Osteoporosis

in geriatrics and women

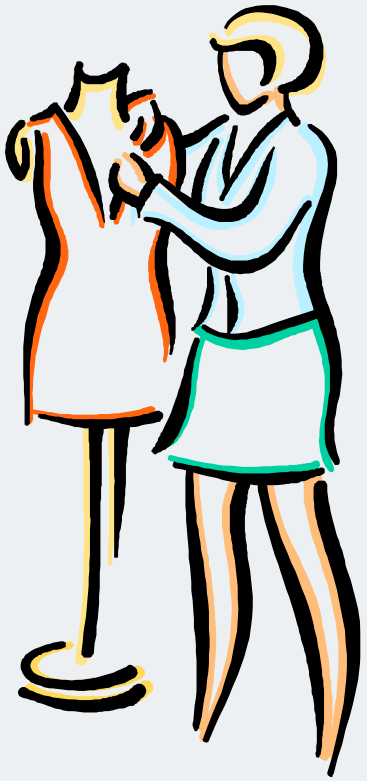
Niayesh Mohebbi

Typical comments from people with osteoporosis

"I've lost six inches in height and none of my clothes fit me anymore."

Comments

“It’s hard to get clothes that look nice when my back is so hunched over.”



Comments

"If somebody had told me sooner what I know now about osteoporosis, none of this might be happening to me!"

CLINICAL MANIFESTATIONS

- Osteoporosis has no clinical manifestations until there is a fracture. (A silent disease)
- Osteoporosis can have profound impacts on physical function and activity.
- The pain, physical limitations, and lifestyle and cosmetic changes caused by osteoporotic fractures can also have serious psychologic effects, including depression, loss of self-esteem, anxiety, fear, anger, and strained interpersonal relationships.

Risk factors

- Age
- Gender
- Race
- Family history
- Small stature
- Low wt
- Early menopause
- Alcohol
- Smoking

Diseases

- RA
- Hyperthyroidism
- Hyperpara
- Cushing synd
- GI disorders
- Cancers
- COPD
- Diabetes
- HIV
- Transplantation
- Cystic fibrosis
- Severe liver disease
- Sex hormone deficiency

medications

- Glucocorticoids
- Anticonvulsants
- Heparin
- TPN
- Thyroid suppl
- AL
- MPA
- Li
- Immunosuppresants
- Loop diuretics
- Chemotherapy
- GnRH agonists

DIAGNOSIS

- Assessment of microarchitecture requires bone biopsy, therefore BMD assessment is the gold standard to diagnose osteoporosis
- T-score
- Z-score
- WHO criteria can not be used in premenopausal women or men under age 50 because the relationship between BMD and fracture risk is not the same in younger women and men

Cont.

- BMD that is 2.5 SD or more below mean BMD for young adult reference population,t score of -2.5 or less
- Osteopenia: -1<T score<-2.5
- As BMD decreases,fracture risk increases with no threshold.

BMD measurement

- Dual energy x-ray absorptiometry (DXA) gives an accurate and precise estimate of BMD
- DXA measurements of the spine and hip
- If pharmacologic therapy is planned, measurement of spine BMD is useful as it shows less variability and can detect responses to therapy earlier than hip BMD
- Diagnosis :lowest T-score measured.

Validated risk factors of fracture

- Advanced age
- Previous fracture
- Long-term glucocorticoid therapy
- Low body weight (less than 58 kg)
- Family history of hip fracture

  Parental history of hip fracture is associated with a two fold increased risk of hip fracture
- Cigarette smoking
- Excess alcohol intake

Risk Factors for Osteoporotic Fracture

Relative Risk ≥ 2 (Major)

- Age > 70
- Menopause < 45
- Hypogonadism
- Fragility Fracture
- Hip Fracture in 1º Relatives
- Glucocorticoids
- Malabsorption
- High Bone Turnover

- Anorexia Nervosa
- BMI < 18
- Immobilization
- Chronic Renal Failure
- Transplantation

Relative Risk 1 - 2 (Moderate)

- Estrogen Deficiency
- Calcium Intake < 500 mg/d
- Primary Hyperparathyroidism
- Rheumatoid Arthritis
- Bechterew Disease
- Anticonvulsants
- Hyperthyroidism
- Diabetes Mellitus
- Smoking
- Excessive Alcohol

Brown J. et al. CMAJ 2002; 167(10 suppl):S1-S34

Maximizing PBM

"Senile osteoporosis is a pediatric disease"

- Nutrition: Ca, Vit D
- Physical activity
- Smoking
- alcohol

Calcium

- **Children 1-3 years old**: 700 mg
- **Children 4-8 years old:** 1,000 mg
- **Children 9-18 years old:** 1,300 mg
- **Adults 19-50**: 1,000 mg
- **Women 51 to 70:** 1,200 mg
- **Men 51 to 70:** 1,000 mg
- **Women & men 71 and over**: 1,200 mg

Maximizing PBM

There is no role for pharmacological therapy as a mean to maximize PBM, except…

- Hormone replacement for deficiency state in children
- GH deficiency
- Pharmacological doses of VitD for anticonvulsant therapy

Minimizing bone loss

Non Pharmacological therapy

- **Ca:** reducing rate of bone loss/trend toward reduction of vertebral fracture
- **Vit D**: absorption of Ca, mineralization of bone, optimal muscle function and balance
- **Physical activity**
- **Smoking:** reduce BMD/increase fracture risk

Physical activity

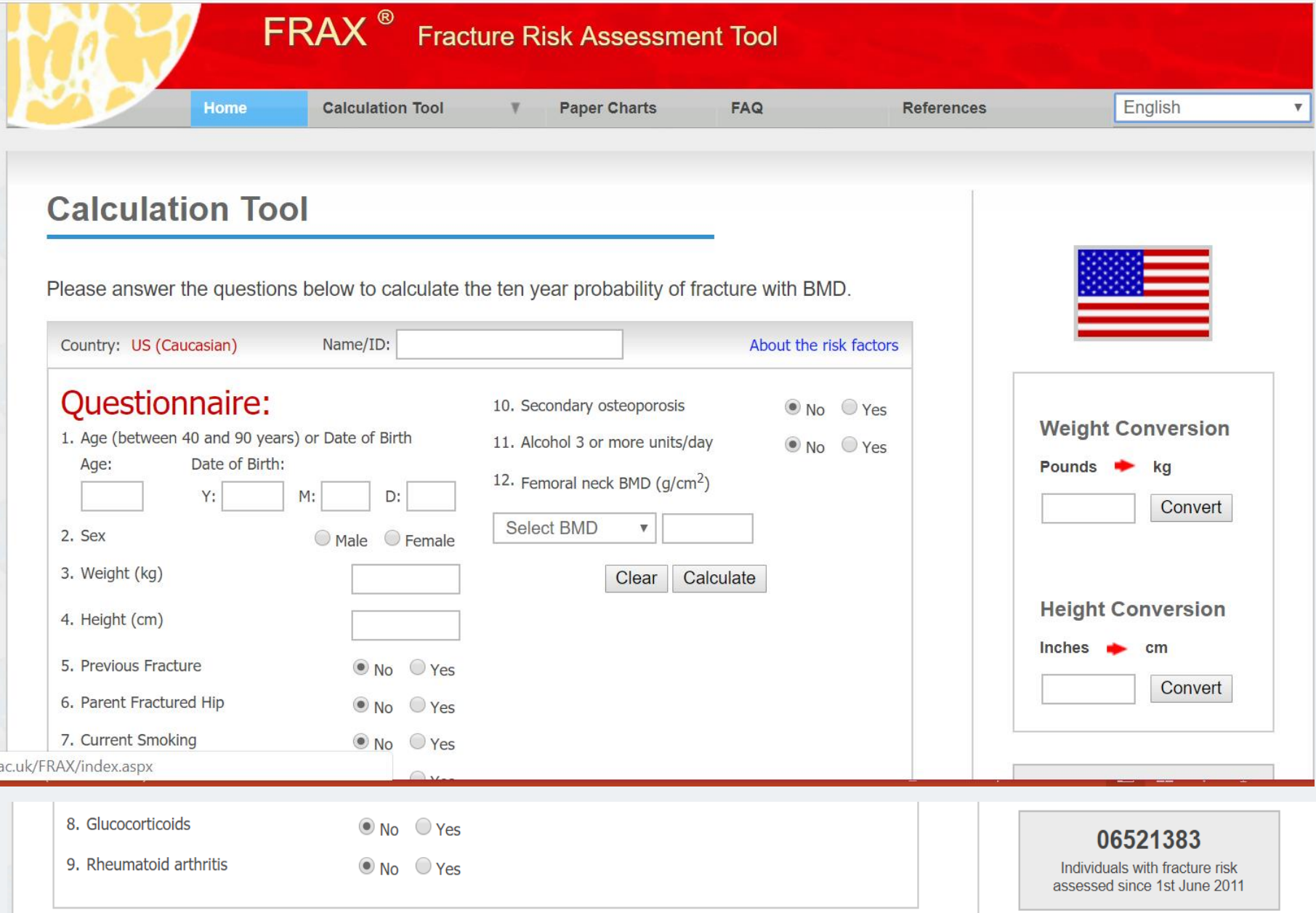
- Weight-bearing exercise is associated with small but significant improvement in BMD in premenopausal and postmenopausal women and in men

- It may also improve muscle tone and reduce the risk of falls

- minimum of 30 minutes of physical activity (such as brisk walking) on most, if not all, days of the week, at least 3 days weekly.

Pharmacologic therapy for:

- Patients with a history of fragility fracture or with osteoporosis based upon bone mineral density (BMD) measurement (T-score ≤-2.5).
- suggest the treatment of high-risk postmenopausal women with T-scores between -1.0 and -2.5. We calculate fracture risk using the World Health Organization (WHO) Fracture Risk Assessment Tool (FRAX) .A reasonable cutpoint that may be cost effective in some settings is a 10-year probability of hip fracture or combined major osteoporotic fracture of ≥3.0 or ≥20 percent, respectively.


FRAX® Fracture Risk Assessment Tool
Home
Calculation Tool
Paper Charts
FAQ
References
English
Calculation Tool
Please answer the questions below to calculate the ten year probability of fracture with BMD.
Country: US (Caucasian)
Name/ID:
About the risk factors
Questionnaire:
1. Age (between 40 and 90 years) or Date of Birth
Age:
Date of Birth:
Y:
M:
D:
2. Sex
Male
Female
3. Weight (kg)
4. Height (cm)
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/cm2)
Select BMD
Clear
Calculate
Weight Conversion
Pounds
kg
Convert
Height Conversion
Inches
cm
Convert
06521383
Individuals with fracture risk assessed since 1st June 2011

Pharmacological therapy

Drugs approved for prevention:

- Estrogen
- Biphosphanates
- Raloxifene
- Denosumab
- Teriparatide
- Calcitonin

WHI

CE (0.625 mg/d)± MPA (2.5 mg/d) reduced the risk of hip, vertebral and other fractures in healthy post menopausal women

- EPT:CHD, stroke,VTE, breast cancer
- ET: stroke, VTE

In the light of WHI data and efficacy of other antiresorptive drugs, EPT should no longer be used solely for prevention or treatment (not FDA approved) of osteoporosis.

Exception:

persistent menopausal symptoms/can not tolerate other drugs

Biphosphonates

- Potent antiresorptive: BMD/fracture

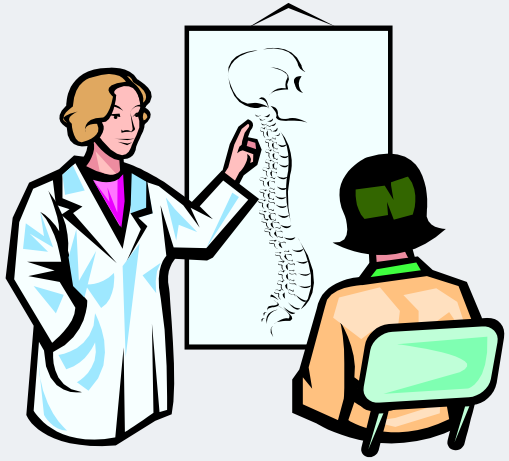
- Prevention doses:

alendronate	5mg/d or 35mg/wk
residronate	5mg/d or 35mg/wk or 75mg on two consecutive days monthly
Ibandronate	150 mg/month

Raloxifene

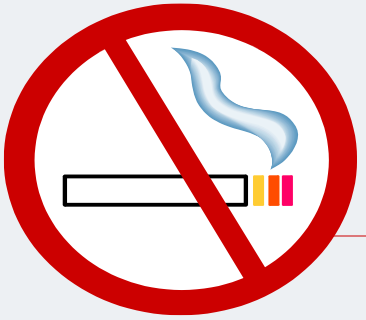
- BMD/vertebral fracture
- Not nonvertebral fracture
- Breast cancer reduction
- No effect on heart disease or endothelium
- Thromboembolic event
- Hot flash

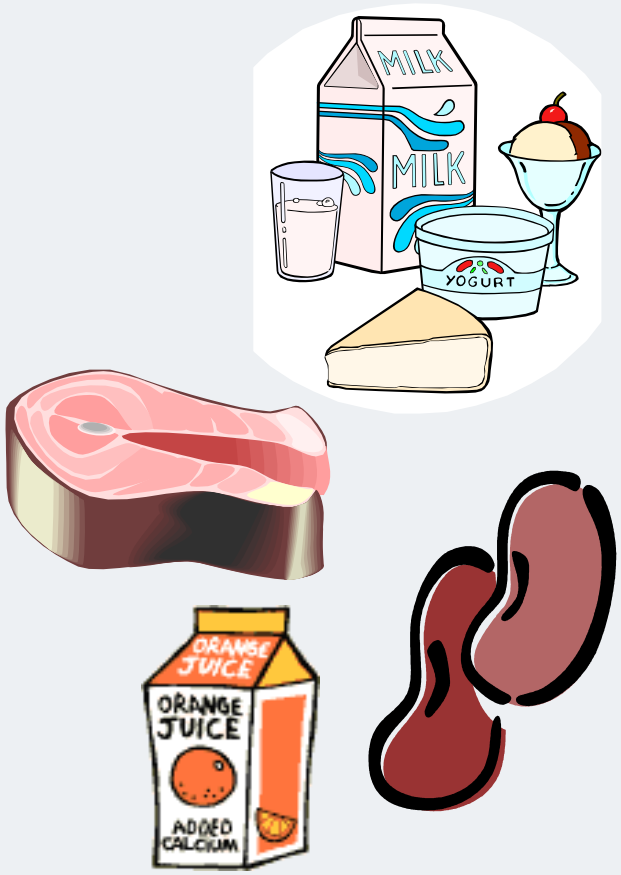
Management of osteoporosis



Non pharmacologic

- **Ca/Vit D:** 1500/800
- **Diet**
- **Exercise**
- **Cessation of smoking**





Common Food Sources of Calcium			
Food	**Serving Size**	**Amount**	**%DV***
Yogurt, fruit, low fat	1 cup	345 mg	35%
Milk, low fat	1 cup	305 mg	31%
Orange juice, calcium fortified	1 cup	300 mg	30%
Sardines, canned with bone	3 ounces	325 mg	33%
Collard greens, boiled	1 cup	266 mg	27%
Cereal, cream of wheat, cooked	1 cup	232 mg	23%
Cheese, cheddar	1 ounce	204 mg	20%
Beans, white, boiled	1 cup	191 mg	19%
Fish, salmon, canned	3 ounces	181 mg	18 %
Soybeans, boiled	1 cup	175 mg	18 %
Cottage cheese, low-fat	1 cup	138 mg	14%
Kale, boiled	1 cup	94 mg	9%
Beans, pinto, boiled	1 cup	79 mg	8%
Almonds	1 ounce	75 mg	8%
Broccoli, boiled	1 cup	62 mg	6%
Figs, dried	2 figs	62 mg	6%
Oranges, raw	1 medium	52 mg	5%

Source: USDA Nutrient Database.

* Daily Value (DV) is the daily reference amount used on food and supplement labels.

Protect Your Bones

Ways to Make Your Home Safer

Biphosphonates

- Inhibit bone resorption
- Prevention & treatment

Alendronate

- Weekly as effective as daily
- Prevention dose half of treatment
- Long term efficacy: at least 10 yrs
- Approved for male osteoporosis/glucocorticoid induced

Alendronate vs Residronate

In the RCT alendronate increased bone density more than residronate at all sites after 12 months but there were no difference in incidence of fracture

Ibandronate

- Monthly(150 mg) appears to improve BMD more than daily(2.5mg)
- 3mg IV every 3months
- Reduces hip fracture risk?

Zoledronic acid

- 5mg once yearly (15 min infusion)
- Increases BMD and reduces fracture risk
- Adverse events: flu-like syndrome, transient hypocalcemia,AF
- Can not tolerate oral

Denosumab

- is an alternative to IV zoledronic acid for women at high risk for fracture (such as older patients) who have difficulty with the dosing requirements of oral bisphosphonates, who prefer to avoid IV bisphosphonates due to side effects (eg, acute phase reaction), or who have impaired renal function.

Biphosphonates

- Poorly absorbed
- Not in active upper GI disease
- Timing of dose
- cLcr> 30-35 ml/min

Bisphosphonates – Missed Dose

- Once weekly alendronate, risedronate
  - Take on morning after remembering, then resume once weekly on regularly chosen day
- Once monthly ibandronate
  - If next dose > 7 days away, take dose the morning following the date remembered
    - Then return to original schedule
  - If next dose < 7 days away, wait until next scheduled dose
    - Must not take two 150 mg tablets within the same week

SERMs – Raloxifene

- FDA-approved for:
  - Prevention and treatment of osteoporosis in postmenopausal women
- Mechanism: tissue-selective activity, acts as an estrogen agonist on bone
  - Estrogen antagonist on breast, uterus

Raloxifene

- Prevention & treatment
- BMD/vertebral fracture
- Breast cancer
- Total & LDL-c
- Vaginal bleeding, endometrial hyperplasia
- VTE
- Less potent antiresorptive agent than alendronate or estrogen

Raloxifene – Dosing/Administration

- For prevention and treatment
  - 60 mg PO once daily
- Can be taken any time of day without regard to meals
- Should supplement with calcium/vitamin D if dietary intake inadequate

Raloxifene – Adverse Effects

- Frequency > 10%
  - Hot flashes
  - Arthralgias
  - Sinusitis
- Frequency 1-10%
  - Chest pain
  - Insomnia
  - Migraines
  - Peripheral edema
  - Diaphoresis

**Has been associated with increased risk of thromboembolism (DVT, PE) and superficial thrombophlebitis; risk is similar to reported risk of HRT

Raloxifene

Contraindications/Precautions

- History of DVT/PE or at high risk
- Cardiovascular disease
- History of uterine/cervical carcinoma
- Discontinue at least 72 hours prior to and during prolonged immobilization

Raloxifene

Not first line

FDA approved

Raloxifene

- Place in Therapy: considered first-line in women who cannot tolerate bisphosphonates and have no contraindications to therapy
- Combination therapy (usually a bisphosphonate with a non-bisphosphonate) can provide additional small increases in BMD when compared to monotherapy
- Impact of combination therapy on fracture rate unknown

Combination therapy

Do not suggest combination of biphos-estrogen or biphos- raloxifene therapy as additional benefit is small

Calcitonin

- FDA-approved for:
  - Treatment of osteoporosis in women who are ≥ 5 years postmenopausal
  - Treatment of Paget's disease of bone
  - Adjunctive therapy for hypercalcemia

Calcitonin

- Peptide composed of 32 amino acids
- Binds to osteoclasts and inhibit bone resorption
- Salmon: high affinity(x40),slow rate of clearance
- Human: less antigenic

Calcitonin

- Routes: SC, IM, Intranasal
- Bioavailability: nasal 25% IM (200 IU~50 IU)
- Adverse Events: N, V, flushing
- Nasal may provide more effective analgesia and less AE than parenteral

Calcitonin – Dosing/Administration

- Intranasal
  - 200 units (1 spray) alternating nares daily
  - Store unopened bottles in refrigerator, protect from freezing
  - Can store open bottles at room temperature for up to 35 days
  - Activate pump of *new* bottles until full spray produced (allow to reach room temperature before priming)
  - Each bottle contains at least 30 doses
- IM/SQ
  - 100 units/every other day (minimum effective dose not well-defined)
  - Should perform skin test prior to initiating therapy
- Should supplement with calcium/vitamin D if dietary intake inadequate

Calcitonin – Adverse Effects

- Most common:
  - Nasal spray: rhinitis (12%), irritation of nasal mucosa (9%), epistaxis (3.5%), sinusitis (2.3%), back pain, arthralgia, headache
  - Injection: nausea (10%), flushing (2-5%)
- Temporarily withdraw use of nasal spray if ulceration of nasal mucosa occurs
- Periodic nasal examinations recommended

Calcitonin

We usually don’t use calcitonin as first line therapy.

- we often administer if **pain** is a predominant problem, switch to other agents once pain has abated

- In combination with other agents for treatment of severe osteoporosis

VitD

- Sustantial vitD deficiency is extremely common
- 25(OH) VitD> 20-30 ng/mL
- 600 IU (1-70 yrs), at least 800 IU/d for 71 yrs and older (max 2000 IU)

VitD

- Attenuate bone loss and decrease fracture rate
- Improve muscle function and reduction in fall risk

Teriparatide

- PTH 1-34
- Anabolic agent (stimulates maturation of preosteoblasts)
- Bone formation: begins within few months and peaks 6-9 mon
- Bone resorption: begins at 6 mon peaks after 12 mon
- Antifracture efficacy is evident only after 6 mon or more

Teriparatide vs biphosphonates

Patients on Biphosphonates will often have increamental improvement in BMD even after 10 yrs, while it appears that BMD changes with PTH tobegin to level off after 18 months

Teriparatide

- PTH increases spine and hip BMD in dose-dependent manner

- Increase in lumbar BMD is greater in first 2 years of treatment than any antiresorptive agent

Combination

- PTH plus alendronate?!

- Start PTH approximately 3months after

PTH (1-34) – Adverse Effects

- Most common
  - Dizziness, rash, nausea, headache, leg cramps, arthralgia, rhinitis, transient hypercalcemia
- S/s of hypercalcemia: nausea, vomiting, constipation, low energy, or muscle weakness
- Most adverse effects in the clinical trials were mild and generally did not lead to the discontinuation of the drug
- Osteosarcoma risk in animals
  - Lead to black box warning by FDA

Teriparatide

Due to potential issues of carcinogenicity, PTH treatment should be limited to those most severely affected and for max of 2 years.

after discontinued an antiresorptive should be used

Teriparatide

- Severe osteoporosis
- Failure of other therapies
- Unable to tolerate or have contraindication to biphosphonates

Strontium ranelate

- (available outside of North America) has been shown to reduce vertebral fracture and, to a lesser extent, nonvertebral fracture.

Monitoring response to therapy

For patients starting therapy, we suggest a follow up DXA of hip and spine at **one year**, if BMD is stable or improving less frequent

Approaches to Monitoring Therapy

- Always important to ask patients about adherence, encourage continuation of therapies to reduce fracture risk
- Monitoring of therapy should be considered, as up to 1/6 of women taking effective therapies continue to lose bone, especially if they smoke
- May measure bone mineral density after 1-2 year of therapy, and if BMD is stable or improved, less frequent monitoring thereafter
- Drugs may decrease a patient's risk for fracture even when there is no apparent increase in BMD

Monitoring response to therapy

BMD that is stable or improving

- No consensus on the optimal frequency and preferred site

- ISCD recommends follow-up BMD testing (DXA spine and hip) when the expected change in BMD equals or exceeds the least significant change (LSG)

Monitoring response to therapy

Decrease in BMD:

- Truly reflects a treatment failure
- Does not necessarily imply inadequate therapy, could be ascribed to measurement error, would repeat BMD one year later, taking action if reaffirmed

Bone turnover markers

- Routine monitoring is not necessary
- conditions that might interfere with drug absorption or efficacy, such as small bowel resections or other types of malabsorption, or for patients who are reluctant to take anti-osteoporosis medications regularly.
- fasting urinary N-telopeptide (NTX) or serum carboxy-terminal collagen crosslinks (CTX) before and three to six months after starting bisphosphonate or other antiresorptive therapy. A decrease of greater than 50 or 30 percent in urinary NTX excretion or serum CTX, respectively, provides evidence of compliance and drug efficacy.

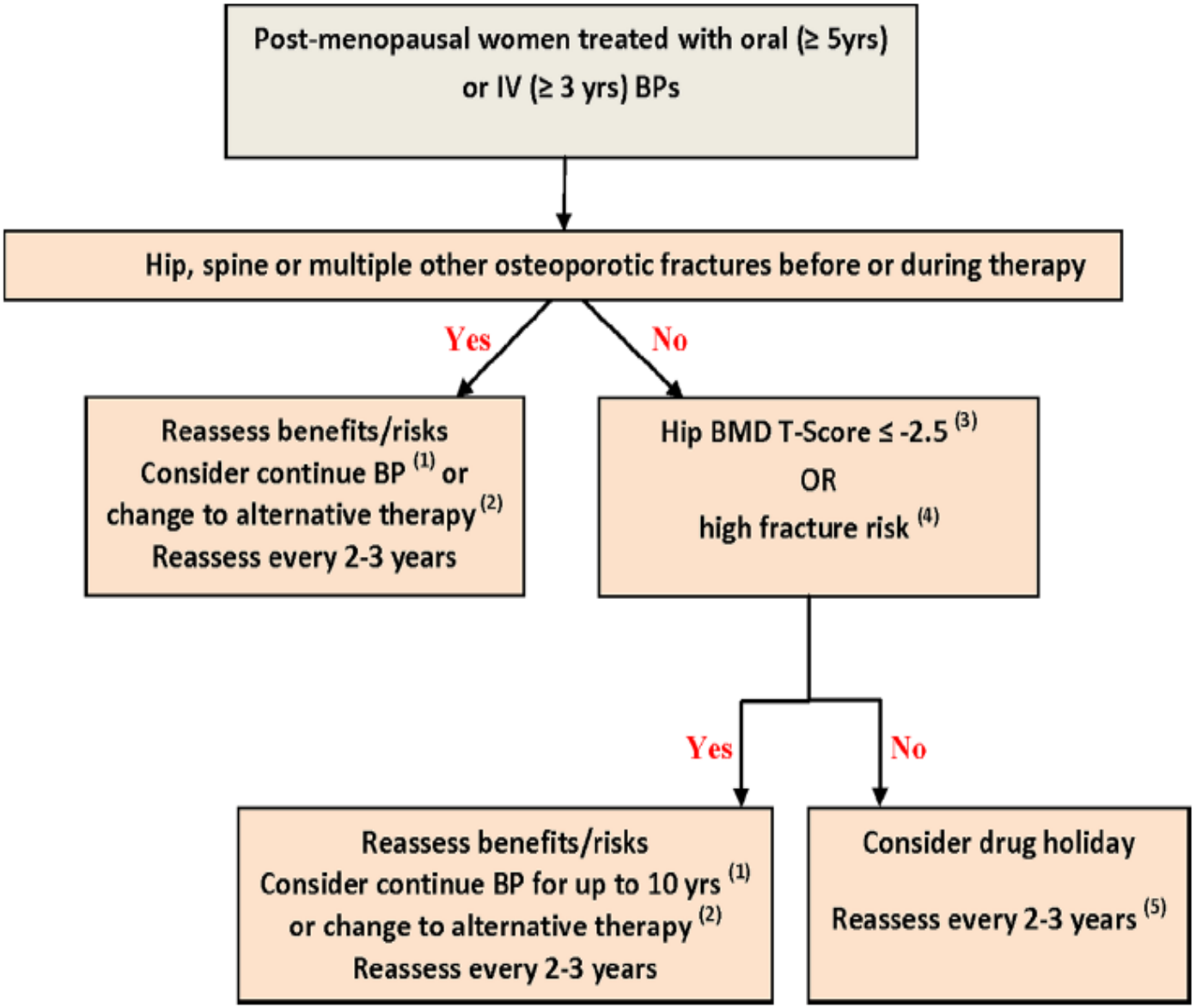
Drugs Approved by the US Food and Drug Administration for Prevention and Treatment of Postmenopausal Osteoporosis

Table 16
Drugs Approved by the US Food and Drug Administration for Prevention and Treatment of Postmenopausal Osteoporosis[a]

	Postmenopausal osteoporosis	
Drug	**Prevention**	**Treatment**
Alendronate	5 mg PO daily 35 mg PO weekly	10 mg PO daily 70 mg PO weekly[b] 70 mg + D[c]
Calcitonin	—	200 IU intranasally once daily, or 100 IU SQ qod
Denosumab	—	60 mg SQ every 6 mo
Estrogen (multiple formulations)	Multiple regimens	—
Ibandronate	2.5 mg PO daily 150 mg PO monthly	2.5 mg PO daily 150 mg PO monthly 3 mg IV every 3 mo
Raloxifene	60 mg PO daily	60 mg PO daily
Risedronate	5 mg PO daily 35 mg PO weekly 150 mg PO monthly	5 mg PO daily 35 mg PO weekly 150 mg PO monthly
Teriparatide	—	20 µg SQ daily
Zoledronic acid	5 mg IV every 2nd y	5 mg IV once yearly

Abbreviations: IV = intravenous; PO = per os; qod = every other day; SQ = subcutaneous.
[a] Please review the package inserts for specific prescribing information.
[b] Fosamax 70 mg is available as both a tablet and a unit dose liquid. Alendronate (generic Fosamax) is available.
[c] Fosamax Plus D is a tablet containing 70 mg of alendronate and 2,800 IU or 5,600 IU of vitamin D for weekly administration.
[d] Risedronate 150 mg once monthly tablet is available.

Approach to the management of PMW on long-term bisphosphonate therapy



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You're never too young or too old to improve your bone health!