ORIGINAL ARTICLE

The FRAX-based Lebanese osteoporosis treatment guidelines: rationale for a hybrid model

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Abstract

Summary We describe our approach to develop FRAX-based osteoporosis treatment guidelines in Lebanon, a country with low-moderate fracture rates. A hybrid assessment algorithm that combines a fixed 10 % intervention threshold until age 70 years, and an age-dependent threshold thereafter, was deemed most suitable.

Introduction The FRAX risk calculator is used to guide intervention thresholds in several national osteoporosis guidelines. This study aimed to describe the approach in developing FRAX-based osteoporosis treatment guidelines in Lebanon, a country with relatively low fracture rates.

Methods We reassessed previous national guidelines combined with an evaluation of age-dependent and fixed FRAX-based intervention threshold models used in the UK, the USA, and Canada. We took into consideration the risk for major osteoporotic fractures (MOF) and the proportions of subjects considered for therapy using such thresholds, before finalizing a model for Lebanon.

Results The new Lebanese guidelines retained the recommendation to treat individuals with fragility fracture at the hip or spine. A femoral neck T-score ≤−2.5 in subjects without fractures was dropped, since it would imply consideration of therapy for individuals with a 10-year risk for MOF of <10 %, up to age 75 years in women. After considering the impact of both age-dependent and fixed intervention thresholds, we chose a new hybrid algorithm, combining a fixed 10 % treatment threshold until age 70 years and an age-dependent threshold thereafter.

Conclusion The Lebanese FRAX-based hybrid model takes into consideration the risk for MOF and the proportions of subjects considered for treatment. This model avoids consideration of drug therapy in a large proportion of younger subjects at low risk for fracture and targets high risk elderly individuals. It was deemed most suitable for Lebanon and may be an option for other countries with relatively low fracture rates.

Keywords Age dependent intervention threshold · Fixed intervention threshold · FRAX · Guidelines · Osteoporosis

Introduction

Osteoporosis is a public health problem affecting women and men, the manifestation of which, namely fractures, is a major contributor to disease burden in aging populations worldwide [1]. Bone mineral density (BMD), expressed as a gradient of risk [relative risk per standard deviation decrease in BMD (RR/SD)], predicts an increased risk of fracture that is comparable across populations [2–4], but the absolute risk of hip fractures may vary by up to 20-fold [5–7]. Furthermore, BMD alone has sub-optimal sensitivity and specificity [8], and the ability to predict fracture risk is improved when BMD is combined with clinical risk factors [9, 10]. Several fracture risk assessment tools have been developed, which incorporate varying numbers of risk factors, with or without BMD [11]. The WHO fracture risk assessment tool, FRAX, is

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a user-friendly, country-specific computer-based fracture probability calculator that incorporates 11 clinical risk factors, with or without BMD at the femoral neck [9]. FRAX estimates the 10-year probability of a major osteoporotic fracture (MOF), defined as hip, clinical spine, humerus or distal forearm fracture, and, separately, hip fracture, taking into account population-specific life expectancy and fracture incidence rates [12]. This risk assessment tool has been calibrated for use in 58 countries worldwide (FRAX website accessed in May 2016 [13]). FRAX has resulted in a major paradigm shift in identifying patients at a high risk for osteoporotic fractures and is used by several organizations to inform intervention thresholds incorporated in the updated osteoporosis guidelines [14, 15].

In this paper, we describe the approach to develop FRAX-based Lebanese osteoporosis treatment guidelines, anchoring them to previous national guidelines, and comparing with FRAX-based osteoporosis guideline models adopted in the UK [16], the USA [17], and Canada [18].

Overview of national FRAX-based osteoporosis guidelines

FRAX-based osteoporosis treatment guidelines agree on recommending drug therapy to high-risk individuals, defined as postmenopausal women and older men who have a history of major fragility fracture, who have a fracture probability above the country-specific intervention threshold, and, for some, in the case of a low hip or lumbar spine T-score [14, 16–18].

Low trauma fractures at the spine and the hip are accepted as warranting treatment in the vast majority of guidelines, including the Lebanese national guidelines. Differences arise among guidelines regarding intervention for patients with fractures at other skeletal sites or who have not experienced fragility fractures [14, 16–18]. To date, three main FRAX-based intervention strategies have been proposed. The original UK model uses a translational approach [16], the National Osteoporosis Foundation (NOF) model uses a clinical and cost-effectiveness approach based on hip fracture risk [17], and the Canadian model is based upon three categories of fracture risk (low, moderate, high) [18]. Other countries have adopted one of these three models, with some variations, based on specific considerations [14].

UK National Osteoporosis Guideline Group model

The UK National Osteoporosis Guideline Group (NOGG) model recommends consideration of pharmacologic therapy for postmenopausal women with a previous fragility fracture, with or without any additional clinical risk factors [16, 19]. Based on this rationale, the NOGG model also proposes to treat a woman with a 10-year risk for MOF or hip fracture

equivalent to or higher than that of a woman with a similar age, BMI of 25 kg/m^2, and history of fracture but no other risk factors, using the UK FRAX calculator [16, 19]. Health economic analyses have confirmed that this approach is cost-effective [12, 20].

US National Osteoporosis Foundation model

The FRAX-informed National Osteoporosis Foundation (NOF) guidelines specify that pharmacological treatment should be considered for postmenopausal women and men over the age of 50 years after a low trauma vertebral or hip fracture, or a BMD diagnosis of osteoporosis, with a T-score of ≤−2.5 at the hip (femoral neck or total hip) or spine [17, 21]. The recommendation to treat patients with prior vertebral or hip fracture was based on evidence from clinical trials, demonstrating fracture risk reduction using pharmacologic therapy in such patients [17]. Individuals with low bone mass (T-score between −1 and −2.5) are also considered for treatment if the 10-year fracture probability with the US FRAX calculator equals or exceeds 20 % for MOF or 3 % for hip fracture. The 3 % hip fracture cutoff was chosen on the basis of cost-effectiveness considerations [22]. The 20 % cutoff for MOF was deemed as equivalent to the 3 % 10-year risk of hip fracture [22].

The Canadian model

The guidelines on the management of osteoporosis in Canada assign individuals to one of three risk categories, based on sex, age, additional clinical risk factors, and femoral neck T-score, using either the Canadian FRAX calculator or the simplified Canadian Association of Radiologists/Osteoporosis Canada (CAROC) tool: low risk (<10 %), moderate risk (10–20 %), high risk (>20 %) [18]. Those who are designated at high risk based upon fracture probability, prior fragility fracture at the hip or spine, or more than one fragility fracture episode warrant consideration for pharmacologic therapy [18]. Those with a T-score of −2.5 or lower at the lumbar spine, total hip, or femoral neck are designated as being at least at moderate risk. Those at moderate risk should be evaluated for additional risk factors, such as spine imaging, to identify occult vertebral fractures (which would identify the individual as high risk) [18]. Individuals at moderate risk with additional risk factors (e.g., rapid bone loss, use of aromatase inhibitors or androgen deprivation therapy) may be offered pharmacologic therapy depending upon patient preferences [18].

Methods

The FRAX-based Lebanese osteoporosis treatment guidelines effort was initiated in 2012 and completed by the beginning of 2014. The guidelines targeted postmenopausal women, and the same approach was applied to men. The process involved reviewing recommendations from previously endorsed national osteoporosis guidelines as initially developed in 2002 [23] and updated in 2007 [24]. It took into account additional information provided by FRAX Lebanon [25], and the models adopted in the UK, USA, and Canada [16–18]. FRAX Lebanon was launched in September 2009 [25], based on the 2007 hip fracture incidence data provided by the Lebanese Ministry of Health (MOH) [6], and WHO life expectancy tables for year 1999. It has been since revised to incorporate updated WHO life expectancy tables for year 2009 [26], resulting in an increase in FRAX derived 10-year fracture risk estimates [27].

We assessed the impact of femoral neck T-score on fracture risk. Since there are no data from prospective Lebanese cohorts allowing such evaluation, we examined the impact of T-scores ranging from −1 to −4, on the 10-year FRAX derived risk for MOF [25], as a function of age (40–90 years), assuming a BMI of 30 kg/m^2 (the average BMI in the older Lebanese elderly population [28, 29]) and no other risk factors.

The most suitable FRAX derived model for Lebanon, a country with a low-moderate rate of fractures [6, 30], was ultimately selected based on age-specific estimates for projected 10-year MOF risk, and proportions of subjects to be considered for drug therapy at thresholds defined either in an age-dependent (NOGG-like) model or fixed threshold (NOF-like) model.

Age-specific intervention thresholds for the 10-year risk of MOF were derived by applying a "NOGG-like" approach to FRAX Lebanon based upon a woman with prior fracture, BMI of 30 kg/m^2, and no other risk factors. Age-specific proportions of women who would be considered for drug therapy were estimated under a "NOGG-like" age-dependent approach in Lebanon. In addition, 10 and 20 % fixed thresholds for MOF were considered in view of their use in the NOF [17] and Canadian guidelines [18], and the proportions of individuals who would be considered for treatment using such thresholds were also estimated.

The initial iteration (2012) implemented for estimating these proportions included subjects with MOF and was applied to both NOF and NOGG-like models. It provides important information to health care authorities/providers in terms of health care costs since all identified individuals would be considered for therapy. The second iteration (2015) excluded individuals with fractures, as they would have been deemed eligible for drug therapy independent of threshold consideration (secondary prevention), and was applied to the NOGG-like model only. Thus, it provides the needed information for the implementation of cost-effectiveness analyses in the setting of primary prevention. Age-specific simulation cohorts were constructed from the prevalence of clinical risk factors and femoral neck bone mineral density to determine the distribution of fracture probabilities as assessed by FRAX [31]. These data were used to estimate the number and proportion of women at or above any given 10-year fracture probability. The simulation model used fracture and death risks specific to Lebanon, and the data was generated by the WHO Collaborating Center, Sheffield team, under the supervision of Professor JA Kanis.

Results

History of fragility fracture

The recommendation to consider drug therapy in patients with a history of fragility fracture at the spine or hip was retained from previous Lebanese guidelines [23, 24]. The presence of more than one fragility fracture episode (other than spine and hip) was added as an indication to consider pharmacologic therapy, given that non-hip non-spine fractures are common, and has been shown to increase the risk of all fractures [32–34].

T-score based thresholds

The previous recommendation to treat individuals with a T-score ≤−2.5 was revisited [23, 24]. The decision to use the WHO diagnostic reference standard [35] as a treatment indication was originally made in consideration of other guidelines at the time [36, 37], and the fact that the BMD-fracture gradient of risk (RR/SD decrease) was similar in Lebanese [23] and western populations [2, 38]. However, it has since become clear that a T-score of −2.5 is a diagnostic, but not necessarily a therapeutic threshold [20]. In women, the 10-year risk for MOF remained below 10 % for a T-score of −2.5 up to age 75 years, and for a T-score of −3 up to age 70 years (Fig. 1). MOF risk would reach 14 % in women with a T-score of −4 at age 65 years. In view of these relatively low MOF risk estimates, even at extremely low T-scores in elderly subjects, a T-score of ≤−2.5 was not retained as a treatment indication in the absence of other risk factors.

A NOGG-like approach applied to Lebanon

We examined intervention thresholds in Lebanese women using a NOGG-like approach. The age-specific intervention thresholds were low, barely exceeding 5 % at age 65 years, and less than 10 % up to age 70 years in women (Fig. 2). These results reflect the low age-adjusted incidence rates of hip fracture in Lebanon compared to other countries such as the UK, the USA, and Canada [5–7]. The proportions of women between ages 50 and
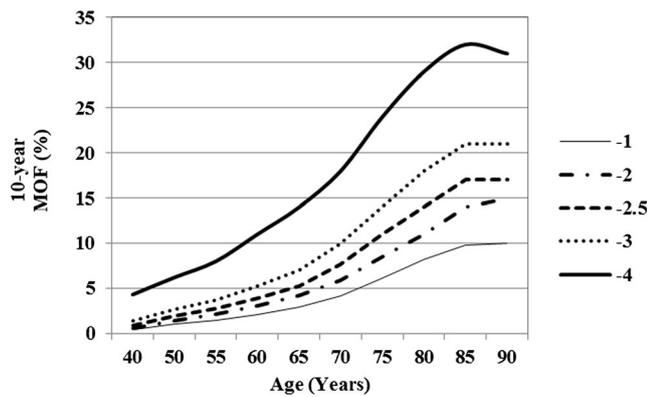
Fig. 1 Age-specific 10-year probability for major osteoporotic fracture (MOF) in FRAX Lebanon, by age and T-score categories, in women with BMI 30 kg/m² and no additional clinical risk factors. The 10-year probability for MOF was calculated, using the Lebanese FRAX online calculator with different femoral neck BMD T-scores, BMI 30 kg/m², and no other risk factors (http://www.shef.ac.uk/FRAX, accessed in April 2016)

85 years estimated to exceed age-specific thresholds varied between 12 and 26 %, if one included women with previous MOF, and between 11 and 18 % after excluding such subjects (Fig. 3, Appendix Table 3). Therefore, applying the original NOGG-like approach to Lebanon would potentially lead to recommendation of drug therapy to a high proportion (11–18 %) of younger women (≤69 years) despite low risk for fracture (10-year MOF risk 1.8–9 %).

Fixed intervention thresholds applied to Lebanon

If one considered a fixed intervention threshold of 10 %, the cutoff between low and moderate risk in the Canadian
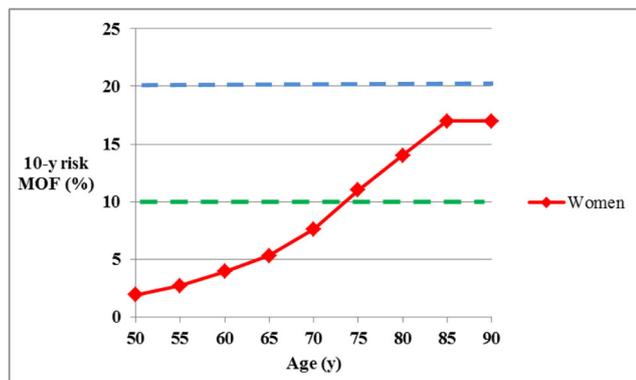

Fig. 2 Age-specific intervention threshold (NOGG-like approach) based on the FRAX-derived 10-year probability of major osteoporotic fracture (MOF), in Lebanese women. The 10-year probability for MOF was calculated, using the Lebanese FRAX online calculator, in women with a history of previous fracture, BMI 30 kg/m², and no other risk factors (http://www.shef.ac.uk/FRAX, accessed in April 2016)

guidelines [18], the estimated proportion of women who would be treated, including those with prior MOF, would be below 6 % up to age 60–64 years, 19 % at age 65–69 years, 41 % at age 70–74 years, and around 80 % at age >85 years (Table 1). If one excluded subjects with prior MOF, the proportions of subjects treated would be even lower, estimated at 1–5 %, up to age 65 years, but would remain relatively high in older age groups. If one considers a fixed threshold of 20 %, the proportions of women who would be treated would be extremely low, and close to 0 % until age 65 years (Table 1). This approach would also recommend treatment to a very low proportion of individuals between the ages of 60 and 70 years, e.g., only 3 % at 65–69 years, although individuals in this age group are considered to be at a significant risk of fracture in general. Indeed, we have shown that 12–20 % of the Lebanese men and women have prevalent moderate to severe vertebral fractures by the age of 70 years [4].

The Lebanese hybrid assessment algorithm

Since the NOGG approach would lead to overtreatment and a fixed intervention threshold led to under-treatment, we evaluated the possibility of a hybrid approach for the Lebanese population. This hybrid model combines a fixed threshold of 10 % in individuals younger than age 70 years whose average risk for fractures is relatively low, with a NOGG-like approach in individuals age
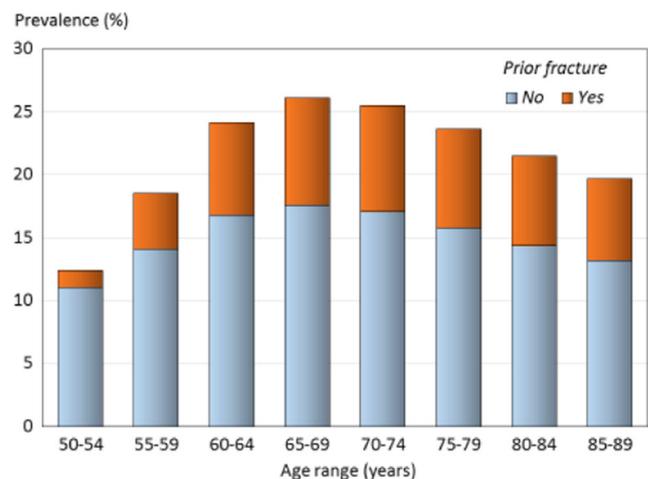

Fig. 3 The proportion of women (prevalence %) exceeding the age-specific intervention threshold (using the NOGG-like approach for major osteoporotic fracture (MOF), by age category. The NOGG-like intervention thresholds were calculated, using the Lebanese FRAX online calculator, in women with a history of previous fracture, BMI 30 kg/m², and no other risk factors (http://www.shef.ac.uk/FRAX; accessed in April 2016)

Table 1 Proportion (%) of Lebanese women in each age group with a 10-year probability for a major osteoporotic fracture (MOF) above the pre-defined fixed thresholds, by 5-year age increments, including women with previous MOF

Age (years)	Proportion (%) of women above 10 %	Proportion (%) of women above 20 %
50–54	0.1	0
55–59	1	<0.1
60–64	6	<1
65–69	19	3
70–74	41	10
75–79	63	22
80–84	77	36
85+	80	43

A BMI of 30 kg/m^2 was used to reflect the average BMI in the Lebanese women above 50 years

The proportions of women above the threshold in each age category were provided by Professor JA Kanis (personal communication) and include subjects with prior fragility fracture

Proportions rounded to the nearest integer

70 years and older (Fig. 4). The fixed intervention threshold below age 70 years would suggest treatment is necessary in a smaller proportion of younger women than if one adopted a NOGG-like approach. Among women older than 70 years, the group at highest fracture risk, the hybrid model suggests consideration of therapy for 10-year MOF risk equal to or higher than 15 % at 75 years, 21 % at 80 years, 27 % at 85 years, and 30 % at 90 years [39].

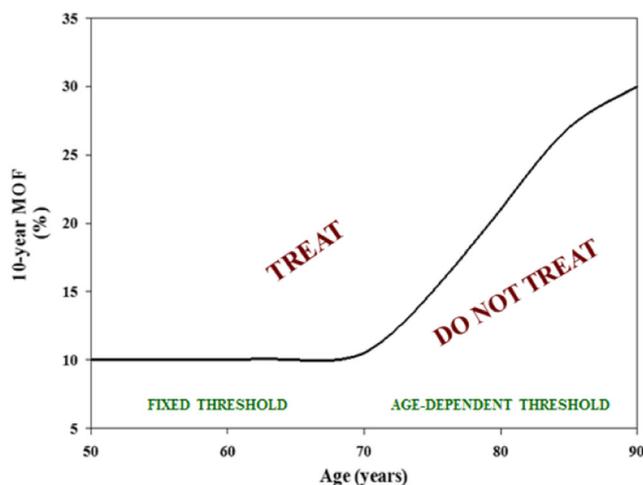The fixed 10 % intervention threshold also allows for a smooth transition from fixed to age-dependent cutoffs,

namely 10 % at 65–69 years and 12 % at 70–75 years, and from a proportion of treated subjects consideration, namely <15 % at age 65–69 years and 17 % at age 70–74 years (Table 2). Using this hybrid model, <5 % of postmenopausal women without fractures would be considered for treatment by age 65 years, and 13–17 % thereafter.

Discussion

The FRAX-based Lebanese guidelines build on previous national guidelines, explore the applicability of various approaches for FRAX-based paradigms to Lebanon, and provide one of the earliest models that considered a hybrid approach, including a fixed and an age-dependent model. This approach took into consideration the risk of MOF and the proportions of subjects considered for treatment using simulation studies applied to FRAX Lebanon.

The only indication to treat retained from the previous Lebanese guidelines was the presence of a fragility fracture at the spine or hip, with the new addition of more than one fragility fracture episode, both in postmenopausal women and older men [39]. The latter was based on the fact that the risk of fracture at all skeletal sites increases in the presence of more than one fragility fracture [32–34, 40], and this is consistent with the Canadian approach [18]. In the UK, any prior osteoporotic fracture would be considered an indication to intervene in postmenopausal women [16], whereas French guidelines identify fractures at

Fig. 4 FRAX-derived intervention thresholds in the Lebanese hybrid model

Table 2 Intervention thresholds and corresponding proportions of women, in each age group, who would be treated under FRAX Lebanon using the proposed hybrid model (fixed 10 % intervention threshold under age 70 with an age-dependent intervention threshold after age 70), by 5-year age increments

Age (years)	Intervention threshold (%)	Proportion (%) of Lebanese women above threshold, including previous MOF	Proportion (%) of Lebanese women above threshold, excluding previous MOF
50–54	10	<5	<5[a]
55–59	10	<5	<5[a]
60–64	10	6	<5[a]
65–69	10	19	<15[a]
70–74	10–14	26	17
75–79	15–20	24	16
80–84	21–26	22	14
85–89	27–30	20	13

Proportions rounded to the nearest integer

[a] Estimates are derived based on simulation cohorts with assumptions for fracture incidence, BMD data, fracture prediction based on BMD, previous fracture, population demography, and mortality

the proximal or distal femur, proximal humerus, proximal tibia, vertebra, pelvis, or three ribs concomitantly, as indications for drug therapy [41]. Indeed, non-spine non-hip fractures constitute over 80 % of osteoporotic fractures and are associated with an increased risk for all fractures. They are treatment responsive, albeit with more modest and variable reduction in fractures rates [32–34, 40].

A T-score ≤−2.5, in the absence of other risk factors, is no longer considered a basis to treat in the Lebanese FRAX-based guidelines, given the low projected MOF risk estimates at this cutoff in both genders, even in elderly individuals. This consideration might be applicable to other countries with similarly low incidence rates of fractures, e.g., those in the Middle East, Southern Europe, and Latin America (Appendix Fig. 5). While the UK and Canada have omitted the use of T-score ≤−2.5 as a stand-alone intervention threshold in the absence of other risk factors [16, 18], guidelines from the NOF [17] and Switzerland [42] still recommend treatment in the presence of a BMD T-score ≤−2.5. France has lowered the T-score intervention cutoff to −3 [41].

All other indications to treat, including the category of "less definite indications for treatment" in the 2002 [23] and 2007 Lebanese guidelines [24], namely for subjects with osteopenia and other risk factors, are now captured within the 10-year MOF FRAX estimate and hybrid assessment algorithm. Such an algorithm, applying a fixed 10 % threshold up to age 70 years, and a NOGG-like age-dependent approach thereafter avoids consideration of drug therapy in low-risk younger individuals, in favor of targeting high risk individuals. This consideration might be applicable to other countries in the Middle East, with similarly low incidence rates of fractures (Appendix Fig. 6).

In the absence of a major fracture history, measurement of BMD is required to inform treatment decision-making and could be selectively used in a subset of subjects at intermediate risk of fracture to further refine fracture risk and decide on therapy [12]. While the NOF and Canadian guidelines require the inclusion of BMD for decision making, when computing 10-year fracture probability with FRAX [17, 18], NOGG restricts the use of BMD testing to a subset of subjects who fall between age-dependent upper and lower limit assessment thresholds [16]. The upper assessment threshold is defined as 1.2 times the FRAX-based NOGG intervention threshold for that age, and the lower assessment threshold is defined as the 10-year fracture risk for MOF in a woman with a BMI of 25 kg/m^2 without any other risk factor. A man or woman with fracture probability exceeding the upper assessment threshold is considered for drug therapy, without BMD testing [16]. The Lebanese guidelines also allow for the use of FRAX in selecting individuals who would benefit from BMD testing. Densitometry is considered in individuals with FRAX derived MOF risk estimates (based on risk factors only) that are close

to the intervention threshold (±4 % margin of error), in order to refine risk estimates and treatment decisions [25].

The International Osteoporosis Foundation website lists osteoporosis treatment guidelines available in 45 countries [14]. The majority include FRAX-based intervention thresholds [14]. Several countries, such as Hungary, Austria, Malaysia, Spain, Taiwan, and Thailand, have adopted the NOF model unchanged, using thresholds of 20 % for MOF and 3 % for hip [14], but no details for such an approach are available in the peer reviewed literature. A few countries, such as Japan [43], China [44], Hong Kong [45], Poland [46], and Switzerland [47], have provided the rationale for the model selected. Japan and Poland considered fracture probabilities that are equivalent to intervention thresholds used in their previous guidelines, such as a BMD T-score ≤−2.5 [43, 46]. The Chinese guidelines set the intervention thresholds at 4 % for MOF and 1.3 % for hip fracture, to yield a proportion treated close to the prevalence of osteoporosis [44]. The Swiss guidelines used a cost-utility analysis [47]. Conversely, guidelines from other countries have explored the use of an age-dependent NOGG-like model to decide on the indication to treat. For example, in Australia, an age-dependent model, based on the 10-year risk of hip fracture resulted in "more realistic treatment rates," compared to the NOF model that would have resulted in recommending treatment to >90 % of individuals above 70 years, and the NOGG model that would have treated only 11 % of these individuals [48]. In France, an age-dependent intervention threshold was used as it matches the increase in fracture risk with age and in the presence of previous fracture [41]. In Belgium, the intervention thresholds (ranging between 7.4 % at 50 years and 30 % at 90 years) were selected to be equivalent to reimbursement cutoffs [49].

The approach adopted in Lebanon was mostly based on clinical judgment, informed by country-specific data as available, and examination of the estimated proportions of individuals for whom treatment would be recommended at various thresholds. A similar consideration was used in the Chinese FRAX-based guidelines [44]. In Lebanon, the 10 % cutoff was chosen in light of its convenience for a smooth transition from a fixed to an age-dependent threshold at age 70, and the proportion of individuals for whom treatment would be recommended. In addition, it is also comparable to cardiovascular cutoffs recently decreased to 7.5 and 10 % in the 2013 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines [50] and 2013 National Institute of Excellence (NICE) guidelines [51], respectively. An inverse-hybrid model, using an age-dependent threshold until age 70 years and a fixed 20 % threshold thereafter, was recently assessed in the UK and deemed to be more equitable to high risk subjects, allowing consideration of therapy for a higher proportion of older women, as compared to the previous NOGG model [52].

Our approach and model suffer from some limitations. These include the assumptions used to allow the calculation of the proportion of individuals with MOF due to the lack of data on incident fractures, other than the hip, thus necessitating the use of hip/non-hip fracture ratios from the Swedish Malmo population as done for the UK and Iceland [12, 53]. However, this is currently the case for many countries with FRAX calculators. Furthermore, due to limited databases and resources, we were unable to conduct cost-effectiveness and quality-adjusted life year analyses. In fact, while more than 40 countries currently have guidelines for the treatment of osteoporosis [14], only the UK [20], USA [54], Switzerland [47], and Greece [55] have published related cost-effectiveness studies. We were also unable to validate FRAX derived estimates with prospective data from Lebanese cohorts at this time. However, a recent systematic review of fracture risk prediction tools underscored that the FRAX calculator had the largest number of externally validated and independent studies, using Western and Asian cohorts [56]. Comparison of FRAX-based guidelines using prospective cohorts has only been implemented in a few countries [57, 58].

Our approach was based on the FRAX Lebanon calculator and on robust hip fracture rates (the 2007 rates were stable over years, unpublished data from the Lebanese Ministry of Health), an important consideration in light of the secular changes in hip fractures in many other countries. In addition, we engaged all concerned stakeholders, through the National Task Force for Osteoporosis and Metabolic Bone Diseases, the Ministry of Health and all concerned specialty societies, with a series of follow-up workshops and case studies at major meetings.

Conclusion

We evaluated the applicability of the UK, US, and Canada FRAX-based guidelines in Lebanon and used them to anchor the FRAX-based Lebanese osteoporosis treatment guidelines. The Lebanese hybrid model avoids consideration of drug therapy in a large proportion of younger subjects at low risk for fracture and targets high risk elderly individuals. It was deemed most suitable for Lebanon and may be an option for countries with relatively low fracture rates, such as countries from the Middle East, Asia, and Latin America.

No model can universally fit the profile and needs of all countries. In addition to fracture risk considerations, country-specific treatment decision must take into account the burden of osteoporosis and its treatment, including drug therapy and health resources, within the context of health care resources, healthcare priorities,

versus other competing non-communicable diseases, and societal willingness to pay. In low to moderate fracture risk countries, with limited resources, a hybrid model may be suitable. Further research investigating the applicability of different models in various countries, guided by prospective cohort data, would help to better identify the most suitable country-specific model.

Appendix

Table 3 Age-dependent FRAX-derived intervention thresholds and corresponding proportions of women, with and without prior major fractures, exceeding these thresholds

Age group (years)	NOGG-like defined intervention threshold (10-year probability MOF)	Estimated proportion (%) of women (including those with prior MOF) above the threshold	Estimated proportion (%) of women with prior MOF above the threshold	Estimated proportion (%) of women without prior MOF above the threshold
50–54	1.8–2.6	12	1	11
55–59	2.8–4	18	4	14
60–64	4.4–5.8	24	7	17
65–69	6.3–9	26	8	18
70–74	9.7–14	25	8	17
75–79	15–20	24	8	16
80–84	21–26	21	7	14
85–89	27–30	20	7	13

The NOGG-like intervention thresholds were calculated, using the Lebanese FRAX online calculator, for a woman with a history of previous fracture, BMI 30 kg/m^2, and no other risk factors (http://www.shef.ac.uk/FRAX; Accessed in April 2016)

Proportions rounded to the nearest integer
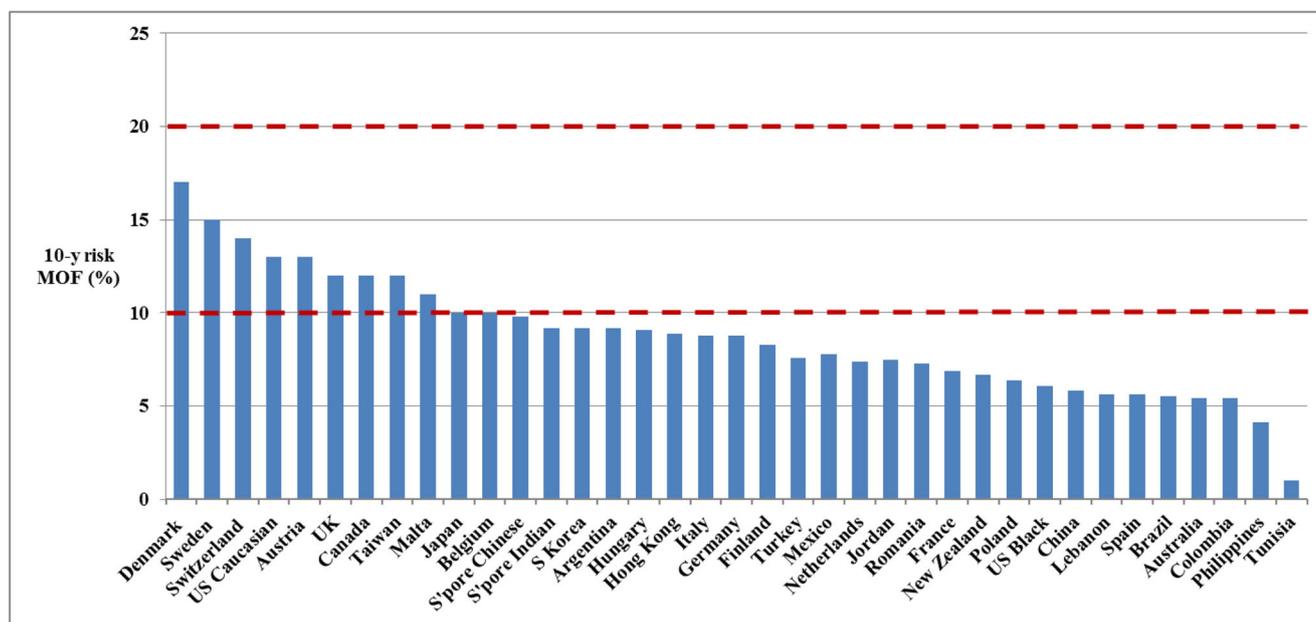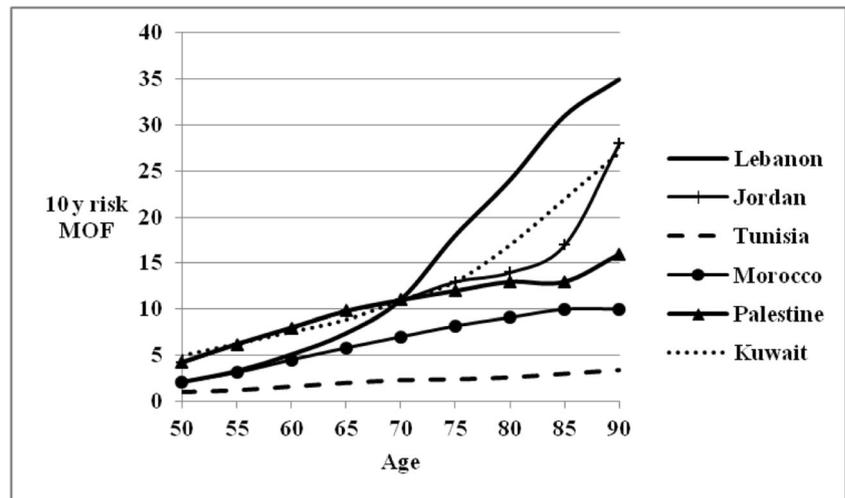
MOF major osteoporotic fracture

Fig. 5 Ten-year probability for major osteoporotic fracture (MOF) by country, in women age 65 years, BMD T-score −2.5, and BMI 25 kg/m^2. The 10-year probability for MOF was calculated, using country-specific FRAX online calculator (http://www.shef.ac.uk/FRAX, accessed in April 2016)

Fig. 6 NOGG-like approach to define intervention thresholds based on the FRAX-derived 10-year probability of major osteoporotic fracture (MOF), in women from Middle East countries. The 10-year probability for MOF was calculated, using country-specific FRAX online calculator (http://www.shef.ac.uk/FRAX, accessed in April 2016)

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