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ORIGINAL ARTICLE

Assessing the risk of osteoporotic fractures: the Ecuadorian FRAX model

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Abstract

Summary The FRAX tool incorporates data on the incidence of fractures and mortality in each country. The epidemiology of fractures changes over time, this makes it necessary to update the specific FRAX model of each population. It is shown that there are differences between old and new FRAX models in older individuals.

Purpose A new FRAX® model for Ecuador was released online in April 2019. This paper describes the data used to build the revised model, its characteristics, and how intervention and assessment thresholds were constructed.

Methods The national rates of hip fracture incidence standardized by age and sex from the age of 40 years for 2016 were used to synthesize a FRAX model for Ecuador. For other major fractures, Ecuadorian incidence rates were calculated using ratios obtained in Malmö, Sweden, for other major osteoporotic fractures. The new FRAX model was compared with the previous model released in 2012. Assessment and intervention thresholds were based on age-specific probabilities of a major osteoporotic fracture equivalent to women with a previous fracture.

Results Fracture incidence rates increase with age. The probability of hip or major fractures at 10 years increased in patients with a clinical risk factor, lower BMI, female sex, a higher age, and a lower BMD T-score. Compared to the previous model, the new FRAX model gave similar 10-year fracture probabilities in men and women age less than70 years but substantially higher above this age. Notwithstanding, there were very close correlations in fracture probabilities between the two models (> 0.99) so that the revision had little impact on the rank order of risk.

Conclusions The FRAX tool provides a country-specific fracture prediction model for Ecuador. This update of the model is based on the original FRAX methodology, which has been validated externally in several independent cohorts. The FRAX model is an evolving tool that is being continuously refined, as the databases of each country are updated with more epidemiological information.

Keywords FRAX model · Hip fracture · Osteoporosis · Ecuador

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Introduction

Osteoporosis is a major public health problem because its most feared consequence, fractures, are a cause of high morbidity, mortality, and health expenditure worldwide [1]. Due to this enormous burden, the assessment of the individual risk of fracture is important so that treatment can be effectively targeted [2].

To calculate the risk of specific fractures in each country, it is necessary to know the epidemiology of hip fractures and/or other major osteoporotic fractures (humerus, forearm, or clinical vertebral fractures), as well as the mortality respective [3].

It is estimated that at the age of 50 years, the remaining lifetime risk of fracture in Sweden is 50% for women and 25% for men [1], but the risk of suffering a hip fracture and other osteoporotic fractures varies markedly worldwide [4, 5].

The difference in the incidence of hip fracture between countries is much greater than the differences between sexes within a country. In fact, a difference in the incidence of hip fractures greater than 10 times has been published in different countries, which is much greater than the measurement errors that occur in such studies [4, 5]: variations of this magnitude have been reported in prospective studies conducted in Europe using a common methodology [6].

The age- and sex-specific risk of death also differ between countries, and this variation contributes to the heterogeneity in the calculations of the fracture probability [7]. Because of this, FRAX models are calibrated for those countries where the epidemiology of fracture and death is known [8].

Information on the epidemiology of fractures in Ecuador is scarce [9, 10], however, recently, information has been updated on the incidence of hip fracture in Ecuador [11, 12]. In 2010, the first version of the FRAX Ecuadorian model was generated for the prediction of risk of osteoporotic fractures and released in January 2012 (https://www.sheffield.ac.uk/FRAX/tool.aspx?country=43); since then the risk of fracture has been evaluated in 23,890 individuals. In 2018, a FRAX model was considered for 7 countries in Latin America, including Ecuador [13], but the heterogeneity of intervention thresholds between countries indicated that, rather than adoption of a global Latin American model, country-specific FRAX models are appropriate. In the present study, the national incidence of hip fractures specific to age and sex in the population of 40 years or older of Ecuador in 2016 is used for the incorporation of a new FRAX model. The development of this new Ecuadorian FRAX model is described and it is used to determine the thresholds of assessment and intervention for the treatment of osteoporosis specific to Ecuador.

Methods

The Republic of Ecuador is located northwest of South America and extends from the latitudes 1° N to 4° S. Mainland Ecuador has 3 continental geographic regions: the coast or littoral of the Pacific, the Andean region of the center of the country (Highlands), and the eastern region (Amazonia). Ecuador also includes an island province, the Galapagos Islands, in the Pacific Ocean. The Ecuadorian population has a high degree of ethnic mixture (white and indigenous race) that shows some variation between the different regions. In 2016, the population of Ecuador was 16,384,534 inhabitants, of which 4,991,258 (30.5% of the total population) were 40 years or older [14]. The Hospital Discharges Yearbook of 2016 was used to extract the information of people age 40 and older hospitalized with the main diagnosis of hip fracture from January 1 to December 31, 2016. The Hospital Discharges Yearbook is part of the National Surveillance System carried out annually by the Instituto Nacional de Estadisticas y Censos del Ecuador (INEC) [15], which records the discharges of all public and private hospitals in Ecuador. The data extracted from the hospital records contain information related to demographic and administrative data, hospital discharge status, and primary discharge diagnosis [15]. The diagnosis of hip fracture was recorded according to the International Classification of Diseases, tenth revision, clinical modification (S72.0-S72.1 and S72.2). The rates of crude incidence, specific age, and sex were calculated for the age groups 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, 90–94, and 95–97 years.

To calculate the incidence rates per 100,000 inhabitants/year, the projection of the Ecuadorian population by age and sex for 2016 prepared by the Economic Commission for Latin America and the Caribbean (CELAC) was used as the denominator [14]. We calculated the incidence standardized by age by the direct method using reference population (40 or more years) for Latin America prepared by the Latin American and Caribbean Demographic Center (CELADE)—Population Division of CELAC, published in 2016 [14]. The statistical analysis of the data was carried out with the EPIDAT computer program. Version 4.2 [www.sergas.es/Saude-publica/EPIDAT]. A value of $p < 0.05$ was considered statistically significant.

The recently published data on hip fracture risk [11] were smoothed using a piecewise linear model with breakpoints at 62, 72, and 92 years of age permitting the calculation of hip fracture risk as a continuous function of age. The incidence of other major osteoporotic fractures (clinical spine, distal forearm, and proximal humerus) was not determined, and it was assumed that age- and sex-specific rates found in Malmö, Sweden [16], were comparable to those of Ecuador. This algorithm has also been used for many of the FRAX models with incomplete epidemiological information [17, 18]. The information available suggests that the pattern of fracture standardized by sex and age is very similar in Europe, Canada, and Australia [19–22]. National mortality rates used data from the UN [23].

Comparison of models

For the purpose of comparing the updated FRAX model and the older version (version 3.5), the probabilities of a major osteoporotic fracture (hip, clinical spine, forearm, and humeral fractures) were computed in men and women at ages 50, 60, 70, and 80 years for all possible combinations of clinical risk factors at BMD T-scores between 0 and −3.5 SD in 0.5 SD steps with a BMI set to 25 kg/m^2 [24, 25]. Thus, we considered all combinations of six risk factors and eight values of BMD giving a total number of 512 combinations. Note that this was not a population simulation but an array of all possible combinations. The correlation between the probabilities derived from the surrogate and authentic models was examined by piecewise linear regression with knots at the probabilities of 10, 50, and 90 percentiles for each age. Tabular data were used to compare probabilities between the two versions at the 10th, 50th (median), and 90th percentile of the distribution of the original model. Differences in the revised model from the original model at these percentiles were expressed as 95% tolerance intervals (TI).

Fracture risk assessment

FRAX was used to determine an intervention threshold defined as the fracture probability at which physicians may decide to intervene. To obtain the intervention threshold with the Ecuadorian FRAX model, we use the approach recommended by the UK National Osteoporosis Guideline Group (NOGG) [26, 27] and the European guidance (ESCEO-IOF) [28]. This approach characterizes the intervention threshold as the probability of age-specific fracture risk equivalent to the 10-year probability of a woman with a previous fragility fracture in a woman with a body mass index equal to 25.0 kg/m^2 and a previous fracture, without BMD and without other clinical risk factors.

Using this same approach, two assessment thresholds were calculated and applied to the intervention threshold previously described. An upper and a lower assessment threshold was defined to delineate a range of fracture probabilities between which a bone mineral density (BMD) test might be recommended. The lower assessment threshold was the probability of age-specific fracture for a woman with BMI equal to 25.0 kg/m^2, without previous fracture, and without clinical risk factors. The upper assessment threshold (UAT) was the threshold probability above which treatment can be recommended without the need to measure BMD [18, 28]. The upper assessment threshold was set at 1.2 times the intervention threshold [18, 28] since almost no individuals are reclassified from high to low risk following BMD measurement when the FRAX fracture probability (calculated without BMD) is 20% or more above the intervention threshold [29, 30].

Results

Incidence of hip fracture

A total of 2205 cases of hip fractures (HF) were recorded in 2016, 677 in men and 1528 in women, aged 40 years or older (M/F = 2.2). In both sexes, the annual incidence per 100,000 people increased with age. The incidence of hip fracture was higher in men than in women up to the age of 60 years and thereafter became much higher in women (almost double in age 70–89 years). The empirical data are shown in Fig. 1 together with the logarithmic regression.

FRAX probability of fracture calculated without BMD

The probability at 10 years of hip fracture increased progressively with age in men and women, even in the absence of other clinical risk factors (Suppl Fig. 1). In contrast with the incidence of hip fracture, the 10-year probability of hip fracture was not higher than that of women at younger ages due to the competing effect of mortality (higher death risk in men).

As expected, the probability of sustaining a major osteoporotic fracture was higher than the probabilities of hip fracture in all ages (Tables 1 and 2). Each of the clinical risk factors contributed independently to the fracture probability (see Tables 1 and 2).

Smoking and alcohol intake were relatively weak risk factors. In women at the age of 80 years, for example, the probability of a major osteoporotic fracture in smokers was 16% higher than women of the same age with no clinical risk factors (6.6/5.7 = 1.16). In the case of increased intake of alcohol, the respective ratio was 1.33. A history of fracture in parents was associated with greater increase in risk ratio risk (2.11 at 80 years). Intermediate probability increases were associated with prolonged use of glucocorticoids, rheumatoid arthritis, and a previous fragility fracture at the age of 80 years.

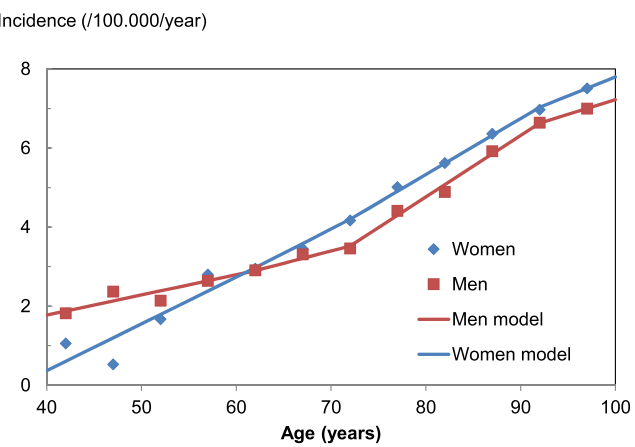

Fig. 1 Hip fracture incidence (yearly rate/100,000) by age and sex. The lines show the logarithmic regression and the symbols the empirical data

Table 1 Ten-year probability of a major fracture (%) in men and women according to the presence of clinical risk factors (CRF) in the absence of BMD. BMI is set at 25 kg/m^2

CRF	Age (years)				
	50	60	70	80	90
Men					
No clinical risk factors	0.4	0.6	1.2	2.7	3.9
Alcohol (3 or more units daily)	0.5	0.7	1.5	3.7	5.3
Rheumatoid arthritis	0.6	0.8	1.8	4.2	6.1
Glucocorticoid use	0.7	0.9	2	4.2	5.8
Current smoking	0.5	0.6	1.3	3	4.3
Family history of hip fracture	0.9	1.1	2	6.2	9.6
Previous fracture	1	1.2	2.3	4.5	6.3
Women					
No clinical risk factors	0.6	0.8	2.2	5.7	7.3
Alcohol (3 or more units daily)	0.7	1	2.8	7.6	9.7
Rheumatoid arthritis	0.8	1.2	3.2	8.6	11
Glucocorticoid use	0.9	1.4	3.8	9.4	11
Current smoking	0.6	0.9	2.5	6.6	7.9
Family history of hip fracture	1.1	1.6	3.7	12	15
Previous fracture	1.2	1.8	4.3	9.5	12

FRAX probability of fracture calculated with BMD

The probability at 10 years of sustaining a major osteoporotic fracture for women without clinical risk factors according to age and T-score is shown in Fig. 2. Up to the age of 80 years, probability of fracture increased with decreasing T-score. Thus, the T-score for any given fracture probability increased with age. For example, in a woman at the age of 50 years without clinical risk factors, a 3.6% probability of sustaining a major osteoporotic fracture required a T-score of − 4 SD. The same fracture probability at the age of 80 years was achieved with a T-score of − 1.5 SD.

Table 2 Ten-year probability of a hip fracture (%) in men and women according to the presence of clinical risk factors (CRF) in the absence of BMD. BMI is set at 25 kg/m^2

CRF	Age (years)				
	50	60	70	80	90
Men					
No clinical risk factors	< 0.1	0.1	0.4	1.4	2.4
Alcohol (3 or more units daily)	< 0.1	0.1	0.6	2.2	3.7
Rheumatoid arthritis	0.1	0.2	0.7	2.5	4.3
Glucocorticoid use	0.1	0.2	0.7	2.5	4
Current Smoking	< 0.1	0.1	0.5	1.9	3.1
Family history of hip fracture	< 0.1	0.1	0.8	4.9	8.2
Previous fracture	0.1	0.3	0.8	2.2	3.8
Women					
No clinical risk factors	< 0.1	0.1	0.6	2.6	3.6
Alcohol (3 or more units daily)	0.1	0.2	1	3.9	5.5
Rheumatoid arthritis	0.1	0.2	1.1	4.5	6.3
Glucocorticoid use	0.1	0.3	1.3	5	6.2
Current smoking	0.1	0.2	0.9	3.6	4.7
Family history of hip fracture	0.1	0.2	1.3	8.8	12
Previous fracture	0.2	0.4	1.3	4	5.6

Comparison of models

The relationship between the probabilities of a major osteoporotic fracture derived from the new and the earlier version of FRAX is shown for women aged 50 to 80 years in Fig. 3 At all ages, there was a close correlation between the two estimates ($r > 0.99$). The revised version gave similar probabilities as the original model at the ages of 50 and 60 years. At the age of 70 and 80 years, the revised version gave higher probabilities than the original model.

In men, the effect of the revision was qualitatively similar to that in women (Suppl Table 1). In the case of hip fracture probability, there was also a close correlation between the two estimates ($r > 0.99$) at all ages. As was the case for a major osteoporotic fracture, the revised version gave higher estimates than the original model at older ages (data not shown).

Intervention thresholds

The fracture probabilities of a major osteoporotic fracture equivalent to a woman with a previous fragility fracture are shown in Fig. 4. The probability increased with age, from 1.2% at age 50 to a peak of 12.6%, at the age of 87 years. The upper and lower assessment thresholds, between which the BMD tests are of greatest value, are also shown.

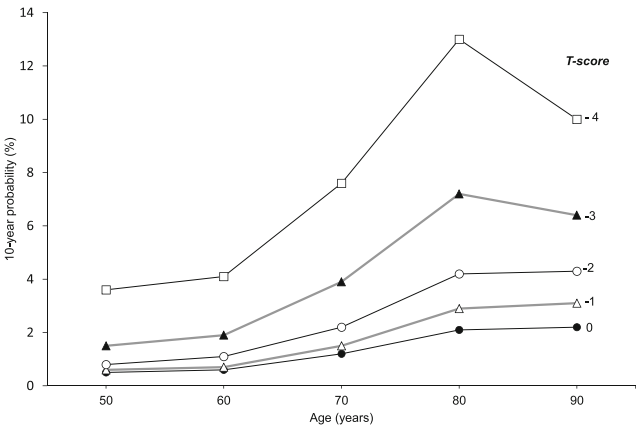

Fig. 2 Ten-year probability of a major osteoporotic fracture for women with a BMI of 25 kg/m2 according to age and BMD T-score for femoral neck BMD in the absence of other clinical risk factors

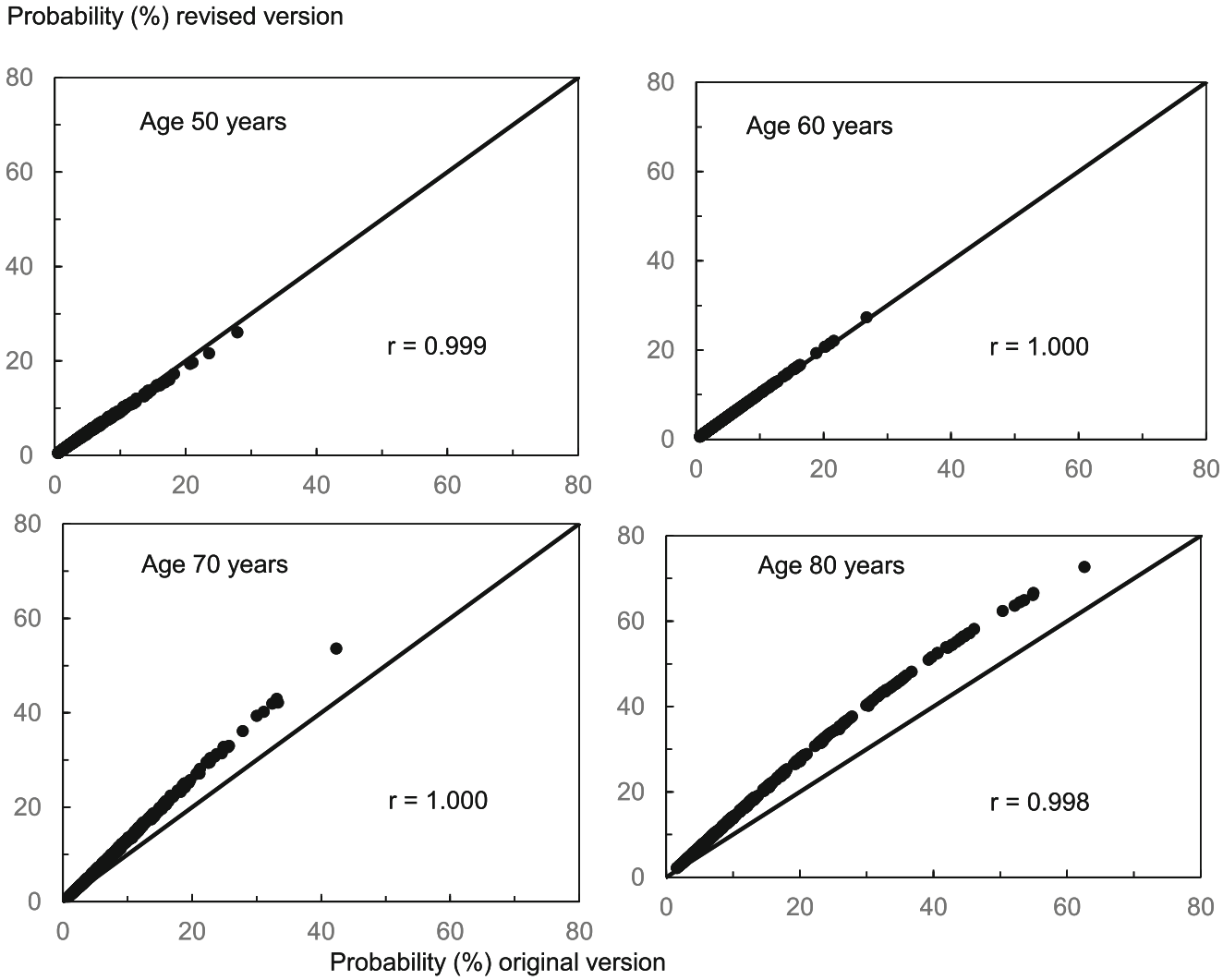

Fig. 3 Comparison of 10-year probability of a major osteoporotic fracture using the original FRAX tool for the Ecuadorian female population and the revised tool for multiple clinical scenarios. The diagonal line indicates the line of identity

Discussion

In this study, the incidence of hip fracture based on recent data from the national population of Ecuador [11] was used to update the FRAX model for Ecuador. This revised model showed similar FRAX probabilities for hip and major osteoporotic fractures at younger ages, but there was a substantial increase in probabilities at older ages in the revised model. Interestingly, while the incidence of hip fracture was higher in men than in women between the ages of 40 to 59 years, the 10-year probability of hip fracture was similar between sexes in this age group; this disparity reflects a higher death risk in men than women in this age group which competes with the fracture hazard in the calculation of probability.

Importantly, the revision had little impact on the rank order of fracture probability. Correlation coefficients between the two models for fracture probability exceeded 0.99 so that one can be accurately predicted from the other; i.e., an individual at the 90th percentile of risk with the original model would still be at the 90th percentile of risk using the revised FRAX tool. However, the identification of higher absolute fracture probabilities at older ages by the revised FRAX model has important ramifications for the potential numbers identified for treatment (for example, if a single threshold value for intervention was to be adopted) and is critically important for health economic analysis.

The present study also describes the application of the new FRAX model to a potential management algorithm for clinical practice. The proposed intervention threshold is based on the fact that many international osteoporosis guidelines recommend intervention in women with a previous fragility fracture [28, 31–33]. From this, it follows that individuals with a fracture probability that is equal to or greater than of women with a previous fragility fracture should be offered treatment even with

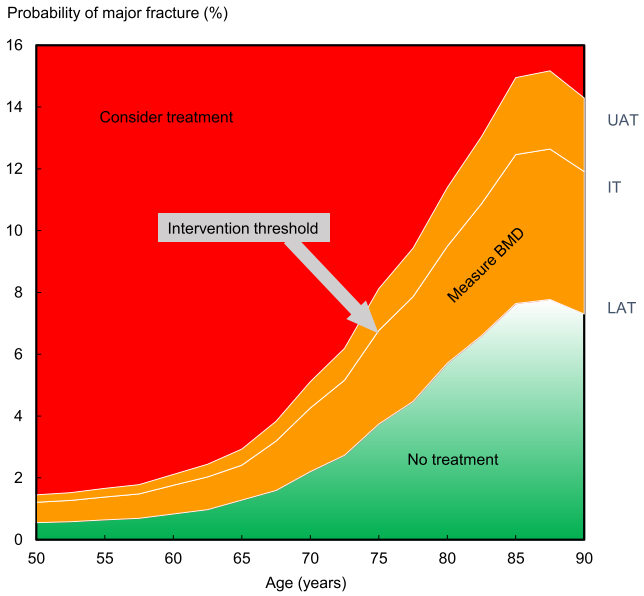

Fig. 4 Assessment guidelines based on the 10-year probability of a major osteoporotic fracture (%). The line within the orange area denotes the intervention threshold (IT). Where assessment is made in the absence of BMD, a BMD test is recommended for individuals where the probability assessment lies between the lower assessment threshold (LAT) and the upper assessment threshold (UAT) in the orange region

no past history of fracture. The intervention threshold is age-specific and ranged from 1.2% at the age of 50 years to 12% at the age of 90 years. According to this, women who have a fracture probability that is equal to or exceeds that of a woman with a previous fracture would be eligible for treatment even in the absence of a previous fracture. For example, a 65-year-old Ecuadorian woman whose mother had a hip fracture and has a T-score of − 2.0 SD has a 2.8% fracture probability that exceeds the risk in a woman of the same age with a previous fracture and without other CRFs (2.5%, BMI of 25 kg/m^2). In contrast, an 80-year-old woman (no clinical risk factors) with a T-score of − 2.5 SD has a fracture probability (5.4%) that is well below the intervention threshold for that age (9.4%). Therefore, intervention thresholds based on fracture probabilities appropriately target treatment to those with a higher age-specific risk rather than those solely with BMD-defined osteoporosis [18]. Measurement of BMD does, however, improve the categorization of patients at high or low risk, and for this reason, the proposed algorithm provides evaluation thresholds for use with BMD so that the latter result can be integrated into a further FRAX calculation. Such a strategy has been shown to identify patients at risk of hip fracture with a much more efficient use of DXA resources than strategies where BMD is measured in all, particularly at younger ages [34]. Furthermore, electronic linkage between FRAX models and national guidelines for assessment and treatment can readily facilitate access by primary care health professionals [35]. A recent primary care–based study has shown a significant reduction in hip fracture incidence using FRAX as a primary care assessment tool to target treatment [36].

The present study has several strengths and limitations. It is based on recent hip fracture data from Ecuador, though the data on hip fracture rates are retrospective and based on only 1 year of observation [11]. However, the information was obtained from official national sources that collect data from all public and private hospitals throughout the country [11], so the results are representative of the entire population of Ecuador. Our study did not have access to information about the incidence of other major fractures (humerus, forearm, or clinical vertebral fractures), so that, as has been done in many other FRAX models, the incidences of these were estimated from the incidence of hip fracture in Ecuador and the relationship between hip fracture and fracture at other sites in Malmö (Sweden) [19, 22]. While unproven that the relationship between the incidence of hip fracture and the incidence of other major fractures is similar in Ecuador and Sweden, this seems to be true for the various countries where this has been tested [20–22].

Conclusions

The FRAX model is an evolving tool that can be continuously refined. While the calculation tool has been stable since its launch in 2008, its calibration is dependent on the adequacy and recency of epidemiological information on fracture and mortality. The revised Ecuadorian FRAX model provides a quantitative estimate of risk fracture that eliminates the uncertainty of the qualitative risk assessment by an individual professional. It incorporates important data on increased fracture rates at older ages. Finally, the analysis provides insight to how this might be translated into clinical practice, in a manner similar to accredited strategies elsewhere, so that inroads can be made in the reduction of the fracture burden in Ecuador.

Research and studies requiring access to public-use surveys and data sets (e.g., INEC) [15] are excluded from the need for approval by an Ethics in Research Committee. Even so, this study was reviewed and approved by the Ethics Committee of the Teaching Hospital of the National Police Guayaquil No. 2.

Compliance with ethical standards

Conflict of interest None.

Ethics statement This study was reviewed and approved by the Ethics Committee of the Teaching Hospital of the National Police Guayaquil No. 2.

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