9-8-2021

Osteoporosis

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Osteoporosis

DFCM Grand Rounds 9.8.21

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Jefferson Health®

HOME OF SIDNEY KIMMEL MEDICAL COLLEGE

Objectives

Review importance of bone health

Define and identify osteopenia and 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

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

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* Washington, DC: National Osteoporosis Foundation; 2014.

Incidence of osteoporosis

- Current estimates are 300 million people with osteoporosis
- 30% of women have osteoporosis
- 1 in 3 women over age 50 will experience an osteoporotic-related fracture
- 1 in 5 men will experience an osteoporotic-related fracture

Sözen T, Özışık L, Başaran N. An overview and management of osteoporosis. Eur J Rheumatol 2017; 4: 46-56

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

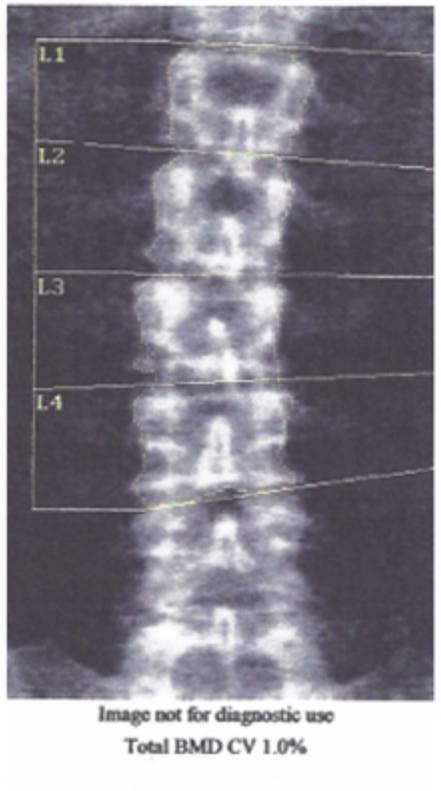
World Health Organization criteria for diagnosing osteoporosis using bone density measurements

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 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%

Other tests to help diagnose osteoporosis?

Single site testing – calcaneal US

- Does correlate with DEXA
- Use as pre-testing before DEXA

Yen Ci , Lin W, Wang,T, et al.Pre-screening for osteoporosis with calcaneus quantitative ultrasound and dual-energy X-ray absorptiometry bone density. www.nature.com/scientificreport. Accessed 9.5.21

Psoas muscle index (PMI)

- Maybe used in the future
- Based on idea of association with sarcopenia and osteoporosis
- Uses CT scan
- Small study out of Japan found correlation of PMI with BMD and fracture risk

Kajiki Y, Tsuji H, Misawa H, et al. Psoas muscle index predicts osteoporosis and fracture risk in individuals with degenerative spinal disease. Nutrition 93 (2022) 111428.

DEXA completed – then what?

Once DEXA completed…

- **Bring in** patient to discuss DEXA results
- 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

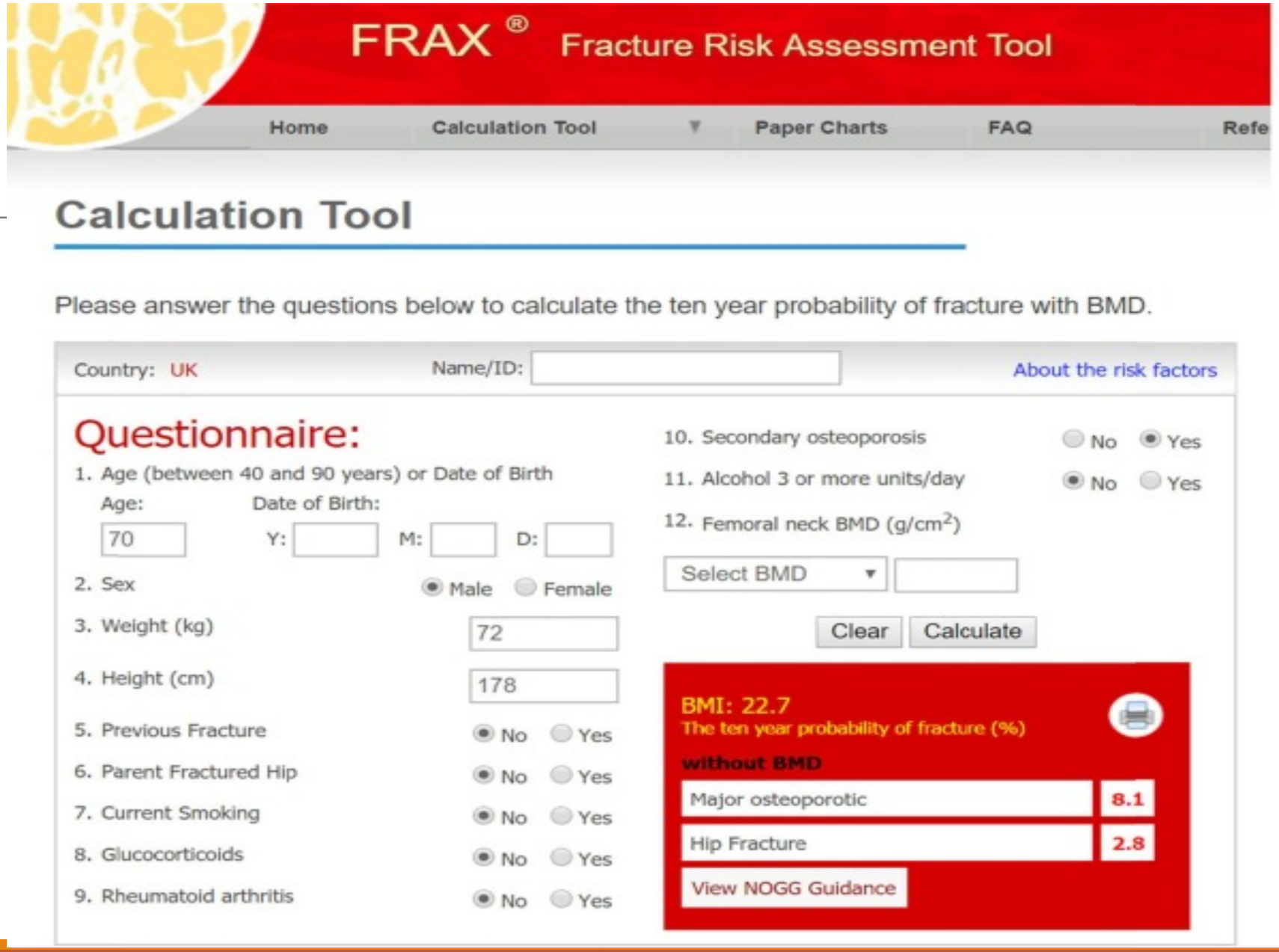
Estimates individualized 10-year probability of hip and major osteoporotic fracture

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:
Date of Birth:
70
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

National Osteoporosis Foundation (NOF) treatment guidelines incorporating FRAX

10-year hip fracture probability ≥3 % or

10-year major osteoporosis-related fracture probability ≥20 %

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

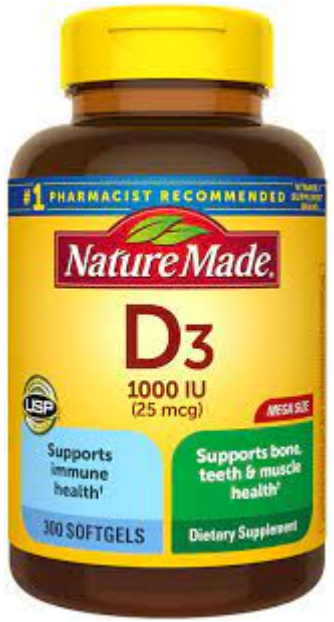
Khosla, S and L. J Melton, Osteopenia, NEJM 356;22 www.nejm.org may 31, 2007.

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

Back extensor strengthening

https://www.youtube.com/watch?v=V3sHGnvnySg

Videos for bone safety

National Osteoporosis Foundation

- Videos for safe lifting – to help protect against vertebral fractures

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 – may help with drug holiday patients

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 approved 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 worse than -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 Paget's 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

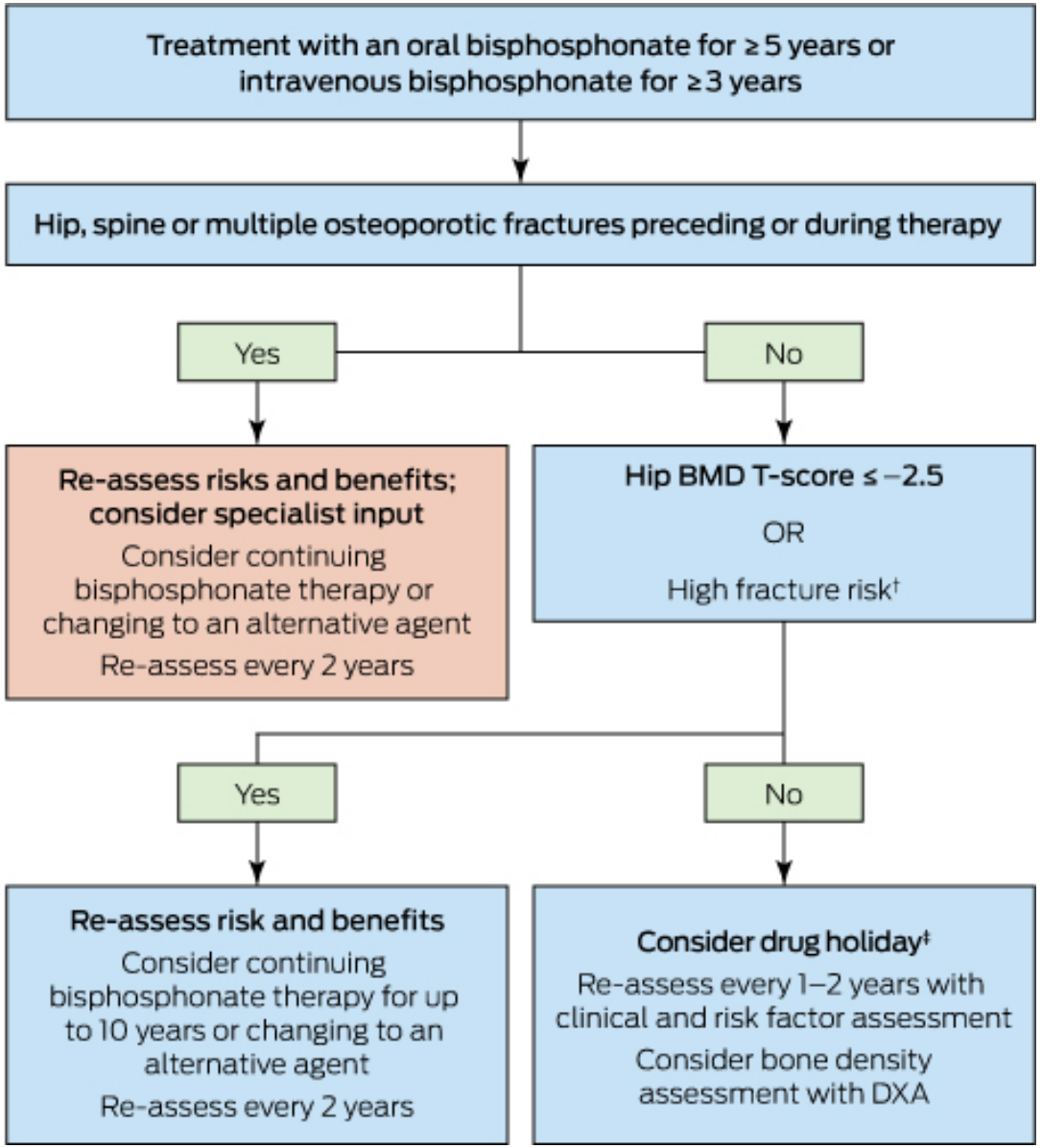
Fallen out of favor due to efficacy data and some question of increased cancer risk (liver)

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

Fun Facts

- Nitrogen-containing bisphosphonates (Fosamax, Actonel) Lower risk of pneumonia by 24% in one study

Sing C,Kiel D, Hubbard R, et al. Nitrogen-Containing Bisphosphonates Are AssociatedWith Reduced Risk of Pneumonia in Patients With Hip Fracture. Journal of Bone and Mineral Research, Vol. 35, No. 9, September 2020, pp 1676–1684.

- *Sleeping less than 5 hours per night is BAD*
  - *Puts women at higher risk for low BMD and osteoporosis*

Ochs-Balcom H,Hovey K,Andrews C, et al. Short Sleep Is Associated With Low Bone Mineral Density and Osteoporosis in the Women's Health Initiative. Journal of Bone and Mineral Research, Vol. 35, No. 2, February 2020, pp 261–268.

Fun Facts

- What about statins and risk of osteoporosis?
  - Recent study found a dose-dependent relationship
  - Low dose statins – less risk of osteoporosis
  - “Reaching the LDL target is the most important thing,” she said. “You should never stop or switch statins because of the risk of osteoporosis.”

NY Times quote from Dr. Alexandra Kautzky-Willer, a professor of medicine at the Medical University of Vienna (senior author on study) Published Oct. 8, 2019Updated Oct. 15, 2019.

*Leutner M, Matzhold C,Bellach L, et al. Diagnosis of osteoporosis in statin-treated patients is dose-dependent. Ann Rheum Dis 2019;**78**:1706–1711. doi:10.1136/annrheumdis-2019-215714*

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 - *medium*

Your patient is 72 and has never had DEXA scan.

She has significant risk factors:

- Still smokes 1/2ppd. Has smoked for 20 years.
- Has COPD – needs steroids intermittently

How much steroid use is considered a risk factor? - Steroid doses taken **by mouth equal to or more than 5mg of prednisone daily taken for more than 3 months** are considered a risk for fracture. (What You Should Know About Steroids and Osteoporosis. https://www.health.ny.gov)

- +her mother had a hip fracture

Case example - *medium*

- You get DEXA scan
- T score of spine = -3.7, T score of femoral neck = -3.2
- FRAX score - Ten year probability of fracture:
  - 23 for major osteoporotic fracture
  - 11 for hip fracture
- What do you recommend?
- Your prescriptions is to start Fosamax 70 mg PO Q week with instructions on how to take properly
  - Full glass of water, first thing in am, not lying back down

Case example - *challenging*

82 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

DEXA scan shows osteoporosis

- Femoral neck T-score -3.8
- FRAX calculator (data 150 pounds, 64 in)
  - Major OP fracture risk = 52
  - Hip fracture risk = 42

This patient is HIGH risk.

Your prescriptions is that as she has been on bisphosphonate x 5 years – would rotate to Prolia.

The Jefferson Landscape

PCPs can manage osteoporosis but should know when/how to refer:

- after the first 5-7 years on treatment or patients with complex history
- When BMD is getting worse despite treatment (to screen for secondary causes, offer other advanced options like Forteo/Tymlos/Evenity)
- When Reclast is considered but there's no available infusion center on site or when BMD indicates severe osteoporosis (T score < -3.5) to discuss Forteo/Tymlos

The Jefferson Landscape

Here at Jefferson both Endocrinology and Rheumatology can help to manage osteoporosis

Rheumatology - All general rheumatology physicians help with osteoporosis management (Drs. Leung, Park, Loizidis, Ponce)

Endocrinology - All see patients with osteoporosis but Dr. Intekhab Ahmed has special interest in this field

Both Endocrinology and Rheumatology share an infusion center in their Center City office (211 S 9th St). They have staff who do prior authorizations for Reclast, get it approved then schedule patients and administer the infusion.

Thank you for Drs. Kiriakidou and Jabour for their input.

Summary

PCPs can have impact through non-pharmacologic counseling:

- Weight-bearing exercise
- Checking vitamin D levels and repleting
- 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