Consensual conclusions from the 1st Multidisciplinary Forum on the Management of Patients with High Risk of Fracture (HRF) due to Osteoporosis

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Summary
On the 12th and 13th of February this year the first Forum on High Risk of Fracture was held in Madrid, coordinated by Prof. Díaz Curiel under the auspices of SEIOMM, and with the sponsorship of Nycomed. Around 100 specialists in rheumatology, traumatology, rehabilitation, geriatrics, units of bone metabolism, internal medicine and endocrinology discussed, from a multidisciplinary perspective, the presentations prepared by the group coordinators based on the review of data published and having been previously discussed in two meetings by the members of the scientific committee. With the difficulties consequent to tackling such a complex theme, a consensus document was developed to reflect the clinical and multidisciplinary reality of the concept of "high risk of osteoporotic fracture". An extract of this document is presented here in summary, with the aim of bringing together the views from the different specialisms involved in the management of disease in this type of at risk patient in our country.
Introduction
In recent decades there has been a significant advance in knowledge related to osteoporosis, the fruits of which are, amongst other things, the definition operative since the year 2000 of the Consensus Conference of the National Institute of Health in the United States1, which defines osteoporosis as a skeletal disease characterised by reduced bone resistance which provokes an increase in the risk of fracture. This definition already makes it clear that low bone density, on the basis of which the disease has come to be diagnosed, is only one of multiple risk factors which are associated with the development of osteoporotic fractures. This allows us to explain that fractures may appear in subjects without densitometric criteria for osteoporosis and, inversely, that many patients with densitometric criteria do not suffer fractures.

Among these risk factors for fracture, female sex, old age, thinness, the presence of previous vertebral or non-vertebral fractures, low bone mass or the presence of diseases or treatments adverse to bone (rheumatoid arthritis or treatment with corticoids for example) have consistently been identified in different studies, systematic reviews and guides to clinical practice1-11. This has allowed the development of models which integrate information relating to different independent risk factors for the development of osteoporotic fractures with those which calculate the absolute risk of fracture in the following few years10,11. This information on the absolute risk of fracture in the following 5 or 10 years has received significant criticism due to its imprecision in some populations but, in any case it implies an advance at a time when giving an absolute value is much more informative for patients and doctors who are not experts in osteoporosis than concepts such as the T-score, the risk gradient or relative risk. These formulae also allow the calculation of thresholds for specific diagnostic interventions – for example a request for densitometry – or therapies – to start a specific treatment – which make them cost-effective.

According to recent studies, it is estimated that in our country there are at present 2,500,000 osteoporotic women and 500,000 osteoporotic men, accounting for 90,000 hip fractures, 500,000 vertebral fractures and 150,000 Colles fractures annually. The estimated costs, solely in the hospital environment, exceed 120 million euros. What is particularly notable is the fact that only 15% of women who have osteoporosis in Spain are being treated, or that almost 50% of people who suffered hip or wrist fracture did not receive any anti-osteoporotic treatment after that fracture. It is necessary therefore to define some risk profiles with which are associated a higher possibility of presenting osteoporotic fractures.

Material and method
On the 12th and 13th of February of this year the first Forum on High Risk of Fracture was held in Madrid under the auspices of SEOIMM, and sponsored by Nycomed. Some 100 experts in rheumatology, traumatology, rehabilitation, geriatrics, bone metabolism units, internal medicine and endocrinology, discussed, from a multidisciplinary perspective, the risk profiles according to each of their specialisms. The members of the scientific committee, in two earlier meetings in previous months, had discussed both the objectives of the Forum – the identification of profiles for high risk of fracture (HRF) – the methodology to be used – review of published evidence – and the introductory presentations which were made in the first part of the Forum.

After the presentations from the group co-ordinators those attending the forum were grouped according to their areas of work: traumatology, rheumatology, rehabilitation and geriatrics and bone metabolism units, where they discussed the evidence presented and reached a consensus within each group. Finally, back in a general session, the agreements reached in each of the groups were discussed and a general consensus reached, which is presented in this article.

Profiles for high risk from the working groups
Traumatology and orthopaedic surgery
The group of experts in orthopaedic surgery and traumatology indicated that although a clear definition of the exact profile and standard for an HRF patient, it would be possible to identify these people satisfactorily in daily clinical practice. It was proposed that the risk factors be stratified into two main groups: key factors (age, life experience, previous osteoporotic fracture and bone mass) and significant factors (independent of bone mass, concentration of vitamin D and falls). An age of 70 years was taken as the cut-off point for which the risk of fracture in the population was clearly raised in the cohorts evaluated. The presence of an earlier fracture is, evidently, one of the factors with most weight in the daily activity of this specialism. What happens also is that the risk of re-fracture after an osteoporotic fracture is not only raised but that this risk almost immediate with subsequent fractures happening in the first few months after the aforementioned fracture. The members of the group established that the presence of ≥ 2 vertebral fractures, or ≥ 2 non-vertebral fractures would be supposed to be HRF. Also considered to be HRF are those subjects with fracture of the hip due to their raised risk of re-fracture. In terms of bone mass, it is estimated that a bone mineral density (BMD) expressed as a T-score below lower than -3 in the hip also indicates HRF. Another factor noted by this group was vitamin D deficiency, with those patients with insufficient vitamin D (25(OH) < 30 ng/ml) older than 70 years of age with more than one vertebral fracture and/or more than one non-vertebral fracture also considered to have HRF. Lastly, the importance of falls (which trigger 90% of fractures of the hip) was also noted. The profiles from this group of HRF patients are shown in Table 1.
They also gave a positive evaluation to the new tools or systems of evaluation (FRAX®, Fracture Index®, FRAMO® and Q-Fracture®) which help the clinician to combine, qualify and quantify this risk factors.

On the management of patients with high risk of fracture, four types of measures to be taken were suggested:
1. Correction of modifiable risk factors.
2. Establishment of non-pharmacological measures (ensuring a sufficient protein-calorific supply, supply of calcium, repletion of levels of vitamin D).
3. Take pharmacological measures (with biphosphonates and/or PTH or its anabolic fragment with non-vertebral anti-fractural efficacy; sequential treatment with PTH or its anabolic fragment + maintenance of antiresorptive drug with non-vertebral anti-fractural efficacy).
4. Adoption of measures to prevent falls.

**In patients with previous fracture. One or more of:**

- Presence of ≥ 2 vertebral fractures
- Presence of ≥ 2 non-vertebral fractures which increase the risk of subsequent osteoporotic fractures
- Presence of one vertebral fracture and one non-vertebral fracture which increases the risk of subsequent osteoporotic fractures
- Existence of a hip fracture
- A patient with fragility fracture and a BMD in the hip < -3 SD should be considered to be HRF.

**In patients with rheumatoid arthritis. One of more of:**

- Postmenopausal women (especially those over 65 years of age)
- BMD similar to that for risk of postmenopausal osteoporosis
- Treated with corticoids at doses higher than 15 mg/day
- High disability index
- Extended illness
- Little physical activity

**In patients without a previous fracture. Two of more of:**

- Age > 70 years
- BMD in hip < -3 SD
- There is more than one major risk factor (parental history of osteoporotic fracture, rheumatoid arthritis, consumption of corticoids at doses > 7.5 mg/day for more than 3 months, early menopause)
- Vitamin D deficiency (< 30 ng/ml)
- Falls: should only be taken into account as a factor triggering an osteoporotic fracture, and not as an intrinsic defining factor for HRF.

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**Rheumatology**

This group of experts has classified the risk factors which are associated in a way that is most consistent with an increase in fractures in their patients into three groups: key (over 70 years of age; previous history of fragility fractures of the hip or vertebrae; intake of glucocorticoids ≥ 7.5 mg/day for three or more months and BMD (T-score) < -3; significant (maternal history of hip fracture; low body mass index (BMI < 20kg/m²), frequent falls in elderly people, low measures of physical activity and functions); and moderate (levels of 25 (OH) vitamin D < 30 ng/ml, some harmful factors related to lifestyle (smoking, excessive consumption of alcohol, sedentary lifestyle or excessive consumption of coffee)). Their consensual proposals for the evaluation of HRF on the basis of age and clinical risk factors are listed in Table 2.

The group indicated also the importance of taking a clinical history, carrying out a complete...
physical examination and a basic study, to discount secondary causes of osteoporosis (haematology with creatinine, calcium, phosphorus, alkaline phosphatase, PTH, TSH, free T4, 25(OH) vitamin D and urinary calcium), in addition to the measurement of BMD and a lateral spinal X-ray. The members of the group also stressed the usefulness of algorithms which estimate the individual risk of osteoporotic fracture such as the aforementioned FRAX® or QFracture®.

One of the most significant contributions of this group has been the identification of sub-groups of rheumatology patients with HRF due to the presence of diseases of their specialism which result in osteoporotic HRF, of which rheumatoid arthritis is the most significant. Finally, the members of this group propose the establishment of recommendations regarding indications for pharmacological treatment in accord with the evaluation of risk; in addition, they indicate that in patients at high risk of vertebral or hip fracture it is necessary to start drug treatment straight away with no delay being justified. In each patient it is necessary to identify and try to correct, if possible, risk and co-morbidity factors involved in osteoporosis, and to give general health promotion advice, to recommend supplements of calcium (1,500 mg/day) and vitamin D (800 UI/day), in addition to the specific treatment: in patients without fractures biphosphonates or anabolics (PTH or teriparatide (TRPT)) may be considered; in patients with anabolic fractures, PTH/TRPT preferably followed by biphosphonates.

Rehabilitation and Geriatrics

The members of this group stressed the absence of a national or international consensus which would allow a current definition of the concept of HRF. However, they indicate that the criteria set by Hamman and Lane, which identify as patients with HRF those which meet at least one of the following conditions: presence of previous osteoporotic fractures, accumulation of multiple risk factors for fractures (chronic secondary causes of osteoporosis, general fragility, history of osteoporotic fractures or high risk of falls due to physical limitations), failure (measured by means of two criteria: appearance of fractures during treatment or loss of BMD) or intolerance to earlier treatment, notable on the part of these specialisms being advanced age, skeletal factors, previous fragility fracture, falls, low body mass index, treatment corticoids, and physical inactivity.

The members of this group also identified, within their usual clinical practice, the presence of some diseases or conditions in which patients with HRF can be indentified. Notable among these are subjects with neurogenic osteoporosis: medullar lesion, ictus, multiple sclerosis, cranial-encephalic trauma and Parkinson’s disease. They also suggested that subjects with three or more falls in the last year be subsidiaries to be studied in order to discount the presence of osteoporosis. It was also highlighted by members of this group that a significant portion of their patients were found already to be in secondary or tertiary prevention due to having suffered fractures and their side effects; However, this group also recognised the advantage which the use of some scales for the calculation of risk of osteoporotic fractures, such as FRAX® and OST-T, even with their limitations, could bring.

Bone Metabolism Units

The Bone Metabolism Units are characterised by their specialisation and their multidisciplinary nature, in dealing with osteoporosis and the prevention of fractures. This group showed that nowadays it is not possible to define unequivocally, unarguably and reproducibly what is high risk of fracture, because it is difficult to establish a hierarchy and specific weight for the very diverse known determinants of the risk of fracture (Figure 1).

The main limitation to defining HRF arises from the difficulty of establishing what is high risk of fracture. Even the different reference guides (such as those of SEIOMM, NICE or NOF) do not manage to fix on one definition of HRF. And it is the fact that the mechanism of producing fractures is multifactorial which reduces considerably the possibilities of defining HRF, given that it is not known how many of these risk factors, and to what degree, are necessary to determine high risk of fracture.

This group cited various scales of transversal risk most commonly used such as Fracture Index®, OST®, FRAMO®, NOF®, ORAI®, SCORE®, ABONE® and more recently, FRAX® or Q-fracture®. Regarding FRAX®, it is indicated that while it presents a promising and sensible approach to dealing with the problem, it is inexact, with clear methodological limitations (not recording falls, and factors such as the degree of consumption of tobacco or alcohol); in addition, the cut-off point is arbitrary and is not based on scientific evidence, is independent in each country, and establishes an inevitable cost/benefit association. In fact in daily practice, the FRAX® scale is used frequently to suspend treatment in patients with low risk. In relation to QFracture®, it is suggested this scale also has inexactitudes and limitations, given that it does not record previous fractures, nor does it take into account family history; in the same way, an absence of a cut-off point is detected, which is also arbitrary and different for each country.

The Bone Metabolism and Internal Medicine Group also said that the only objective estimation of high risk which has been published is for a specific database (that used for QFracture®), which situates the 90th percentile of absolute risk of fracture of this cohort at 8.75% at 10 years in women and 2.11% in men, but there are no data which guarantee the applicability of these findings to Spain or to other countries. However, it was recognised that we all have a subjective perception of what it is to be “high risk”, and it is the case that the risk factors which lead to this concept are perfectly well established, their relative risk values being well known. What is more, it is assumed that the existing risk scales, especially FRAX® and Qfracture®, are useful tools to be used in a contexts
Table 2. Profile of High Risk of Fracture (HRF). Rheumatology Group

**Factors associated with HRF:**

- Advanced age > 70 years
- Previous fragility fracture (symptomatic or asymptomatic)
- Low BMD < 3 SD
- Maternal history of hip fracture
- Taking of corticoids (≥ 7.5 mg/day for more than 3 months)
- Low weight (BMI < 19 kg/m²)

**Special and common situations in rheumatology patients**

- Chronic inflammatory diseases with persistent activity
- Rheumatic polymyalgia and/or giant cell arteritis
- Transplant (distinguishing between pretransplant and postransplant)
- Frequent use of treatments which induce osteoporosis

**HRF in patients with rheumatological diseases**

**Steroidal osteoporosis:**
- Daily dose of corticoids higher than 15 mg
- Period of treatment longer than one year

**Rheumatoid arthritis:**
- Postmenopausal women (especially those over 65 years of age)
- BMD similar to that for risk postmenopausal osteoporosis
- Treated with corticoids at doses higher than 15 mg/day
- High disability index
- Extended disease
- Little physical activity

**Ankylosing spondylitis**
- Patient with a disease of more than 10 years standing
- Male > 30 years, treated with corticoids
- Acute loss of BMD in the first 5 years, with an extended disease
- Episodes of lumbago in the last 6 months
- Associated inflammatory intestinal disease

**Systemic ermatose lupus:**
- Postmenopausal woman, with a longstanding disease
- Started after the age of 30
- Little exposure to the sun
- Use of sun filter,
- Low BMD in hip

**Systemic schlerosis:**
- Age > 50 years
- Woman
- Early menopause
- Body mass index < 25
- Use of systemic corticoids

**Rheumatic polymyalgia/Giant cell arterisis**
- Age > 60 years
- Functional limitation (little physical activity)
- Use of systemic corticoids (high accumulated dose)
- Loss of strength
- Reduced BMD
**Table 3. Profile for High Risk of Fracture (HRF). Geriatrics Group**

<table>
<thead>
<tr>
<th>Factors associated with HRF: The greater the number of factors the higher the risk:</th>
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<tbody>
<tr>
<td>1. Age: given that the patients are older than 75 years of age by definition, and in practice, almost all are older than 80 years of age, this is a risk factor which is always present in our daily clinical practice, which means that any other factors which we indicate are associated with this one.</td>
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<tr>
<td>2. Low bone mineral density (BMD): given point 1, a T-score &lt; -2.5 in the hip is an indicator of a patient with HRF.</td>
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<tr>
<td>3. Previous fragility fracture, vertebral (clinical or radiological) or non-vertebral (above all, hip).</td>
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<tr>
<td>4. Treatment with steroids at doses higher than 7.5 mg, for more than 3 months.</td>
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<tr>
<td>5. Older people with falls: numerous factors related to falls are associated with risk of fracture: repeat falls, changes in the neuromuscular function of lower limbs (MMII) (an Up and go test and a test of walking speed are proposed for its evaluation), changes in balance and poor vision. In these patients the presence of bone fragility should be assessed, since the risk of fracture is much greater when falls are associated with osteoporosis (carry out a lateral dorsolumbar spinal X-ray, and densitometry, if necessary).</td>
</tr>
<tr>
<td>6. Fragile older people: These are older people at risk from falls and osteoporosis. They are very frequently seen in the daily practice of geriatrics. They are patients with low weight, malnutrition, sarcopenia, instability, easily fatigued, inactive. Patients with these characteristics should be evaluated in relation to the risk of fracture and taking into account the general situation of the patient, in order to propose which diagnostic tests and which therapeutic approach is most appropriate.</td>
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<tr>
<td>7. Other risk factors: frequent pathologies in geriatrics which are also associated with HRF:</td>
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<tr>
<td>- Dementia, above all, moderate stages with wandering and other conduct disorders.</td>
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<td>- Longstanding Parkinson’s disease</td>
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<td>- Patients with ictus</td>
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<tr>
<td>There are also drug treatments which appear to be associated with falls or which promote bone fragility:</td>
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<tr>
<td>- Anticonvulsants, above all phenytoin, primidone</td>
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<tr>
<td>- Long-acting benzodiazepines</td>
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<td>- Neuroleptics</td>
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**Special and common situations in rehabilitation and geriatry patients**

1. Medullar lesion: (above all in the first two years).
2. Cerebrovascular accident: shows a specific osteoporotic pattern, predominantly on the hemiplegic side and more intense in higher limbs. Many risk factors for falls concur (73% suffer at least one fall in the first 6 months after an ictus) and are subject to treatment which could lead to an increased risk of fractures (anticoagulants, anticonvulsive drugs). Early treatment is advised. |
| 3. Multiple sclerosis: it should be considered in itself as an independent risk factor for the development of osteoporosis, in addition to being associated with other risk factors such as immobility, an increase in number of falls, the continual use of corticoids and vitamin D deficiency. |
| 4. Parkinson’s disease: The risk of hip fracture is 5 to 10 times greater (this being more significant from the fifth year after diagnosis). Patients with osteoporosis and Parkinson of ≥ 6 years standing with high risk of falls and low BMI may be considered as having HRF. |
| 5. Patients with cranial-encephalic trauma: they show a high risk of fracture, usually accumulating numerous factors which predispose them to loss of bone mass and falls. |
| 6. Patients with amputation of lower limbs: with many factors which facilitate loss of bone mass and lead to falls, although it has not yet been possible to define what is their HRF profile. |
| 7. Older people: in general they show a higher incidence and concurrence of risk factors for low BMD and falls, associated with an increase in the rate of hip fractures, such as advanced age, previous fragility fractures, radiological evidence of vertebral deformity, reduced height or thoracic kyphosis, low BMI, falls, pluripathology (including disease with high risk of fractures, like ictus), the use of drug treatments which carry risk (steroids, anticonvulsive), insufficient levels of vitamin D, insufficient intake calcium, fragility and reduction in physical activity. |
| 8. Fragile older people: the presence of at least 3 out of 5 of the following factors: weight loss (> 4.5 kg in one year), subjective tiredness, weakness, low walking speed and low physical activity. They have higher risk of hip fractures and of falls. If there is osteoporosis confirmed by densitometry, drug treatment should be initiated. |
In any case, a very low BMD (T-score < -3) can help determine a high risk of fracture, but only provided it is associated with other variables of increased risk such as age > 70 years, intake of corticoids at a dose > 7.5 mg/day, early menopause, frequent falls, previous existence of at least one vertebral fracture, family history of fractures,...

**Conclusions**

For doctors involved in the diagnosis and treatment of osteoporosis it is absolutely necessary, and a priority, to determine those patients who have the highest risk of fractures, given that such an occurrence has serious clinical and socioeconomical repercussions. Starting from this reality, this forum has attempted to make an approach to the problem of defining HRF, with the intention of marking a starting point which allows, at least, the definition of the essentials which this area of research should cover in the next few years. In any case, to be able to count in this forum on rheumatologists, traumatologists, doctors of internal medicine, rehabilitators, geriatricians and bone specialists to share their perceptions is already in itself a success. In conclusion, although with the data available it is not possible to define from risk factors a profile for high risk of fracture, advanced age, personal and family history of fractures, as well as very low bone mass, among others, contribute significantly to this increase risk, although each specialization involved in the management of the pathology has a different view as a function of the characteristics of the patients who visit them.

Table 4. Profile of High Risk of Fracture (HRF). Bone Metabolism Units Group

<table>
<thead>
<tr>
<th>Highly relevant, first level:</th>
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<tbody>
<tr>
<td>• Age &gt; 70 years</td>
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<tr>
<td>• BMD (T-score) in femoral neck &lt; -3</td>
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<td>• Previous existence of at least 2 vertebral fractures or 1 hip fracture</td>
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<th>Relevant, second level:</th>
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<tr>
<td>• More than 2-3 falls a year</td>
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<tr>
<td>• Use of oral corticoids at doses of 7.5 mg/day, for at least 3 months</td>
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<tr>
<td>• BMI &lt; 19 kg/m²</td>
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<tr>
<td>• Family history of hip fractures</td>
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<tr>
<td>• Consumption of tobacco &gt; 10 cigarettes/day</td>
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Figure 1. Factors involved in the development of osteoporotic fractures
**Bibliography**