# Post-Menopausal Female and Male Osteoporosis

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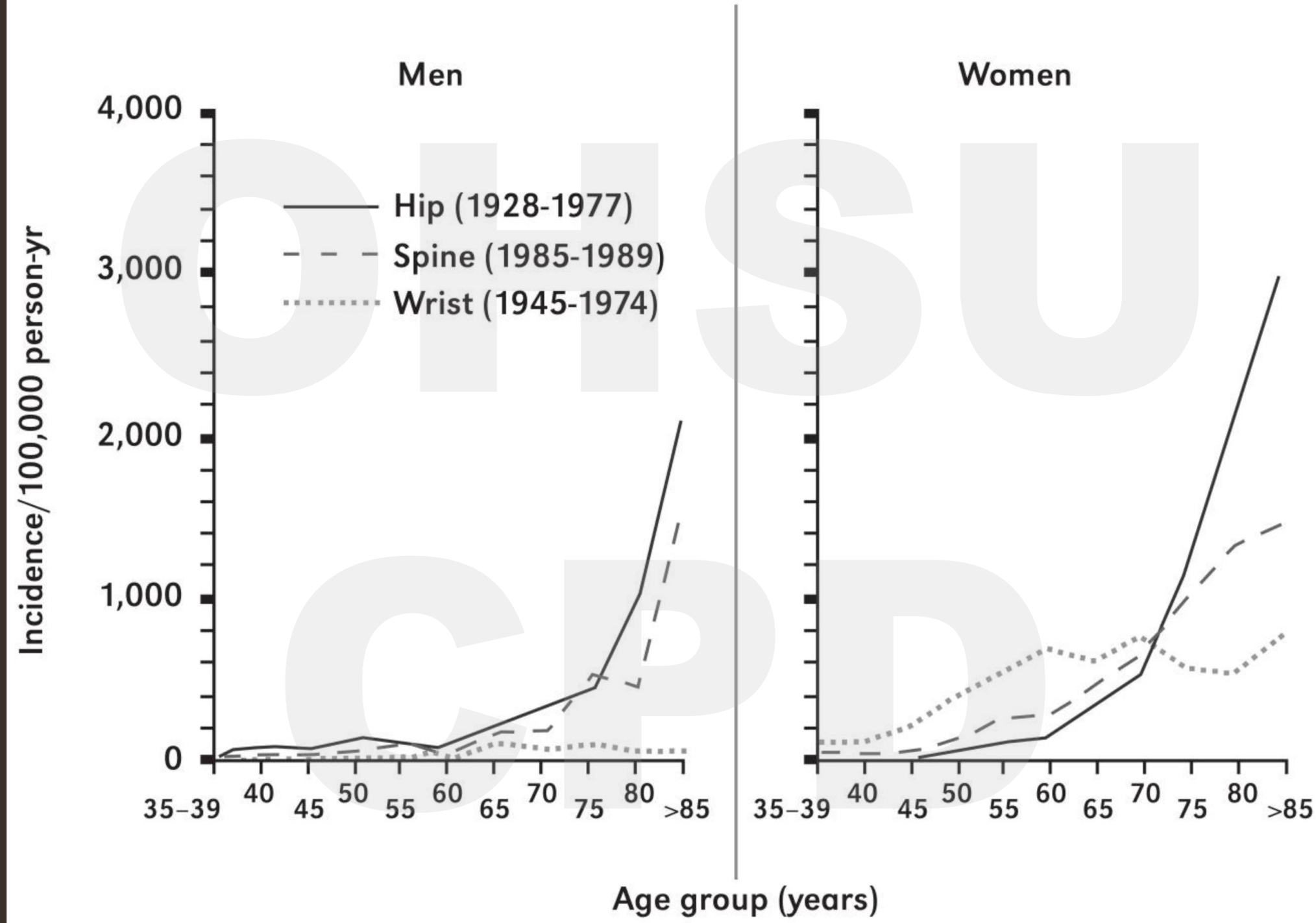
## Table 4-1 Lifetime Risk of Fracture at Age 50 Years

| Type of fracture | White women | White men |
|---|---|---|
| Hip (%) | 17.5 | 6.0 |
| Vertebra(%) | 15.6 | 5.0 |
| Forearm (%) | 16.0 | 2.5 |
| Any of the three (%) | 39.7 | 13.1 |

Source: Cummings and Melton 2002.

1.5 million osteoporotic fractures per year (70% female)


Men
Women
4,000
3,000
2,000
1,000
0
Incidence/100,000 person-yr
Hip (1928-1977)
Spine (1985-1989)
Wrist (1945-1974)
35–39
40
45
50
55
60
65
70
75
80
>85
Age group (years)

# The 'Women's Disease' That Also Strikes Men

By LAURIE TARKAN

## Osteoporosis does not discriminate, but that message is lost on many doctors.

Dick Richards of Anderson, Calif, goes for his physical every year, and his doctor jots down his height and weight The doctor does not react to the fact that each year Mr Richards is shorter.

Maybe he never looks back over Mr Richards' file to compare, or if he does notice the change, he does not think twice about it

After all, although losing height is a symptom of osteoporosis, a disease of weakening bones, most doctors do not associate the disease with men

Mr Richards had also been complaining of back pain since he was in his 40's, but he dismissed it as a part of getting old, and his doctors simply dismissed it, even though men with osteoporosis are susceptible to microfractures of the spine, and therefore back pain

Mr Richards also broke his left arm in three places when he was 46, but the accident stemmed from an accident, so again nobody suspected a more insidious bone problem.

So Mr Richards thinks it was just luck that his H M O switched him to a female doctor who was more aware of women's disorders

When he went for his physical examination at age 52, the new doctor reviewed his charts and ordered a bone mineral density test The test revealed that he had severe osteoporosis, meaning that his bones had become so porous that they were 10 times as likely to break as those of other men of his age

Now 57, and almost four inches shorter than his peak height of 5 feet 11 inches tall, Mr. Richards has to avoid activities that involve a risk of falling or injury, and he can no longer partake in the ranching activities he has done all his life

When his daughter went in for a physical recently and told her doctor that her father had osteoporosis, the doctor tried to correct her, saying, "you mean your mother has osteoporosis "

When a disease is more common in one sex, it is not unusual for the less-affected sex to get overlooked

men get it at a younger age than women, it was deemed a man's disease, and for years women were neither included in the clinical studies nor educated about their risks

And it has happened with osteoporosis, which is considered a disease of postmenopausal women, or more familiarly, a little old ladies' disease Of the 10 million people in this country with osteoporosis and the 18 million with low bone mass, 80 percent are women

"It's clear that the burden of osteoporosis and fractures is greater in women, and what has happened is that has overshadowed a smaller but very significant problem in men," said Dr Eric Orwoll, professor of medicine at Oregon Health Sciences University

The lifetime risk for a man's having a fracture of the hip, the spine or the forearm, the most troubling consequence of osteoporosis, is 13 percent or about 1 in 8 That is also the same risk for prostate cancer and about the same as a woman's risk of getting breast cancer

Osteoporosis can be a debilitating and fatal disease Fractures of the spine lead to stooped posture, loss of height, chronic pain and can cause compression of the lungs and stomach

And, one-third of men who suffer hip fractures will die within a year

Though the disease does manifest itself later in life in men than women, it is not much later

Fractures start to increase around age 60 in women, in men, they increase between 65 and 70, said Dr L Joseph Melton, an epidemiologist at the Mayo Clinic in Rochester, Minn Osteoporosis-related fractures can occur earlier in men and women

The lack of awareness among physicians

Shane Young for The New York Times

Dr. Eric Orwoll, above, says the strong link between osteoporosis and women often leads to overlooking the problem in men. Signs of osteoporosis in Dick Richards, right, were missed for years.

Courtesy of Dick Richards

treatment Osteoporosis, known as the "silent disease," often has no symptoms until the bones are so compromised that a minor trauma causes a fracture

Because there are no early warning signs, awareness of the risk factors and the use of bone density tests are critical to catching it early and preventing further bone loss

As awareness of osteoporosis in postmenopausal women has grown, it has become more common for them to get routine bone density tests, though many experts say it is not common enough

Men, though, are rarely given bone density tests, unless they have severe symptoms like spine or hip fractures And even when

# 63 year old post-menopausal woman

- Fractured left shoulder (proximal humerus) at age 61 while walking her dog. Her first fracture
- Menopause age 51, No history of estrogen replacement therapy
- Bone Density T-score
  - Lumbar spine: - 2.8
  - Total hip: -2.4
  - Femoral neck of hip: -1.8
- No history of steroid therapy, kidney stones, cancer

# PMH / MEDS

- GERD
- Hypertension
- Insomnia
- Surgical History
  - Shoulder fracture repair
  - C-section

- Omeprazole 40 mg BID
- Amlodipine 5 mg daily
- Trazodone 50 mg bedtime
- Calcium with Vitamin D daily
- Multivitamin daily
- B Complex daily

# SH / FH / ROS

- Wine nightly, no tobacco/drugs
- Lives with husband and dog
- Active lifestyle
- Yogurt every morning

- Father had curved spine
  - No hip fracture
- Mother died age 58 (breast cancer)

- ROS

+ back pain

+ bloating

# Physical Exam

- BP 116/70 P 78 R 12 Pain 0 Weight 124 lbs Height 61.5 inches
- Gen: appears well
- EENT: no goiter, stable dentition
- CV: Reg
- Lungs CTA
- Abd: Soft, + BS
- MS: no spine pain to palpation, no kyphosis
- Skin: no bruising
- Psych: intelligent and conversational

# Bone Specific History / Exam Details

- Age of menopause
  - Premature is less than 45 yo (FRAX risk assessment)
- History of kidney stones
  - Hypercalciuria
- Daily dairy consumption
  - Calcium intake
- Proton Pump Inhibitor
  - Type of calcium supplement
- Parental history of HIP FRACTURE specifically
  - FRAX risk assessment
- Spine assessment on exam
  - Imaging workup
- Dental assessment on exam
  - Drug safety

# Diagnosis of Osteoporosis (women and men)

- 1) Clinical Judgment: Fragility fractures, general frailty
- 2) Bone density
  - T-score less than -2.5 at spine, total hip, or femoral neck of hip
- 3) Fracture Risk Assessment Tool (FRAX) – Free calculator
  - 20.0 % or greater 10 year risk of any osteoporotic fracture

  OR
  - 3.0 % or greater 10 year risk of hip fracture

# Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

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

## Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth
   Age: 63 Date of Birth: Y: M: D:
2. Sex ○ Male ● Female
3. Weight (kg) 56.3
4. Height (cm) 156.2
5. Previous Fracture ○ No ● Yes
6. Parent Fractured Hip ● No ○ Yes
7. Current Smoking ● No ○ Yes
8. Glucocorticoids ● No ○ Yes
9. Rheumatoid arthritis ● No ○ Yes
10. Secondary osteoporosis ● No ○ Yes
11. Alcohol 3 or more units/day ● No ○ Yes
12. Femoral neck BMD ($g/cm^2$)

T-Score -1.8

Clear Calculate

BMI: 23.1
The ten year probability of fracture (%)
with BMD

| | |
|---|---|
| Major osteoporotic | 15 |
| Hip Fracture | 2.0 |

### Weight Conversion

Pounds → kg

124 Convert

### Height Conversion

Inches → cm

61.5 Convert

**07721254**
Individuals with fracture risk assessed since 1st June 2011

# Diagnosis of Osteoporosis - YES

- 1) Clinical Judgment: Fragility fractures, general frailty
- 2) Bone density
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  - 20.0 % or greater 10 year risk of any osteoporotic fracture

  OR
  - 3.0 % or greater 10 year risk of hip fracture

# Clinical Pearl

- FRAX most useful in patients with osteopenia on bone density
  - T-score of -1.0 to -2.4 at spine, total hip, or femoral neck of hip
- Identifies patients with osteoporosis based on fracture risk
  - Parental history of hip fracture important data point
- Provides assurance that fracture risk is not elevated
  - Avoids over treatment
- Always calculate using the ‘Caucasian’ setting as FRAX underestimates fracture risk in Blacks, Asians, and Hispanics

# Osteoporosis Workup (women and men)

- Highly Recommended
  - Complete Metabolic Panel (corrected calcium for low albumin)
    - Corrected Calcium = 0.8 * (4 – Albumin) + Measured Calcium
  - Phosphorus
    - Rare disorders of low phosphorus, osteomalacia
  - Vitamin D (25 – OH)
  - PTH (parathyroid level)
  - TSH
- General recommendation
  - Magnesium
  - CBC
  - Spine x-ray (abnormal exam finding or more than 1.5 inches height loss)
  - 24 hour urine calcium (kidney stones = hypercalciuria?)
- Not Recommended
  - Bone turnover markers (NTX, CTX)
  - Vitamin D (1,25 – OH)

# Osteoporosis Treatment - Calcium

- A vital component of care!
- Total daily MINIMUM = 800 mg from all sources combined
  - Dairy plus supplements
  - Maximum intake = 2000 mg
- Assume 250 mg of calcium for every serving of dairy
  - Soy, almond, and coconut milk must say FORTIFIED on the package
- Leafy green vegetables are a potential source of calcium
  - Collard Greens: 250 mg / cup
  - Turnip greens: 200 mg /cup
  - Kale / Bok Choy: 150 mg / cup
  - Spinach contains oxalate which will impede absorption of calcium
  - All other greens contain < 150 mg / cup (broccoli, okra, swiss chard, peas)

# Osteoporosis Treatment - Calcium

- Supplement to a level of 800 mg daily if required with tablets/caplets/chews/liquid/powder
- Will not cause a heart attack
- Calcium carbonate – most common form
  - 1 serving = 1 tablet will provide 500-600 mg calcium
  - Take with food
- Calcium Citrate – enhanced absorption over calcium carbonate
  - 1 serving = 2 tablets will provide 500 mg calcium
- Jarrows Bone Up™, Osteoblend™ are acceptable
  - Large serving size (3-6 tablets) to provide 500-800 mg calcium

# Clinical Pearl

- Our patient on proton pump inhibitor therapy (over 40 mg daily)
- Reduces absorption of calcium carbonate
  - H2 blockers (ranitidine, famotidine) not a concern
- Confirm her supplement and switch to Calcium Citrate based regimen
  - Citracal™ is my personal favorite
- Other conditions to consider calcium citrate
  - Post gastric bypass
  - Crohns or Inflammatory bowel disease
  - Gluten intolerance

# Osteoporosis Treatment – Vitamin D

- Goal Vitamin D (25 – OH) level
  - Optimal: 30 – 80 ng/ml (no difference between 34 and 68 ng/ml)
  - 20 ng/ml is absolute minimum
- 4000 IU (international units) daily from all supplement sources is safe and effective
- Add on 50,000 IU prescription dose weekly for 8 weeks to boost very low baseline levels (< 15 ng/ml)
- Check level after 6-8 weeks of repletion
- 6000 – 8000 IU daily are needed for some patients
  - No toxicity until over 100 ng/ml

# Clinical Pearl

- Vitamin D3 (cholecalciferol) is the standard vitamin D supplement
  - Human/animal form
- Vitamin D2 (ergocalciferol) is plant based form
  - Same mechanism of action as D3 but shorter half-life
    - Vegan preferred
  - Prescription 50,000 IU capsule is Vitamin D2 – short term use
- Some labs report out Vitamin D3 (25-OH) and Vitamin D2 (25-OH) values
  - This is absurd, the total value (D3 (25-OH) + D2 (25-OH)) is what matters

# Osteoporosis Treatment - Exercise

- Best weight bearing exercise program:

- Oregon State University Better Bones and Balance Program
  - $15.00 workout DVD

  - https://extension.oregonstate.edu/bbb/better-bones-balancer-store#dvd

# Our Female Patient

- Ca 8.8 mg/dl Phos 2.8 mg/dl Cr 0.6 mg/dl
- Vitamin D (25 – OH) : 24 ng/ml
- PTH 82 pg/ml
- TSH Normal

- Stop calcium carbonate
- Start calcium citrate 500 mg daily (serving size = 2 tablets daily)
- Start Vitamin D3 2000 unit capsule daily
- Maintain MVI and Yogurt intake
- Provide DVD order form

- CALCIUM, VITAMIN D, WEIGHT BEARING EXERCISE ARE THE FOUNDATIONS OF BONE HEALTH
  - Ensure that all three elements are addressed in your patient prior to medical therapy

# Osteoporosis Treatment (women and men) Medications: Bisphosphonates

- Bisphosphonates enter bone matrix and inhibits osteoclast cells (bone eating cells)
  - Known as ANTI-RESORPTIVES
- 1) Alendronate 70 mg tablet by mouth once weekly
  - Generic for Fosamax™
  - No role for Actonel™ (risedronate) nor Boniva™ (ibandronate)
- Empty stomach, water only, no lying down for 30 minutes
  - Complex rules and GI side effects main barrier to usage
- Reduces spine, hip, and other fractures (humerus, radius, rib etc..)
- A first line agent

# Osteoporosis Treatment (women and men) Medications: Bisphosphonates

- 2) Reclast™ (zoledronic acid) 5 mg infusion
- Once yearly
- 100% adherence, no gastrointestinal side effects
  - inexpensive
- Excellent fracture prevention
- Post infusion reaction 1 – 5 days post therapy
  - Flu like symptoms
  - Acetaminophen, hydration, rest

# Our female patient

- Use of high dose proton pump inhibitor ( > 40 mg daily)
  - Concern for ulcers, Barrett's esophagus, esophageal strictures
- Would avoid oral bisphosphonate (alendronate)
- Recommend IV zoledronic acid

# Clinical Pearl

- Mild GERD not contraindication to oral alendronate
  - Safe to try for 4-8 weeks to assess GI side effects
- Caution patients on post infusion reaction to zoledronic acid infusion
- Ensure normal calcium levels and calcium intake
- Ensure normal vitamin D (25 – OH) level and vitamin D intake
- Minimum GFR for bisphosphonates: 40 ml/min
  - Calculate via Cockcroft-Gault equation
    - Accounts for weight, gender, age, and creatinine (MDRD does not account for weight)
    - Persons less than 100 lbs will have low GFR despite normal creatinine

# Osteoporosis Treatment (women and men) Medications: Prolia™ (denosumab)

- Inhibits osteoclast signaling (only agent with this mechanism of action)
  - Classified as an anti-resorptive, like bisphosphonates
- 60 mg subcutaneous injection every 6 months
  - Must be in health care setting, not for patient self injection
- Superb spine, hip, and other fracture prevention
  - Similar to Reclast™ (zoledronic acid)
- Alternative for those with adverse reaction to bisphosphonates
  - Myalgias, infusion reaction
- Minimum GFR is 30 ml/min (excellent choice for CKD)
- Expensive, requires insurance pre-authorization
- Ensure adequate calcium and vitamin D intake

# Osteonecrosis of the Jaw - ONJ (bisphosphonates and denosumab)

- Very rare: 1 in 10,000 patient-years
  - Fear of this adverse event not sufficient to avoid osteoporosis therapy
- Precautions
  - Poor dentition (you will know it when you see it)
  - History of radiation therapy to jaw/mouth
  - No regular dental care (unless full dentures)
  - Planned dental extraction or root canal
- Dental clearance not required
- No lab tests nor imaging available to predict, monitor for ONJ

# Surveillance / Monitoring of Therapy

- Bone density after 1 year of therapy
  - Same or improved values
    - No declines over 5 %
- CMP / Vitamin D yearly on bisphosphonates
- CMP prior to each denosumab injection (every 6 months)

# Duration of Therapy (women and men)

- Alendronate: Not to exceed 5 years of continuous therapy
- Zoledronic acid: Not to exceed 3 years of continuous therapy
- Prolonged bisphosphonate exposure increases risk of atypical mid-femur shaft fractures
  - 1/1000 risk after 8 years of therapy
- Can restart therapy after 2 year drug holiday
- Denosumab: Safety data up to 10 years (20 injections) continuously
  - Therapy cessation associated with accelerated bone loss

# Specialized Agents (women and men)

- Forteo™ (teriparatide) and Tymlos™ (abaloparatide)
- Parathyroid hormone analogs
  - Stimulate osteoblasts (bone forming cells) – termed an ANABOLIC agent
- Extremely effective with trabecular bone (spine bone mass)
  - Symptomatic compression fractures
  - T-score less than -3.0 at spine
- 2 year limit of use due to warning regarding osteosarcoma)
  - Pagets disease of bone, radiation therapy, unexplained elevation of alk phos levels
- Daily subcutaneous injection
- Very expensive, requires insurance pre-authorization
- Must be followed by an anti-resorptive agent to maintain gains

# Specialized Agents (women only)

- Evenity™ (romosozumab) – sclerostin inhibitor
  - Sclerostin inhibits bone formation
  - 210 mg subcutaneous injection every 30 days
- Inhibiting an inhibitor results in powerful anabolic agent
- Black box warning of increased risk of heart attack or stroke
  - Limited to 1 year of therapy
- Unclear where it currently fits in treatment paradigm
  - Alternative to teriparatide or abaloparatide
    - No osteosarcoma risk

# Hormone Therapy

- Estrogen (+/- progesterone) does prevent fractures
- Reserved for postmenopausal women requiring treatment for menopausal symptoms

- Testosterone does increase bone mineral density but not shown to prevent fractures
- Reserved for older men with hypogonadal symptoms

- Osteoporosis drugs can be used in addition to hormone therapy

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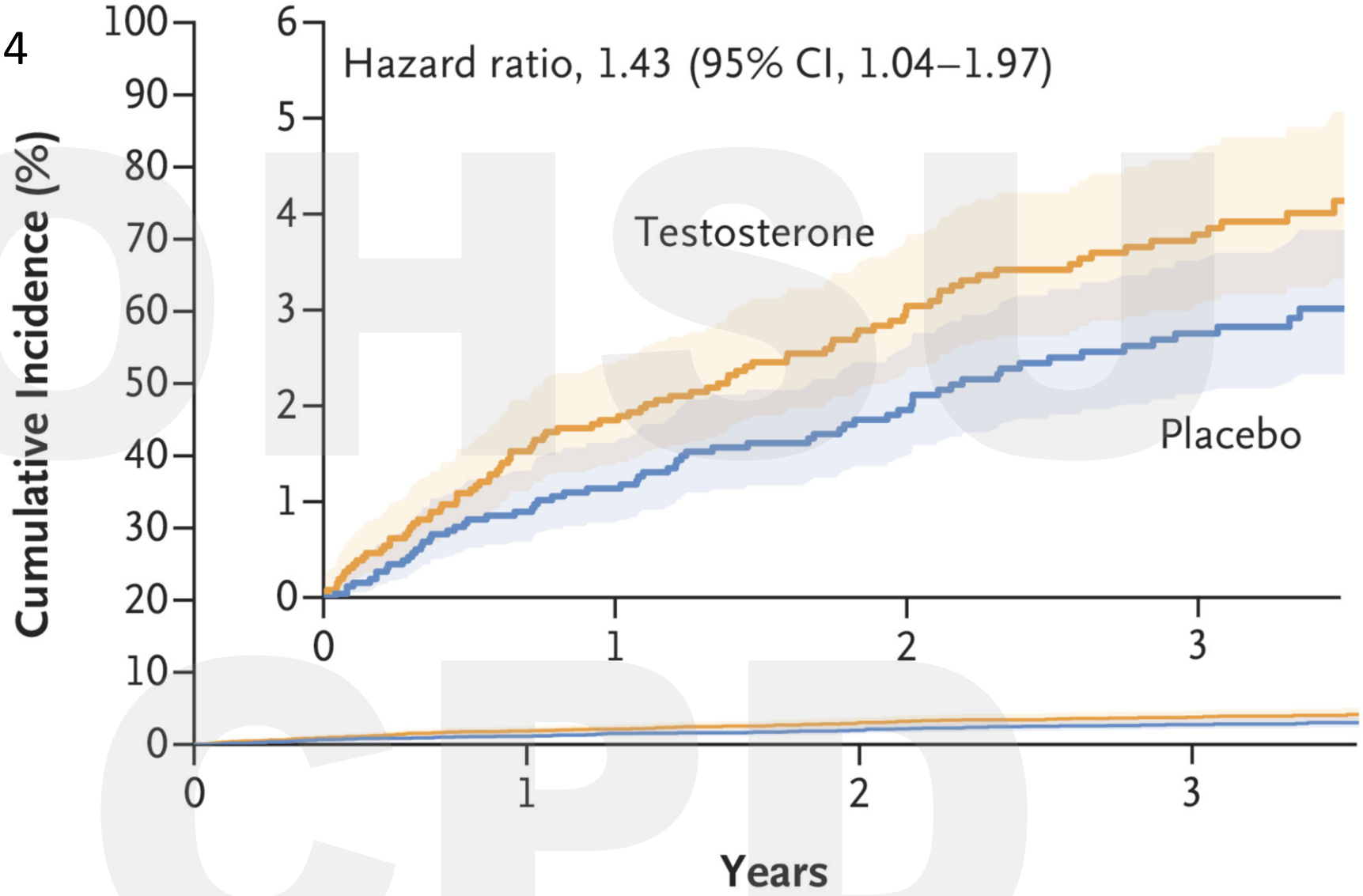


**No. at Risk**

| | | | | |
|---|---|---|---|---|
| Testosterone | 2601 | 2332 | 1812 | 1369 |
| Placebo | 2603 | 2335 | 1812 | 1354 |

# Summary

- Calcium, Vitamin D, and weight bearing exercise are the foundations of bone health
  - Must be present for medical therapy to succeed
- Use calcium supplements to *supplement* to 800 mg of calcium daily
- Calculate FRAX score for patients with osteopenia
- Alendronate PO, zoledronic acid IV, and denosumab SQ are the primary osteoporosis agents
- Bisphosphonates (alendronate/zoledronic) have duration limits
- ONJ is a rare adverse effect
- Hormone therapy for symptom relief not osteoporosis therapy