Osteoporosis Update

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THIS IS MODERN MEDICINE

The Burden of Fragility Fracture

- A public health problem
  - 50% W and 20% M >50 yo
  - 2 million fragility fractures/US
  - > ½ million in the UK
- Global burden of hip fracture
  - ↑ 20% by 2030
  - double by 2050
- Consequences can be severe
  - Chronic pain
  - Disability
  - Mortality
  - Health care expenditure

Burge et al, JBMR 2007

Underdiagnosed and Undertreated

Primary prevention

- 49% W recommended to have DXA will have it

Secondary prevention

- Only 14% who sustained hip fracture get treated subsequently
- Risk of subsequent fracture highest 1-2 years after fracture
- 32% will have another fracture within 5 years

Sing et al, Jour Bone Mineral Res 2023, National Committee for Quality Assurance, The State of Health Care Quality 2022

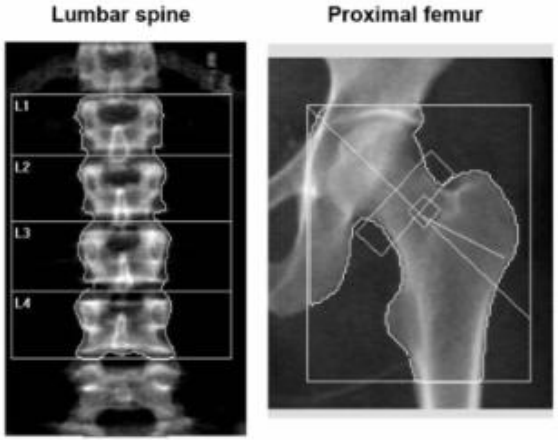
Who to Screen?

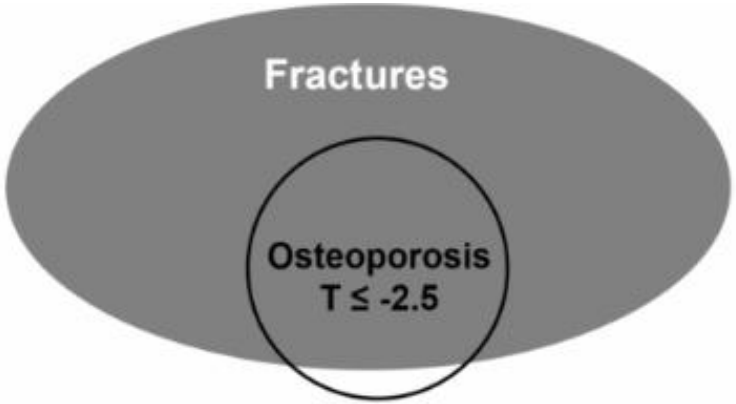
- All postmenopausal women ≥65 years
- Postmenopausal women & men ≥50 years with risk factors
- No guideline consensus for screening in men ≥70
- Routine screening not recommended for adults ≤ 50
  - Strong risk factors
  - Prior low-trauma fractures
  - Suspected secondary causes

How to Screen?

Dual-energy x-ray absorptiometry (DXA)

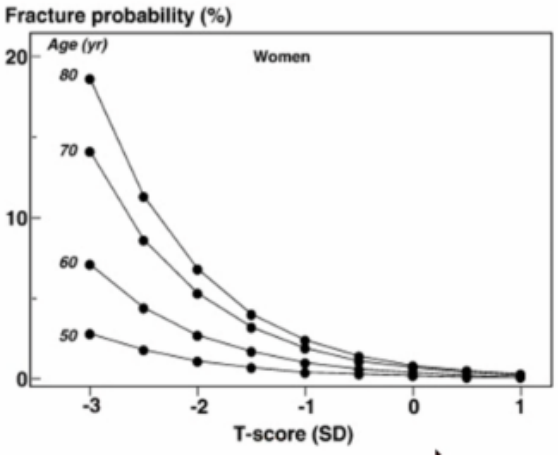
- 1 Std dev decrease in age-adjusted BMD → 2-fold increase in fracture risk
- Essential to identify fracture risk





Osteoporosis Risk Factors

- Age
- Previous fractures
- Family history
- Physical exam
  - Low BMI
  - Height loss/kyphosis
- Lifestyle
  - Low calcium diet
  - Alcohol
  - Active smoking
  - Frailty/fall risk
- Medications
  - Glucocorticoids
  - GnRH agonist
  - Aromatase inhibitors
  - Anti-convulsants



- Endocrine
  - Hyperthyroidism
  - Hyperparathyroidism
  - Early menopause
  - DM
  - Hypogonadism
- GI disorders
  - IBD
  - Celiac disease
  - Gastric bypass
- Other
  - Rheumatoid arthritis
  - CKD
  - Eating disorders
  - Post transplant bone loss

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FRAX: Fracture Risk Assessment Tool

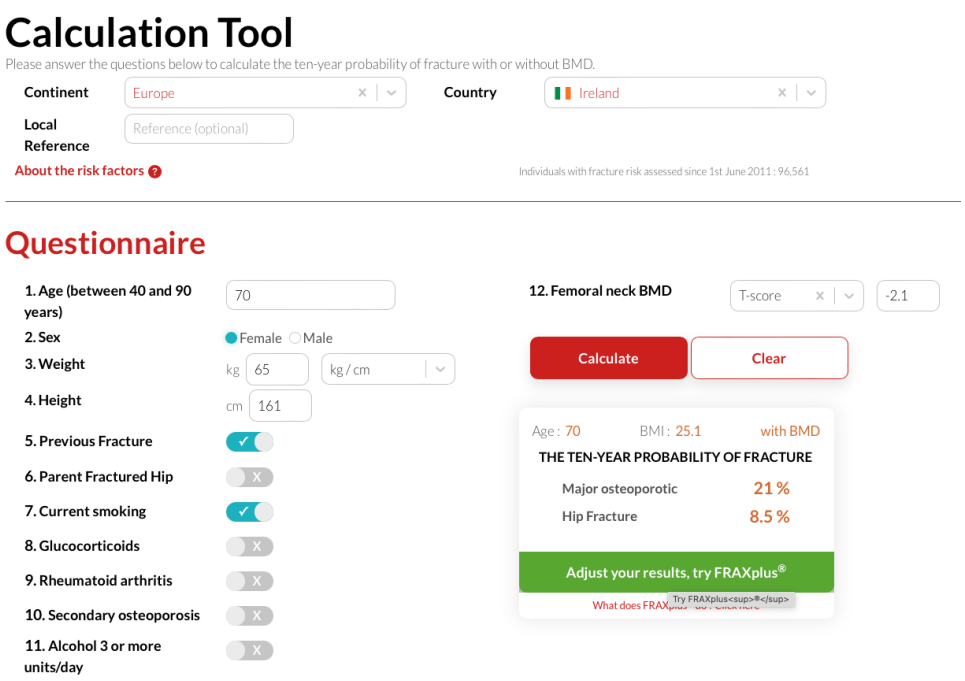
- Calculates 10-year probability of hip fracture & major osteoporotic fracture (MOF)
- Stratify patient risk in treatment naïve osteopenic patients

FRAX limitations

- GC dose dependency
- BMD Discordance
- Frailty and falls
- Recency of fracture

FRAXplus

- Adjust for falls, high-dose steroids, T2D, discordant BMD
- If on GC ≥ 7.5 mg:
  Hip fracture x 1.20
  MOF x 1.15



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Investigate Secondary Causes

- When to suspect secondary cause
  - Younge age
  - Very low T score
  - Atypical fracture pattern
  - Absent classical risk factors
  - Underlying conditions
  - Medications
- All patients
  - Bone profile
  - Renal function
  - FBC
  - 25-OH Vitamin D
  - PTH
- Targeted
  - TFT
  - Testosterone
  - SPEP
  - tTG antibody
  - CTD screen

Treatment

Lifestyle & non-pharmacological management

- Address risk factors (fall risk, inflammatory disease control, GC exposure, etc)
- Ca 1000-1500 mg from all sources
- Vit D 800 IU/day
- Exercise – weight bearing and resistance
- Lifestyle: stop smoking, limit EtOH to <2 units/day

Treatment - Pharmacologic Intervention

Anti-resorptive drugs

- Bisphosphonates
- Denosumab
- Raloxifene
- HRT, *recent update NOGG 2024*

Anabolic drugs

- Teriparatide
- Abaloparatide
- Romosozumab

Bisphosphonates

Oral Agents

- Alendronate weekly
  - 50-60% vertebral, 20-25% non vertebral
- Risedronate weekly
  - 40-50% vertebral, 30-40% non vertebral
- Ibandronate monthly
  - 50-60% vertebral, **limited non-vertebral fracture reduction**

IV agents

- Zoledronic acid q12mo
  - 70% vertebral, 40% non vertebral
- Ibandronate q3mo

Avoid if eGFR <30-35 ml/min
Correct Vit D deficiency
Oral preparation
Avoid in esophageal pathology
Osteonecrosis of jaw
Atypical femur fracture

Osteonecrosis of Jaw

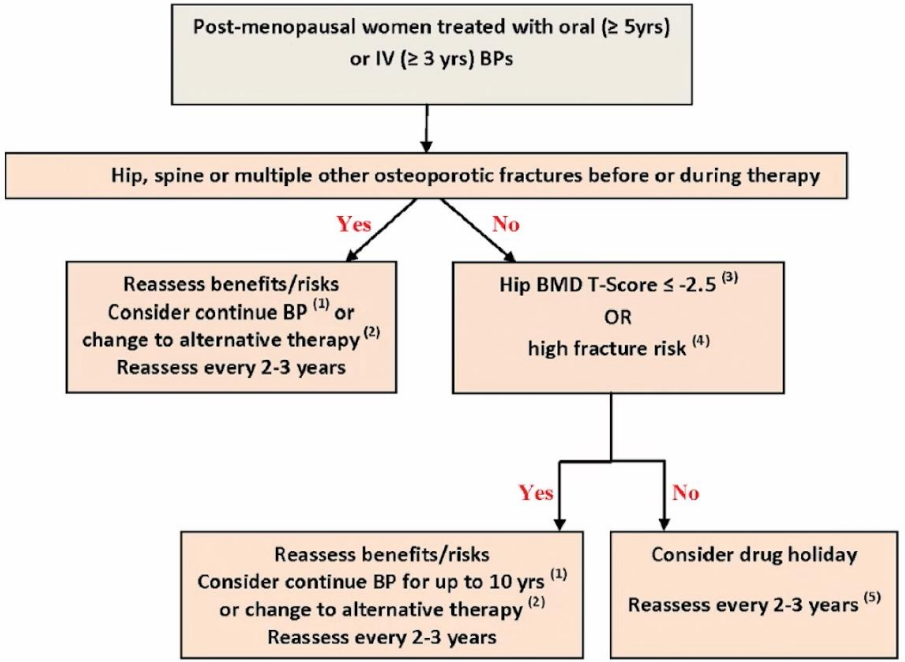
- <1 per 100,000 patient-years
- Risk factors
  - Dose and duration of therapy
  - IV administration
  - Dental extraction, implants, poorly fitted dentures
  - Anti-cancer treatments, GC smoking, DM
- Prevention
  - Pre-treatment screening
  - ?Treatment pause prior to extraction

Atypical Femur Fracture

- 3 in 100,000 patient-years
- Transverse subtrochanteric fracture at lateral cortex
- Prodromal thigh or groin pain common
- Up to 1/3 bilateral
- Risk factors
  - Duration of therapy
  - GC use
  - Asian ethnicity

Khan et al,, JBMR 2015, Shane et al ASBMR 2nd Task Force, JBMR 2014

Bisphosphonate Drug Holiday



Adler et, JBMR 2016

Denosumab

- Humanized Ab to RANKL
- 6-montly SC injection
- No renal toxicity or GFR adjustment
- Short acting
- BMD loss by 1 year after discontinuation

Hypocalcemia
Osteonecrosis of jaw
Atypical femur fracture

Anabolic Agents

- Teriparatide and abaloparatide – recombinant PTH receptor agonist
- Activate PTH receptor
- Anabolic effect on bone
- Significant cost
- Daily injection for 18-24 months
- Must be followed by an anti-resorptive
- Indicated for very high-risk fracture
    - T-score <-3.5
    - T-score <-2.5 + fragility fracture
    - Multiple risk factors
    - Failed/intolerance to previous

Hypercalcemia
Hyperparathyroidism
Renal stones
Osteosarcoma RFs

Romosozumab

- Newest anabolic agent
- Humanized monoclonal Ab against Sclerostin (suppresses bone formation)
- Inhibits RANK → decrease bone resorption
- Monthly SC injection x12 months
- PMO, very high risk
- Benefits in men not yet approved

Stoke or MI in last 12mo
At risk for CV event
Hypocalcemia

Conclusion

- Fragility fractures are a major public health burden
- Timely intervention can prevent fractures and disability
- A major treatment gap persists – GP awareness and patient identification are key to reducing fracture-related morbidity and mortality
- Decision to treat should not be based on T-score alone
- Long-term safety monitoring, drug holidays, and reassessment are essential components of safe osteoporosis management

Thank you

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