Osteoporosis is a systemic skeletal disease characterized by low bone mass and deterioration of bone microarchitecture leading to fractures secondary to minimal trauma. Vertebra, hip and forearm are common sites of these fragility fractures. The frequent association between fragility fractures and an increase in morbidity and mortality makes osteoporosis a huge socioeconomic and public health burden for many countries. This chronic bone disorder affects mainly postmenopausal women but can also develop in older man. It is calculated that at the age of 50 years, the lifetime fracture risk is 50% for women and 25% for men.

Predictions based on epidemiological studies reveal a continuous increase in the world’s population, probably reaching approximately 7.5 to 10.5 billion people by the year 2050. It is noteworthy that Latin America and the Caribbean region account for 9% of this global population. Brazil, the biggest country in Latin American (LATAM), is the fifth most populous country in the world and accounts for 32% of the individuals in this region. The International Osteoporosis Foundation (IOF) published, in 2012, a large epidemiological report – the Latin America Regional Audit – that gathered information from a literature search and/or provided by key opinion leaders on the burden of osteoporosis in 14 countries from Latin America. Firstly, this Audit showed that, although the current percentage of people 50 years of age and older lies between 13 and 29% in those countries, it is estimated that by 2050 these figures will be 28 to 49% with a 280% increase in the 70 and over population. The aging of these populations is a matter of concern due to the many diseases that mainly affect older people, including osteoporosis and its related fragility fractures. In LATAM, the current data on osteopenia and osteoporosis is scarce, but some studies bring good epidemiological information. Based on these, models for the FRAX calculation tool regarding the absolute risk for fragility fractures were constructed for 6 countries in LATAM: Argentine, Brazil, Chile, Colombia, Ecuador and Mexico.

FRAX® is a computer-based algorithm developed by the Centre for Metabolic Bone Diseases, University of Sheffield Medical School, UK, first released in 2008 (http://www.shef.ac.uk/FRAX) 3,4. The algo-
rithm, calculates the 10-year probability of a major fracture (hip, clinical spine, humerus, or wrist) and the 10-year probability of hip fracture in postmenopausal women and men aged 50 years or older.

Fracture risk is readily calculated from age, body mass index (BMI) and dichotomized (yes or no) clinical risk factors (CRFs) comprising prior fragility, parenteral history of hip fracture, current tobacco smoking, long-term oral glucocorticoid use, rheumatoid arthritis, other causes of secondary osteoporosis, and alcohol consumption. Rheumatoid arthritis and long-term use of glucocorticoids are risk factors independent of their action on BMD, the other secondary causes of osteoporosis considered in the algorithm are assumed to influence the increased risk for fracture by their lowering of BMD.

The bone mineral density (BMD) of the femoral neck can be optionally entered to enhance fracture risk prediction, but the FRAX algorithm output can be calculated without this information. If available, the inclusion of BMD in the calculation of fracture probability improves the accuracy of the assessment but it is most needed in individuals in whom fracture probabilities lie close to an intervention threshold. This is defined as the fracture probability at which physicians may intervene.

Fracture probability differs greatly in different parts of the world, and the FRAX calibration has been made individually for each country where the epidemiology of hip fracture and death is published. The FRAX model is unique because unlike other algorithms, fracture probability is computed by taking the risk of fracture and the risk of death into account. The inclusion of risk of death is important because individuals with an immediate probability of death are less likely to suffer from fractures than those with longer life expectancy. In addition, some risk factors affect the risk of death as well as the risk of fracture. Examples include increasing age, low BMI, low BMD, long-term use of glucocorticoids, and smoking.

The association between risk factors and fracture risk has been made individually for each country where the epidemiology of hip fracture and death is published. The FRAX model is unique because unlike other algorithms, fracture probability is computed by taking the risk of fracture and the risk of death into account. The inclusion of risk of death is important because individuals with an immediate probability of death are less likely to suffer from fractures than those with longer life expectancy. In addition, some risk factors affect the risk of death as well as the risk of fracture. Examples include increasing age, low BMI, low BMD, long-term use of glucocorticoids, and smoking.

Data from four Brazilian epidemiologic studies (table below) were collected and analyzed to obtain national data on the incidence of hip fracture and mortality. These studies have been conducted in the cities of Porto Alegre located in the South, Marilia in the Southeast, and Sobral and Fortaleza in the Northeast regions of the country.

The studies from Porto Alegre, Marilia, and Sobral were retrospective and the Fortaleza study was prospective.

The development and validation of the Brazilian FRAX model followed the method universally used for this tool. The risk factors used in the Brazilian model were based on a systematic set of meta-analyses of worldwide population-based cohorts and validated in independent cohorts with over a million patient-years of follow-up (please see reference 9 for more information).

For the clinicians, FRAX provides a quantitative estimate for fracture risk and, thereby eliminates the
uncertainty of an individual’s practitioner qualitative assessment of risk.

Regarding the intervention thresholds, the approach recommended by the National Osteoporosis Guideline Group (NOGG) in the UK 15,16 was used in the Brazilian FRAX model. This methodology sets the intervention threshold at the age-specific fracture probability equivalent to women (or men) with a prior fragility fracture. Where access to BMD testing is limited, FRAX can be calculated using BMI and the use of BMD can be optimized by only testing those individuals in whom probabilities are close to the intervention threshold at the age-specific fracture probability. Where access to BMD testing is limited, FRAX can be calculated using BMI and the use of BMD can be optimized by only testing those individuals in whom probabilities are close to the intervention threshold 15,17,18. In this way, testing is confined to individuals at high (or low) risk with reasonable likelihood to be reclassified at low (or high) risk on the basis of the BMD test. Following this approach, two assessment thresholds were calculated and applied to the intervention threshold described above:

The threshold probability below which neither treatment nor a BMD test should be considered (lower assessment threshold).

The threshold probability above which treatment may be recommended without the need for BMD (upper assessment threshold).

The results of this calculation were displayed in figures showing the fracture probabilities equivalent to women (or men) with a previous fragility fracture in the FRAX Brazil model. These figures will be soon available for clinical use in the website of the Brazilian Medical Association.

FRAX represents a significant advance in the assessment of both women and men at risk of osteoporosis-related fractures and allows the tailoring of pharmacological interventions to high-risk subjects. However, it has limitations and must be used only as a guideline. The practitioner clinical judgment will, and should, supplant any calculated value. Furthermore, it is a tool in evolution, being refined as the databases are updated with more epidemiological information.

REFERENCES