Osteoporosis: Assessing Risk

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Learning Objectives

- Participants will recognize patients that need to be evaluated for osteoporosis based on risk factors
- Participants will implement guidelines to diagnose osteoporosis
- Participants will identify fragility fractures and apply those principles to diagnosing osteoporosis
- Participants will select which of their male patients should be evaluated for osteoporosis

Evidence Reviewed

ACP Clinical Guidelines, 2017 and 2023

USPSTF Guidelines, 2018

Endocrine Society Clinical Practice Guidelines, 2019/2020

NIH Osteoporosis and Related Bone Diseases National Resource Center, 2018

American Association of Family Physicians

Bone Health and Osteoporosis Foundation

Epidemiology

- 10.2 million Americans >/=50 yo have osteoporosis (ACP)
- About 43 million Americans in the same age group have osteopenia and are at risk of developing osteoporosis
- 1.5 million Americans have fracture from osteoporosis
- 50% of postmenopausal (PM) women will have an osteoporotic fracture
- Over 70% of all fractures occur in women (USPSTF)

Impact of Osteoporosis (OP)

- 20-30% increased mortality 1yr after hip fracture (USPSTF)
  - Even with treatment
  - 1 in 3 men will die in a year
    - Higher mortality in men
    - Men are offered less treatment to prevent fractures than women (ACP)
    - Age is an important indicator for mobidity/mortality in men
      - Men 80yo = women 65yo
- 500,000 hospitalizations
- 180,000 nursing home admits
- Projected cost $25billion by 2025 (ACP 2017)
- Hip fractures impact all parts of life

Patient Case

74yo F with no past medical history. Menopausal since age 50. Does not take any medications or supplements. BMI 27. Had a borderline normal DXA bone density test at age 65yo. Up to date on vaccines. What further information would be helpful in determining this patient's risk for osteoporosis?

Modifiable Risk Factors for OP

- Alcohol- >4 drinks men, >2 women
- Caffeine- >2.5 cups/day
- Tobacco
- Immobilization and inactivity
- Vit D deficiency
- Low calcium intake
- Low body weight- <128lb

Non- modifiable Risk Factors

- Family hx of fracture
- Personal hx of fracture
- Hormone deficiency
- Age
- White or Asian ethnicity
- Female sex
- Postmenopausal (PM)
- Rheumatoid arthritis
- Chronic kidney, lung, stomach, or intestinal disease
- Hyperparathyroidism

Medications

- Steroids
- Anticoagulants
- Anticonvulsants
- Aromatase inhibitors
- Chemotherapy
- GnRH agonist

Patient Case, cont'd- Individual Risk Factors

- Drinks 12-24oz of diet soda per day
- Dairy intake 8oz of skim milk a few days per week
- Mom had significant stooping/kyphosis in her later years
- Pt broke left wrist 8 years ago
- Pt broke right wrist 6 months ago- saw ortho, nonoperative

What stands out to you?

Patient Case Question

What next step would you take?

- Start Vitamin D/Calcium supplement and encourage weight bearing exercise
- Order a DXA bone density test
- Presume osteoporosis and treat
- Not sure, don't want to commit, ask someone else

What next step would you take?

Start Vitamin D/Calcium supplement and encourage weight bearing exercise

0%

Order a DXA bone density test

0%

Presume osteoporosis and treat

0%

Not sure, don't want to commit, ask someone else

0%

What next step would you take?

Start Vitamin D/Calcium supplement and encourage weight bearing exercise

0%

Order a DXA bone density test

0%

Presume osteoporosis and treat

0%

Not sure, don't want to commit, ask someone else

0%

Screening with DEXA in Women

- USPSTF- screen for OP with DXA in women 65yo and older (B)
  - Screen for OP with DXA in women <65yo who are at increased risk of OP- risk factors/risk assessment tool (B)
  - Re-screen every 4-8yr
- BHOF- women >/=65yo
  - PM women with risks
  - Serial bone mineral density (BMD)
- ACP- recommends against monitoring during treatment- weak evidence
- Endocrine Society- women >/= 65yo OR PM women 50+ with risk factors

Screening in Men

- USPSTF- Insufficient evidence to screen men
- BHOF- DEXA for men >/= 70yo, men 50-69yo with risk factors
- ACP- offer tx to men who have clinical OP to reduce vertebral fx
- Endocrine Society- Men >/= 70yo
    - Men 50-69yo with additional risk factors

Assessing OP Risk

- Several tools exist- SCORE, ORAI, OSIRIS, OST, FRAX
- Independent of bone mineral density (BMD)
- USPSTF suggests performing DXA on women <65yo if their fracture risk equals 8.4% (avg fracture risk for a 65yo white woman)

OSTEOPOROSIS AND FRACTURE RISK EVALUATION

A tool for primary care providers

US version

WHEN SHOULD YOU PRESCRIBE TREATMENT?

- **Is your patient 50 or older with a hip or vertebral fracture?**
  - Yes → Does your patient have one or more risk factors for osteoporotic fracture? – see list on the right
    - No → Discuss preventative measures and consider re-evaluation of patient in 2-3 years
    - Yes → **BMD(DXA) AND/OR risk assessment by FRAX®:**[1,2]
      - T-score ≤ -2.5 **or**
      - Osteopenia with fracture of proximal humerus, pelvis, or wrist **or**
      - FRAX® risk above recommended treatment threshold (≥3% for hip fracture or ≥20% for major osteoporotic fracture)

      → **Treat**
  - No → **Treat**
- Is your patient a postmenopausal woman or man aged 50 or older?
  - Yes → Does your patient have one or more risk factors for osteoporotic fracture? – see list on the right
    - No → Discuss preventative measures and consider re-evaluation of patient in 2-3 years
    - Yes → **BMD(DXA) AND/OR risk assessment by FRAX®:**[1,2]
      - T-score ≤ -2.5 **or**
      - Osteopenia with fracture of proximal humerus, pelvis, or wrist **or**
      - FRAX® risk above recommended treatment threshold (≥3% for hip fracture or ≥20% for major osteoporotic fracture)

      → **Treat**

Discuss benefits versus risk of treatment
Discuss specific anti-osteoporosis medications, calcium and vitamin D supplementation, fall risk assessment and prevention, as well as future care

Final shared treatment decision between patient and provider

Refer to country-specific guidelines for treatment options

RISK FACTORS FOR OSTEOPOROSIS & FRACTURES

- ☐ **Previous non-hip, non-spine fractures over the age of 50. Toes, fingers, nose and skull not included.**
- ☐ Parental history of osteoporosis and fractures (especially hip fractures)
- ☐ Loss of height as an adult (>4 cm or 1.5 in)
- ☐ Rheumatoid arthritis and inflammatory diseases
- ☐ Hyperthyroidism and hyperparathyroidism
- ☐ Diabetes
- ☐ Glucocorticoid excess
- ☐ Hypogonadal states
  - Estrogen deficiency or amenorrhea (other than pregnancy)
  - Early natural or surgical menopause (age 45 or less)
  - Low testosterone in men
- ☐ Digestive and gastrointestinal diseases (including malabsorption, lactose intolerance, celiac)
- ☐ Cancer (especially prostate and breast)
- ☐ High risk medications
  - Androgen deprivation therapy
  - Aromatase inhibitors
  - Glucocorticoids (prednisone and others)
  - Proton Pump inhibitors
  - Seizure medications (lithium, depakote)
  - Selective serotonin reuptake inhibitors
  - Thiazolidinediones
- ☐ Lifestyle factors – smoking, falls, excessive alcohol intake, immobility

KEY MESSAGES IN BENEFIT VERSUS RISK DISCUSSION

- Fractures are serious and impact health as well as survival. In addition, serious side effects from medications are very rare. The benefits/side effects differ by medication and should be explained (see side panel) without losing sight of the severe consequences of fractures we are trying to prevent.
- The significant health consequences of fractures must be considered, including pain, reduced mobility, need for assistive walking devices, loss of independence, reduced quality of life and complications such as infection, cardiovascular events, thromboembolic disease and death.
- Drug summaries and package inserts list all side effects, but do not mention how rare many of these are.
- Patients may have major concerns with regard to a particular side effect – the reasons for this should be explored and reassurance provided if appropriate.
- For each atypical femoral fracture potentially caused, 50 osteoporotic fractures may be prevented[5].
- Consider evaluation for secondary causes including CBC, CMP, 25-hydroxy vitamin D, 24 hour urine calcium.
- Osteoporosis is a chronic disease, just like diabetes and hypertension We can effectively treat and reduce the risk for fracture, but do not cure it. As such , it will require lifelong attention.

NOTES ON USE OF THIS TOOL

- This tool is intended to aid clinicians in communicating with patients about risk assessment and prevention of osteoporotic fractures.
- Note that the bone infographics can be shaded to represent key statistics, e.g. risk of fracture, risk of side effects, proportion of fractures prevented.

References:
1. https://www.sheffield.ac.uk/FRAX/
2. US guidance (NOF): https://my.nof.org/bone-source/education/clinicians-guide-to-the-prevention-and-treatment-of-osteoporosis
3. Khan, J Bone Miner Res, 2015. 30(1).
4. Dell, J Bone Miner Res, 2012. 27(12).
5. Adler, J Bone Miner Res. 2016. 31(1)

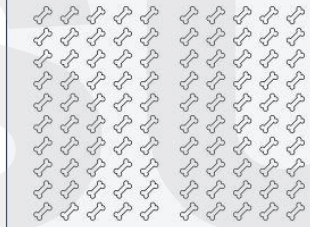
OSTEOPOROSIS AND FRACTURE RISK EVALUATION

A tool for primary care providers

US version

RELATIVE RISK REDUCTION IN FRACTURE WITH ANTI-RESORPTIVE TREATMENT*

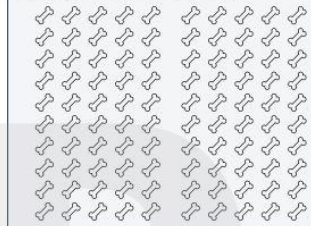
Spine: 60%
Hip: 40%
Non-spine: 25%



*hormone therapy, bisphosphonates and Denosumab

What does my percentage risk mean?

Probability of fracture: _____% (e.g. FRAX®)



COMMON SIDE EFFECTS

- **Bisphosphonates**
  - By enteral route: mild gastro-intestinal disturbances
  - By IV: flu-like symptoms - acute and transient bone and muscle pain, as well as fever
- **SERM**
  - Leg cramps and hot flushes

INFREQUENT SIDE EFFECTS

- **SERM**
  - Deep venous thromboembolism
- **Denosumab**
  - Skin rashes and infections
  - Hypocalcemia
- **Anabolics**
  - PTH and PTHrP analogs
    - Hypercalcemia
    - Nausea
    - Dizziness and headache
    - Hypercalciuria
  - Romosozumab
    - Rare cardiovascular events

CONSEQUENCES OF FRACTURE

- **Overall decrease in quality of life including:**
  - Pain
  - Loss of independence
  - Immobility
  - Premature death
- **Huge impact not just on the patient, but also on caregivers, family and friends**

Risk of rare side effects with anti-resorptives

Probability of osteonecrosis of the jaw: 0.001%[3]
Probability of atypical femur fractures: 0.001%[4]

Probability of these rare side effects is minimal compared to the risk of fracture.

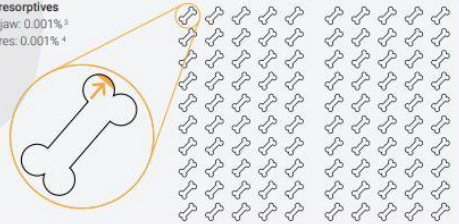


Table 2. Characteristics of Clinical Risk Assessment Tools for Osteoporosis[a]

Tool	Risk Factors	Scoring	Frequently Used Threshold for Increased Osteoporosis Risk
OST	Weight, kg	(kg − y) × 0.2	<2
	Age, y		
ORAI	Age, y		≥9
	≥75	15	
	65-74	9	
	55-64	5	
	45-54	0	
	Weight, kg		
	<60	9	
	60-69	3	
	≥70	0	
	No current estrogen use	2	
OSIRIS	Age, y	−0.2 × age	<1
	Weight, kg	0.2 × weight	
	Current estrogen use	2	
	Prior low-impact fracture	−2	
SCORE	Non-black race	5	≥6
	Rheumatoid arthritis	4	
	Prior rib/wrist/hip fracture	4 for each type of nontraumatic rib/wrist/hip fracture after age 45 y (max 12)	
	Never used estrogen	1	
	Age, y	3 × first digit of age	
	Weight, lb	−1 × weight divided by 10	
FRAX	Age, y	Refer to website[b]	9.3% (major osteoporotic fracture)[c]
	Sex		
	Weight, kg		
	Height, cm		
	Previous fracture		
	Parental hip fracture		
	Current smoking		
	Glucocorticoid use		
	Rheumatoid arthritis		
	Secondary osteoporosis		
	Alcohol consumption ≥3 U/d		

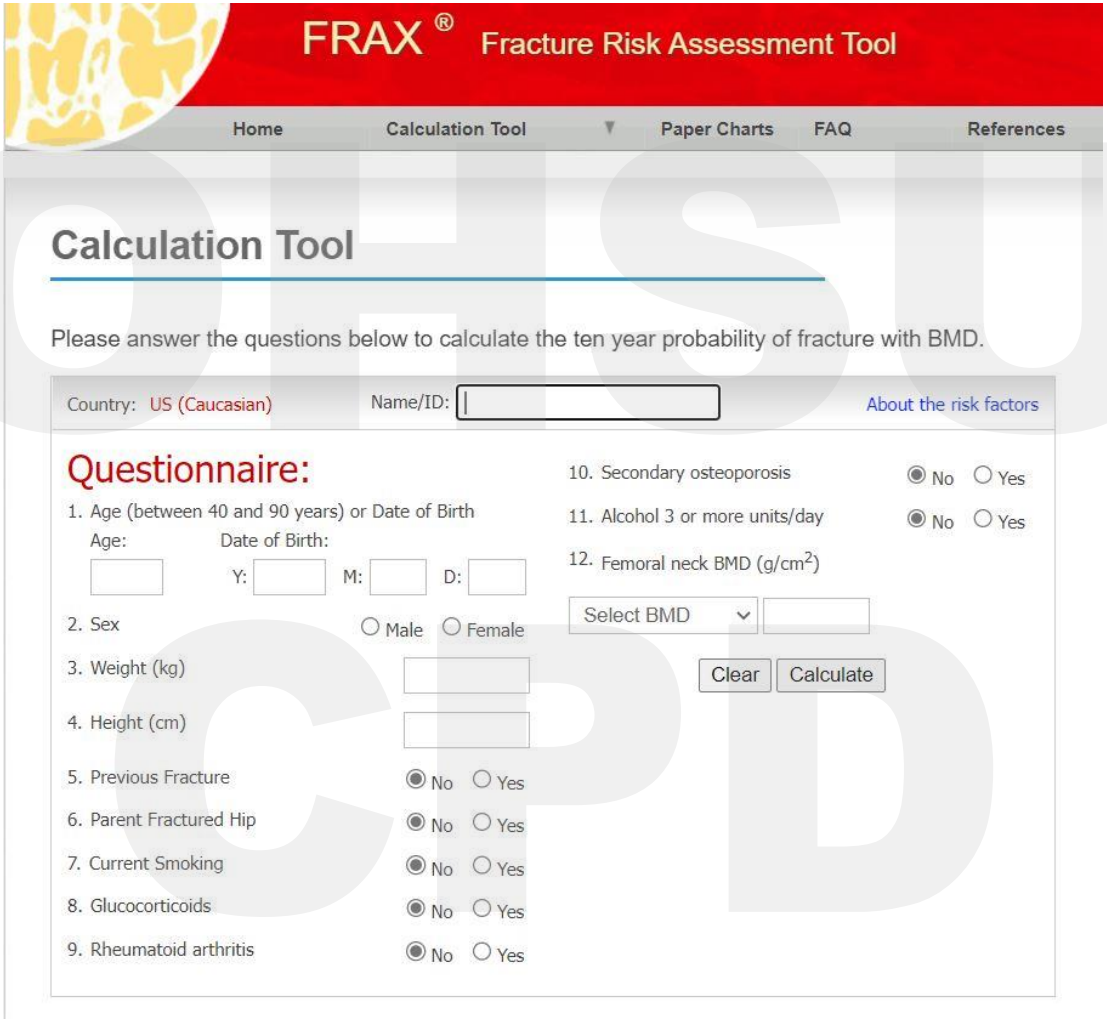
Abbreviations: FRAX, Fracture Risk Assessment Tool; ORAI, Osteoporosis Risk Assessment Instrument; OSIRIS, Osteoporosis Index of Risk; OST, Osteoporosis Self-Assessment Tool; SCORE, Simple Calculated Osteoporosis Risk Estimation.

[a] Table adapted from Chen S.J, et al.[42]

[b] Refer to https://www.sheffield.ac.uk/FRAX.

[c] 9.3% represents the 10-y major osteoporotic fracture risk in a 65-y-old white woman without any other risk factors in the United States, as calculated in 2011. Currently, FRAX calculates this risk to be 8.4%.

frax.shef.ac.uk/FRAX/tool.aspx?country=9



Fragility Fracture

- Any fracture at age 50yo or older is concerning for recurrent fractures
  - Especially in the first year after a fracture
  - Even a traumatic fracture
  - Sign or symptom of OP
  - T score less helpful in predicting fracture than current fracture
- Vertebral fractures increase risk of more vertebral fractures by 5x and hip fracture by 2-3x (BHOF)
- These patients are underdiagnosed and undermanaged for osteoporosis (BHOF)
- Start treatment for OP for any recent fracture, without BMD (Endocrine Society)
  - 2 weeks after hip fracture (Horizon trial)

Case Continued

74yo F with no PMH coming in for follow up. Moderate caffeine intake.
Recent wrist fracture.
Wt- 77kg
Ht- 170cm
Let's assess her fracture risk

- OST- 0.6- Low risk
- ORAI- 9- needs DEXA
- OSIRIS- -1.4- intermediate group- 39% in this group had OP
- SCORE- 14- increased risk for OP
- FRAX- 24% risk of fracture in 10 years

Case Question

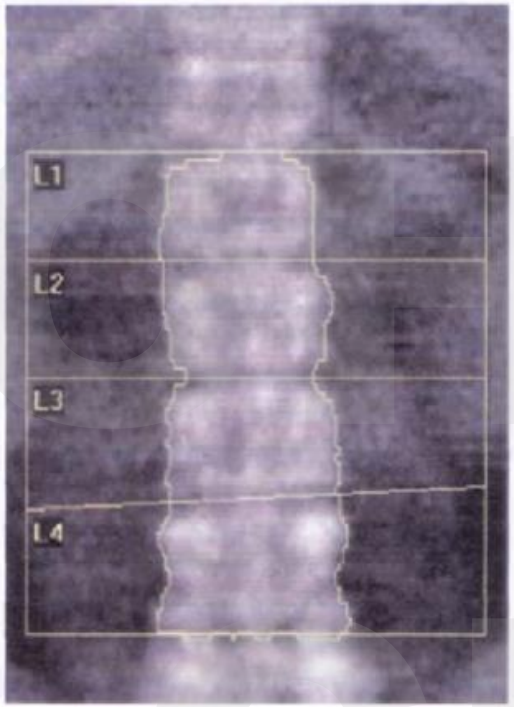
Based on her multiple risk calculators, what next steps do you want to do?

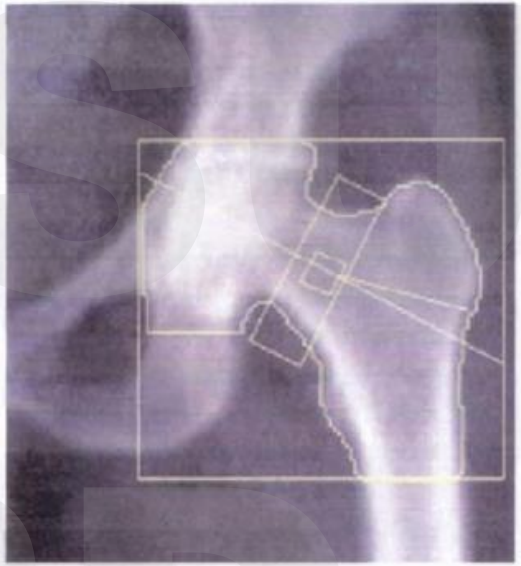
- Labs only
- Labs and DEXA
- Labs and Treatment
- Referral to osteoporosis expert

Based on her multiple risk calculators, what next steps do you want to do?

Based on her multiple risk calculators, what next steps do you want to do?

Densitometria óssea da coluna lombar e do colo do fémur. | Download Scientific Diagram (researchgate.net)





DXA Results Summary:

Region	Area (cm^2)	BMC (g)	BMD (g/cm^2)	T-score	PR (%)	Z-score	AM (%)
L1	9.97	6.54	0.657	-2.4	71	-0.7	89
L2	11.95	9.61	0.805	-2.0	78	-0.1	98
L3	13.28	10.11	0.761	-2.9	70	-0.9	88
L4	15.95	13.85	0.868	-2.3	78	-0.2	98
Total	**51.14**	**40.11**	**0.784**	**-2.4**	**75**	**-0.4**	**94**

DXA Results Summary:

Region	Area (cm^2)	BMC (g)	BMD (g/cm^2)	T-score	PR (%)	Z-score	AM (%)
Neck	**5.27**	**3.91**	**0.743**	**-1.0**	**87**	**0.7**	**112**
Troch	9.25	5.61	0.606	-1.0	86	0.2	104
Inter	17.82	20.06	1.125	0.2	102	1.3	121
Total	32.34	29.57	0.914	-0.2	97	1.1	118
Ward's	1.08	0.58	0.537	-1.7	73	0.7	119

Diagnosing Osteoporosis

- EITHER Fragility fracture OR low BMD on DEXA
  - OP on DEXA OR Osteopenia + FRAX score
  - FRAX score gives 10yr total fracture risk or hip fx, cutoff- 20% and 3%
- Osteopenia= T score between -1.0 and >-2.5
- Osteoporosis= T score </= -2.5
- T score used for men and women older than 50yo
- Once diagnosed with OP, always have OP

Vertebral Radiographs

- Look for fragility fracture- vertebral fractures are the most common type of fracture and underdiagnosed
- BHOF recommends performing XR
  - If T</= -1.0 in women 65yo or older or men 80yo or older
  - All women >/=70yo and men >/=80yo without T score
  - PM women and men >/=50yo with fragility fx
  - PM women and men >/=50yo with loss of height of >/=4cm or 1.5in total
    - Or 0.8in in a year
  - Recent or continued long-term steroid therapy

Secondary OP

- OP caused by something besides aging and hormone loss
- Up to 30% of cases of OP are secondary
- When OP diagnosed, perform history and physical and lab work up for secondary causes of OP
  - 25 OH vit D, BMP, TSH
- BHOF- consider more in depth evaluation
  - PTH, Total T, SPEP, etc

Non- Pharmacologic Treatment

- Insufficient evidence for physical activity
  - CDC recs 120-300min per week of mod intensity aerobic activity, weight training, and balance training
- Fall prevention
  - USPSTF recommends exercise and PT- weight bearing and balance training
  - Identify fall risks
  - Hip protectors
  - Review med list for polypharmacy/high risk medication
- Counsel on modifiable risk factors

Table 9. Excercise Recommendations	
WEIGHT-BEARING EXERCISES	30 minutes on most days of the week. A 30-minute session or multiple sessions spread out throughout the day.
MUSCLE-STRENGTHENING EXERCISES	Two to three days per week. Can be done all at once or in multiple short sessions, full body or one body part per day. (For example arms one day, legs the next and trunk the next.)
BALANCE, POSTURE AND FUNCTIONAL EXERCISES	Every day or as often as needed. Focus on area of most need: If patient has fallen, balance exercises should be emphasized. If patient's spine is bent, focus should be on posture exercises. If patient has trouble climbing stairs or getting up from the couch, he/she should do more functional exercises. These exercises can be performed at one time

Reprinted from "Exercise for Strong Bones" published online by the National Osteoporosis Foundation at nof.org. (NOF, 2015)

Safehip Soft Hip Protector - Active Women, Small - Item #929154 (berktree.com)

Calcium and Vitamin D

- No international consensus on a reference range for vit D- somewhere around 20-30ng/ml
- Endocrine Society- calcium 1000-1200mg/d, goal vit D of 30, daily vit D 1000-2000IU daily
- BHOF- ensure adequate calcium in the diet (1000-1200mg), goal vit D 30-50, supplement to achieve those levels
- NIH- calcium 1000-1200mg/d, Vit D 600-800IU/d
- ACP- appropriate cal/vit D are needed, no dose specifics
    - Excess can cause hypercal or nephrolithiasis
- AAFP recommends a balanced diet of protein, fruits/veg, calcium and Vit D
- USPSTF- rec against calcium/vit D supplementation for primary prevention of fracture in older women
    - Insufficient evidence for supplementation in men or premenopausal women

Table 6. Calcium-Rich Foods (Patient Handout Included in this Toolkit)

PRODUCE	SERVING SIZE	ESTIMATED CALCIUM*
Collard greens, frozen	8 oz.	360 mg
Broccoli rabe	8 oz.	200 mg
Kale, frozen	8 oz.	180 mg
Soy Beans, green, boiled	8 oz.	175 mg
Bok Choy, cooked, boiled	8 oz.	160 mg
Figs, dried	2 figs	65 mg
Broccoli, fresh, cooked	8 oz.	60 mg
Oranges	1 whole	55 mg
SEAFOOD		
Sardines, canned with bones	3 oz.	325 mg
Salmon, canned with bones	3 oz.	180 mg
Shrimp, canned	3 oz.	125 mg
DAIRY		
Ricotta, part-skim	4 oz.	335 mg
Yogurt, plain, low-fat	6 oz.	310 mg
Milk, skim, low-fat, whole	8 oz.	300 mg
Yogurt with fruit, low-fat	6 oz.	260 mg
Mozzarella, part-skim	1 oz.	210 mg
Cheddar	1 oz.	205 mg
Yogurt, Greek	6 oz.	200 mg
American Cheese	1 oz.	195 mg
Feta Cheese	4 oz.	140 mg
Cottage Cheese, 2%	4 oz.	105 mg
Frozen yogurt, vanilla	8 oz.	105 mg
Ice Cream, vanilla	8 oz.	85 mg
Parmesan	1 tbsp	55 mg
FORTIFIED FOOD		
Almond milk, rice milk or soy milk, fortified	8 oz.	300 mg
Orange juice and other fruit juices, fortified	8 oz.	300 mg
Tofu, prepared with calcium	4 oz.	205 mg
Waffle, frozen, fortified 2 pieces	2 pieces	200 mg
Oatmeal, fortified	1 packet	140 mg
English muffin, fortified	1 muffin	100 mg
Cereal, fortified	8 oz.	100-1,000 mg
OTHER		
Mac & cheese, frozen	1 package	325 mg
Pizza, cheese, frozen	1 serving	115 mg
Pudding, chocolate, prepared with 2% milk	4 oz.	160 mg
Beans, baked, canned	4 oz.	160 mg

**The calcium content listed for most foods is estimated and can vary due to multiple factors. Check the food label to determine how much calcium is in a particular product.*

FOOD	SERVING SIZE	VITAMIN D CONTENT
Canned salmon (with bone)	1 can (369 grams)	2816 IU
Salmon, fresh roasted	1/2 filet	815 IU
Canned tuna (in oil, drained)	3 ounces	229 IU
Whole milk (cow)	1 cup	124 IU
Soy milk (Silk brand plain)	1 cup	119 IU
Low fat milk (1%)	1 cup	117 IU
Orange juice (fortified)	1 cup	89 IU
Kellogg's All-Bran Cereal (original)	1/2 cup	51 IU
Egg, whole, hard boiled	1 large	44 IU
Spinach souffle	1 cup	42 IU
Mushrooms (fresh, shitake)	1 cup	41 IU
Cheddar Cheese	1 ounce	7 IU

Pharmacologic Treatment

- Goal of treatment: depends on the person- no fractures, stable BMD, or increasing BMD
- Bisphosphonates
  - Alendronate, Risedronate, Zoledronic Acid
- RANK Ligand Inhibitors
  - Denosumab
- Sclerostin inhibitors
  - Romosozumab
- Peptide Hormones (anabolic)
  - Teriparatide, Calcitonin
- Estrogen therapy
  - Estrogen or SERMs- reloxifene

From ACP

Table. Medications Licensed in the United States for Treatment of Osteoporosis

Drug Name (Class)	Route; Frequency	Types of Fractures Examined in Randomized Clinical Trials at Long-Term Follow-up (>36 mo)				Average Annual Medicare Spending Per Beneficiary in 2019	FDA Warning
		Hip	Clinical Vertebral	Any Clinical	Radiographic Vertebral		
Antiresorptive drugs							
Alendronate (bisphosphonate)*†‡	By mouth (tablet or solution); once a day (10 mg) or once a week (70 mg)§	Yes	No	Yes	Yes	$793-$1306 (brand-name); $39 (generic)	Upper gastrointestinal irritation; osteonecrosis of the jaw; atypical femur fractures; severe bone, joint, and muscle pain
Risedronate (bisphosphonate)*†‡	By mouth; once a day, once a week, or 2 d in a row once per month§	Yes	No	No	Yes	$2036-$2732 (brand-name); $604 (generic)	Upper gastrointestinal irritation; osteonecrosis of the jaw; atypical femur fractures; severe bone, joint, and muscle pain
Ibandronate (bisphosphonate)*‡	By mouth; once a month§	No	No	No	Yes	$1379 (brand-name); $220 (generic)	Upper gastrointestinal irritation; osteonecrosis of the jaw; atypical femur fractures; severe bone, joint, and muscle pain
Zoledronate (bisphosphonate)*†‡	Intravenous; once a year§	Yes	Yes	Yes	Yes	$855 (brand-name); $316-$987 (generic)	Osteonecrosis of the jaw; atypical femur fractures; severe bone, joint, and muscle pain
Denosumab (RANK ligand inhibitor)†‖	By injection (subcutaneous); every 6 mo¶	Yes	Yes	Yes	Yes	$1913-$12 241 (brand-name)	Dermatologic reactions and serious infection, including skin infections; suppression of bone turnover contributing to adverse outcomes, such as osteonecrosis of the jaw, atypical fractures, and delayed fracture healing
Anabolic drugs							
Abaloparatide (parathyroid hormone–related protein)‖	By injection (subcutaneous); once a day	No	No	Yes**	Yes**	$9873 (brand-name)	Hereditary osteosarcoma disorders††
Teriparatide (recombinant human parathyroid hormone)‖‡‡	By injection (subcutaneous); once a day	Yes**	Yes**	Yes**	Yes**	$22 156 (brand-name)	Hereditary osteosarcoma disorders††
Romosozumab (sclerostin inhibitor)‖	By injection (subcutaneous); once a month for 12 mo§§	No	Yes**	Yes**	Yes**	$5574 (brand-name)	Cardiovascular risk Stroke history or risk‖‖
Estrogen agonist on bones							
Raloxifene (selective estrogen receptor modulator)*‡	By mouth; once a day	Yes	Yes	Yes	Yes	$1730 (brand-name); $593 (generic)	Stroke history or risk Thromboembolism history or risk¶¶

Bisphosphonates

- Alendronate, risedronate, zoledronic acid- reduce fx at all sites
- Considered first line for men and women (ACP)
- Mechanism of action
  - Inhibits osteoclastic activity
- Directions
  - oral - take with water, sitting up for 30 min
  - IV- yearly
- Length of therapy
  - Unknown, consider stopping after five years for oral and 3yr for IV
- Not recommended with CrCl <30-35mL/min

Adverse Effects

- Common
  - GI- gastritis/GERD, uveitis/episcleritis, hypocalcemia
- Zoledronic acid
  - hypocalcemia, influenza like illness, uveitis, episcleritis, arthralgias, headache
- Risks with prolonged use
  - Osteonecrosis of the jaw and atypical femur fracture

Denosumab (Prolia)

- Mechanism of action
  - Monoclonal Ab inhibits RANKL-> formation and activity of osteoclasts
- Reduces vertebral, nonvertebral, hip fx
- Subcut q6mos
- Considered second line medication
- Side effects
  - Infections, cellulitis, rash, back and extremity pain, hypersensitivity, osteonecrosis of the jaw, hypocalcemia, atypical femur fracture
- Cessation of therapy results in rebound severe bone turnover until about 2yr post cessation leading to multiple fractures

Very High Risk

- Per ACP
  - Older age
  - Recent fracture
  - Multiple fractures
  - Multiple OP risk factors
  - Failed other therapies

Romosozumab (Evenity)

- Monoclonal antibody inhibits sclerostin
  - Sclerostin causes bone turnover
- Increases BMD more than alendronate and teriparatide (BHOF)
- Reduces vertebral and other fractures, but not hip (ACP)
- Being utilized as first choice in women at very high risk (ACP)
- Subcut monthly (2 injections at a time) for 1 year and then transition to bisphosphonate or denosumab
  - Less effective after 1 year
- Side effects/warnings- increased MI, stroke, CV death
  - Hypocalcemia, osteonecrosis of the jaw, atypical femur fracture
- Contraindicated in people with stroke or MI in the last year

Teriparatide

- Recombinant human parathyroid hormone
- Reduces vertebral and nonvertebral fractures but not all fracture types (hip)
- Consider as first choice (interchangeable with remosozumab) for women at very high risk (ACP) and then transition to bisphosphonate or denosumab
- Side effects
  - GI, headache, hypercalcemia, renal, dizziness, palpitations

Raloxifene

- Selective Estrogen Receptor Modulator
- ACP can't recommend for or against
- Considerable risks- hot flashes, VTE, CVA
- Prevents vertebral fractures only

Abaloparatide

- Parathyroid hormone related peptide
- ACP can't recommend for or against
- Side effects
  - GI, headache, hypercalcemia, renal, dizziness, palpitations

Calcitonin

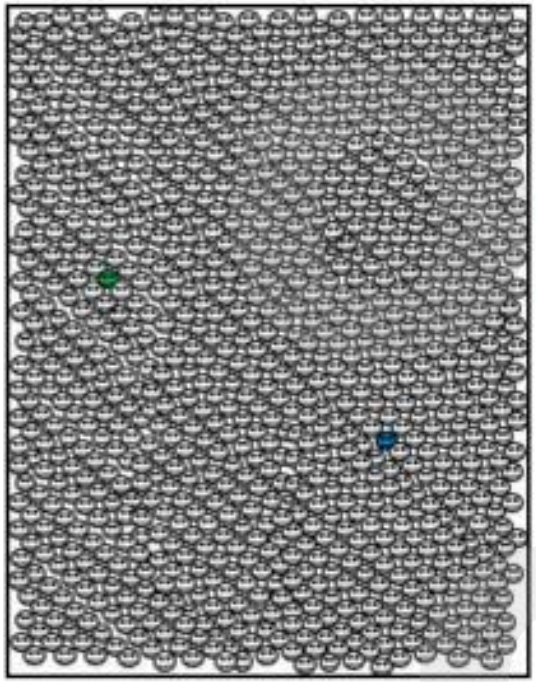
- Antiresorptive
- Reduces vertebral fracture only
- Modest analgesic properties
- No longer recommended by ACP

Bisphosphonate Duration of Therapy

- Unclear evidence regarding duration of therapy and monitoring
- In 15yr, 10% normal/mild osteopenia develop OP- T>-1.49
- T -1.5 to -1.99- 10% develop OP in 5yr
- T -2 to -2.49- 10% develop OP in 1yr
- High risk patients likely benefit from more than 5yr of treatment
- BHOF- drug holiday 5yr oral, 3yr IV bisphos
- IF high risk for fracture- T <-2.5 or fracture during treatment:
    - 10yr for oral bisphosphonate, 6yr IV bisphos

Osteonecrosis of the Jaw (ONJ) and Atypical Femur Fracture (AFF)

- ONJ
  - Rare- associated with bisphosphonate and denosumab- 1-10/100,000
  - Slightly increased over baseline population
  - Associated with treatment over 5 years
  - Dental care may help prevent osteonecrosis
  - More common in those receiving high doses for cancer
- AFF
  - Rare- associated with bisphosphonates, denosomab, romosozumab
  - Unclear if associated with duration of use
  - Femoral shaft fracture
  - Preceded by thigh/groin pain
  - Associated with treatment >3 years but more commonly 7yr



THE RISK OF ADVERSE EVENTS WITH OSTEOPOROSIS MEDICATION

Out of 1,000 people on osteoporosis medication for 5 years:

- <1 may have osteonecrosis of the jaw (.01/1000)
- <1 may have a atypical femur fracture (.16/1000)

THE RISK OF FRACTURE WITHOUT OSTEOPOROSIS MEDICATION

Out of 1,000 women:

- 500 will suffer a fracture without t reatment for osteoporosis during their lifetime.

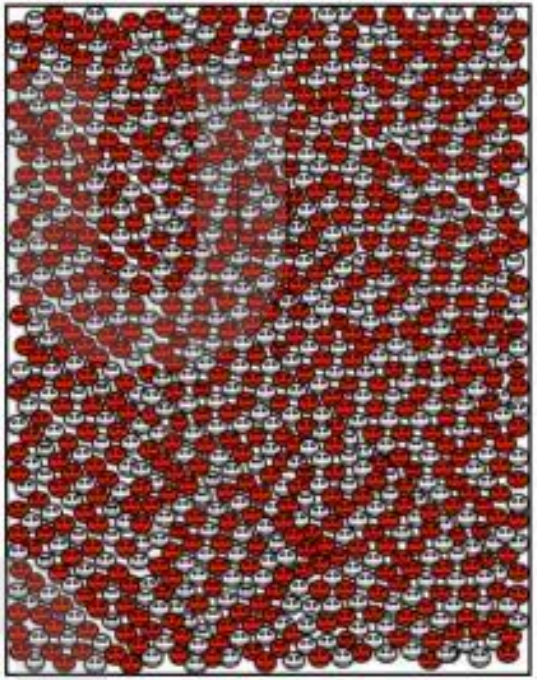


Figure 3. For most people, it is easier to understand relative risks when they are represented graphically, as they are in this representation comparing data on incidence of rare adverse events and incidence of (common) osteoporosis-related fracture.

Case Outcome

- 74yo F with recent wrist fracture went to her doctor. Received a bone density test- did not know the results. Was started on alendronate and calcium. She is not sure the length of treatment or when she will be tested again.

Take Home Points

- Take action on patients with fracture at 50yo or older
- Consider risk factors in patients younger than 65yo, use risk calculators to identify those who need to be screened earlier
- Consider which male patients you might screen and/or treat
- Bisphosphonates are first line treatment in those eligible

ACP
American College of Physicians

Treatments to Reduce Fractures in Postmenopausal Females With Primary Osteoporosis

Recommendations

RECOMMENDATION: ACP recommends that clinicians use bisphosphonates for initial pharmacologic treatment to reduce the risk of fractures in postmenopausal females diagnosed with primary osteoporosis (strong recommendation; high-certainty evidence).

RECOMMENDATION: ACP suggests that clinicians use the RANK ligand inhibitor (denosumab) as a second-line pharmacologic treatment to reduce the risk of fractures in postmenopausal females diagnosed with primary osteoporosis who have contraindications to or experience adverse effects of bisphosphonates (conditional recommendation; moderate-certainty evidence).

RECOMMENDATION: ACP suggests that clinicians use the sclerostin inhibitor (romosozumab, moderate-certainty evidence) or recombinant PTH (teriparatide; low-certainty evidence), followed by a bisphosphonate, to reduce the risk of fractures only in females with primary osteoporosis with very high risk of fracture (conditional recommendation).

RATIONALE: Bisphosphonates had the most favorable balance among benefits, harms, patient values and preferences, and cost among the examined drugs in postmenopausal females with primary osteoporosis and should be used as first-line treatment. Denosumab also had a favorable long-term net benefit, but bisphosphonates are much cheaper than other pharmacologic treatments and available in generic formulations. Evidence showed that the benefits of recombinant PTH (teriparatide) or the sclerostin inhibitor (romosozumab) may have outweighed harms compared with placebo in a select population of postmenopausal females (mean age >74 years) with osteoporosis and very high risk for fracture. Bisphosphonates were associated with higher risk for osteonecrosis of the jaw and atypical femoral fractures. Teriparatide may have resulted in no difference in risk for serious adverse events but probably increased the risk for withdrawal due to adverse events in RCTs after 36 months.

Patient Population
Postmenopausal females diagnosed with primary osteoporosis

Interventions Compared With Placebo
Bisphosphonates (alendronate, risedronate, zoledronate), denosumab, teriparatide, abaloparatide, romosozumab, raloxifene

Key Outcomes Assessed at 12–36 and ≥36 Months
Hip fracture, any clinical and clinical vertebral fractures, radiographic vertebral fractures, harms (serious adverse effects and treatment withdrawal due to adverse effects)

Resources

- American College of Physicians. (2023). *Pharmacologic Treatment of Primary Osteoporosis or Low Bone Mass to Prevent Fractures in Adults: A Living Clinical Guideline From the American College of Physicians*. (acpjournals.org)
- US Preventive Services Task Force. Screening for Osteoporosis to Prevent Fractures: US Preventive Services Task Force Recommendation Statement. *JAMA.* 2018;319(24):2521–2531. doi:10.1001/jama.2018.7498
- Richard Eastell, Clifford J Rosen, Dennis M Black, Angela M Cheung, M Hassan Murad, Dolores Shoback, Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society Clinical Practice Guideline, *The Journal of Clinical Endocrinology & Metabolism*, Volume 104, Issue 5, May 2019, Pages 1595–1622, https://doi.org/10.1210/jc.2019-00221
- Osteoporosis International (2022) 33:2049–2102 https://doi.org/10.1007/s00198-021-05900-y
- Densitometria óssea da coluna lombar e do colo do fémur. | Download Scientific Diagram (researchgate.net)
- Centers for Disease Control and Prevention. Physical activity and health. https://www.cdc.gov/physicalactivity/basics/pa-health/index.htm. Updated February 13, 2018. Accessed Jan, 2024.
- Lyles KW, Colo´ n-Emeric CS,Magaziner JS, Adachi JD, Pieper CF, Mautalen C, Hyldstrup L, Recknor C, Nordsletten L, Moore KA, Lavecchia C, Zhang J, Mesenbrink P, Hodgson PK, Abrams K, Orloff JJ, Horowitz Z, Eriksen EF, Boonen S; HORIZON Recurrent Fracture Trial. Zoledronic acid and clinical fractures and mortality after hip fracture. N Engl J Med. 2007;357(18): 1799–1809.
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- Safehip Soft Hip Protector - Active Women, Small - Item #929154 (berktree.com)