**General Practitioner and FRAX® (computer-based algorithm)**

Raffaella Michieli 1
Anna Maria Carraro 2

1 National Secretary, Italian College of General Practitioner, Firenze, Italy
2 General Practitioner, Dolo (Venezia), Italy

Address for correspondence:
Raffaella Michieli, MD
Via Fusinato 32
30174 Mestre (VE), Italy
Phone: +39 3386076480
E-mail: michieli.raffaella@simg.it

Summary

Osteoporotic fractures became the most important cause of disability and an increasing burden to the public health costs in Italy and in many regions of the world. Health professionals play a central role in identifying people at high risk of osteoporosis and osteoporotic fractures. However, it is important to have available methods that allow to identify patients showing high risk of fragility fractures, with lower costs and high sensitivity than those currently adopted, e.g. Dual Energy X-ray Absorptiometry (DEXA).

The computer-based algorithm (FRAX®) developed by WHO shows some barriers in primary care, for instance the difficulty to access this tool by General Practitioners (since it is not available in their DATABASE). Moreover, since the incidence of fracture and the prevalence of associated risk factors change over time, risk prediction algorithms need to be dynamic, so that they can be remodelled over time. In Italy, the Health Search - CSD Longitudinal Patients Database (HSD) could potentially provide the data needed to support the development and validation of an applicable prediction tool in primary care.

In this framework we aim to develop and validate a prognostic score for osteoporotic fractures in Italian General Practice and to establish a risk map.

KEY WORDS: osteoporosis; fractures; prevention; Health Search Database (HSD); FRAX.

Osteoporosis is a relevant issue in the context of public health systems since, due to the progressive population ageing, osteoporotic fractures became the most important cause of disability and an important increasing burden to the public health costs in Italy and in many regions of the world (1).

Health professionals play a central role in identifying people at high risk of osteoporosis and osteoporotic fractures. Many patients may already be suffering from the ‘silent disease’ without knowing, as osteoporosis can progress without any signs or symptoms. For General Practitioners there is a real opportunity to improve the investigation of patients and combat the progression of the disease. Their role consists in applying the best practice approach in:

- identifying, diagnosing, treating and managing, in a timely and accurate manner, men and women who are at low, medium, high risk of fracture;
- identifying, diagnosing, treating and managing, in a timely and accurate manner, men and women who have been diagnosed with at least one minimal trauma fracture;
- reducing the progression of such individuals to a second fracture;
- optimizing patients and their access to information, understanding of the condition and involvement in its management in order to help patients improve their health status.

In the current process of population ageing, it was estimated that in 2020 about 4.7 millions women will be affected by osteoporotic fractures and that, in the same year, the potential cost of osteoporotic hip fractures will increase by 80% compared to current cost. The “Studio Epidemiologico sulla Prevalenza di Osteoporosi” (Osteoporosis Prevalence Epidemiology Study), carried out in Italy in 2002 considering 6811 postmenopausal women (age: 40-80) and 4981 men (age: 60-80), estimated that 23% of women and 14% of men are affected by osteoporosis. Women showed a risk of being affected by osteoporosis 4 times higher than men. Moreover, 50% of women and 12.5% of men aged >50 ys were subjected to at least one fracture in their life (2).

According to a study based on 2002 data, the total costs (hospitalization, rehabilitation, disability retirement found and indirect costs) of hip fractures in patients older than 65 ys reached, in Italy, the value of 1075 millions €, considering an estimated number of fractures greater than 80000. Thus the impact of the disability connected to hip fractures on the Italian National Health System is close to that related to the coronary heart disease (3).

Common sites for osteoporotic fracture are the hip, spine, proximal humerus and distal forearm. These fractures are repetitive and characterized by an increasing seriousness over time. Among them, the most serious are hip fractures, since they are associated with limited functional recovery, and they cause reduction of social activity, mortality and disability (4). In such fractures, death occurs in 20% of patients within the first year after fracture, enduring disability in 30% of them, 40% can’t walk autonomously, 80% can’t conduct daily activities autonomously (5).

Another study carried out in Italy (6) assessed the survival probability of men and women in the years following a hip fracture and compared such results to the general population. This study showed that, after two years a hip fracture occurs, the survival probability is reduced by 50% in men and slightly less in women; life expectancy is significantly lower than the general population.
Hence, these results suggest that it is necessary to develop actions aimed at reducing disability and related health costs, by means of the prevention of primary fractures, as well as their treatment and rehabilitation.

In this framework it is important to develop methods aimed at identifying patients showing high risk of fragility fractures, an objective that deserved a wide international consensus. Indeed, although Bone Mass Density (BMD) measurement at the femoral neck with Dual Energy X-ray Absorptiometry (DEXA) is a strong predictor of the osteoporotic fracture risk (7) and it is useful for the decision to begin a following pharmacological osteoporosis therapy, there have been several issues associated with its use as a clinical diagnostic test.

Moreover such approach cannot be efficiently used as exclusive screening tool in primary care because of its relevant cost and low sensitivity (8). Accordingly, less expensive and more practical methods for assessing individuals at high, medium and low risk of osteoporotic fractures is a health care requirement. Therefore in recent years several researches aimed at identifying factors other than BMD that might be able to predict the fracture risk were carried out.

In this context the WHO has identified seven clinical risk factors (previous fragility fracture, parental history of hip fracture, current smoking, glucocorticoid treatment, alcohol intake 3 or more units daily, low body mass index, rheumatoid arthritis) that in conjunction with age and sex would be able to assess fracture probability, independently from BMD (8). A further objective of WHO was to develop a computer-based algorithm (FRAX®) to determine an absolute fracture risk score in general practice that could be independent from BMD. This prediction tool has a higher sensitivity and allows General Practitioners to be more appropriate in detecting patients at low, medium, high risk of fracture (9), as well as in defining which intervention threshold should be adopted for the prevention of fragility fractures (10).

However FRAX® shows some barriers in primary care; first of all the difficulty to access to this tool by General Practitioners (that should use it in their daily practice), since it is not available in their DATABASE.

Furthermore, since the incidence of fracture and the prevalence of associated risk factors change over time, the methods to derive the risk prediction algorithms need to be dynamic, so that they can be remodelled over time.

In Italy, the Health Search - CSD Longitudinal Patients Database (HSD) could meet such requirement. It is an Italian General Practice (GP) database that comprises data given by computer-based patient records of a selected group of over 900 Primary Care Physicians (PCPs). PCPs voluntarily agreed to collect patient information and to attend specific training courses for data entry. The HSD contains patients’ demographic details that are linked through the use of an encrypted code with clinical records (diagnoses, referrals, and tests results), drug prescriptions (drug name, date of the filled prescription, and number of days’ supply), prevention records, hospital admissions, and the date of death. To be considered for participation in epidemiological studies, PCPs should meet “up-to-standard” quality criteria pertaining to the levels of coding, prevalence of well-known diseases, mortal-

### Table 1 - Multivariable Poisson regression of the association between baseline clinical characteristics and 5-year fracture risk in women (12).

<table>
<thead>
<tr>
<th></th>
<th>All fractures</th>
<th>Hip fractures</th>
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</thead>
<tbody>
<tr>
<td><strong>Demographic characteristics</strong></td>
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<tr>
<td>Age strata</td>
<td></td>
<td></td>
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<tr>
<td>&lt;=60</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>65-69</td>
<td>1.68 (1.58-1.78)</td>
<td>2.77 (2.32-3.30)</td>
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<tr>
<td>&gt;=70</td>
<td>3.19 (3.02-3.37)</td>
<td>13.27 (11.37-15.50)</td>
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<tr>
<td><strong>FRAX® factors</strong></td>
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<tr>
<td>History of fracture</td>
<td>1.90 (1.75-2.06)</td>
<td>2.21 (1.93-2.52)</td>
</tr>
<tr>
<td>Use of corticosteroids</td>
<td>1.69 (1.42-2.01)</td>
<td>1.80 (1.34-2.43)</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>1.25 (1.07-1.46)</td>
<td>1.28 (0.97-1.69)</td>
</tr>
<tr>
<td>BMI &lt;=20</td>
<td>1.42 (1.23-1.63)</td>
<td>2.01 (1.61-2.50)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>1.08 (0.97-1.20)</td>
<td>1.13 (0.91-1.39)</td>
</tr>
<tr>
<td><strong>Other possible risk factors</strong></td>
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<tr>
<td>Osteoporotic diagnosis</td>
<td>1.42 (1.35-1.49)</td>
<td>1.30 (1.19-1.43)</td>
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<tr>
<td>Gastrointestinal disease</td>
<td>1.17 (1.10-1.25)</td>
<td>1.13 (1.00-1.29)</td>
</tr>
<tr>
<td>Chronic hepatic disease</td>
<td>1.33 (1.19-1.48)</td>
<td>1.38 (1.13-1.68)</td>
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<tr>
<td>Depression</td>
<td>1.24 (1.14-1.35)</td>
<td>1.36 (1.17-1.57)</td>
</tr>
<tr>
<td>COPD</td>
<td>1.22 (1.10-1.34)</td>
<td>1.24 (1.04-1.46)</td>
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<td><strong>Pharmacotherapy</strong></td>
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<tr>
<td>Anticonvulsants</td>
<td>1.49 (1.32-1.70)</td>
<td>1.61 (1.28-2.01)</td>
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</tbody>
</table>
ty rates, years of recording and the evaluation of missing values (11). A number of studies have been published confirming the research validity of the HSD information in conducting epidemiological research. It is also worth mentioning that the HSD allows to trace with accuracy large part of the major risk factors related to the occurrence of osteoporotic fractures. In fact, a study carried out in 2012 based on the use of primary care data, confirms a higher incidence of osteoporotic fractures among females when compared with males, as well as in the older population strata. Moreover, predictors of osteoporotic fractures were those expected to be identified by FRAX® algorithm in a general practice setting as well (12). When this study was initiated, 500 PCPs homogeneously distributed across all Italian areas, covering a patient population of 1,088,229 individuals, fitted the up-to-standard quality criteria (Table 1). All these elements suggest that, considering the clinical utility of a simple risk score for the assessment of absolute fracture risk among osteoporotic patients, its assessment and validation in the Italian HSD could potentially provide an applicable prediction tool in primary care.

With this approach we aim to develop and validate a prognostic score for osteoporotic fractures in Italian General Practice and to establish a risk map. The next steps of the project will be:

1) to assess the incidence of primary osteoporotic fractures and risk factors in 5-10 ys follow up (i.e. dynamic cohort of active patients, age 45-90 ys, included in the lists of the 700 general practitioners belonging to the network of health search);
2) to establish a predictive risk score for osteoporotic fractures by defining two distinct populations, a “derivation” population (used to assess initial osteoporotic fractures incidence risk scores and hazard ratios associated to the factor of risk) and a “validation” population used to test the multivariate model;
3) to validate the predictive risk scores by comparing predicted and observed risk in the validation population as well as indicators of model discrimination/efficiency (e.g. D-statistic, R², ROC, etc.) and test it in the validations population.

This is a challenging project but it is essential in order to improve the appropriateness of General Practitioner in osteoporosis therapy and the prevention of fragility fractures.

References