FRAX, NICE and NOGG

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Disclosures

- Research funding and/or honoraria and/or advisory boards for:
  - ActiveSignal, Amgen, Bayer, Boehringer Ingelheim, GE Lunar, GSK, Hologic, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, Servier, Synexus, Tethys, UCB, Warner Chilcott
Issues to be discussed

• A little background on FRAX
• NICE and FRAX
  ○ Nowt on NICE and NOGG
• Setting assessment and intervention thresholds
• Practical implementation
What is the intended use of FRAX®?

- Osteoporosis is a common disease
  - It should largely be managed in primary care.
- Experts in osteoporosis are used to integrating information derived from multiple risk factors, but
  - most primary care physicians in many countries have little expert knowledge.
  - It is this constituency for which FRAX® is primarily designed
- To increase awareness and knowledge of osteoporosis and to initiate appropriate treatment in patients at highest risk of fracture.
FRAX web usage 2012-13 in Europe
Issues to be discussed

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  o Nowt on NICE and NOGG
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Calculation Tool

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

**Country:** UK

**Name/ID:**

**Questionnaire:**

1. Age (between 40 and 90 years) or Date of Birth
   - Age: 65
   - Date of Birth: [Y: ] [M: ] [D: ]

2. Sex
   - Male
   - Female

3. Weight (kg)
   - 61

4. Height (cm)
   - 156

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]

**BMI:**

- **BMI:** 25.1
- **The ten year probability of fracture (%):**
  - **without BMD:**
    - Major osteoporotic: 16
    - Hip Fracture: 3.1
  - View NOGG Guidance

**Weight Conversion**

- Pounds ➝ kg
  - [Convert]

**Height Conversion**

- Inches ➝ cm
  - [Convert]
Fracture risk assessment models

<table>
<thead>
<tr>
<th></th>
<th>Garvan</th>
<th>Qfracture</th>
<th>FRAX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Externally validated</td>
<td>Yes (a few countries)</td>
<td>Yes (UK only)</td>
<td>Yes</td>
</tr>
<tr>
<td>Calibrated</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Applicability</td>
<td>Unknown</td>
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<td>Falls as an input</td>
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<td>Yes</td>
<td>No</td>
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<tr>
<td>BMD as an input variable</td>
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<td>No</td>
<td>Yes</td>
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<tr>
<td>Prior fracture as an input</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Family history as an input</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Output</td>
<td>Incidence</td>
<td>Incidence</td>
<td>Probability</td>
</tr>
<tr>
<td>Treatment response assessed</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
NICE SCG Fracture Risk Assessment

- Consider assessment of fracture risk in all women aged 65 years and over and all men aged 75 years and over.
  - Interpret with caution if aged over 80 years, because predicted 10-year fracture risk may underestimate short-term fracture risk.
- Consider fracture risk in women <65 years and men <75 years if they have any of the following risk factors:
  - previous fragility fracture
  - current or frequent use of oral glucocorticoids
  - history of falls
  - family history of hip fracture
  - causes of secondary osteoporosis
  - low BMI (<18.5 kg/m²)
  - smoking >10 cigarettes per day
  - alcohol intake > recommend units
- Do not routinely assess fracture risk in people <50 years unless major risk factors (e.g. GC use, untreated premature menopause, previous fragility fracture).
Further NICE Recommendations

• Use either FRAX (without a BMD value) or QFracture to calculate 10-year predicted absolute fracture risk when assessing risk of fracture.

• Do not routinely measure BMD to assess fracture risk without prior assessment using FRAX (without a BMD value) or QFracture.
Risk factors in QFracture-2012

• Age
• Sex
• Ethnicity
• Body mass index
• Smoking status
• Alcohol use
• Use of corticosteroids
• Parental history of hip fracture/osteoporosis
• Prior osteoporotic fracture (wrist, spine, hip, or shoulder)
• Rheumatoid arthritis or SLE
• History of falls
• Dementia/Nursing or care home residence
• Type 1 or Type 2 diabetes
• Cancer
• Asthma or COPD
• Cardiovascular disease
• Chronic liver disease
• Chronic kidney disease
• Parkinson's disease
• Gastrointestinal malabsorption
• Epilepsy or use of anticonvulsants
• Use of antidepressants
• Endocrine problems (thyrotoxicosis, hyperparathyroidism, Cushing’s)

http://qfracture.org; Hippisley-Cox & Copeland, BMJ 2012;344:e3427
Further NICE Proposed Recommendations

• Use either FRAX (without a BMD value) or QFracture to calculate 10-year predicted absolute fracture risk when assessing risk of fracture in people of between 40 and 84 years.

• Do not routinely measure BMD to assess fracture risk without prior assessment using FRAX (without a BMD value) or QFracture.
Absolute risk values are not the same

Woman with prior fracture, BMI 24, no other CRFs

- Qfracture-2012 (Major)
- Qfracture-2012 (Hip)
- FRAX (Major)
- FRAX (Hip)
Further NICE Proposed Recommendations

BMD and Intervention Thresholds

• Following risk assessment with FRAX (without a BMD value) or QFracture, consider measuring BMD with DXA in people whose fracture risk is in the region of an intervention threshold for a proposed treatment, and recalculate absolute risk using FRAX with the BMD value.

• Consider measuring BMD with DXA before starting treatments that may have a rapid adverse effect on bone density (for example, sex hormone deprivation for treatment for breast or prostate cancer).

• It is out of the scope of this guideline to recommend intervention thresholds.
  
  o Healthcare professionals should follow local protocols or other national guidelines for advice on intervention thresholds.
Issues to be discussed

• A little background on FRAX
• NICE and FRAX
  ○ Nowt on NICE and NOGG
• Setting assessment and intervention thresholds
• Practical implementation
Case Finding Strategies

RCP 1999

- CRFs
- BMD
  - T-score < -2.5
  - Treat

National Osteoporosis Guideline Group 2008

- CRFs
  - FRAX
    - High
      - Treat
    - Intermediate
    - Low
      - Treat
      - BMD
        - FRAX
          - High
          - Low
Consider treatment

Measure BMD

No treatment

Consider treatment

Intervention threshold

No treatment

Compston et al, Maturitas (2009); 62(2):105-8; www.shef.ac.uk/NOGG
Postmenopausal women ≥75yrs

Postmenopausal women ≤75yrs Men >50 yrs

Exclude secondary causes

Treat with alendronate

If not tolerated, other bisphosphonates or strontium ranelate or raloxifene

Ca and vit D supplements Falls assessment/Rx Lifestyle advice

Postmenopausal women and men >50 yrs with ≥1CRF

FRAX®(± BMD) & NOGG

High fracture probability

Low fracture probability

Reassure Lifestyle advice

CRF=clinical risk factor; BMD=bone mineral density; Ca=calcium; vit=vitamin; Rx=treatment
Proportion of population treated
Women in the UK aged 60-64 years

- Prior fracture
- No fracture

<table>
<thead>
<tr>
<th>Category</th>
<th>Proportion of population (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOGG</td>
<td>30</td>
</tr>
<tr>
<td>NOGG with BMD in fracture</td>
<td>15</td>
</tr>
</tbody>
</table>
Issues to be discussed

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Incorporating GC dose into clinical practice

Calculation Tool

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

Country: UK
Name/ID: 

**Questionnaire:**
1. Age (between 40 and 90 years) or Date of Birth
   - Age: 63
   - Date of Birth: 
2. Sex
   - Male
3. Weight (kg)
   - 69
4. Height (cm)
   - 167
5. Previous Fracture
   - No
6. Parent Fractured Hip
   - No
7. Current Smoking
   - No
8. Glucocorticoids
   - No
9. Rheumatoid arthritis
   - No
10. Secondary osteoporosis
    - No
11. Alcohol 3 or more units/day
    - No
12. Femoral neck BMD (g/cm²)

**Weight Conversion**
- Pounds to kg

**Height Conversion**
- Inches to cm

**BMI:** 24.7
- The ten year probability of fracture (%)
- Without BMD:
  - Major osteoporotic: 17
  - Hip Fracture: 4.0

View NOGG Guidance

01206780
Individuals with fracture risk assessed since 1st June 2011
Diabetes Manitoba Cohort

FRAX underestimates fracture risk in patients with diabetes
Giangregorio et al, JBMR 2012
Options around taking diabetes into consideration in FRAX

• Clinical judgement
  • e.g. a patient with diabetes below but close to a FRAX-based intervention threshold, the physician might recommend treatment.

• Use RA as a surrogate for diabetes

Leslie et al, JBMR 2012 27: 2231–2237
Distribution of LS-FN discordance
Reclassification across the NOGG threshold after LS discordance adjustment

<table>
<thead>
<tr>
<th>FRAX</th>
<th>Below threshold</th>
<th>Above threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Below threshold</td>
<td>15 161</td>
<td>166</td>
</tr>
<tr>
<td>Above threshold</td>
<td>262</td>
<td>2 904</td>
</tr>
</tbody>
</table>

Reclassified = 2.3%
Summary

• NICE has endorsed the use of FRAX or QFracture in the assessment of fracture risk.

• Clinical utility requires assessment thresholds, integration of BMD, intervention thresholds and demonstration of reversibility of risk.

• Targeting scans to those at or near the intervention threshold is an efficient use of resources.

• The FRAX/NOGG approach addresses these requirements