BURNING QUESTIONS ON...

UNDERSTANDING FRAX AND THE ASSESSMENT OF FRACTURE RISK IN PRIMARY CARE IN 2016

Nearly 50% of women will experience a fracture following the menopause, meaning predicting the risk factors and taking positive preventative action can improve the quality of life of thousands of women. FRAX is a key tool in the fight against osteoporosis and this article considers how it can be used, its strengths and limitations

EV McGloskey
Centre for Metabolic Bone Diseases,
University of Sheffield, Sheffield
UK

NC Harvey
MRC Lifecourse Epidemiology Unit,
University of Southampton,
Southampton UK

JA Kavis
Institute for Health and Aging,
Catholic University of Australia,
Melbourne, Australia

Q Why do we need to prevent fragility fractures?

A Osteoporosis, and its resulting fractures, is such a common disease that the responsibility for long-term management largely resides within primary care. Nearly 50% of women will experience a fracture following menopause, while nearly 20% of men over the age of 50 years will also experience a fracture. It has been estimated that approximately 536,000 fragility fractures occurred in the UK in 2010, comprising 79,000 hip fractures, 66,000 clinical vertebral fractures, 69,000 forearm fractures and 322,000 other fractures (i.e. fractures of the pelvis, rib, humerus, tibia, fibula, clavicle, scapula, sternum and other femoral fractures). Fractures have major adverse effects on quality of life in terms of pain and disability, in addition to presenting a considerable burden to the National Health Service. Hip fractures still account for more than 20% of all orthopaedic bed occupancy. In 2010, fractures accounted for the loss of 158,700 quality-adjusted life years (QALYs) at an estimated cost of £3.3 billion; new fractures accounted for three quarters of this cost with most of the remainder reflecting long-term post-fracture care, while pharmacological interventions to reduce fracture risk comprised only 2%. With an aging population, the cost to society and individuals of treatment, rehabilitation and premature mortality is set to increase. When accounting for demographic projections, the annual number of incident fractures is predicted to increase by 27% by 2025, representing an increase of 146,000 fractures, including an additional 23,000 hip fractures per annum. Despite the current and increasing burden, the majority of women and men at high fracture risk do not yet receive active treatment.

Nearly 50% of woman will experience a fracture following menopause, while nearly 20% of men over the age of 50 years will also experience a fracture
A How should you choose a fracture risk tool?

Experience from other disease areas, such as cardiovascular disease and diabetes, suggest that the availability of risk calculators and their linkage to clinical guidelines can broaden GPs' knowledge and awareness of disease areas, as well as enhancing the targeting of further assessments and treatment to those most in need, i.e. at appropriately high risk. In 2012, NICE recommended the use of two fracture risk assessment tools, namely FRAX and QFracture. It is important to note that this recommendation does not mean that the tools are equivalent (Table 1); indeed, there are marked differences in the magnitude of their output values, particularly in regard to major osteoporotic fractures, and the weight given to individual risk factors (e.g. prior fracture).

**TABLE 1: TABLE DOCUMENTING THE MAIN DIFFERENCES IN THE QFRACTURE AND FRAX TOOLS IN THE UK**

<table>
<thead>
<tr>
<th></th>
<th>QFracture</th>
<th>FRAX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Externally validated</td>
<td>Yes (UK only)</td>
<td>Yes, internationally</td>
</tr>
<tr>
<td>Calibrated</td>
<td>Yes (hip fractures only)</td>
<td>Yes</td>
</tr>
<tr>
<td>Applicability</td>
<td>UK</td>
<td>58 countries</td>
</tr>
<tr>
<td>Falls as an input variable</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>BMD as an input variable</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Intervention thresholds and guidance</td>
<td>No</td>
<td>Yes (NOGG)</td>
</tr>
<tr>
<td>Outcome</td>
<td>Hip, forearm, spine, shoulder</td>
<td>Hip, forearm, spine, humerus</td>
</tr>
<tr>
<td>Outcome metric</td>
<td>Incidence</td>
<td>Probability</td>
</tr>
<tr>
<td>Interchangeable</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Equivalent outputs</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

NOGG. National Osteoporosis Guideline Group

For example, fracture events at sites other than the hip were poorly recorded in the databases used to generate QFracture so that, given a similar risk profile as a patient in FRAX, the apparent incidence of major osteoporotic fractures is substantially lower than that generated by FRAX. The latter is calibrated to the incidence of such fractures in the UK, so that if all the UK population was assessed by FRAX, the number of major osteoporotic fractures observed would be equal to that predicted by the calculator. The low prior fracture rates in the QFracture databases results in the algorithm predicting an increase in fracture rate of approximately 10% or less in the presence of a prior fracture, whereas the same variable in FRAX increases the predicted risk by almost two-fold. These, and other differences, have been addressed in more detail elsewhere and mean that QFracture outputs cannot be used with guidance and thresholds that are based on FRAX outputs.

The major benefit of the ability to assess absolute fracture risk is that it enables the targeting of treatment on this basis rather than the use of BMD alone.
Q What are the practicalities of FRAX and how does the calculation work?

The FRAX tool is available in a number of formats; the web-based calculator ([www.shef.ac.uk/FRAX](http://www.shef.ac.uk/FRAX)) (Figure 1) is probably the most widely used globally and in the UK, but the tool is also available as an app on smartphones (iPhone, Android or Windows) and is embedded in the software of most makers of bone densitometers. FRAX is also available within SymionOne software for use in primary care in the UK. At a practice or CCG level, a number of external IT companies have developed software that can extract the relevant data for the FRAX calculation, process and clean this data and then generate the individual FRAX probabilities for importing back into the clinical database. The most obvious deficit within these data is the availability of information on a parental history of hip fracture so that this question needs to be addressed prospectively when interviewing the individual patient in the surgery or clinic.

In addition to age, gender and BMI, the calculation is based on seven easily collected, dichotomous clinical risk factors comprising prior fracture, parental history of hip fracture, prior glucocorticoid use, a diagnosis of rheumatoid arthritis, a known cause of secondary osteoporosis, current smoking and a daily alcohol intake of three or more units. More detailed guidance around these risk factors is provided on the website and within the smartphone apps. The calculation generates the probability of a hip fracture alone or a major osteoporotic fracture (wrist, spine, humerus or hip) in the next 10 years. The measurement of femoral neck bone mineral density (BMD) can also be added to the calculation in selected patients as suggested by NICE and implemented through the National Osteoporosis Guideline Group (NOGG) guidance (see below); the weight given to some of the other risk factors (e.g. BMI) is altered in the presence of BMD as the measures are correlated. Indeed, in a patient with secondary osteoporosis (other than rheumatoid arthritis or exposure to glucocorticoids), the risk factor does not contribute any further weight to the calculation in the presence of the BMD result since the conservative assumption is made that most causes of secondary osteoporosis influence fracture risk by impacting on BMD. Finally, FRAX calculates a probability of fracture that also takes into account the impact of various risk factors (age, BMI, smoking, etc.) on mortality; thus, at the upper extremes of age, the probability of fracture actually shows a decrease as the likelihood of death surpasses that of fracture.

Q How do I know when to refer for a BMD scan and when to treat?

The FRAX tool on the website and smartphones has a direct link to guidance produced by NOGG, a link that can be used at the discretion of the clinician. The NOGG guidance has been supported by a number of clinical and patient societies ([www.shef.ac.uk/NOGG](http://www.shef.ac.uk/NOGG)) including the Royal College of Physicians, the Primary Care Rheumatology Society and National Osteoporosis Society. A recent survey of website activity suggests that at least 1,200 calculations take place per week on the FRAX website each day in the UK, with over 700 of these completing the link through to NOGG guidance. NICE guidance recommends that fracture risk should be assessed by FRAX prior to deciding whether a BMD assessment is necessary and this is handled by a 3-colour “traffic-light” graph on the NOGG website (Figure 2). One immediate benefit of electronic and web-based guidance, including the traffic light graph, is that changes in guidance can be implemented easily. Proposed changes to the NOGG graphs are under discussion. BMD scans are recommended in those with FRAX probabilities lying within the “amber” area on the graph.

![Figure 1. The FRAX questionnaire and results for a 76-year-old woman, BMI 21.4 and a positive parental history of hip fracture. The output can be linked to NOGG guidance directly through the button which appears in the red results box when the calculation is complete.](http://www.shef.ac.uk/FRAX)

![Figure 2. NOGG guidance graphs showing the result (as an “x”) from the subject in Figure 1. A BMD measurement is recommended before deciding the need for therapy.](http://www.shef.ac.uk/FRAX)
What are the benefits and limitations of FRAX?

The major benefit of the ability to assess absolute fracture risk is that it enables the targeting of treatment on this basis rather than the use of BMD alone, replicating approaches in cardiovascular disease and other areas of clinical medicine. The tool is designed primarily for use in primary care, concordance between decisions reached using the combination of FRAX and NOGG and decisions made in a specialised osteoporosis clinic is high (approximately 73%), suggesting that the tool can be used to provide a high quality of care where osteoporosis care has perhaps been lacking before. Indeed, the tool has an important educational role as well as being a risk calculator. A further benefit is that several studies have shown in retrospective analyses of clinical trials that patients identified at high risk of fracture by FRAX, with or without the inclusion of BMD, show reductions in fracture incidence during treatment with a number of osteoporosis therapies. Importantly, the results of a study to look at the use of FRAX as a screening tool for fracture risk in women aged 70-85 years in the UK will be published soon.

Like all such clinical tools, FRAX has limitations and these have been discussed in more detail with the two most frequently cited limitations relating to the lack of a prior fall as a risk factor and the handling of other clinical risk factors dichotomously (yes/no) rather than taking the dose or severity into account, for example the glucocorticoid dose, number of prior fractures and levels of alcohol or cigarette consumption. Although prior fall is not enquired for specifically, the risk is partially captured by other variables including age, prior fracture, alcohol use and glucocorticoid use. It has been estimated that the probability of fracture may be underestimated by about one-third in those with a history of falls, but this needs confirmation in future analyses; in the meantime, it would be prudent to take a history of falls into account in a patient with a FRAX probability that lies below but near to an intervention threshold so that skeletal protection could be initiated alongside measures to decrease fall risk. With regard to the patient with multiple fractures, there may be no need for the use of a tool such as FRAX as treatment is usually indicated in postmenopausal women or older men with such a finding, particularly if multiple vertebral fractures are present; it is important to exclude causes of secondary osteoporosis in such circumstances as well as managing the fracture risk. Finally, the NOGG guidance has been adapted to incorporate some impact of higher doses of glucocorticoids on fracture probability. It is important to remember that while we need to be aware of the limitations of new tools, we must not forget that there were similar or indeed greater limitations to the techniques that preceded such tools in clinical practice, e.g. the limitations of the use of BMD as the only decision-making tool in the management of osteoporosis.

CONCLUSION

The availability of the FRAX tool and associated NOGG guidance enhances the management of osteoporosis in primary care in the UK. The needs for education and increased awareness continue alongside increasing ease of access to and implementation of the tool and guidance in GP software systems. The potential to impact beneficially on the burden of fractures is significant and the approach should provide dividends for the NHS and patients in the future.

References


BJFM Challenge answers
(see pages 4-5)

1. C (see pages 12-15)
2. D (see pages 12-15)
3. D (see pages 12-15)
4. C (see pages 12-15)
5. A, E (see pages 19-23)
6. B (see pages 19-23)
7. A (see pages 24-25)
8. A, B, D, E (see pages 24-25)
9. A (see pages 27-29)
10. A (see pages 27-29)
11. E (see pages 30-32)
12. D (see pages 30-32)
13. B (see pages 30-32)
14. D (see pages 30-32)