Osteoporosis challenges

Wendy Holden Consultant Rheumatologist
Osteoporosis challenges

• Who should have a fracture risk assessment?
• Who to treat?
• Drugs, holidays and unusual adverse effects

• Fracture liaison service?

• New DMARD shard-care guidelines
The size of the problem

• 1 in 2 women and 1 in 5 men >50 will sustain a fragility fracture

• 50% of fractures are preventable

• After fragility fracture at HHFT only 20% have appropriate care

• Adherence with bisphosphonates 1 year after hip fracture 15-30%
Spinal fractures - A silent epidemic

• 2/3 vertebral fractures are silent

• 1 vertebral fracture increases risk of further fracture by 4.5, especially if symptomatic

• Loss of adult height > 5cm is an important warning sign
Who should have fracture risk assessed?

Good news and bad news…
Tips on FRAX and requesting DXA

• DXA and FRAX usually not indicated < 50 unless:
  • Fragility fracture
  • Significant corticosteroids (x2 risk fracture at any BMD – dose-dependent)
  • Untreated premature menopause

• Most people will not need repeat DXA before 3-5 years
• Repeat DXA over 75 not usually needed
UK National Osteoporosis Guidelines Group suggest:

- Assess fracture risk using FRAX in:

  - All postmenopausal women and men ≥ 50 years with one or more risk factors or a BMI ≤ 19kg/m²
Risk factors for osteoporotic fracture

- Previous **fragility** fracture, particularly of the hip, wrist and spine including radiographic vertebral fracture (fall from standing height – not stress fractures, fingers or scaphoid)

- Parental history of hip fracture (less than 80)

- Current glucocorticoid treatment (any dose, oral for ≥ 3 months)

- Current smoking

- Alcohol intake of 3 or more units daily
Risk factors for osteoporotic fracture

• Secondary causes of osteoporosis including:
  • Rheumatoid arthritis
  • Untreated hypogonadism in men and women
  • Prolonged immobility
  • Organ transplantation
  • Type I diabetes
  • Hyperthyroidism
  • Gastrointestinal disease
  • Chronic liver disease
  • Chronic obstructive pulmonary disease

• Falls
Determining fracture risk

Bone density
Bone strength
Fracture risk

Images: People exercising with weights, X-ray of a pelvis, medical equipment.
Assessing fracture risk - FRAX
www.shef.ac.uk/FRAX

• Men and women 40-90
• Better predictor of fracture than BMD alone but not perfect
Who should have treatment?

It depends on their fracture risk....

(probably most people who have had a fragility fracture)
Look at the T-score
(Z-score is for young adults)

Beware of spinal osteoarthritis and severe spinal osteoporosis
Who should have treatment?

- Treatment recommended when T score is $<-2.5$
- But fracture risk strongly depends on age and other risks
- Most fractures occur in osteopenic range (-1 to -2.5)
JD age 77

Results Summary:

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Total BMD CV 1.06%, ACF = 1.029, BCF = 0.992, TH = 4.382
Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

**Questionnaire:**

1. Age (between 40 and 90 years) or Date of Birth
   - Age: [ ] 77 [ ] Y: [ ] M: [ ] D: [ ]
2. Sex
   - Male [ ] Female [ ]
3. Weight (kg)
   - 54
4. Height (cm)
   - 172
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)
    - Hologic [ ] 0.563 [ ] T-score: -2.5

**Risk factors**

For the clinical risk factors a yes or no response is asked for. If the field is left blank, then a "no" response is assumed. See also notes on risk factors.

The risk factors used are the following:

1. **Age**
2. **Sex**
3. **Weight**
4. **Height**
5. **Previous Fracture**
6. **Parent Fractured Hip**
7. **Current Smoking**
8. **Glucocorticoids**
9. **Rheumatoid arthritis**
10. **Secondary osteoporosis**
11. **Alcohol consumption**
12. **Femoral neck BMD**

**BMI:** 18.3

**The ten year probability of fracture (%) with BMD**
- Major osteoporotic fracture: 11%
- Hip Fracture: 7.9%

If you have a TBS value, click here: Adjust with TBS

Print tool and information

04565585
Individuals with fracture risk assessed since 1st June 2011

www.nos.org.uk

National Osteoporosis Society
Intervention Threshold

Major Fracture - 10 year fracture probability

Hip - 10 year hip fracture probability

Legend:
- Red: Treat
- Green: Lifestyle advice and reassure

Prednisolone daily dose (or equivalent):
- ≥7.5mg daily
- 2.5-7.5mg daily
Management after fragility fracture

• Investigations
  All people after fragility fracture

• > 75
  No need for DXA
  Bisphosphonate + Ca/Vitamin D

• < 75
  DXA

T score > -1
  Reassure and general measures

T score -1 to -2.5
  General measures

T score < -2
  Consider treatment especially if vertebral fracture

T score below – 2.5
  Bisphosphonate + Ca/Vitamin D
Drugs and osteoporosis
Calcium and Vitamin D

• Both essential to reduce fracture risk

• Increased risk MI in women given 1000 mg calcium daily – studies contradictory

• If adequate dietary calcium, can just replace Vitamin D

• Optimal Vitamin D level unclear - at least 50 nmol/L
  • Vitamin D₃ (colecalciferol) 20 micrograms (800 Units) daily

• Fultium D₃
Calcium – daily intake 700 – 1300mg

Can be skimmed
Shake up soya milk

- 4 figs = 500 mg
- Ice cream
- Hot chocolate
If vitamin D < 50 nmol/L

• Give 300,000 IU total - for example
  • 50,000 IU weekly x 6
  • 60,000 IU weekly x 5

• IM Vitamin D doesn’t work and may increase fracture risk

• After high dose, resume 400-800 IU daily

• Routine recheck of serum vitamin D not necessary
Bisphosphonates

• Alendronic acid, risedronate, ibandronate, zoledronate
• All reduce bone resorption
• All very effective – reduce fracture risk by 50% or more

• Risedronate very fast to work- choice for steroid-induced OP

• Absorption of oral bisphosphonates only 6%
• Vital to ensure taken correctly
• Adherence very low – 15 - 30% 1 year post hip fracture
Why is bisphosphonate adherence so low?

• Bisphosphonate administration instructions are complicated
• Many drugs interfere with absorption
• No tangible benefits to patients – understanding “fractures”
• Worry about adverse effects – especially GI, dental and dentists

(Should everyone after fracture just have zoledronate?)
Osteonecrosis of the jaw

“My dentist said I mustn’t have that treatment”

“My dentist said my jaw would rot”

“My dentist said that with that treatment I have to have my tooth out at the hospital”

“I eat lots of cheese”
Osteonecrosis of the jaw related to medication

2 distinct patient groups

**Osteoporosis**
- zoledronate 5mg annually 3 years
- denosumab 60mg 6monthly 5-10 years

**Risk of ONJ**
- 1 in 10,000 to 1 in 100,000 (orals)
- 1 in 1000 to 1 in 10,000 (zol or denosumab)

**Cancer**
- zoledronate 4mg monthly
- denosumab 120mg monthly

2% at 30 months
FRiSCy ONJ guidance

• Risk is 1 per 10,000 to 100,000 on OP drug
• Risk is 1 per 1000 extractions for osteoporosis

• Advise dental check up but do not delay bone therapy

• If need dental work, aim to be healed by time of next denosumab/ zoledronate

• Could avoid extractions - let the tooth fall out
• Implants similar risk
Atypical femoral fractures

For every 137 hip fractures prevented > 1 AFF caused...

- 1 in 60,000 after 2 years bisphosphonate
- 1 in 800 after 8 years
- Most have prodromal thigh pain and periosteal reaction before fracture
- Minimal risk with 5 years treatment
Advice on atypical fractures

• Bisphosphonates are very effective & atypical fractures are rare

• No patient guidance so remain alert to new thigh pain in patients on bisphosphonates

• Any type of bisphosphonate for at least a year + within the last 12 months

• Anterior thigh or groin pain and is dull or aching

• If suspect atypical fracture request AP and lateral x-rays (of both sides) of the full femur and consider stopping the bisphosphonate
Denosumab

- Continues to improve BMD with every dose
- Now green drug
- 60mg s/c injection every 6 months
- Safe if eGFR < 30 but can cause hypocalcaemia

- Correct hypocalcaemia and Vitamin D deficiency before each injection
- Periodic monitoring of calcium if renal impairment (after 2-3 weeks)
Drug holidays

General agreement that there should be a treatment break

No consensus on duration
Probably has to be individual advice
Drug holidays

Oral bisphosphonates
5 years on 2 years off, then FRAX +/- DXA
10 years on 2 years off if high risk

High risk means:
• Over 75
• Hip or multiple fractures
• BMD still < 2.5 after 5 years or pre-treatment < 4
• Current corticosteroids

If fracture on treatment:
• Check adherence
• Switch to zoledronate or denosumab
• Re-start the clock

If lose BMD and adherent or fracture after 1 year and adherent:
Switch to denosumab or zoledronate
Drug holidays

Zoledronate – very long half life – longer holidays probably OK

3 years on 3 years off
6 years on 3 years off if high risk

High risk means:

• Over 75
• Hip or multiple fractures
• BMD still $< 2.5$ after 5 years or pre-treatment $< 4$
• Current corticosteroids
Denosumab “off” effect
Denosumab – 1 year after stopping

- A year after stopping denosumab – observational study
- 8/82 had at least one clinical fracture
- 4/82 multiple vertebral fractures
- 1/82 had a Hip fracture

McClung Osteoporosis International 2017
No holiday for denosumab

**Denosumab**

5 years on then reassess FRAX +/- DXA

10 years on if high risk

After denosumab – zoledronate, oral bisphosphonate, strontium or continue denosumab

**High risk means:**

- Over 75
- Hip or multiple fractures
- BMD still < 2.5 after 5 years or pre-treatment < 4
- Current corticosteroids

If fracture on treatment:
- Check adherence
- Switch
- Re-start the clock
Approximate treatment costs

- Alendronate (generic) £53.56
- Risedronate (generic) £264.63
- Zoledronate (iv) £283.74 + infusion costs
- Denosumab (s/c) £366 (in primary care)
- Teriparatide (s/c) £7000 for 2 year course
When to refer to secondary care

• Pre-menopausal women with fragility fracture
• Men under 60 with fragility fracture

• Multiple fragility fractures and osteopenia
• Fractures after 1 year if compliant on treatment

• Fragility fractures with complex medical conditions
• Very low BMD (< - 3-4 ish)
DMARD monitoring – new guidelines

• Coming very soon and much easier!

• Hospital should:
  • Perform relevant screening bloods
  • Initiate DMARD
  • Repeat prescriptions for 2-3 months
  • Request and check blood results during this period
  • Request and check blood results if dose has changed

• Hospital should be very clear when asking GPs to take over prescribing and monitoring

• Physical shared-care agreement no longer exists
Recommended monitoring for new DMARDs

- FBC, Cr (or GFR), ALT, albumin every 2 weeks until stable dose for 6 weeks
- Then monthly FBC, Cr or GFR, ALT, albumin for 3 months
- Then FBC, Cr or GFR, ALT, albumin at least every 12 weeks

- For dose increases - FBC, Cr or GFR, ALT, albumin every 2 weeks until stable dose for 6 weeks then back to previous schedule

- Combination DMARDs will still need monthly monitoring
DMARD monitoring

• Primary care responsibilities:

• Continue prescribing and monitoring once requested

• Report any adverse events to the specialist and stop treatment on their advice or immediately if urgent need
Thresholds at which to discontinue treatment and contact rheumatology for urgent review:

- WCC<3.5 x10^9/L
- Neutrophils<1.6 x10^9/L
- Unexplained eosinophilia>0.5 x10^9/L
- Platelets<140 x10^9/L
- MCV<105
- ALT>100 units/L
- Unexplained fall in albumin
- Creatinine>30% above baseline +/- GFR<60
Questions?

wendy.holden@hhft.nhs.uk
Management in primary care – Investigations

- FBC and ESR
- High ESR – measure immunoglobulins and Bence-Jones protein
- Renal, bone biochemistry and LFT
- Serum 25 – OH Vitamin D
- Parathyroid hormone if calcium raised or Vitamin D low

- TSH
- Coeliac screen (TTG)
- Serum testosterone, SHBG

- Lateral lumbar and thoracic X-rays, especially if > 5cm height loss
General management – bone health

• Maximise peak BMD – before age 30
• Nutritional advice – calcium, Vitamin D, protein intake
• Weight-bearing exercise, resistance exercise, balance
• BMI – both low and high

• Smoking
• Alcohol – especially men
• Falls
• Minimise relevant drugs especially high dose PPI
• Adherence with bisphosphonates
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Total BMD CV 1.06%, ACF = 1.029, BCF = 0.992, TH = 7.559
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2. Sex
   - Male  Male  Female

3. Weight (kg)
   - 54

4. Height (cm)
   - 172

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)
    - Hologic  0.563

**BMI:** 18.3

The ten year probability of fracture (％) with BMD

- Major osteoporotic: 11
- Hip Fracture: 7.9

**Risk factors**

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Intervention Threshold

Major Fracture - 10 year fracture probability

Hip - 10 year hip fracture probability

- **Treat**
- **Lifestyle advice and reassure**

Prednisolone daily dose (or equivalent):
- ≥7.5mg daily
- 2.5-7.5mg daily
DXA challenges...

- DXA calculates BMD using area, not volume – surrogate measure of density
- Can’t compare results on different machines
- Can’t compare if > 5kg weight gain or loss
- Osteoarthritis of lumbar spine artificially raises spinal BMD
What’s New?- Safety


Medicines Evidence Commentary and DTB December 2016, Vol 54, Issue 12

- A European nested case-control study including 92,163 cases and 8,246,403 controls found that current use of any non-steroidal anti-inflammatory drug (NSAID) increased the risk of admission to hospital for heart failure by nearly 20% compared with past use.

- The study suggests a dose-response effect with very high doses of etoricoxib and diclofenac more than doubling the risk of admission to hospital for heart failure.

- Prescribers should continue to follow MHRA prescribing advice on use of NSAIDs, and base prescribing on assessment of a person’s individual risk factors (including cardiovascular and gastrointestinal).

- NSAIDs should be avoided in people with heart failure or those at high risk of heart failure.

- If an NSAID is needed it should be used at the lowest effective dose for the shortest possible time and reviewed regularly.

http://dtb.bmj.com/content/54/12/134
What’s New?- Safety

Methotrexate reminder

Following a recent situation, it has come to the attention of the Medicines Management Team that there is more than one brand of methotrexate injection. It is important that the patient is familiar with the use of the device provided.

- The hospital’s clinicians have a tendency to recommend methotrexate injection generically and this is then inadvertently transcribed on to the patient’s medication record.
- Prescribers receiving requests from secondary care to prescribe methotrexate (any formulation) are reminded to check the CCG’s current shared care guidelines (available on our website). This includes information on
- what to prescribe and how, and the responsibilities for monitoring these patients.
- The scg for methotrexate clearly states that the words Metoject® must appear somewhere on the prescription for the injection, as this is the device that the hospital has been using.
- Plus the volume to be administered is not the same between the different brands-
  - Zlatal® contains methotrexate 25mg/ml soln for inj in pre-filled syringe, compared to
  - Metoject® contains methotrexate 50mg/ml soln for inj in pre-filled syringe.