Fracture-risk calculators: Has their time come?

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See related research article by Langsetmo and colleagues, page E107

Osteoporotic fractures occur in 30%–50% of postmenopausal women and 10%–20% of older men, causing substantial morbidity, mortality and cost to society. Prevention of osteoporotic fractures is an important component of health care that relies on the accurate prediction of who is likely to sustain a fracture. Although predicting events is not easy, models that predict fracture have been developed and then validated in external populations. In this issue, Langsetmo and colleagues[1] report the results of their validation study of one such model involving a Canadian cohort. We review the history of fracture prediction and discuss the use of fracture-risk calculators.

In 1994, a study group sponsored by the World Health Organization (WHO) recommended that postmenopausal women be grouped into four diagnostic categories of fracture risk (normal, osteopenia, osteoporosis and severe osteoporosis) based on bone mineral density T-scores and history of fracture.[2] Those recommendations were widely adopted and led to measurement of bone mineral density occupying a central place in strategies for fracture prevention. Nevertheless, numerous other risk factors for fracture exist (many of which are independent of bone mineral density),[3] and most osteoporotic fractures occur among women who do not fulfill the WHO criteria for osteoporosis.[4] For these reasons, models that integrate other risk factors for fracture in addition to bone mineral density might improve our predictive ability.

Predictive models have been reported for numerous conditions, but only a small proportion have entered clinical practice. Before clinical use, a model must be validated in populations different from those in which it was developed. Two key factors should be considered: discrimination and calibration. Discrimination is the ability of the model to distinguish between people with and without the outcome. It is assessed by the area under the receiver operating curve (or equivalent C statistic); a value of 1 indicates a perfect model, greater than 0.8 indicates excellent performance, 0.6 to 0.8 indicates moderate performance, less than 0.6 indicates weak performance, and 0.5 indicates performance no better than chance.[5] Calibration is a measure of the goodness of fit of the model, and is assessed by comparing observed risk with predicted risk in a cohort divided by quintiles or deciles of predicted risk, and in subgroups defined by relevant clinical factors.[5]

Langsetmo and colleagues[1] describe a carefully conducted validation study of an absolute risk calculator for fracture developed from the Dubbo Osteoporosis Epidemiology Study[6] in Australia. The Dubbo calculator incorporates four clinical risk factors (age, sex, history of fractures and recent falls) with bone mineral density to produce estimated five- and ten-year risks of hip and osteoporotic fracture. The authors report that the Dubbo calculator has moderate predictive ability (greater for hip fracture than the broader category of osteoporotic fracture), is generally well-calibrated and is an improvement on the existing WHO recommendations[2] and, in men, the Canadian Association of Radiologists recommendations.[10]

A more widely known fracture-risk calculator is FRAX. A recent validation study of the country-specific FRAX-Canada tool involving the Manitoba Bone Density Program cohort showed similar findings, with good calibration and moderate predictive ability that was greater for hip fracture than major osteoporotic fracture.[6]

Absolute risk calculators for fracture have theoretical and practical advantages over earlier category-based systems. Fracture risk is expressed as a continuum, removing the somewhat arbitrary categorizations that otherwise occur. Clinically relevant reclassification of risk occurs, particularly in two settings: younger people with low bone mineral density but no clinical risk factors often have low risk of fracture over the short to medium term, whereas older people without osteoporosis by WHO criteria often have

Key points

- Absolute risk calculators improve fracture-risk prediction and should be used in clinical practice.
- Calculators should be validated in local cohorts before clinical use.
- Both validated in Canada, the Dubbo and FRAX-Canada calculators are suitable choices for assessing fracture risk in older Canadians.

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a high risk of fracture, especially if other clinical risk factors are present. Such reclassifications should alter prescribing practice. For these reasons, together with the improved performance in men, absolute fracture risk calculators are likely to supercede the current recommendations of the Canadian Association of Radiologists.[10]

The calculators have limitations. They have only moderate predictive ability, which is greater for hip fracture than osteoporotic fracture. However, their predictive ability is similar to that of other risk calculators, such as the Framingham cardiovascular risk calculator.[8] Even moderately predictive calculators are useful in clinical practice and may outperform the risk assessments of clinicians.[5] In addition, the calculators do not provide confidence intervals for the risk estimates, and they report estimates to one decimal place, creating the impression of greater precision than exists. Different country-specific FRAX tools can give markedly different estimates, highlighting the importance of local validation before use.[9]

Use of absolute risk for prediction of fracture will focus attention on treatment thresholds for fracture prevention. Using the Dubbo calculator, 90% of people older than age 80 years have an estimated ten-year fracture risk of greater than 20%,[1] which is defined by the Canadian Association of Radiologists as high risk.[10] Similarly, the National Osteoporosis Foundation guidelines for osteoporosis management recommends pharmacologic treatment in 93% of women older than age 75 years.[11] Despite classification as high-risk, most people in both of these situations will not sustain a fracture during the short to medium term. Calculating absolute risk reductions may help better inform patients of potential treatment benefits.

Keeping in mind their limitations, absolute risk calculators for fracture represent an important advance in fracture prediction and should be used in clinical practice. How should clinicians in Canada choose between the Dubbo and FRAX-Canada calculators? A comparison of the features of each is presented in Table 1. The performance of the calculators appears similar. Both calculators can be used without bone mineral density values, but their predictive ability drops noticeably.[7,9] FRAX uses more variables than the Dubbo calculator, but the additional variables do not increase its predictive ability[9,12] and add to the complexity and time needed to use the calculator. The equations of the Dubbo algorithm are freely available[1] and can be incorporated into computer software, whereas the FRAX algorithm has not been published. Notwithstanding these differences, either calculator appears suitable for use in assessing fracture risk in older Canadians.

Table 1: Comparison of the Dubbo and FRAX fracture risk calculators

Feature	Dubbo	FRAX
Model development		
Cohort(s)	Single cohort in Australia	20 cohorts worldwide
Externally validated	Yes	Yes
Model performance in Canadian cohort		
Discrimination		
Hip fracture	Excellent	Excellent
Osteoporotic fracture	Moderate	Moderate
Calibration	Good	Good
Parameters of model		
Can be used without bone mineral density values	Yes	Yes
Number of variables	5	11
Access to calculator		
Simplified paper tables	Yes	Yes
Web-based calculator	Yes	Yes
Published equations or algorithm	Yes	No

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