Personalised assessment of fracture risk

Which tool to use?

Tuan V Nguyen

OSTEOPOROSIS and its consequence of fragility fracture impose a significant public health burden and primary health problem in Australia. It is not widely appreciated that patients with a fragility fracture, especially hip fracture, have an increased risk of premature mortality.[1] Primary care physicians play a key part in the treatment and prevention of fracture and thereby save lives by assessing and managing high-risk individuals.

We have developed and implemented the world's first tool for personalised assessment of fracture risk, called the Garvan Fracture Risk Calculator (hereby 'Garvan').[2] In subsequent years, the Fracture Risk Assessment Tool (FRAX) was developed and implemented for clinical use.[3] Currently, The Royal Australian College of General Practitioners (RACGP) recommends that either Garvan or FRAX can be used for assessing fracture risk for treatment decision.

However, in a recent analysis,[4] Stuckey et al have pointed out that there is discrepancy in fracture risk estimates between Garvan and FRAX. As stated by Stuckey et al, the discrepancy could affect treatment decision: 'there are many instances when treatment may be recommended, as per the RACGP and Osteoporosis Australia guidelines, if the Garvan risk calculator is used but not if the FRAX calculator is used'. Here, we offer some explanations for the discrepancy and propose a solution going forward.

First, some discrepancy is expected, because the input risk factors in Garvan and FRAX differ. FRAX includes rheumatoid arthritis and glucocorticosteroid use as predictors, whereas Garvan does not, because these factors are correlated with bone mineral density. Garvan takes into account the number of falls – a key risk factor for hip fractures – in the prediction of risk; FRAX does not currently take falls into account. Garvan considers prior fracture as a quantitative variable (ie number of fractures), whereas FRAX considers prior fracture as a binary variable (ie yes/no). Thus, for an individual with two (or more) prior fractures, Garvan would predict a higher risk of subsequent fracture than for an individual with one prior fracture. By contrast, FRAX treats the two individuals as having equal risk.

FRAX was developed using multiple cohorts with different durations of follow-up, and not all cohorts had mortality data. FRAX's predicted risk is adjusted for competing risk of mortality, but how the adjustment is made has not been published. Garvan was developed using data from the Dubbo Osteoporosis Epidemiology Study, where the sequential events of fracture, refracture and death for every individual have been directly monitored. Hence, the predicted risk inherently represents the probability of sustaining fracture among those at risk during their specific remaining lifetime.

Second, the Garvan model's predicted risk is more consistent with actual risk than FRAX's. In the Geelong Osteoporosis Study, Garvan underestimated fracture risk by approximately 25% in women and 19% in men, and FRAX underestimated it by 55% in women and 66% in men.[5] In the New Zealand cohort, Garvan predicted almost 100% of fracture cases, but overpredicted hip fracture risk by 50%, while FRAX underestimated fracture risk by 50% (Table 1).[6] In the Canadian Multicentre Osteoporosis Study, the Garvan model's predicted risk closely matched that observed in the population over time.[7] As high-risk individuals would be recommended for treatment under any circumstance, the overestimation by Garvan has no negative clinical impact.

Third, the Garvan model's predicted risk is consistent with clinical decision. In an Australian cohort of 531 individuals aged 70 years and older, Garvan correctly identified who would be indicated for treatment or required a dual-energy X-ray absorptiometry scan in 88% of the cases,[8] which is slightly higher than FRAX (83–84%). In a Polish cohort of 218 men with a prior fracture, Garvan identified 82% as 'high risk' for treatment, whereas

Table 1. Comparison of predicted fractures between the Garvan Fracture Risk Calculator ('Garvan') and Fracture Risk Assessment Tool (FRAX) models in Australian and New Zealand populations

	Predicted/observed any fractures*		Predicted/observed hip fractures*	
Study	**Garvan**	**FRAX**	**Garvan**	**FRAX**
Holloway-Kew et al[5]				
Women	139/184 (0.75)	52/115 (0.45)	50/42 (1.19)	20/42 (0.48)
Men	88/109 (0.81)	26/73 (0.36)	21/17 (1.23)	10/17 (0.59)
Bolland et al[6]				
Women	276/279 (0.99)	121/229 (0.53)	86/57 (1.51)	43/57 (0.75)

**Numbers in parentheses represent the ratio of predicted values over observed values*

Table 2. Comparison of consistency with clinical decision between the Garvan Fracture Risk Calculator ('Garvan') and Fracture Risk Assessment Tool (FRAX) models

	Consistency with clinical decision	
Study	**Garvan**	**FRAX**
Inderjeeth et al[8]	88%	83–84%
Pluskiewicz et al[10]		
Prior fracture	93%	72%
Pluskiewicz et al[9]		
Prior fracture	82%	8%
Osteoporosis	74%	9.5%

FRAX identified only 8%.[9] Moreover, among 251 men with osteoporosis, Garvan would recommend 74% for treatment, but FRAX would recommend only 9.5.[9] The same trend was observed in women (Table 2).[10]

At present, Australian primary care physicians are faced with the question of which fracture risk assessment tool should be used. As Segal's law states, 'A man with a watch knows what time it is; a man with two watches is never sure'. We should not burden doctors with two fracture risk assessment models. Given the aforementioned findings, it could be argued that the Garvan model is more clinically relevant for primary care physicians for personalised assessment of fracture risk.

Author

Tuan V Nguyen FAHMS, Professor and Director, Centre for Health Technologies, University of Technology Sydney, NSW

Competing interests: TVN is a developer of the Garvan tool that is mentioned in the article.

Funding: None.

Provenance and peer review: Not commissioned, externally peer reviewed.

Correspondence to:
tuanvan.nguyen@uts.edu.au

References

1. Bliuc D, Nguyen ND, Milch VE, Nguyen TV, Eisman JA, Center JR. Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women. JAMA 2009;301(5):513–21. doi: 10.1001/jama.2009.50.
2. Nguyen ND, Frost SA, Center JR, Eisman JA, Nguyen TV. Development of a nomogram for individualizing hip fracture risk in men and women. Osteoporos Int 2007;18(8):1109–17. doi: 10.1007/s00198-007-0362-8.
3. Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E. FRAX and the assessment of fracture probability in men and women from the UK. Osteoporos Int 2008;19(4):385–97. doi: 10.1007/s00198-007-0543-5.
4. Stuckey B, Magraith K, Opie N, Zhu K. Fracture risk prediction and the decision to treat low bone density. Aust J Gen Pract 2021;50(3):165–70. doi: 10.31128/AJGP-04-20-5363.
5. Holloway-Kew KL, Zhang Y, Betson AG, et al. How well do the FRAX (Australia) and Garvan calculators predict incident fractures? Data from the Geelong Osteoporosis Study. Osteoporos Int 2019;30(10):2129–39. doi: 10.1007/s00198-019-05088-2.
6. Bolland MJ, Siu AT, Mason BH, et al. Evaluation of the FRAX and Garvan fracture risk calculators in older women. J Bone Miner Res 2011;26(2):420–27. doi: 10.1002/jbmr.215.
7. Langsetmo L, Nguyen TV, Nguyen ND, et al. Independent external validation of nomograms for predicting risk of low-trauma fracture and hip fracture. CMAJ 2011;183(2):E107–14. doi: 10.1503/cmaj.100458.
8. Inderjeeth CA, Raymond WD. Case finding with GARVAN fracture risk calculator in primary prevention of fragility fractures in older people. Arch Gerontol Geriatr 2020;86:103940. doi: 10.1016/j.archger.2019.103940.
9. Pluskiewicz W, Adamczyk P, Franek E, et al. FRAX calculator and Garvan nomogram in male osteoporotic population. Aging Male 2014;17(3):174–82. doi: 10.3109/13685538.2013.875991.
10. Pluskiewicz W, Adamczyk P, Franek E, et al. Ten-year probability of osteoporotic fracture in 2012 Polish women assessed by FRAX and nomogram by Nguyen et al – Conformity between methods and their clinical utility. Bone 2010;46(6):1661–67. doi: 10.1016/j.bone.2010.02.012.

correspondence **ajgp@racgp.org.au**