017 Dec;105:11-17. doi: 10.1016/j.bone.2017.08.003. Epub 2017 Aug 5.

# Discontinuation of Denosumab Therapy

- For patients at low risk, a decision to discontinue denosumab could be made after 5 years,
  - Bisphosphonate therapy should be considered to reduce or prevent the rebound increase in bone turnover.
- Continuation of denosumab can also be considered until results from ongoing trials become available.
- Denosumab should not be stopped without considering alternative treatment
  - To prevent rapid BMD loss and a potential rebound in vertebral fracture risk.

**Discontinuation of Denosumab therapy for osteoporosis: A systematic review and position statement by ECTS.**
Tsourdi E[1], Langdahl B[2], Bone. 2017 Dec;105:11-17. doi: 10.1016/j.bone.2017.08.003. Epub 2017 Aug 5.

# Effects of SERMS (Estrogen agonist/antagonists)

- SERMS exert estrogen like effects on the skeleton
- Decrease bone turnover
- Increase bone density, but to a lesser degree than with bisphosphonates
- Decrease risk of vertebral fracture
- No hip or non-vertebral fracture

Ettinger B, et al.,JAMA.1999; 282:637-85

# Raloxifene

- Pros
  - Osteoporosis prevention
  - No endometrial or breast stimulation
  - LDL reduction
- Cons
  - No current non-vertebral fracture data (e.g. hip)
  - No effect on vasomotor symptoms
  - Thrombosis
  - Effects on cholesterol are modest
  - Leg cramps

# Anabolic Agents

- Unique from other treatments because they are bone building through increased osteoblast activity
- Effects diminish quickly after discontinuing therapy
- Teriparatide
  - Increases BMD up to 13% at spine and to a lesser degree at hip[1,2]
  - Correlates to 72% relative risk reduction of new vertebral fractures[3]
- Abaloparatide
  - Increases BMD at all sites
  - Relative risk reduction of 86% for new vertebral fractures and 43% for nonvertebral fractures[4]


1. Neer RM, et al. *N Engl J Med.* 2001;344(19):1434-1441.
2. Marcus R, et al. *J Bone Miner Res.* 2003;18(1):18-23.
3. Bouxsein ML, et al. *J Bone Joint Surg Am.* 2009;91(6):1329-1338.
4. Miller PD, et al. *JAMA.* 2016;316(7):722-733.

# Effects of Parathyroid Hormone

- Stimulates osteoblast activity preferentially
- Increases bone turnover and creates a positive bone balance
- Improves trabecular microarchitecture and increases cortical thickness
- Increases bone mass
- Decreases risk of vertebral and nonvertebral fractures
- Requires daily injections

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

# Parathyroid Hormone

- Pros
  - Osteoporosis treatment
  - Reduction in risk of vertebral and nonvertebral fractures
  - May be used in conjunction with other OP therapies (e.g. anti-resorptive)
- Cons
  - Osteosarcoma risk?
  - Long-term use not established
  - Long-term safety not established
  - Hip fracture prevention?
  - Daily sq injections
  - Nausea, headache, etc.

# Teraparatide

- FDA approved 2002
- Recombinant human parathyroid hormone analog (1-34), [rhPTH(1-34)] indicated for:
  - Treatment of postmenopausal women with osteoporosis at high risk for fracture
  - Increase of bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture
  - Treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy at high risk for fracture
- Self administered subcutaneous infection for 2 years followed by bisphosphonate therapy
- Carries a label warning regarding osteosarcoma

# Abaloparatide

FDA approved 4/28/17

- Indicated for:
  - Treatment of postmenopausal women with osteoporosis at high risk for fracture defined as:
    - A history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy
- Lab-made copy of part of the human parathyroid hormone-related protein (PTHrP)
- Daily subcutaneous injection
- Recommended for two years and followed with bisphosphonates for several years
- Carries a label warning regarding osteosarcoma
- Side effects include nausea, dizziness, and vomiting

# New Agent: Romosozumab

Not yet FDA approved:

- Monoclonal antibody that binds sclerostin
  - **Increases bone formation**
  - **Decreases bone resorption**
  - Rapid onset of fracture reduction, in the first 6 months
- Adverse events were balanced in the 12 and 24 month studies between placebo and treatment groups
- One atypical fracture and 2 cases of osteonecrosis of the jaw in the treatment group

Felicia Cosman, M.D., Daria B. Crittenden, M.D., Jonathan D. Adachi, M.D., et al, Romosozumab Treatment in Postmenopausal Women with Osteoporosis, N Engl J Med 2016; 375:1532-1543

# American College of Physicians Recommendations

| | Drug | Length of use | BMD monitoring during treatment |
|---|---|---|---|
| First-line therapy | Alendronate, risedronate, zoledronic acid, denosumab | 5 y | No |
| Second-line therapy | Individualize to patient | | |

- Recommend against the use of raloxifene or menopausal hormone therapy to treat osteoporosis
- Omitted anabolic agents from recommendations

Qaseem A, et al. *Ann Intern Med.* 2017;166(11):818-839.

# American Association of Clinical Endocrinologists and American College of Endocrinology Recommendations

| | Drug | Length of use | BMD monitoring during treatment |
|---|---|---|---|
| First-line therapy | Alendronate, risedronate, zoledronic acid, denosumab | Bisphosphonates:<br>High risk, 10 y<br>Low risk, consider drug holiday after 5 y | Every 1-2 y until BMD is stable or individualize to risk |
| Second-line therapy | Ibandronate, raloxifene | | |
| Very high fracture risk or failed bisphosphonate therapy | Anabolic agent teriparatide | 2 y | |

- Raloxifene or menopausal hormone therapy may be a reasonable option in select patients

Camacho PM, et al. *Endo Prac*. 2016;22(suppl 4):1-42.

# Addressing Recent Controversies in the Treatment of Osteoporosis

# Addressing Recent Controversies

- Long term use of bisphosphonate therapy
- Bisphosphonate therapy and the occurrence of fractures of the subtrochanteric or diaphyseal femur
- Osteonecrosis of the jaw (ONJ)

# Bisphosphonates

- Concerning adverse effects:
  - Osteonecrosis of the jaw
    - Risk 1:1,000 to 1:263,000
    - Not associated with treatment duration
    - Potential risk factors include poor oral hygiene, glucocorticoid therapy, and chemotherapy
  - Atypical femur fractures
    - Risk increases with longer therapy duration
    - Subtrochanteric and diaphyseal femoral fractures
- Bisphosphonates accumulate in the bone, so drug holidays are recommended to reduce long-term risk

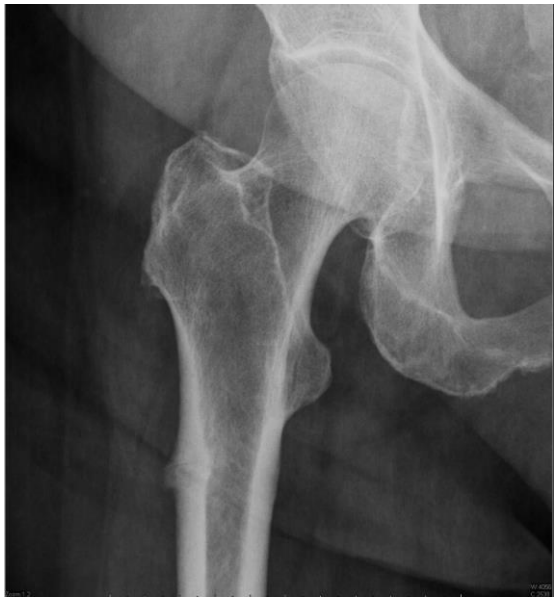


Image from ScienceSource

McClung M, et al. *Am J Med.* 2013;126(1):13-20.

# Addressing Recent Controversies

- Treatment decisions require risk and benefit discussions
- What was acceptable risk previously, may no longer be acceptable
- If disease state risk is high: *fracture*
  - Risk of rare complications may be outweighed

# Long-Term Use of Bisphosphonates

New guidance: American Society for Bone and Mineral Research (ASBMR):

- Long-term treatment with medications reduces the likelihood of fractures in women at high risk
- Reassess for risk after 5 years of oral treatment and after 3 years of IV treatment
- Women at high risk for fractures should continue oral treatment up to 10 years and IV treatment up to 6 years with intermittent follow-up
- Women whose risk of fractures decreases after 3 to 5 years should stop treatment and be reassessed ever 2 to 3 years
- If have fracture during treatment continue bisphosphonate or switch to alternative therapy and reassess every 2 to 3 years

Adler RA, et al. *J Bone Miner Res*. 2016;31(1):19-35.

# Use of Drug Holidays in Women Taking Bisphosphonates

- The duration and length of the holiday should be based on clinical judgment

**Individualize based on risk/benefit assessments**

Diab D, Watts N, Use of Drug Holidays in Women Taking Bisphosphonates, NAMS Practice Bulletin, Released April 1, 2013.

# Drug Holiday Recommendations

| Risk level for fracture | Initiate drug holiday | Therapy during holiday | Length of holiday |
|---|---|---|---|
| Low risk | After 5 y of stability on oral treatment or after 3 y with intravenous zoledronic acid | None | Individualize to patient risk |
| High risk and remains at high risk | After 10 y of oral therapy or after 6 y for intravenous zoledronic acid | Consider teriparatide or raloxifene | Individualize to patient risk |

Camacho PM, et al. *Endo Prac*. 2016;22(suppl 4):1-42.

# Fracture Risk In Patients On Drug Holiday

- Retrospective chart review of 401 patients with osteopenia or osteoporosis on drug holiday from 2004 to 2013
- 15.4% developed a fracture during follow-up
- Yearly incidence of fracture ranged from 3.7 to 9.9% during years 4 and 5
- Majority of fractures occurred at the wrist, foot, ribs, and spine
- Mean age of the fracture group was higher then the nonfracture group
- Researchers recommend further assessment of drug holiday in terms of initiation and length

Bindon B, Adams W, Balasubramanian N, Sandhu J, Camacho P. Osteoporotic fractures during bisphosphonate drug holiday. *Endocr Pract* 2018;24(2):163-169. doi: 10.4158/EP171975.OR

# Summary

- Osteoporosis is under diagnosed and preventative care is under utilized
- Current practice requires dialogue between patient and practitioner in regards to individual risk and risk and benefits of therapeutic options
- Treatment strategies must be individualized to obtain greater compliance to therapy
- Practitioners will need to stay current while treatment recommendations continue to be reviewed and possibly changed

# Cases

BMD

FRAX

The Art of Managing Osteoporosis and Fracture Prevention!

# Case #1

- 72 year old Caucasian woman
- Non-smoker
- F.H. Osteoporosis in Mother
- Negative for secondary causes of osteoporosis

BMD:
LS Total: -1.3
Hip: Neck - 0.8
Total -0.4

Country : US (Caucasian) Name / ID :

About the risk factors

# Questionnaire:

1. Age (between 40-90 years) or Date of birth

Age: 72

Date of birth: Y: 1937 M: D:

2. Sex ○ Male ◉ Female

3. Weight (kg) 74.84

4. Height (cm) 165.1

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 per day ◉ No ○ Yes

12. Femoral neck BMD (g/cm²)

Hologic 0.758 **T-score: -0.8**

Clear Calculate

BMI **27.5**

**The ten year probability of fracture (%)**

| | |
|---|---|
| Major osteoporotic | 19 |
| Hip fracture | 3.0 |

# Case #2

- 52 year old Caucasian
- Non-smoker
- Negative for secondary causes of Osteoporosis

BMD
LS Total: -1.5
Hip: Neck -2.2
Total -2.1

Country : US (Caucasian) Name / ID : About the risk factors

# Questionnaire:

1. Age (between 40-90 years) or Date of birth

Age: 52 Date of birth: Y: 1956 M: D:

2. Sex ○ Male ◉ Female

3. Weight (kg) 58.97

4. Height (cm) 167.64

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 per day ◉ No ○ Yes

12. Femoral neck BMD (g/cm²)

Hologic 0.610 **T-score: -2.1**

Clear Calculate

BMI 21.0

The ten year probability of fracture (%)

| | |
|---|---|
| Major osteoporotic | 7.5 |
| Hip fracture | 1.5 |

# Case #3

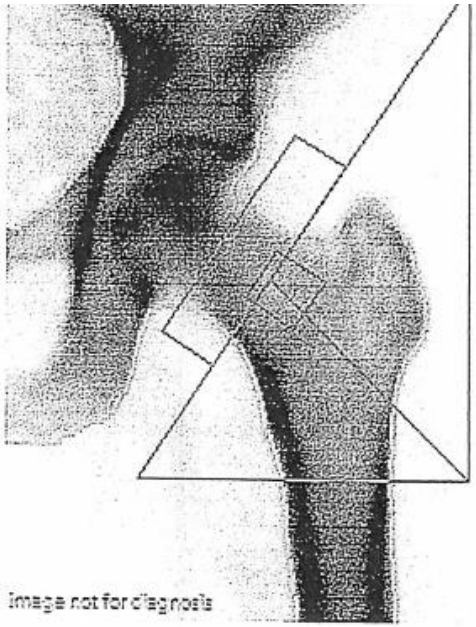
82 yo woman

LS: normal with -0.9

Hip: Moderate low bone mass (Osteopenia) -2.0

Patient has never been treated with pharmacologic therapy. She denies problem with swallowing, GERD or known esophagus problem. She has mild CKD and is being followed by a nephrologist.

# Would you treat this patient? What would you prescribe?




| | |
|---|---|
| **Major Osteoporotic Fracture:** | **22.5%** |
| **Hip Fracture:** | **6.4%** |
| **Population:** | USA (Caucasian) |
| **Risk Factors:** | History of Fracture (Adult) |

*FRAX is a trademark of the University of Sheffield Medical School's Centre for Metabolic Bone Disease, a World Health Organization (WHO) Collaborating Centre

# Case #4

- 63 yo woman has a family history of breast cancer in her Mother.
- Bone density test
  - LS: T-score -2.4
  - Hip: -1.6 at femoral neck
- Does she have osteoporosis?
- Is it important to look at her FRAX score?
- What are her options for therapy?

# Case #4

- Pt prefers to take Raloxifene and starts the medication
- What risk factors are important to identify for this patient?
- The patient has her bone density repeated in 2 years and stays on her Raloxifene
- 2 years later her BMD shows a T score of -2.5 in the femoral neck
- What will you do about her treatment plan?
- Will she stay on Raloxifene?

# Case #5

73 yo woman recently diagnosed with osteoporosis

- Bone Density Test
  - Hip -2.5, LS -0.4
- H/O Gerd/esophagitis
- Normal kidney function
- Pt states that she is planning to have a tooth implant once she is able to use dental insurance after 1/2020

What will your management plan be?


**National Osteoporosis Foundation**

# QUESTIONS?

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