



# Keeping Your Bones Strong During and After Cancer Treatment

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Bay Area Cancer Connections

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# Disclosures

- Scientific Advisory Board member, Crinetics Pharmaceuticals

# Outline

- The importance of bone health
- Effects of cancer treatment on bone health
- Optimizing bone health through diet and exercise
- Medications to improve bone strength

# Perspectives on breast cancer and bone

## Doctor

Optimizing bone health during treatment for breast cancer



## Scientist

New approaches to preventing breast cancer bone metastases



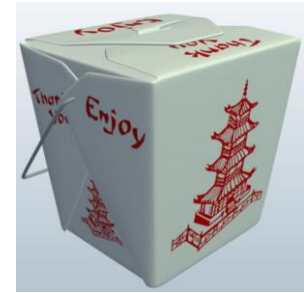
## Patient



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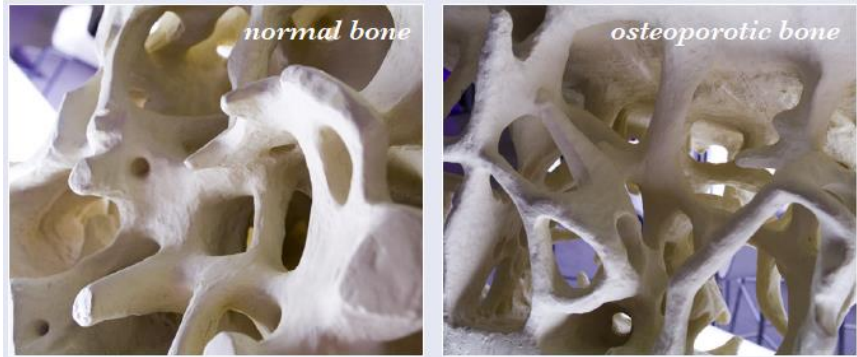
# Take-home messages

- Fractures due to osteoporosis are serious but preventable
- Your risk of fracture depends on many factors
- Cancer treatments can cause bone loss
- Lifestyle changes can slow but not reverse bone loss
- When used properly, osteoporosis medications are safe and effective



# What is osteoporosis?

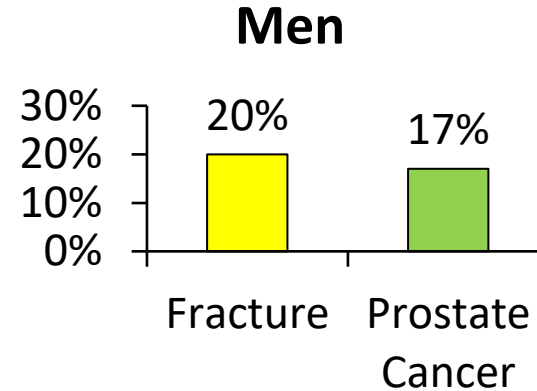
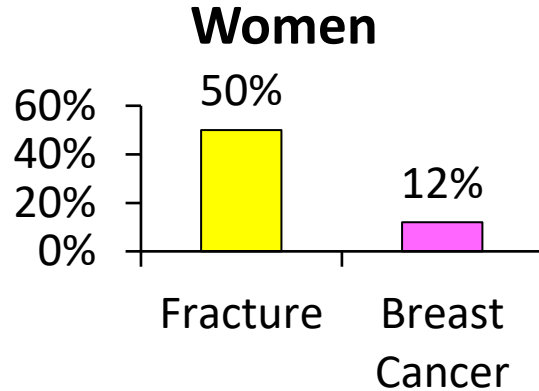
- “Porous bone”
- A decrease in bone mass leading to increased fragility and likelihood of fracture



IOF WOD 2012 report

# Osteoporosis in perspective

Lifetime risk at age 50



There are 5500 fractures a day in the US due to osteoporosis...



Photo by J. Wu



[2million2many.org](http://2million2many.org)

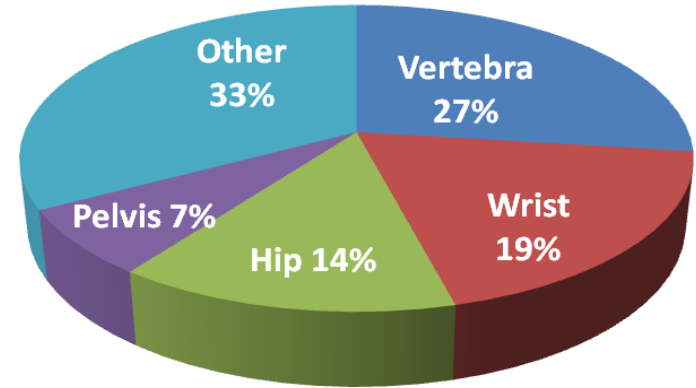
...that's **2 million**  
fractures a year.



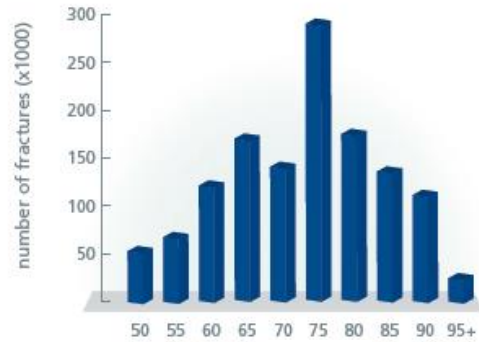
# Osteoporosis is a major public health problem

- Affects 10 million Americans (80% women)
- 2 million fractures per year
- Direct costs \$17 billion per year

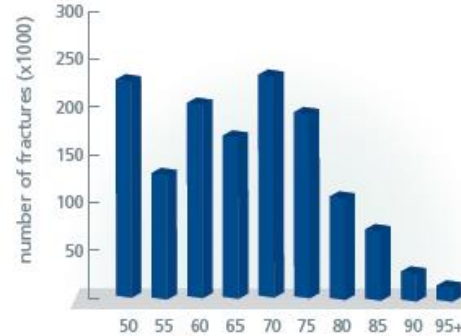
**Types of fractures**



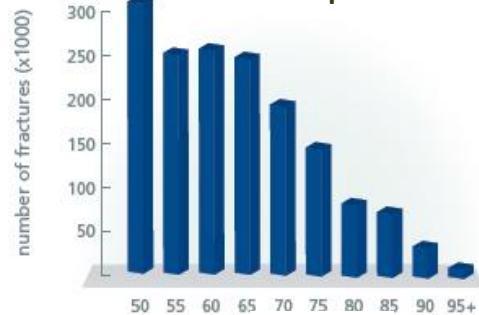
# Fracture patterns change with age



Hip



Spine



Wrist

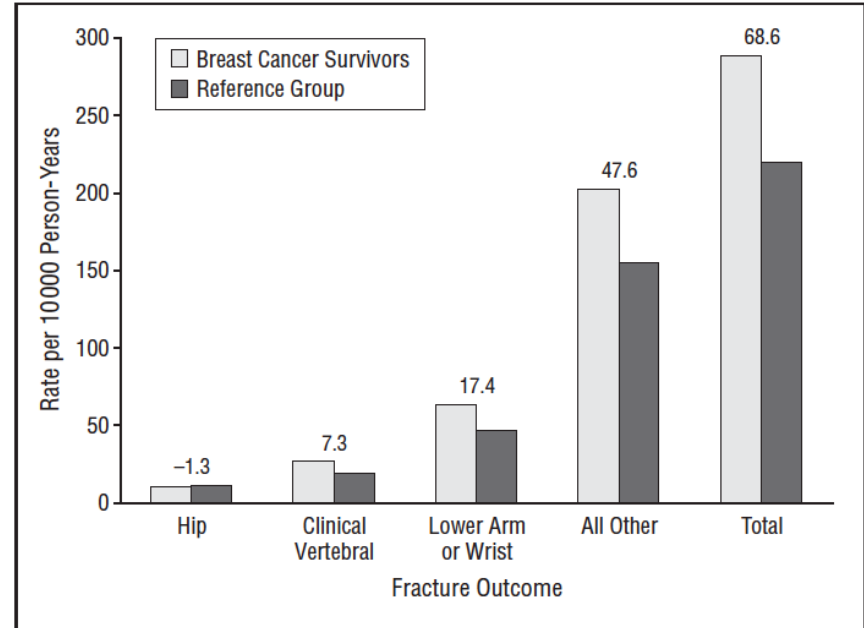


Shoulder

IOF WOD 2012 report

# Osteoporosis is common in breast and ovarian cancer

- Women with breast and ovarian cancer are at risk for bone loss from:
  - Chemotherapy
  - Premature menopause
  - Endocrine therapy
  - Radiation therapy



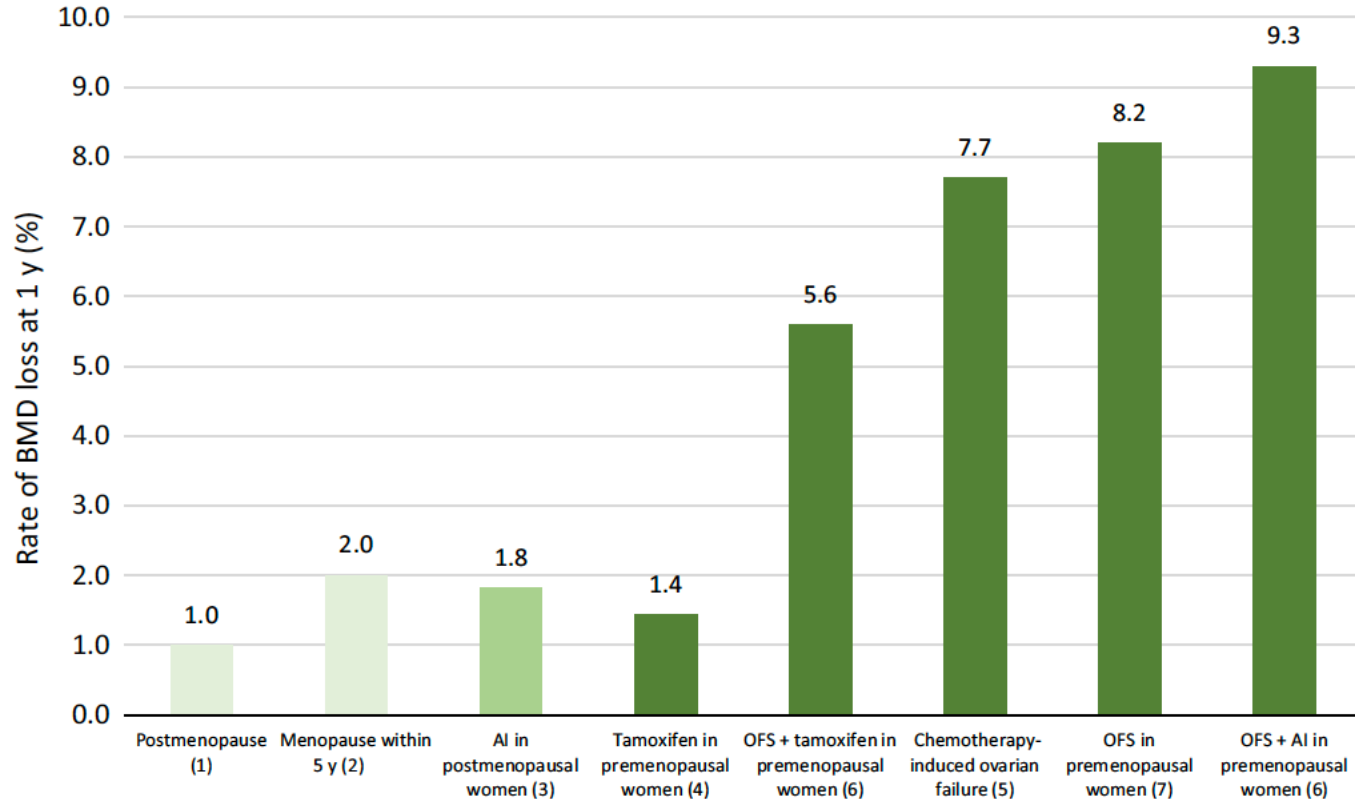
Chen, Arch Int Med 2005

# Endocrine therapy for breast cancer

- 80% of breast cancers express estrogen receptor (ER) and/or progesterone receptor (PR)
- Sources of estrogens
  - Pre-menopause – ovaries
  - Post-menopause – aromatization of adrenal androgens
- Endocrine therapy
  - Selective estrogen receptor modulators (tamoxifen)
  - Aromatase inhibitors (anastrozole, exemestane, letrozole)
  - GnRH agonists (goserelin, leuprolide)
  - Anti-estrogen (fulvestrant)



# Endocrine therapy for breast cancer can lead to substantial bone loss



Grossman, Clin  
Endo 2018

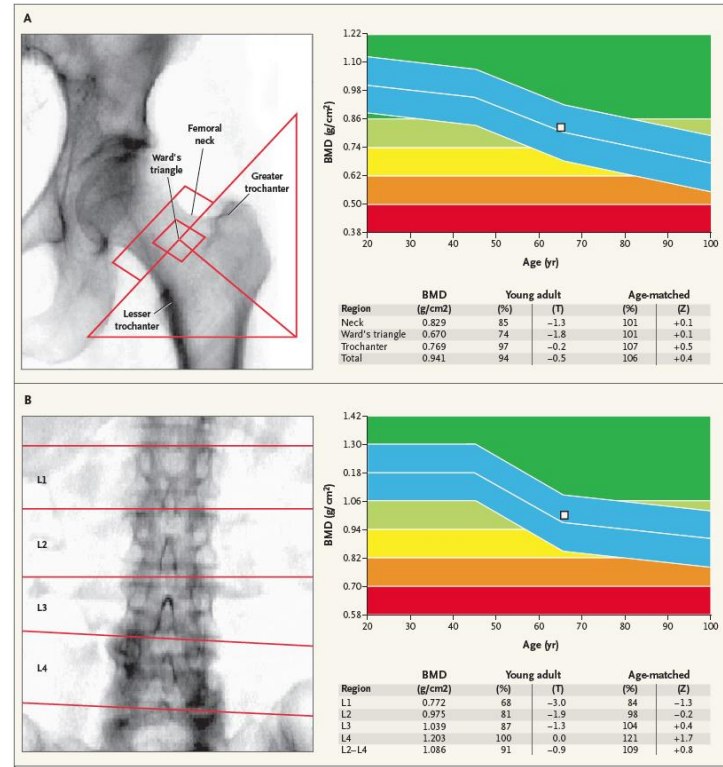


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# Risk factors for bone loss

- Age
- Previous fracture
- Glucocorticoid therapy
- Family history of osteoporosis (especially a parent with a hip fracture)
- Low body weight
- Tobacco use
- Excessive alcohol intake
- Rheumatoid arthritis
- Secondary osteoporosis

# What is a bone density scan?

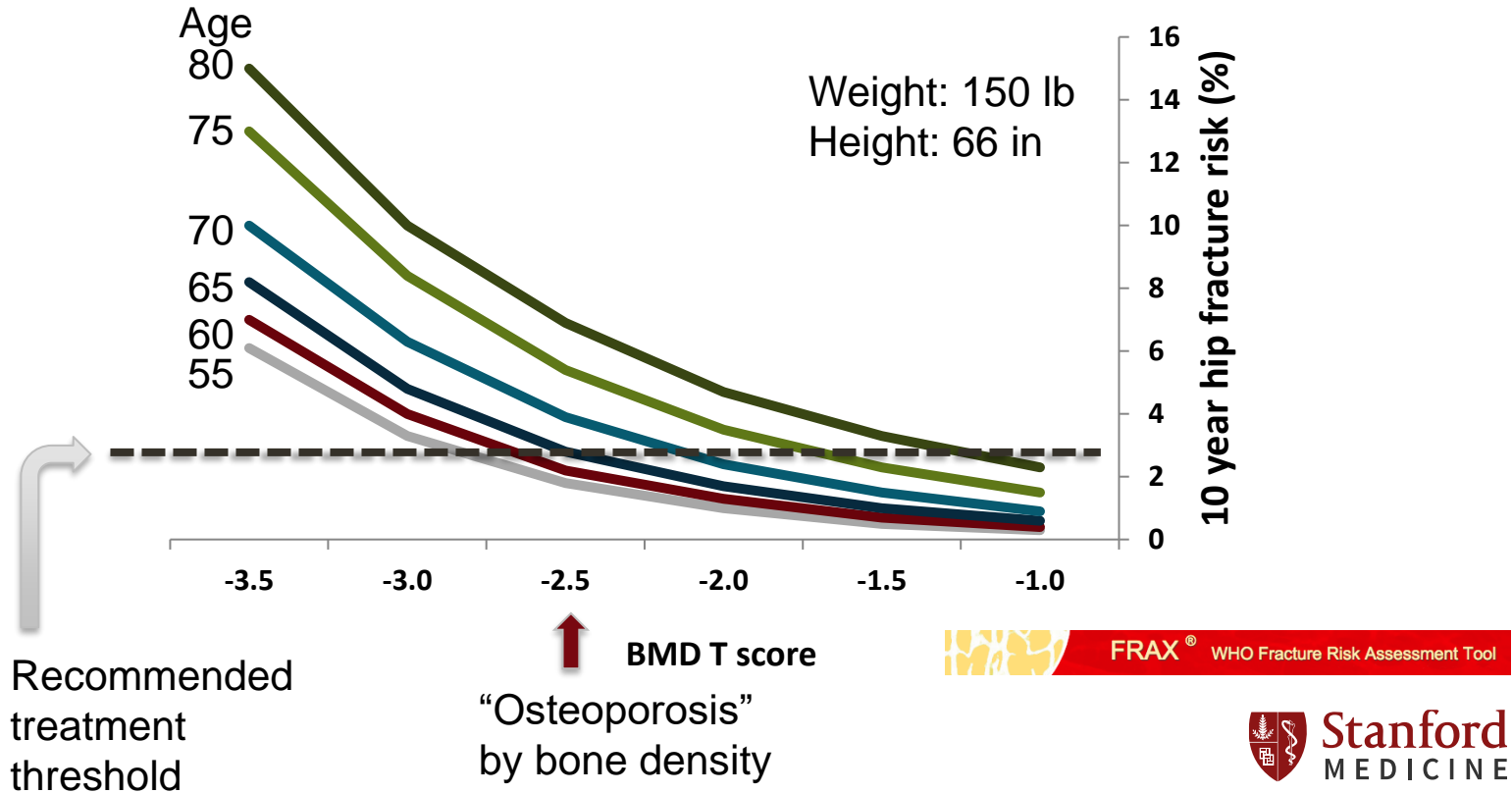


Raisz, NEJM 2005



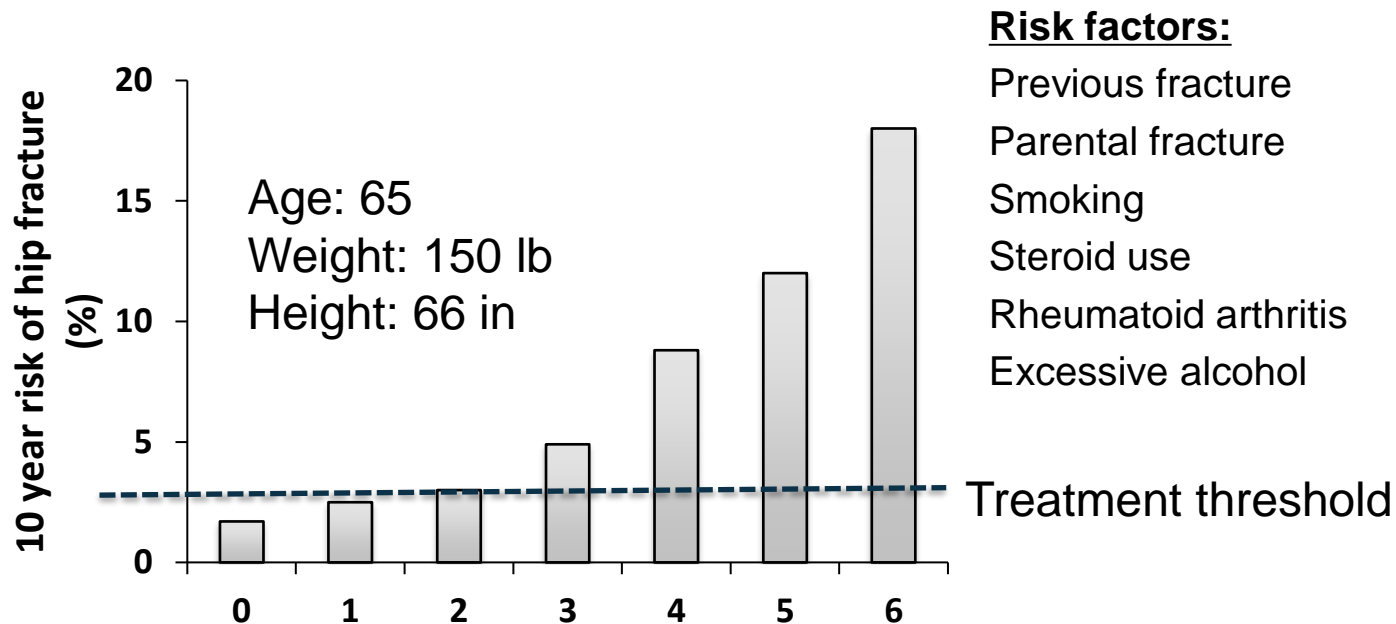
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# Fracture risk depends on BMD and age





# Fracture risk increases with the number of risk factors



# Who should have a bone density test?

- General recommendations
  - Women age 65 and older and men age 70 and older
  - Younger postmenopausal women and men ages 50–69 with clinical risk factors
  - Anyone with a low-trauma fracture after age 50
  - Adults with a condition (e.g., rheumatoid arthritis) or taking a medication (e.g., glucocorticoids) associated with bone loss

# Who should have a bone density test?

- Cancer-specific recommendations
  - All postmenopausal women
  - Premenopausal women on ovarian suppression and aromatase inhibitor
  - Premenopausal women on tamoxifen?

# How can I improve my bone health?

## Recommendations of the Surgeon General's Report on Bone Health

- Get enough calcium and vitamin D
- Be physically active
- Reduce your risk of falls
- Maintain a healthy weight
- Do not smoke
- Limit alcohol use
- Talk with your doctor about medicines you are taking that could weaken bones



# How much calcium?

- Goal 1000-1200 mg daily
- Dietary sources
  - Milk, 1 cup = 302 mg
  - Yogurt, 1 cup = 300 mg
  - Cheddar cheese, 1.5 oz = 306 mg
  - Fortified orange juice, 1 cup = 260 mg
  - Canned salmon, with bones = 181 mg
  - Cottage cheese, 1 cup = 138 mg
  - Broccoli, 1 cup = 90 mg
- Supplements
  - No more than 500 mg at a time
  - If you are taking acid blocking medication, calcium citrate is recommended
  - Otherwise, calcium carbonate is fine



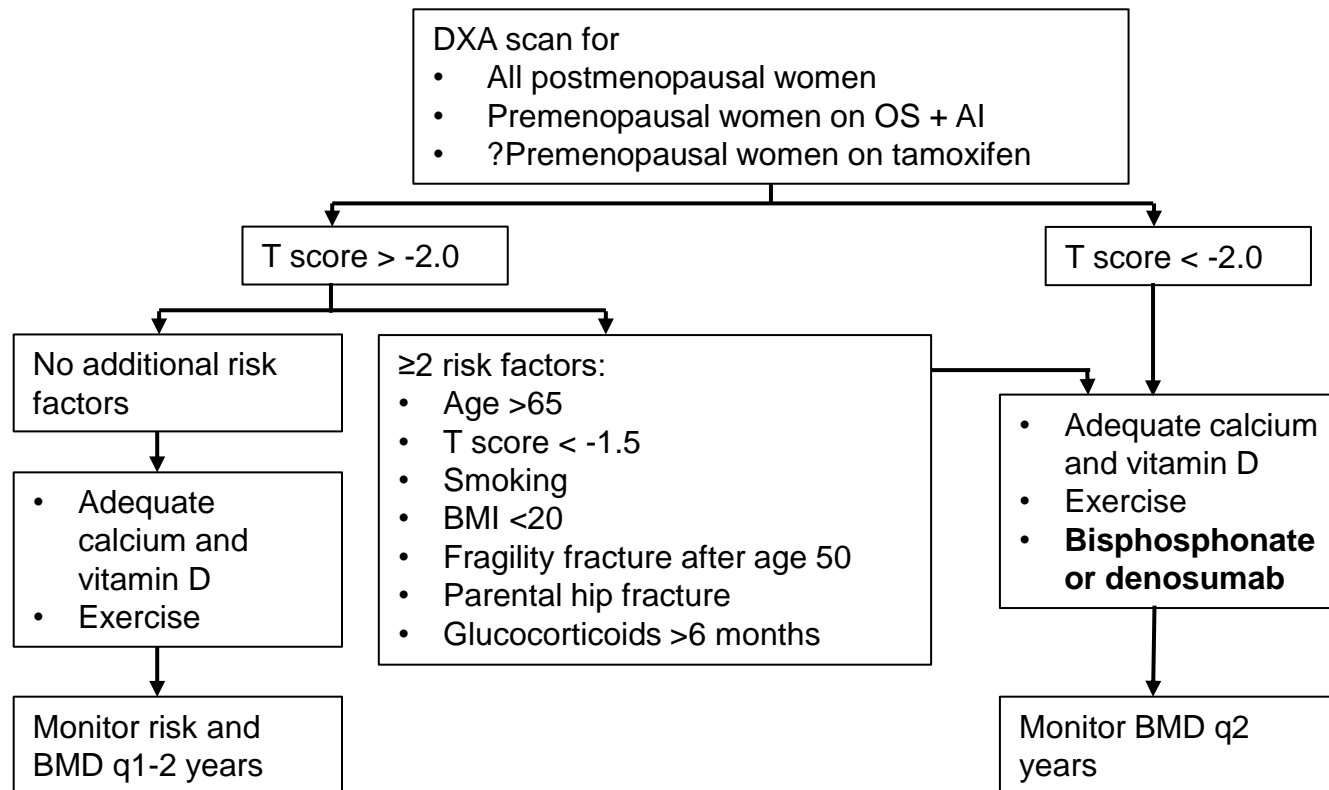
# How much vitamin D?

- Vitamin D – goal 800-1000 IU a day
  - Vitamin D2 (ergocalciferol) is a plant-based supplement
  - Vitamin D3 (cholecalciferol) is produced in the skin, animal-based

# Physical activity

- At least 150 minutes of moderate or 75 minutes of vigorous activity a week
- Strength training 2-3 times per week
  - Weights or resistance
- Balance and flexibility are also important
- Bone Health and Osteoporosis Foundation recommendations:
  - <https://www.bonehealthandosteoporosis.org/preventing-fractures/exercise-to-stay-healthy/>

# Management of bone loss during endocrine therapy for breast cancer



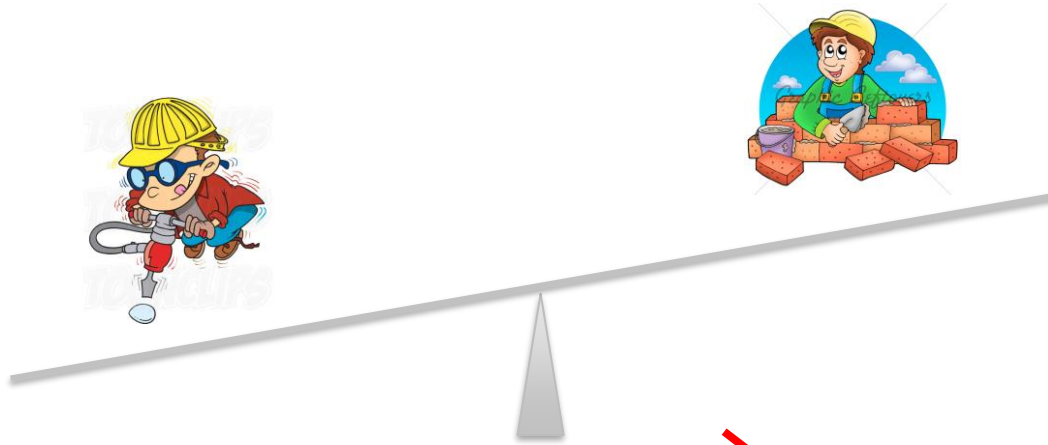
Modified from Hadji,  
J Bone Onc 2017



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# Medications for treating osteoporosis



## **Prevent bone breakdown:**

Selective estrogen receptor  
modulators (SERMs)

Bisphosphonates

Denosumab (anti-RANKL MAb)

## **Promote bone formation:**

Teriparatide (PTH)

Abaloparatide (PTHrP)

Romosozumab (anti-  
sclerostin MAb)



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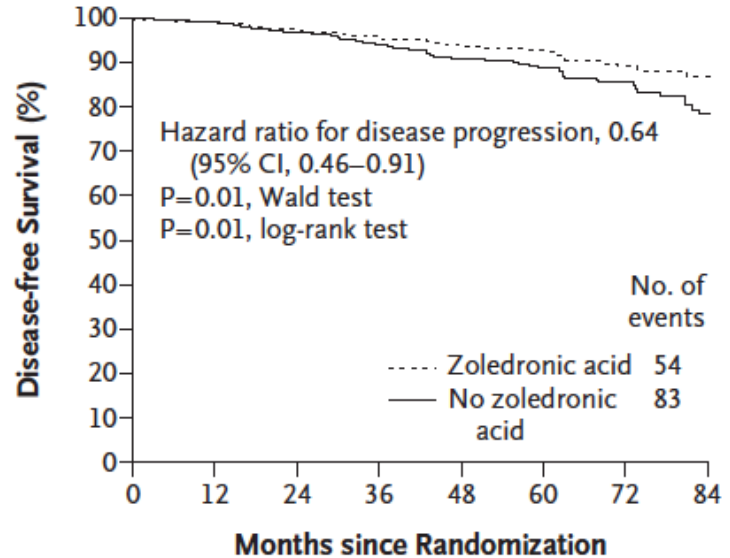
# Osteoporosis medications used in patients undergoing cancer treatment

Class	How given	Pros	Cons
Oral bisphosphonates: <ul style="list-style-type: none"><li>• <b>Alendronate</b> (Fosamax)</li><li>• <b>Risedronate</b> (Actonel)</li><li>• Ibandronate (Boniva)</li></ul>	<ul style="list-style-type: none"><li>• Weekly tablets (except Boniva which is monthly)</li></ul>	<ul style="list-style-type: none"><li>• Safe and effective</li></ul>	<ul style="list-style-type: none"><li>• Heartburn</li><li>• Use with caution in kidney disease</li><li>• Boniva has not been shown to reduce all fracture types</li></ul>
IV bisphosphonate: <ul style="list-style-type: none"><li>• <b>Zoledronic acid</b> (Reclast)</li></ul>	<ul style="list-style-type: none"><li>• Intravenous infusion once a year</li></ul>	<ul style="list-style-type: none"><li>• Convenient</li></ul>	<ul style="list-style-type: none"><li>• Use with caution in kidney disease</li><li>• Mild flu-like reaction can occur</li></ul>
Anti-RANKL monoclonal antibody: <ul style="list-style-type: none"><li>• <b>Denosumab</b> (Prolia)</li></ul>	<ul style="list-style-type: none"><li>• Injection every 6 months</li></ul>	<ul style="list-style-type: none"><li>• Marked increase in BMD</li><li>• Can be used in kidney disease</li></ul>	<ul style="list-style-type: none"><li>• Cannot be stopped abruptly</li></ul>



# There may be a survival benefit with IV zoledronic acid for postmenopausal women

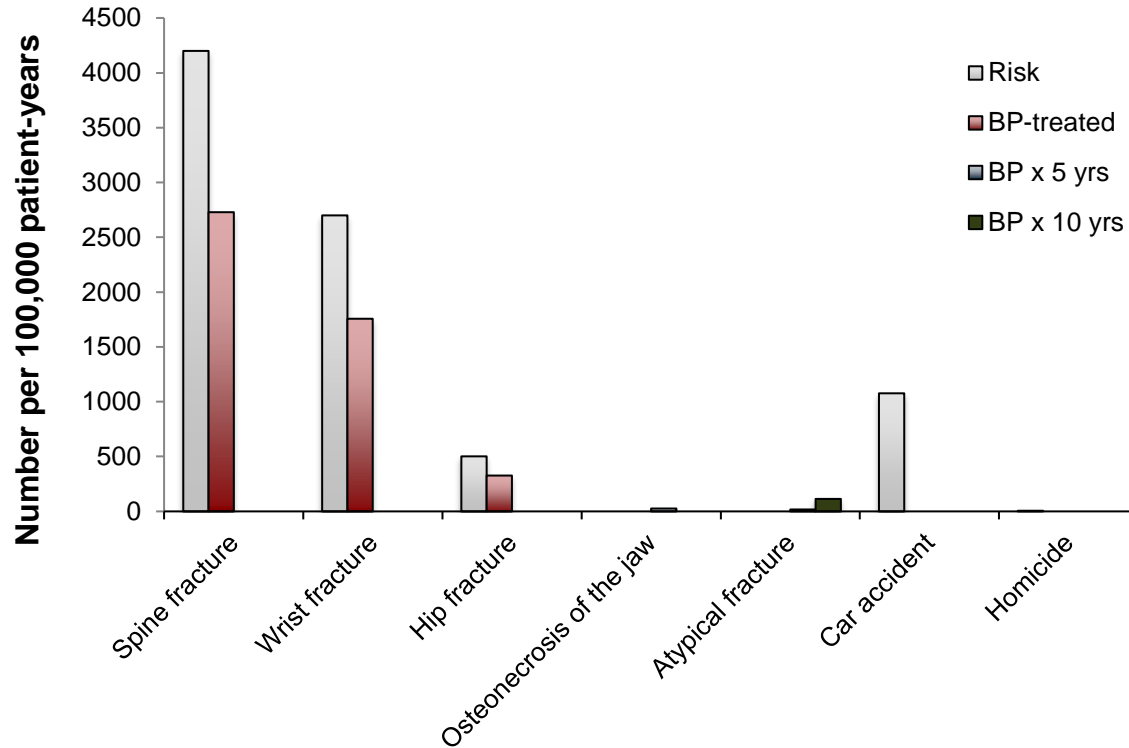
- ASCO: adjuvant bisphosphonate therapy should be discussed with postmenopausal patients
- Of the recommended options only IV zoledronic acid (Reclast, Zometa) is available in the US
- Adjuvant denosumab (Prolia, Xgeva) is not recommended



# Common concerns about medications

- “I prefer natural remedies to taking medication.”
- “I am very sensitive to medications.”
- “I’ve read that osteoporosis medications can be dangerous.”
- “I have a mother/sister/aunt/friend that took this medication and had an unpleasant side effect.”

# What are the benefits vs. risks of treatment?



Modified from Adler, JBMR 2016

# What are the benefits vs. risks of treatment?

Over 10,000 patient-years

Number of preventable fractures:



Number of cases of:



Osteonecrosis of the jaw



Atypical fractures (5 years)



Atypical fractures (10 years)



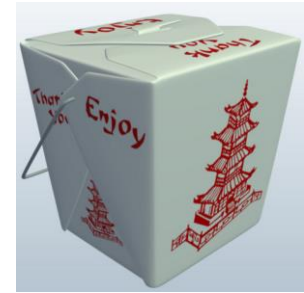
In the appropriate patients, the benefits of 5 years of bisphosphonate treatment far outweighs the risk.

# Lowering the risks of treatment

- Get regular dental care and practice good oral hygiene
- Consider drug holidays if the risk of fracture is low enough
- Let your provider know about medications before undergoing dental procedures
- Denosumab (Prolia, Xgeva) should not be stopped abruptly
- Risks are greater at higher doses (for example for management of cancer metastases to bone)

# Take-home messages

- Fractures due to osteoporosis are serious but preventable
- Your risk of fracture depends on many factors
- Cancer treatments can cause bone loss
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