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ORIGINAL ARTICLE

Age-dependent assessment thresholds to optimize patient care in a resource-limited setting: an analysis based on the Sri Lankan FRAX model

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Abstract

Summary Age-dependent upper and lower assessment thresholds help categorizing women aged 40 years or more according to their fracture risk, independent of BMD information.

Introduction Age-dependent assessment thresholds of the FRAX algorithm help stratifying men and women aged 40 years or more according to their fracture risk. This allows clinicians to decide on those who require interventions without BMD assessment and those who require BMD input for further assessment.

Methods Intervention thresholds were defined by 10-year probabilities of a major osteoporotic fracture (MOF) and hip fracture (HF) considering a woman with a BMI of 25.0 kg/m^2 having a prior fragility fracture but no other clinical risk factors. The lower assessment thresholds (LAT) were set at 0.8 times the 10-year probabilities of a MOF and HF in a woman with a BMI of 25.0 kg/m^2, without previous fracture or other clinical risk factors. The upper assessment thresholds (UAT) were set at 1.2 times the intervention thresholds of MOF and HF. Fracture probabilities were estimated for the age range of 40–80 years, without BMD input. These values were applied to a group of women who underwent DXA for clinical reasons in a single center.

Results The LATs of MOF and HF varied from 0.7 to 8.8% and 0.1 to 3.7%, from 40 to 80 years, respectively. The corresponding values for UATs were 2.5 to 21.6% and 0.3 to 8.4%. ITs of MOF and HF varied from 2.1 to 18% and 0.2 to 7%, respectively. When applied to a group of 315 postmenopausal women who underwent DXA for clinical indications, 22.9% of women were above the UATs (high-risk category) while 8.6% were below the LATs (low-risk category). The proportion of women in the intermediate category who require BMD for further assessment was 68.6% (95% CI 59.7 to 77.5%).

Conclusions In nearly one-third of women aged 40 years or more, the decision to treat or not to treat can be achieved without BMD estimation. The remaining two-thirds will require a BMD assessment for further evaluation.

Keywords FRAX · Intervention thresholds · Osteoporosis · Sri Lanka.

Introduction

The current osteoporosis management pathways pay more attention to the assessment of fracture risk than the diagnostic categorization based on bone mineral density (BMD) estimations [1]. Although BMD is a strong predictor of fracture risk, the combination of BMD and clinical risk factors is a better predictor of fracture than BMD alone [2, 3]. The current fracture risk assessment algorithms such as fracture risk assessment calculator (FRAX), Garvan, and QFracture are built on this principle but they vary in the manner and number of risk factors incorporated [1]. The FRAX is used in 72 different countries or territories in the world, and in countries such as the USA, South Africa, and Singapore, the models have been

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modified to suit different ethnicities (https://www.sheffield.ac.uk/FRAX/index.aspx).

Country-specific FRAX models are preferred as they generate more accurate predictions based on local fracture and mortality data [4, 5]. Local FRAX models should be supplemented with intervention thresholds appropriate to the particular country or ethnic group in order to facilitate rational decision-making in the management of osteoporosis [5]. Intervention thresholds have been developed in many countries using different methods and principles [5].

Since FRAX has been designed to estimate fracture probabilities on clinical risk factors alone without BMD input, this facility can be used in countries or regions with restricted access to dual-energy x-ray absorptiometry (DXA) service [6]. The FRAX performs equally well in predicting fracture with and without BMD information [6, 7]. In addition to country-specific FRAX models, some countries have developed intervention thresholds in order to optimize patient care and streamline the use of DXA services. These guidelines help clinicians make decisions on preventive measures for a sizable proportion of patients without the need for DXA evaluation at the point of care [8, 9]. Adhering to this principle, Nagendra found that only 31% of patients require DXA evaluation before making the final decision [10]. Similar observations have been made by others too [11, 12].

This approach is based on clinical reasoning introduced in the UK by the National osteoporosis guideline group (NOGG) [2, 8] and followed in subsequent analyses [9, 13, 14]. The method provides an upper assessment threshold according to age, above which preventive measures are advocated without DXA evaluation. The low assessment thresholds demarcate those who neither require DXA evaluation nor preventive medications. Those in the intermediate zone require BMD estimation before making the final decision.

DXA facility in Sri Lanka is only limited to 3–4 major cities and the majority of clinicians in the country have either no access or only limited access to the facility. Furthermore, no major improvement in the DXA availability has occurred in the country in the recent past. Hence, it is important to provide guidance for clinicians, especially those who have no access or limited access to DXA, to make rational decisions in the management of patients suspected to have a high fracture risk. Furthermore, such guidance will help streamlining DXA referrals and optimal utilization of limited DXA services in the country. The objective of this study was to provide such guidance that suit the local setting.

Methods

We used the method introduced in the UK by the National osteoporosis guideline group (NOGG) and endorsed by the National Institute for Health and Care Excellence (NICE). This methodology is based on the proposition that if a postmenopausal woman with a prior fragility fracture requires treatment to prevent subsequent fracture without the need of BMD or regardless of other clinical risk factors; then, a same-age woman without a fracture but having the same fracture probability should also be treated in the same manner. Based on this principle, 10-year probabilities of major osteoporotic fracture and hip fracture were estimated for a woman of 25 kg/m^2 BMI with a prior fragility fracture and no other clinical risk factors, without BMD information. These were considered the intervention thresholds. Two additional sets of thresholds were also calculated as follows. These calculations were done using the Sri Lankan FRAX model which has been built on fracture data from surrogate populations and age-specific mortality data from Sri Lanka.

1) Lower assessment thresholds: these were calculated considering a postmenopausal woman of BMI 25 kg/m^2 without prior fragility fracture or other clinical risk factors. These values were multiplied by 0.8 to achieve the lower assessment thresholds. Neither BMD assessment nor specific treatment was considered necessary for those with fracture probabilities below these values (low-risk zone).
2) Upper assessment thresholds: these were set at 1.2 times the intervention thresholds estimated earlier. Those with fracture probabilities above these values do not require BMD assessment to initiate specific treatment (high-risk zone).

Women with fracture probabilities in the intermediate zone, between the two assessment thresholds, need BMD evaluation before the initiation of specific treatment. These values were applied to a group of treatment naïve postmenopausal women who were referred to the DXA unit at Teaching Hospital, Karapitiya, Galle Sri Lanka, for the measurement of BMD and evaluation of fracture risk before treatment initiation and they were classified into three groups according to the assessment thresholds: above the upper assessment thresholds, below the lower assessment thresholds, and in between the two thresholds.

Of the 315 women, 10 were found to have previous low-trauma fractures (three forearm and seven vertebral). Fifteen patients had active rheumatoid arthritis and 10 were on oral glucocorticoids. Eight patients gave the parental history of hip fracture and while 12 were on chemotherapy for breast cancer.

Teaching Hospital, Karapitiya is a state-run tertiary health care institute which provides DXA facility for the entire Southern province of the country. This facility is available, free of charge, to all clinicians in the region. The population in the Southern province consists of mixed ethnicity, almost proportionate to the country's ethnic composition

and the majority of social determinants of health such as the proportion of people below the national poverty line, literacy rate, and social habits such as smoking and alcohol consumption are similar to national figures.

Results

The major osteoporotic fracture and hip fracture intervention thresholds between 40 and 80 years ranged from 2.1 to 18% and 0.2 to 7%, respectively. The lower assessment thresholds of major osteoporotic fracture ranged from 0.7 to 8.8% between 40 and 80 years while hip fracture lower assessment thresholds ranged from 0.1 to 3.7%. The major osteoporosis fracture upper assessment thresholds ranged from 2.5 to 21.6% between 40 and 80 years while the corresponding figures of hip fracture were 0.3 to 8.4% (Table 1).

Figure 1 shows the three zones (low, high, and intermediate risk) according to the major osteoporosis fracture probability. Similarly, Fig. 2 shows the three zones defined according to the hip fracture risk. The upper line demarcates high-risk women who qualify for specific treatment based on fracture risk calculated with clinical risk factors without BMD input. Similarly, the lower line demarcates those who neither require pharmacologic interventions or BMD assessment. Those in the intermediate zone need reassessment with the inclusion of BMD and reclassification according to Figs. 3 and 4. Figure 3 shows the high- and low-risk zones according to major osteoporotic fracture risk after recalculation while Fig. 4 shows the two zones for hip fracture risk.

The above thresholds were applied to a group of postmenopausal women ($n=315$) who underwent DXA to assess fracture risk due to clinical indications (age: mean 65 and SD 11 years). When both major osteoporosis fracture and hip fracture risk were taken into consideration, 22.9% of women were in the high-risk category while 8.6% were in the low-risk category (total of 31.4%). The proportion of women in the intermediate category who require BMD for further assessment was 68.6% (95% CI 59.7 to 77.5%).

When intervention thresholds were applied, all those above the upper assessment thresholds were found to be above the intervention thresholds while those below the lower assessment thresholds remained below the intervention thresholds. In the intermediate group, 24% were found to be above the intervention threshold.

Discussion

This study was designed to provide a guide for clinicians in Sri Lanka who have limited access to DXA to estimate the fracture risk of postmenopausal women and especially to select those who require DXA evaluation before making the final decision. Apart from optimizing the use of limited DXA facility by reducing the number of referrals, these guidelines will help clinicians make treatment decisions for a sizable proportion of women without a delay. We observed that in 31% of patients the decision to treat or not to treat can be reached locally with the facility to access the Sri Lankan FRAX algorithm at the point of care. A study in India reported that by applying similar principles, the number of referrals can be reduced to 32.2% [10]. A similar analysis in the UK by Kyriakos et al. found that only 32% of women require BMD testing when the current NOGG age-dependent thresholds were applied [15]. Comparatively, the proportion of women who require BMD assessment observed in the current analysis is significantly higher. The risk profile of participants of different studies is likely to vary due to the variations in the prevalence of clinical risk factors including fracture and criteria used by clinicians to select patients for BMD estimations. This could partly explain the differences observed between the outcomes of studies.

The use of risk categorization based on clinical risk factors is possibly more cost-effective. Johansson et al.

Table 1 Intervention thresholds and assessment thresholds of a woman of 25 kg/m^2 BMI according to the Sri Lankan FRAX model

Age	Major fracture LATs	Hip fracture LATs	Major fracture UATs	Hip fracture UATs	Major fracture ITs	Hip fracture ITs
40 years	0.7	0.1	2.5	0.3	2.1	0.2
45 years	0.7	0.1	2.5	0.4	2.1	0.3
50 years	1.0	0.1	3.2	0.5	2.7	0.4
55 years	1.6	0.2	5.3	1.0	4.4	0.8
60 years	2.8	0.5	8.9	2.2	7.4	1.8
65 years	4.6	1.0	14.4	3.8	12.0	3.2
70 years	6.4	1.8	18.0	5.5	15.0	4.6
75 years	7.8	2.6	20.4	7.1	17.0	5.9
80 years	8.8	3.7	21.6	8.4	18.0	7.0

LAT, lower assessment thresholds; *UAT*, upper assessment thresholds; *IT*, intervention thresholds

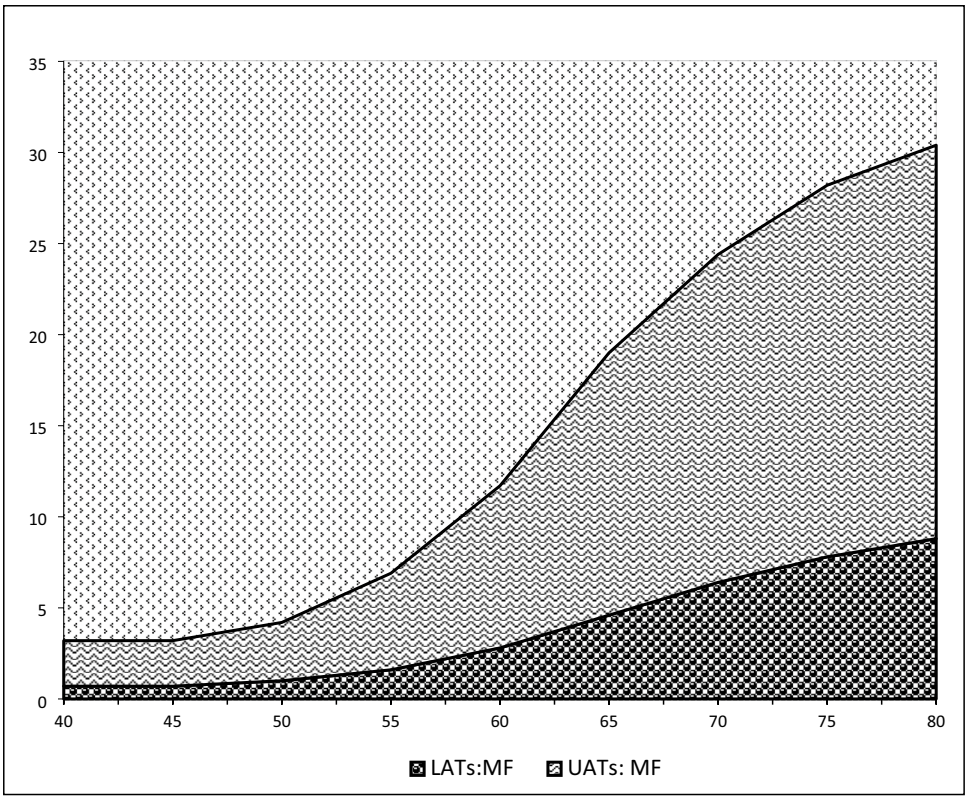

Fig. 1 Age-dependent upper assessment thresholds (UAT) and lower assessment thresholds (LAT) of major osteoporotic fracture

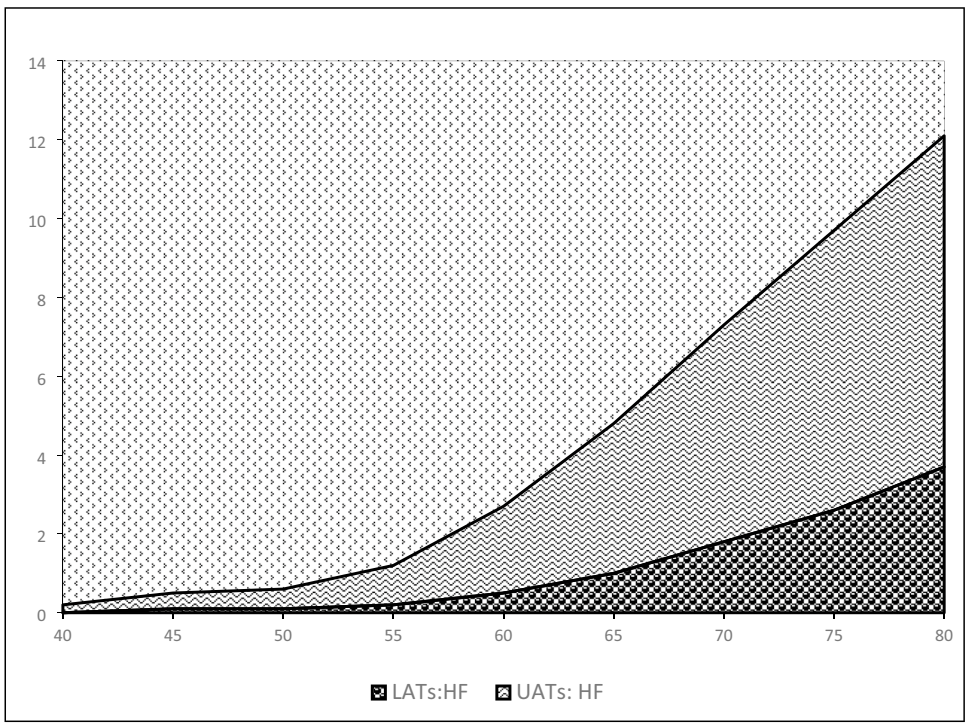

Fig. 2 Age-dependent upper assessment thresholds (UAT) and lower assessment thresholds (LAT) of hip fracture

in the UK observed that compared to the Royal College of Physicians, London strategy, the NOGG strategy based on age-dependent intervention thresholds uses BMD resources more efficiently with lower costs per hip fracture averted [16]. It is important to examine the cost-effectiveness of these assessment and intervention

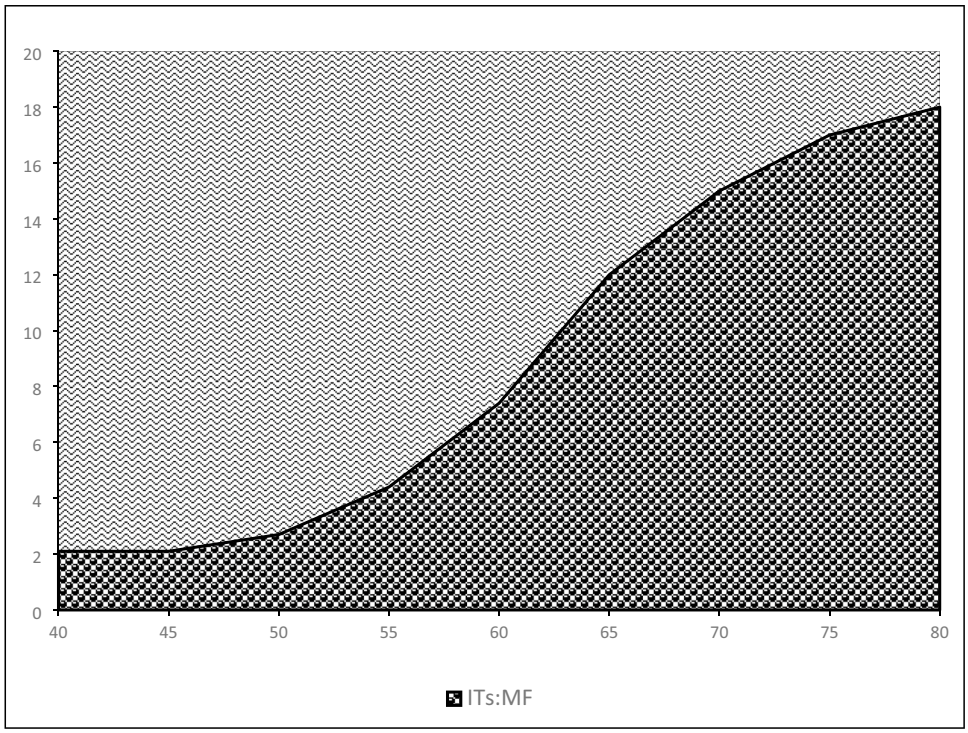

Fig. 3 Age-dependent intervention thresholds (IT) of major osteoporotic fracture

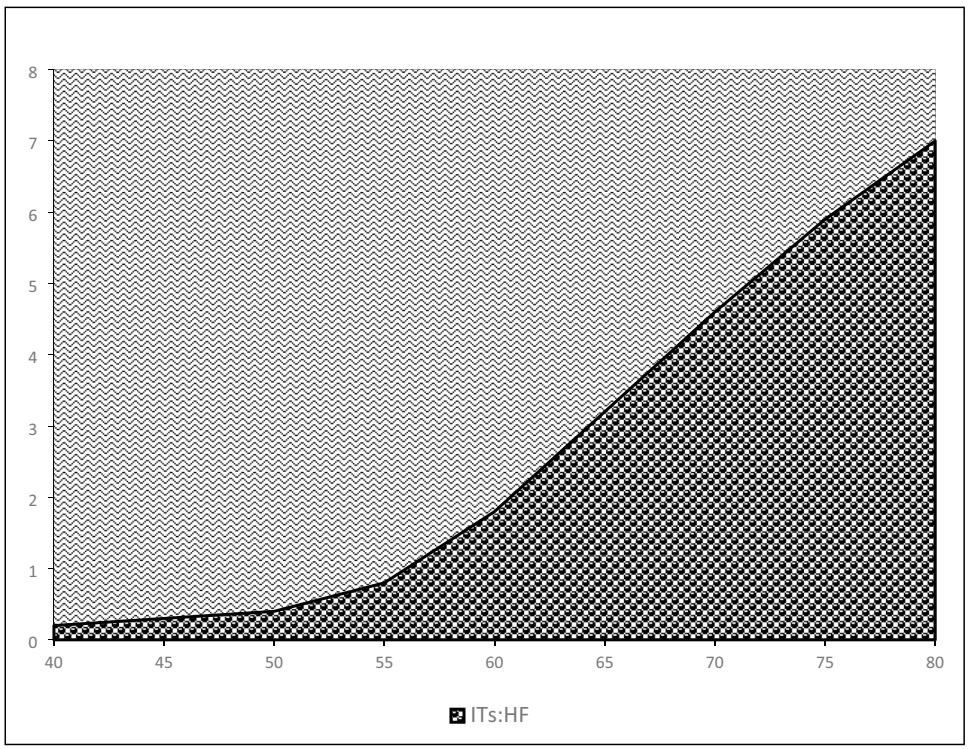

Fig. 4 Age-dependent intervention thresholds (IT) of hip fracture

thresholds when applied in different clinical settings in the country.

In defining the lower assessment thresholds, the current study deviated from previous studies of similar nature [8–10] by lowering the thresholds by 0.2 (multiplied by 0.8). This was done to prevent possible confusion among clinicians owing to the already existing intervention thresholds recommended in 2020. The guidance in

2020 recommended fixed intervention thresholds of 9% for major osteoporotic fractures and 3% for hip fractures, regardless of age, and we found the unadjusted lower assessment thresholds in the current analysis to exceed these values beyond 75 years of age. Furthermore, we believe that the downregulated lower assessment thresholds provide a more conservative approach to patient assessment and clinicians will be more confident in not treating women in the low-risk category. The lowering of lower assessment thresholds by 0.2 did not make a significant impact on the categorization of subjects. If the lower assessment thresholds were not adjusted, five women could have been added to the intermediate group. They, however, remained below the intervention thresholds.

Although it is possible to determine the fracture risk of postmenopausal women and initiate pharmacologic treatment without BMD assessment, clinicians may prefer to have BMD measurement in the initial assessment of patients. A survey among 84 orthopedic surgeons in India, most respondents preferred BMD assessment in the initial patient assessment [17]. Pickney et al. found that patients who could recall DXA results correctly had a better medication adherence compared to those who were not able to recall [18]. Higher awareness of DXA results in the initial assessment is linked with greater belief in treatment benefits and medication adherence [19]. Furthermore, effective patient management requires an access to the DXA facility. The efficacy of interventions needs to be monitored and that requires either serial BMD or bone marker assessments. According to the IOF Inadequate Responders Working Group, replicate BMD testing helps identifying treatment failures early [20].

Despite the clear advantages in the management of osteoporosis, the restricted availability of DXA, especially in developing countries, still prevails. According to the Asia Pacific audit on osteoporosis sponsored by the IOF in 2014, the availability of DXA in most of Asian countries is a serious concern [21]. Nearly 7 years after the audit, the availability of DXA in Sri Lanka is limited to a few major cities and the majority of clinicians in Sri Lanka have either no access or have only a very limited access to the facility. This situation is unlikely to change in the immediate future as osteoporosis is not a health priority in the country.

The results of the current study will help clinicians understand the risk categorization better and the charts provided can be used to educate patients regarding their fracture risk. A similar approach is used in cardiovascular risk charts developed by the WHO for developing countries [22]. These color-coded charts are used both in the risk assessment and patient education in the primary care settings in the country. Studies have shown that graphical presentation can be used to enhance comprehension of diseases and medication adherence especially among people with limited health literacy [23].

Many countries have developed country-specific guidelines based on the same principle in the current study. These include NOGG in the UK [8], Nagendra in India [10], and Lesnyek et al. in eight Eurasian countries [9]. It is intuitive to believe that a postmenopausal woman with an average BMI with a low energy fracture should receive osteoporosis-specific treatment regardless of other clinical risk factors and BMD information. In order to be more conservative in this recommendation, the thresholds estimated were upgraded (multiplied by 1.2) in defining the high-risk category.

We believe that the findings of this study can be applied to Sri Lankan men of the same age range as well. Compared to women, studies on osteoporosis in men in Sri Lanka are sparse. Previous studies have shown that FRAX-based fracture thresholds should be the same for men and women of the same age [24] as the cost-effectiveness of osteoporosis medications are similar in both genders [2].

This study included data only from one center and this can be seen as a limitation of the study. Since the DXA facility is provided free of charge and available for all clinicians in the area, the DXA unit included in this analysis serves a wide range of patients: from children to older adults. Therefore, we believe that the results can be generalized to the rest of the country.

In conclusion, this study helps clinicians in resource-limited areas in Sri Lanka in assessing fracture risk of women of 40–80 years and making therapeutic decisions without BMD information in nearly 31% of them at the point of care. It also helps identifying those who require BMD estimations and this in turn would help in the proper utilization of limited DXA facility available in the country. The same thresholds published in this study can be applied to men of 40–80 years in selecting them for specific preventive treatment.

Declarations

Conflicts of interest None.

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