

# FRAX First – Pragmatic Approach in Resource Poor Settings

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## Abstract

**Background:** Fracture Risk Assessment Tool (FRAX) is a fracture prediction tool that uses clinical risk factors with or without bone mineral density (BMD). BMD is difficult to obtain in resource-limited setting. Hence, we aimed to compare fracture risk prediction by FRAX without BMD (FRAX) and FRAX with BMD (FRAX/BMD). **Objective:** We intended to determine if FRAX and FRAX/BMD would produce identical predictions for 10-year probability of hip fracture and major osteoporotic fracture (MOF). We also desired to study the risk factors that could help to identify the similarity of risk prediction. **Materials and Methods:** A retrospective review of patients who underwent BMD measurement and FRAX assessment was conducted. Men and women >50 years of age with osteopenia and osteoporosis according to the World Health Organization (WHO) definition at one or more sites were included. FRAX prediction scores were calculated with and without BMD using the FRAX India tool. **Results:** Of 239 subjects, 207 (86.61%) had identical fracture risk predictions with or without BMD in FRAX estimation. Mean age was lower ( $P = 0.009$ ), whereas body mass index (BMI), hip BMD, spine BMD, and history of previous fracture were higher ( $P = 0.005$ ,  $P < 0.001$ ,  $P < 0.001$ , and  $P = 0.02$ , respectively) in the identical prediction group. **Conclusion:** In our study, FRAX provided fracture risk prediction alike FRAX/BMD in most of the cases. FRAX is a good predictor of fractures especially in younger patients with higher BMI. Therefore, we conclude that FRAX is an effective tool to predict osteoporotic fracture risk and would be an inexpensive alternative when access to dual-energy X-ray absorptiometry (DXA) is limited.

**Keywords:** Fracture risk, fracture risk assessment tool, osteoporosis

## INTRODUCTION

Osteoporosis has been characterized as a skeletal disorder of reduced bone strength resulting in greater bone fragility and fracture. In 2013, it was estimated that around 50 million people in India were either osteopenic or osteoporotic.<sup>[1]</sup> With increasing longevity of Indian population, this problem may reach epidemic proportions.<sup>[2]</sup> Indian studies have also shown that osteopenia was more prevalent than osteoporosis among postmenopausal women and men.<sup>[3,4]</sup> Annual incidence of hip fractures were observed to be 163 and 121 per 1,00,000 per year in women and men, respectively, in Rohtak, a North Indian district with only slight female preponderance, but early occurrence compared to Caucasians.<sup>[5]</sup> Prevalence of radiographic vertebral fractures in Delhi was reported to be 17.9% similar to the western population.<sup>[6]</sup>

Diagnosis of osteoporosis and osteopenia is made with Dual-energy X-ray Absorptiometry (DXA) which is the main diagnostic modality. However, it is not flawless and has fallacies including errors of precision and accuracy, lack

of clinical risk factors, assessment of bone quality, and use of Caucasian reference database. Since treatment is based on fracture risk, the World Health Organization (WHO) introduced a Fracture Risk Assessment Tool (FRAX) in 2008 for estimating the 10-year probability of hip fracture and other major osteoporotic fractures (MOF).<sup>[7]</sup> The bone mineral density (BMD) of femoral neck is an optional variable in this tool. Treatment is recommended if 10-year risk of fractures is >20% for MOF and >3% for hip fracture according to the National Osteoporosis Foundation (NOF). Unfortunately, FRAX too has limitations as it does not consider nutritional status, vitamin D deficiency, bone turnover markers, lumbar spine BMD, and other secondary causes.

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But in resource-constrained settings especially rural areas, availability, accessibility, and cost of DXA make BMD estimation an impractical screening tool. Further, when frequency of estimating fracture risk increases as time taken for osteopenic individuals to develop osteoporosis is longer,<sup>[8]</sup> it seems to be an unsustainable component of FRAX. Earlier studies have shown that FRAX could produce identical fracture risk prediction like FRAX/BMD.<sup>[9-11]</sup> Hence we aimed to determine if FRAX and FRAX/BMD would produce identical predictions for 10-year probability of hip fracture and MOF in our population. We also intended to identify risk factors that suggest different risk prediction.

## MATERIALS AND METHODS

This was a retrospective study in which individuals who underwent BMD measurement and FRAX scoring at Sri Ramachandra Medical Centre, Chennai during the time period July 2016 to December 2017 were included. Men and women >50 years of age with osteopenia and osteoporosis according to the WHO definition at one or more site were included in this study. Those who have already received treatment with the US Food and Drug Administration (USFDA) approved drugs for osteoporosis were excluded. Height and weight were measured using standard medical scales. Femoral neck BMD and T-score were obtained from the DXA scanner. DXA was done using the same machine for all the subjects (GE Lunar Prodigy Advance enCORE™ Version 13.60). FRAX/BMD and FRAX prediction values were calculated using the FRAX India tool (<https://www.sheffield.ac.uk/FRAX/tool.aspx>). Subjects were separated into two groups, Group A and B. Subjects who received identical treatment recommendation from FRAX calculation with and without BMD were categorized into Group A. Those who received a different treatment recommendation with and without BMD were included in Group B. Identical treatment recommendation is defined as a 10-year probability of MOF <20% and hip fracture <3% with or without BMD as well as MOF >20% and hip fracture >3% with or without BMD.

### Statistical methods

Continuous variables are expressed as mean ± standard deviation (SD) and categorical variables are expressed as percentages. Comparison of group means was done using the Student's t-test and one-way analysis of variance (ANOVA) in the case of three groups. Correlation between the variables was tested using the Spearman's correlation coefficient. Statistical analysis was done using the Stata version 15.

## RESULTS

Subjects who met our inclusion criteria were 239 in which 125 (52.3%) were women. Eighty-nine subjects (37.2%) were between 50–59 years, 105 (44%) were between 60–69 years, 41 (17.2%) subjects were between 70–79 years,

and only 4 (1.6%) subjects were >80 years of age. BMD alone as defined by T-score – 2.5 or lower at one or more site recommended therapy in 84 out of 239 subjects (35.1%). FRAX and FRAX/BMD made identical fracture risk prediction for 207 out of 239 subjects (86.61%). The inclusion of BMD in FRAX calculation did not change the fracture risk prediction in these 207 subjects, of which 18 (8.7%) met treatment cut-off according to the NOF recommendation. Of the 32 subjects (13.39%) for whom BMD inclusion showed different fracture risk prediction, 21 (65.62%) met treatment threshold criteria. These 21 subjects were not considered as treatment requiring by FRAX calculation. Sixty-one (29.5%) individuals had osteoporosis in Group A, whereas 23 (71.9%) had osteoporosis in Group B. Data on fracture location were unavailable and hence further analysis was not possible. The demographic differences between the study groups are shown in Table 1. Mean age was lower ( $P = 0.009$ ) in the identical prediction group, whereas body mass index (BMI), hip BMD, spine BMD, and a history of previous fracture were higher ( $P = 0.005$ ,  $P < 0.001$ ,  $P < 0.001$ , and  $P = 0.02$ , respectively). Other risk factors like gender, current smoking, alcohol intake, rheumatoid arthritis, and secondary causes did not show statistically significant difference between the groups.

**Table 1: Comparison of clinical risk factors between the identical prediction group (Group A) and different prediction group (Group B)**

Parameters	Group A	Group B	P
Frequency	207 (86.61%)	32 (13.39%)	
Age	62.01 (7.8)	65.84 (6.91)	0.009
Sex			
Female	106 (51.2%)	19 (59.4%)	0.39
Male	101 (48.8%)	13 (40.6%)	
BMI	26.59 (4.74)	24.10 (3.8)	0.005
Hip BMD	0.82 (0.1)	0.70 (0.11)	<0.001
Spine BMD	1.00 (0.15)	0.86 (0.15)	<0.001
Previous fracture			
No	172 (83.1%)	21 (65.6%)	0.02
Yes	35 (16.9%)	11 (34.4%)	
Current smoking			
No	190 (91.8%)	26 (81.3%)	0.06
Yes	17 (8.2%)	6 (9.4%)	
Alcohol			
No	189 (91.3%)	29 (90.6%)	0.9
Yes	18 (8.7%)	3 (9.4%)	
Rheumatoid arthritis			
No	182 (87.9%)	24 (75%)	0.049
Yes	25 (12.1%)	8 (25%)	
Secondary causes			
No	189 (91.3%)	27 (84.4%)	0.22
Yes	18 (8.7%)	5 (15.6%)	
Bone status			
Osteopenia	146 (70.5%)	9 (28.1%)	<0.001
Osteoporosis	61 (29.5%)	23 (71.9%)	

## DISCUSSION

Our study shows that FRAX alone provides identical fracture risk prediction with or without BMD in 86.61%. When FRAX was included in therapeutic decision making along with BMD, 26.4% did not qualify for treatment compared to BMD alone. Higher hip and spine BMD in identical risk group would likely be due to the increased frequency of osteopenia in this group compared to larger number of osteoporosis in the other group. Previous fractures were more in the different risk group probably due to the increased occurrence of osteoporosis. The results of this study suggest that inclusion of BMD to the FRAX fracture risk prediction model did not alter the treatment recommendation in most subjects evaluated for fracture risk. This makes FRAX a useful initial tool in the evaluation of osteoporosis in resource-constrained countries.

In a similar retrospective study involving 36,730 women and 2873 men >50 years of age, Leslie *et al.* showed that the FRAX prediction of high risk fractures was associated with osteoporosis proving that FRAX is an efficient predictor.<sup>[12]</sup> A prospective study from USA including 150 patients also proved that FRAX alone predicts the fracture risk identical to FRAX with BMD in 84% of the study population (postmenopausal women and men >50 years of age).<sup>[9]</sup> An Indian study from the Himalayan state with 125 participants also concluded that FRAX may be used to predict 10-year probability of major osteoporotic fractures and hip fracture in the absence of DXA facility in resource-limited setting.<sup>[11]</sup> Our study finding also supports this approach. However, another retrospective study from Mumbai showed that the risk of MOF increased slightly and risk of hip fracture increased significantly when BMD was included in FRAX calculation in postmenopausal women.<sup>[13]</sup> Addition of femoral neck T-scores to the FRAX tool in Asian Indian men living in the United States also showed an increase in the 10-year probability of MOF.<sup>[14]</sup>

The therapeutic intervention threshold used in this study is recommended by the NOF and is based on the Indian version of the FRAX tool that uses data of Singapore Indians. Treatment thresholds may have to be lowered considering the lower BMD in Asians and Indians compared to Caucasians.<sup>[15]</sup> Therefore, we recommend larger prospective studies with customized Indian treatment cut-offs before establishing that FRAX alone would be a good screening tool. Inclusion of postmenopausal women <50 years of age could have increased the number of women studied and might have shown more information.

## CONCLUSION

In our study, FRAX provided fracture risk prediction alike FRAX/BMD in most of the cases. FRAX is a good predictor

of fractures especially in younger patients with higher BMI. Therefore, we conclude that FRAX is an effective tool to predict osteoporotic fracture risk and would be an inexpensive alternative when access to DXA is limited.

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## Conflicts of interest

There are no conflicts of interest.

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