Osteoporosis

Eastern Shore Medical Symposium 2021

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Jefferson Health®

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Conflicts of Interest

- Serve on the Board of The Hill at Whitemarsh (a continuing care retirement community)
- Serve as Chair of ADGAP (Association of Directors of Geriatric Academic Programs)
- No financial conflict with either

Objectives

- Review importance of bone health
- Define osteopenia and osteoporosis
- Learn how to identify osteopenia and osteoporosis
- Identification of risk factors for osteoporosis
- Learn treatment options for osteopenia
  - how to counsel patients
  - How to use FRAX calculator to assist with treatment decisions
- Learn treatment options for osteoporosis
  - Become familiar with treatment guidelines and options

Bone health

- Why so important?
- Prevent fractures
- Maintain quality of life and potentially postpone frailty
- Be able to continue with activities you enjoy

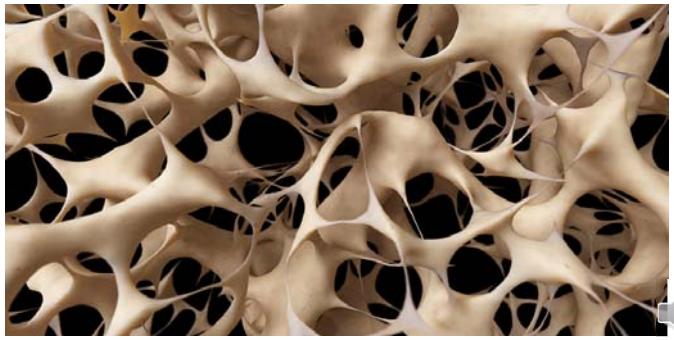
Bone health

- Be able to continue with instrumental activities of daily living (IADLs)
  - Activities central to ability to live on own: shopping, using telephone, managing medications, managing finances, preparing meals, housekeeping, transportation, laundry
- Be able to continue with activities of daily living (ADLs)
  - Core activities needed to live on own: bathing, dressing, grooming, feeding, toileting, and transferring

What is osteoporosis?

- Defined by National Osteoporosis Foundation (NOF) as:
  - Chronic, progressive disease with:
  - Low bone mass
  - Deterioration of microarchitecture of bones
  - Increased bone fragility
  - Increased fracture risk

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



Who should get screened?

- USPSTF – grade B recommendation:
  - All women 65 and over
  - Women 60 and over with at least one risk factor
- USPSTF – Insufficient evidence (Grade I) for screening in men
- *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 Downloaded From: https://jamanetwork.com/ on 05/02/2021*
- National Osteoporosis Foundation (NOF) for men
  - Men over age 70
  - Younger men with one or more risk factors (www.nof.org accessed 5.8.21)

Risk factors for osteoporosis

- Low body weight (<70 kg, 154 pounds)
- Smoking
- Family history
- Low physical activity
- *Released on AHRQ Web site on September 17, 2002, and an abridged version of this recommendation also appeared in Ann Intern Med. 2002;137(6):526-528.*

Calculating risk – ORAI scale

Parameter	Finding	Points
age in years	>= 75	15
	65 – 74	9
	55 – 64	5
	45 - 54	0
weight in kilograms	< 60	9
	60 – 69	3
	>= 70	0
current estrogen use	no	2
	yes	0

- DEXA should be done if the woman has a total score >= 9. (range 0-26)
- https://www.physio-pedia.com/The_Osteoporosis_Risk_Assessment_Instrument_(ORAI)

DEXA scan

- DEXA scan measurement cornerstone for making diagnoses of osteopenia or osteoporosis

Defining osteopenia and osteoporosis

originally defined by WHO working group in 1994

TABLE 1

World Health Organization criteria for diagnosing osteoporosis using bone density measurements

CATEGORY	T SCORE
Normal	Not more than 1.0 standard deviations (SD) below the young adult mean
Osteopenia	Between 1.0 and 2.5 SD below the young adult mean
Osteoporosis	More than 2.5 SD below the young adult mean
Severe or established osteoporosis	More than 2.5 SD below the young adult mean with a fracture

image obtained from
https://www.clevelandclinicmeded.com/medicalpubs/ccjm/Jan06/watts.htm4/25/21

DEXA report

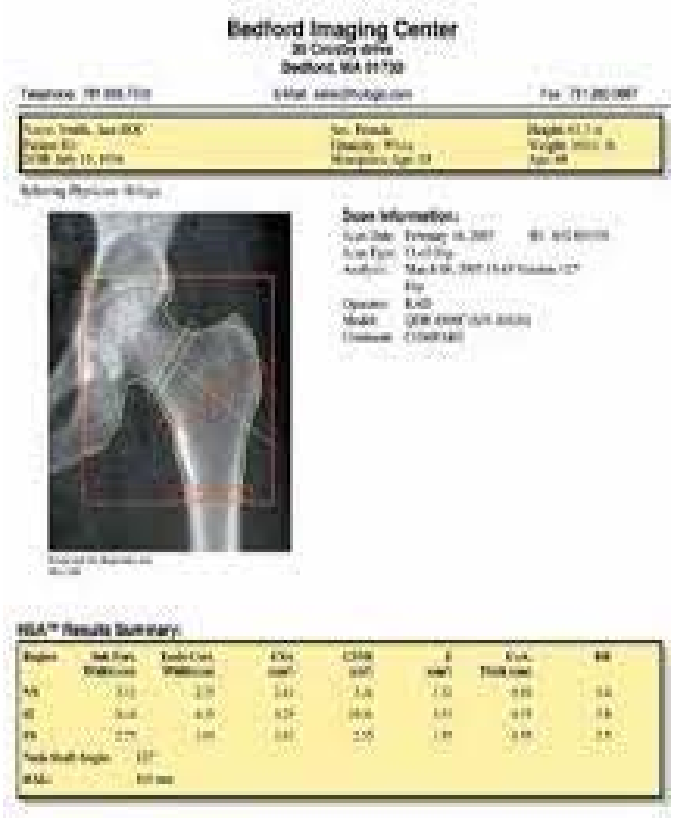
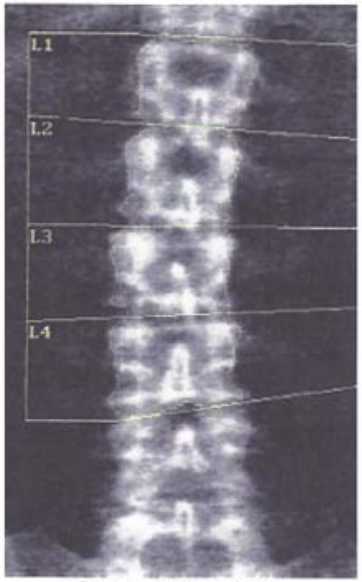


Image from Hologic Bone Densitometry and the Evolution of DXA Tao Wu, Clinical Science Manager, Hologic Asia Pacific Hologic, Inc.

DEXA scoring

image from osteoporosisinstitute.org accessed 4/25/21



DXA Scan Information:

Example of a DXA scan showing a T score lower than -2.5 indicating osteoporosis

Results Summary:

Total BMD:	0.766 g/cm²	T score:	-2.6
Peak reference:	73%	Z score:	-1.1
Age matched:	86%		

Region	Area [cm²]	BMC [g]	BMD [g/cm²]	T score	%PR	Z score	%AM
L1	12.06	7.45	0.617	-2.8	67%	-1.5	79%
L2	13.15	10.12	0.770	-2.3	75%	-0.9	88%
L3	12.71	10.65	0.838	-2.2	77%	-0.7	91%
L4	14.66	12.08	0.824	-2.7	74%	-1.1	87%
Total:	52.59	40.30	0.766	-2.6	73%	-1.1	86%

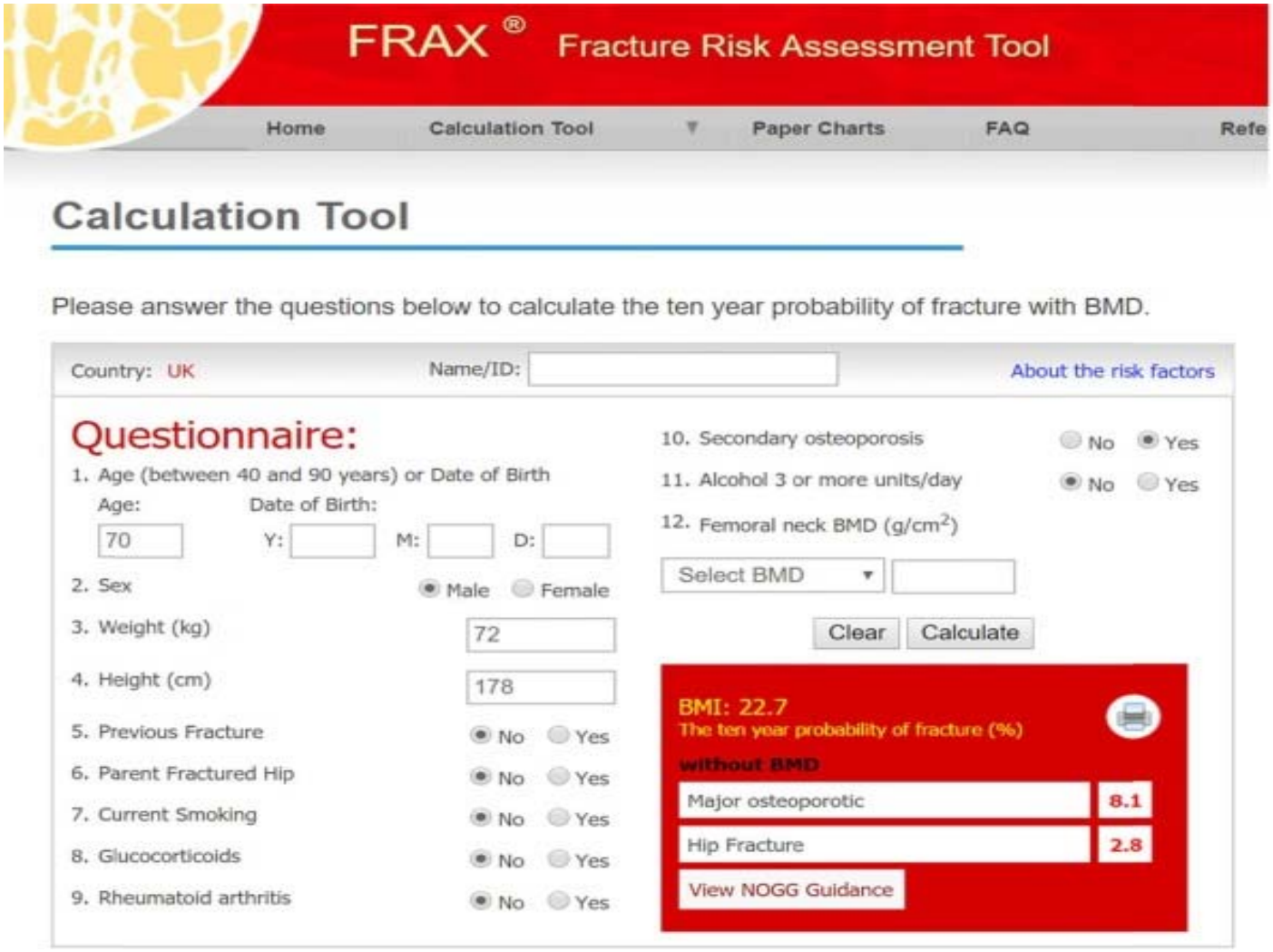
DEXA completed – then what?

- Once DEXA completed –
  - Use FRAX calculator (in some places on the DEXA report)
  - then discussion about treatment options

FRAX (Fracture Risk Assessment Tool)

- Originally released in 2008
- Has country-specific algorithms
- Based on risk factors and DEXA scores
- Estimates individualized 10-year probability of hip and major osteoporotic fracture
- Website: http://www.shef.ac.uk/FRAX
- Approx. 3 million visits / year
- FRAX incorporated into over 80 guidelines

A decade of FRAX: how has it changed the management of osteoporosis? Kanis JA, Harvey NC, Johansson H, et al. Aging Clinical and Experimental Research (2020) 32:187–196.


FRAX ® Fracture Risk Assessment Tool
Home
Calculation Tool
Paper Charts
FAQ
Refe
Calculation Tool
Please answer the questions below to calculate the ten year probability of fracture with BMD.
Country: UK
Name/ID:
About the risk factors
Questionnaire:
1. Age (between 40 and 90 years) or Date of Birth
Age:
70
Date of Birth:
Y:
M:
D:
2. Sex
Male
Female
3. Weight (kg)
72
4. Height (cm)
178
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
BMI: 22.7
The ten year probability of fracture (%)
without BMD
Major osteoporotic
8.1
Hip Fracture
2.8
View NOGG Guidance

National Osteoporosis Foundation (NOF) treatment guidelines incorporating FRAX

Initiate pharmacologic treatment:

–hip or vertebral (clinical or asymptomatic) **fractures**

–T-scores ≤−2.5 at the femoral neck, total hip, or lumbar spine by DXA (**osteoporosis**)

– In postmenopausal women and men age 50 and older with low bone mass (T-score between −1.0 and −2.5, **osteopenia**) at the femoral neck, total hip, or lumbar spine by DXA and a **10-year hip fracture probability ≥3 % or a 10-year major osteoporosis-related fracture probability ≥20 %** based on the USA-adapted WHO absolute fracture risk model (Fracture Risk Algorithm (FRAX®); www. NOF.org and www.shef.ac.uk/FRAX)

Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int (2014) 25:2359–2381

Osteopenia

- Think of osteopenia like pre-diabetes, pre-HTN
- An opportunity to slow or even stop progression to osteoporosis
- Initiate ***core prevention measures*** for all
- Consider initiation of pharmacologic measures

Osteopenia – core prevention measures

- Calcium recommendations
    - 1200 – 1500 mg per day for postmenopausal women
- Vitamin D recommendations
    - 400-800 IU daily for postmenopausal women
    - Goal is to achieve vitamin D level > 25-30 ng/ml

Khosla, S and L. J Melton, Osteopenia, NEJM 356;22 www.nejm.org may 31, 2007.

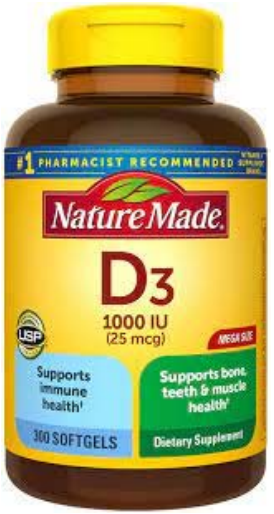
- Now vitamin D popular for other reasons (immune health discussion in COVID) – 1000-2000 IU daily dosing

Osteopenia – core prevention measures

- Vitamin D repletion works
  - Meta-analysis of 25 studies of vitamin D repletion
  - Statistical decrease in vertebral fractures
  - Trend towards non-vertebral fractures

Papadimitropoulos E, Wells G, Shea B, et al ,2002.

Endocrine Reviews 23(4):560–569.



Osteopenia – core prevention measures

- Weight bearing exercise
  - National osteoporosis foundation (www.nof.org)
  - High impact – dancing, running, tennis…
  - Low impact – elliptical machine use, walking…
- Muscle strengthening
  - Lifting weights, use of bands…

Osteopenia – core prevention measures

- Exercise – what does the literature tell us?
  - “Combined exercise and group exercise programs, including weight-bearing activities, balance training, jogging, low-impact loading, high magnitude exercise, muscle strength, and simulated functional tasks, are advised to…at least preserve BMD.
  - However the combination of exercise should be tailored on the patient’s clinical features.
  - No agreement exists on the best protocol in terms of duration, frequency, and the type of exercises to be combined. The most relevant effect was detected at the spine.”
  - *Benedetti MG,Furlini G, Zati A, et al, BioMed The Effectiveness of Physical Exercise on Bone Density in Osteoporotic Patients. Research International. 2018, https://doi.org/10.1155/2018/4840531*

Osteopenia – core prevention measures

- Exercise recommendations – common sense
  - Adults should perform 150 to 300 minutes of moderate physical activity each week (www.aafp.org)
  - National osteoporosis foundation has developed safe movement and exercise videos (https://www.nof.org/patients/treatment/exercisesafe-movement/)
    - 4 main goals:
    - Walking program 3-5 times per week, 40 minutes each time
    - Balance program
    - Muscle strengthening program
    - Specific focus on back extensor strengthening

Videos for bone safety

- National Osteoporosis Foundation
  - Videos for safe lifting – to help protect against vertebral fractures
  - (https://www.nof.org/patients/treatment/exercisesafe-movement/)

- We are going to look at how to lift groceries from trunk of car.
  - https://vimeo.com/showcase/4034464

Osteopenia – pharmacologic measures

- Determine FRAX score
- Consider pharmacologic treatment if **10-year hip fracture probability ≥3 % or a 10-year major osteoporosis-related fracture probability ≥20 %**
- Have a RAB (risk, alternative and benefit) discussion with each patient
- **Non-pharmacologic measures only and follow up DEXA in 2 years vs initiating pharmacologic measures early as preventive measure**

Osteopenia – markers of bone turnover

- Thought that measuring markers of bone turnover might help with decision around pharmacologic therapy – but jury still out
- Patients with high turnover are (in theory) at higher risk for fractures
  - Markers of resorption:
    - urinary or serum C-terminal and N-terminal telopeptides of type I collagen
  - Markers of formation:
    - bone-specific alkaline phosphatase, osteocalcin ,and N-terminal propeptide of type I collagen

Khosla, S and L. J Melton, Osteopenia, NEJM 356;22 www.nejm.org may 31, 2007.

Osteopenia – pharmacologic measures

- What are the pharmacologic options for osteopenia?
  - Bisphosphonates – aldendronic acid (Fosamax), ibandronic acid (Boniva), risendronic acid (Actonel), zoldenronic acid (Reclast)
  - SERMs – raloxifene (Evista)
  - Estrogen therapy
- The use of pharmacologic agents with osteopenia remains controversial

Osteopenia management – what do the guidelines tell us?

- **National Osteoporosis Foundation**

Initiate pharmacologic treatment: “In postmenopausal women and men age 50 and older with low bone mass (T-score between −1.0 and −2.5,osteopenia) at the femoral neck, total hip, or lumbar spine by DXA and a 10-year hip fracture probability ≥3 % or a 10-year major osteoporosis-related fracture probability ≥20% based on the USA-adapted WHO absolute fracture risk model (Fracture Risk Algorithm (FRAX®); www.NOF.org and www.shef.ac.uk/FRAX)”

Cosman F, de Beur SJ, LeBoff MS, et al. Clinician’s Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int (2014) 25:2359–2381

Osteopenia management – what do the guidelines tell us?

- **ACP guidelines**
- *"clinicians should make the decision whether to treat osteopenic women 65 years of age or older who are at a high risk for fracture based on a discussion of patient preferences, fracture risk profile, and benefits, harms, and costs of medications."*

Qaseem A, Forciea MJ, McLean RM, et al. Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update From the American College of Physicians. Annals of Internal Med. June 6, 2017

Osteopenia – what's practical

- Initiate lifestyle recommendations in all:
  - Calcium
  - Vitamin D
  - Weight-bearing exercises – and give NOF website as resource for exercise videos
  - Calculate FRAX score and look at T-score
    - If T score close to – 2.5 and FRAX score over 3% for hip and 20% for major then have discussion about RABs of treatment vs f/u DEXA in 2 years

Osteoporosis

- **Rule out secondary causes**
  - Basic work up includes:
  - serum 25-hydroxyvitamin D
  - calcium
  - Creatinine
  - thyroid-stimulating hormone

Jeremiah MP, Unwin BK MD, Greenawald MH, et al. Am Fam Physician. 2015;92(4):261-268.

- ***Use of Z-score*** *– is the age-matched comparison – if abnormal can indicate secondary cause*

Osteoporosis

- Same non-pharmacologic treatment options
- Pharmacologic treatment options
  - Most guidelines recommend initiating pharmacologic measures when DEXA t score > -2.5
  - More controversy around stopping point

Bisphosphonates

- Aldendronate (Fosamax)
  - 70 mg per week
- Efficacy data good - reduces the incidence of spine and hip fractures by about 50 % over 3 years in patients with a prior fractures
- Ibandronate (Boniva)
  - 150 mg per month and 3 mg every 3 months by IV
- Efficacy data similar for vertebral fractures but not with non-vertebral fractures

Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int (2014) 25:2359–2381

Bisphosphonates

- Risedronate (Actonel)
  - 35 mg weekly or 150 mg monthly tablet)
- Efficacy data - Risedronate reduces the incidence of vertebral fractures by 41 to 49 % and non-vertebral fractures by 36 % over 3 years
- Zoledronic acid (Reclast)
  - 5 mg by intravenous infusion over at least 15 min once yearly for treatment and once every 2 years for prevention
- Efficacy data - reduces the incidence of vertebral fractures by 70%, hip fractures by 41 %, and nonvertebral fractures by 25 % over 3 years

Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int (2014) 25:2359–2381

Bisphosphonates

- Cautions
  - Cannot be used with GFR <30
  - Osteonecrosis of jaw – more of an issue with IV
  - Atypical femur fractures
    - These tend to occur if used bisphosponates for > 5 years
    - Have higher threshold if patient complaining of thigh pain to image
    - Suspect that changes in bone quality and fracture repair process by bisphosphonates has been implicated (*Saita Y, Ishijima M, Kaneko K. Atypical femoral fractures and bisphosphonate use: current evidence and clinical implications. Ther Adv Chronic Dis. 2015, Vol. 6(4) 185–193*)

Teriparatide (Forteo)

- Parathyroid hormone analog, anabolic activity
- 20 mcg SQ daily
- Efficacy data – decreases both vertebral and non-vertebral fractures

Crandall CJ, Newberry SJ, Diamant A, et al. Comparative effectiveness of pharmacologic treatments to prevent fractures: an updated systematic review. Ann Intern Med. 2014;161(10):711-723.

- Use maximum of 2 years
- Black box waring – increased risk of osteosarcoma in rats, avoid in patients with increased risk of osteosarcoma including Pagets disease, unexplained high alkaline phosphatase

Denosumab (Prolia)

- Prolia
  - Human monoclonal Ab – inhibits osteoclast activity
  - 60 mg SQ q 6 months
  - Max of 3 years therapy
  - Efficacy data – effective for vertebral and non-vertebral fracture reduction

Crandall CJ, Newberry SJ, Diamant A, et al. Comparative effectiveness of pharmacologic treatments to prevent fractures: an updated systematic review. Ann Intern Med. 2014;161(10):711-723.

Raloxefine (Evista)

- Selective estrogen receptor modulator (SERM)
- Raloxefine (Evista) 60 mg PO daily
- Efficacy data – only effective at reducing vertebral fractures

Crandall CJ, Newberry SJ, Diamant A, et al. Comparative effectiveness of pharmacologic treatments to prevent fractures: an updated systematic review. Ann Intern Med. 2014;161(10):711-723.

- *Increased vasomotor symptoms*
- *Increased blood clot risk*
- *Decreases breast cancer risk*

Jeremiah MP, Unwin BK MD, Greenawald MH, et al. Am Fam Physician. 2015;92(4):261-268.

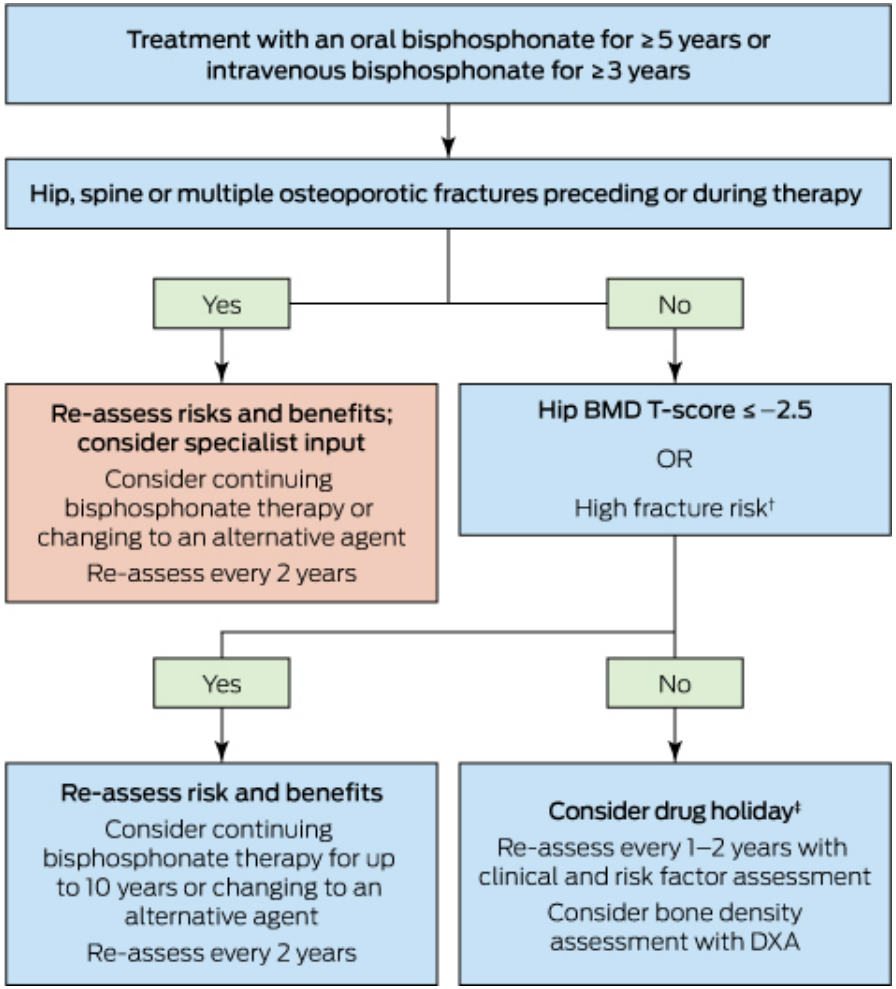
Calcitonin nasal spray

- 200 units (one spray) in one nostril daily
- Efficacy data – benefits vertebral risk only
- Fallen out of favor due to efficacy data and some question of increased cancer risk

Overman RA, Borse M, Gourlay ML. Salmon calcitonin use and associated cancer risk. Ann Pharmacother. 2013;47(12):1675-1684.

Deciding how long to treat

- Now accepted to have a RAB discussion about on-going use of bisphosphonates after 5 years of treatment (3 years for Reclast)
  - To help you stratify – DEXA, fracture hx, consider bone turnover markers
  - Decide if low risk – use DEXA (if now t scores > -2.5), no fracture
  - If low risk – can do drug holiday and monitor with DEXA q 2 years
  - If high risk – can opt to continue bisphosphonate or rotate therapy to Prolia or Forteo
  - When to end drug holiday – if worse BMD, fracture or bone turnover markers indicate high turnover



https://www.mja.com.au/journal/2016/205/4/osteoporosis-treatment-missed-opportunity

Newer agents

- romosozumab (Evenity)
  - monoclonal antibody
  - blocks the effects of the protein sclerostin
  - works mainly by increasing new bone formation
  - 210 mg SQ q month x 12 months
  - Warning about increased risk of MI, CVA, cardiovascular death in one report

Feyza Sancar, PhD. Caution With New Osteoporosis Drug. JAMA May 21, 2019 Volume 321, Number 19

- Abaloparatide (Tymlos)
  - Parathyroid hormone analog, anabolic activity

Case example - easy

- 68 year old female patient of yours is over due for DEXA based on care gap analysis
- No significant risk factors
- You order DEXA
- DEXA scan shows osteopenia
  - T-score -2.0
  - FRAX calculator (data 150 pounds, 64 in)
    - Major OP fracture risk = 12%
    - Hip fracture risk = 2%
- Your prescription is for healthy lifestyle changes – vitamin D repletion, weight-bearing exercises

Case example - challenging

- 80 year old patient with osteoporosis who has been on Fosamax x 5 years. No prior fractures. Hx of COPD requiring steroids often. +parent with hip fracture
- You order DEXA
- DEXA scan shows osteoporosis
  - T-score -3.5
  - FRAX calculator (data 150 pounds, 64 in)
    - Major OP fracture risk = 71
    - Hip fracture risk = 64
- This patient is HIGH risk. Having been on bisphosphonate x 5 years – would rotate to Prolia.

Summary

- PCPs can have impact through non-pharmacologic counseling:
  - Weight-bearing exercise
  - Checking vitamin D levels and depleting
  - Adequate daily vitamin D – 1000 IU daily
- Using DEXA scan in women 65 years and over
- Considering FRAX in osteopenia for RAB discussions

Summary

- Bisphosphonates first line – then denosumab (Prolia) or teraparatide (Forteo) as options
- Bisphosphonates – consider d/c at 5 years of therapy
- Calcitonin and raloxefene (Evista) – little (to no) use
- Not much new in terms of pharmacologic agents

Summary

- Non-pharmacologic, healthy lifestyle measures are the bread and butter for osteoporosis and fracture prevention
- PCPs can help in delaying frailty through fracture prevention and helping maintain fitness/activity levels
- Add the NOF website and safe exercise videos to our patient education materials