Sensitivity, specificity, positive and negative predictive values of the criteria for indicating a bone densitometry in the Evaluation of Medical Techniques and Research in Cataluña

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ABSTRACT

The Catalan Agency for Health Technology Assessment and Research (AETIM) proposed, in 2001, criteria for performing a bone densitometry (BD) for use in the consultations of the public health system. Objective: To determine the sensitivity, specificity, positive predictive value and negative predictive value of the criteria to indicate BD. Material and methods: Five groups of volunteers (premenopausal women aged 46 to 65 years, postmenopausal women aged 46 to 65 years, postmenopausal women aged >65 years and men 46 to 65 years and >65 years) underwent BD and a questionnaire on risk factors. The results obtained with the AETIM criteria are related to criteria for indication of BD proposed by the World Health Organization (1999 and 2003 criteria), the National Osteoporosis Foundation (1998 and 2010 criteria) and the International Committee of Clinical Guidelines on Osteoporosis. Results: Criteria from the Catalan Agency have low sensitivity to detect both low bone mass (T index <−1) and osteoporosis (T index <−2.5); specificity varied according to the group. The positive predictive value is low, but the negative predictive value for osteoporosis is high in all groups (except for postmenopausal women aged >65 years). The remaining criteria have a high negative predictive value and, in women, good sensitivity and low specificity, especially for identifying patients with osteoporosis. Conclusion: Catalan Agency criteria are useful for selecting patients who would not need BD, but lack sufficient sensitivity to identify individuals with low bone mass. The other criteria also have a high negative predictive value for osteoporosis, and a better sensitivity.

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Sensibilidad, especificidad y valor predictivo positivo y negativo de los criterios de indicación de densitometría ósea de la Agencia de Evaluación de Tecnologías e Investigación Médicas de Cataluña

RESUMEN

Objetivo: La Agencia de Evaluación de Tecnologías e Investigación Médicas (AETIM) de Cataluña propuso en 2001 unos criterios de indicación de densitometría ósea (DO) para su uso en las consultas del sistema sanitario público. El objetivo fue conocer la sensibilidad, la especificidad, el valor predictivo positivo (VPP) y valor predictivo negativo (VPN) de los criterios de indicación de DO de la AETIM.

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Introduction

Bone mineral density (BMD) is one of the parameters to gain better insight into the risk of fracture and bone densitometry with dual energy X-ray (DXA) is the technique of choice to measure it. Although risk of fracture estimation appears to be the best way to establish an intervention, DXA is still the most commonly-used tool in clinical practice to start treatment. The indication for DXA has been based on identifying low bone mass and osteoporotic fracture risk factors. Different guides have been based on this proposal, although only a few have been validated.4-11 So as to rationalise the use of DXA in our community, the Agencia de Evaluación de Tecnologías e Investigación Médicas (AETIM) (Agency for Health Technology Assessment and Research) proposed a model based on a combination of high- and medium-risk fracture factors to establish a cut off point for BMD indication.12 Although this model tries to identify individuals at a high risk of fracture, in clinical practice it is being used to identify individuals with DXA indication.

The aim of this study was to ascertain the clinical use of the AETIM guide in selecting individuals with low bone mass. Likewise, results obtained from the guides of the National Osteoporosis Foundation (NOF) from 1998,15 the International Committee for Osteoporosis Clinical Guidelines (ICOCG)16 and the 1999 World Health Organisation (WHO) from 199917 in the same population group were compared. New criteria from NOF (NOF 2010)18 and WHO (WHO 2003)19 were presented subsequent to the study design and were also analysed with the data collected.

Material and method

A transversal, multi-centre study to ascertain the sensitivity, specificity, positive predictive value (PPV) and the negative predictive value (NPV) of the indication criteria for bone densitometry by AETIM (Table 1). These data were used to identify patients with low bone mass, carried out on a random sample of patients who were over 45 years old and who attended programmed visits at primary care surgeries and out-patient departments for rheumatology in the metropolitan area of Barcelona. Results were compared to the indications of other guides (Table 2, Table 3, and Table 4).

So as to avoid any deviations due to age, gender or (in women) menstrual state, the volunteers were divided into 5 groups: males from 46 to 65 years old, males older than 65 years old, pre-menopausal females from 46 to 65 years old, post-menopausal females from 46 to 65 years old and females over 65 years old. Patients were included into each group between the months of February and July, until there were at least 40 volunteers in each of them. The number of volunteers for each group was calculated from two previous studies on the prevalence of bone densitometry indication for each criteria, carried out in the same care areas.20,21 Therefore, in primary care, bone densitometry indication was 36.3% for people over 18 years old who went for consultation and 45.0% for the rheumatology out-patient department (for males from 46 to 65 years old in primary care and rheumatology consultations, 11.3% and 14.5% respectively; for males>65 years old, 35% and 59.3%; for women from 46 to 65 years old, 35.4% and 43.6%; and for women>65 years old, 63.6% and 67.5%).

The first person over 45 years old who attended the consultation each day was considered eligible. This individual would be surveyed and afterwards would be asked for his/her agreement to carry out a bone densitometry. If they accepted, no further people would be surveyed until the next day. If they rejected a bone densitometry, then the next one on that day’s list would be questioned and so forth until one of them agreed to participate. Due to the study logistics,
with a delay in notification of the volunteers included, groups with greater attendance had more volunteers.

The data for each volunteer were collected at the time of consultation, by an interview and clinical history review, and these were completed when the densitometry was carried out. A normalised questionnaire was used with the risk factors included in each bone densitometry indication guide (which was completed with the available data at the time of consultation). To make uniform interpretation of the criteria easier, a consensus meeting was held with all the study participants, where criteria to interpret the variables without very clear definitions were established, and which have been previously published.22,23 No additional tests other than bone densitometry were carried out, so only those factors known at the time of the interview were taken into account.

There were a total of 437 people surveyed and 311 agreed to have a BMD determination by densitometry (the rest declined and were excluded from the study). Three females were excluded as their hormonal state was unknown. At the end of the recruitment period, there were 46 pre-menopausal females aged 46 to 65 years old, 103 post-menopausal females aged 46 to 65 years old, 58 females older than 65 years old, 59 males aged 46 to 65 years old and 42 males older than 65 years old. Out of all the patients, 224 (72.7%) were recruited in primary care surgeries and the rest in rheumatology outpatient departments.

The bone densitometry was carried out at the Bone Metabolism Unit of Hospital Universitario de Bellvitge, using Hologic QDR-1000 apparatus. The spinal column (segment L2-L4) and femoral neck BMD were measured, and the T index was calculated in relation to the normal Spanish population values21 for each location. The worst of the two values was used to classify the volunteer as normal, osteopenic or osteoporotic according to the WHO classification criteria.23 The same classification criteria were used for all groups. The sensitivity, specificity, PPV and NPV for each of the guides and different T-score values were calculated from the results obtained.

Informed written consent was requested from each patient to carry out bone mass determination by DXA. The study was accepted by the ethics committee of Fundación Jordi Gol i Gorina.

**Results**

There were 308 people included in the study. The mean age ± standard deviation (SD) of pre-menopausal females from 46 to 65 years old was 49.8±2.9 years, that of post-menopausal females from 46 to 65 years old was 56.4±4.8 years, that of females over 65 years old was 72.1±4.8 years, that of males from 46 to 65 years old was 56.5±5.3 years and of males over 65 years old it was 72.7±5.2 years. The mean age ± SD of the 3 females aged 46 to 65 years old whose menstrual state was unknown was 53.5±2.6 years old.

In Table 5, sensitivity, specificity, PPV and NPV for each group and guide are presented.

The indications from NOF, WHO and ICOCG include an age above 65 years old to carry out a densitometry. For this reason, the sensitivity in the post-menopausal female group>65 years old is 100% and the specificity, 0%. The PPV corresponds to the proportion of females with a T-score <-1 and -2.5, with sensitivity and specificity of 82.76% and 50.00% respectively. In a similar way, WHO indications include menopause among the criteria to carry out a bone densitometry. It is for this reason that in the two groups of post-menopausal females sensitivity is 100% and specificity 0%, while PPV is 52.43% in females<66 years and 82.76% females>65 years old for a T index<-1, and 16.30% and 50.00%, respectively, for a T-score<-2.5. It is not possible to calculate the NPV in any of these cases.
The results obtained using the AETIM guide show low sensitivity in all groups for osteoporosis detection and variable specificity according to the groups. This means that it does not comply with the requirements for an efficient test, which must have high sensitivity (to detect all positive cases) and high specificity (to reduce the number of false positives). The NPV for osteoporosis is high in all groups, except in post-menopausal women who are older. In contrast, PPV for osteoporosis is low in all groups. These results indicate good ability to select individuals who would not need to have a bone densitometry, especially in the less usual groups (pre-menopausal females and males) and coincides with the results observed in other studies and other decision guides and metaanalyses.

This study also shows the results of other densitometry indication guides in scientific literature used at the time of the AETIM guide publication, as well as later guides. The values obtained in post-menopausal females in our sample are similar to those obtained by Mauck et al, except for the sensitivity and specificity of the population<65 years old. This difference could be explained by the different origin of the sample. Mauck et al is based on the general population, while in our case we use only that fraction that consult with their doctors.

Guides have appeared in the last few years with criteria for bone densitometry indication, so as to optimise the performance of this technique in its clinical application. The criteria include risk factors of low bone mass or fracture that relate them to a decrease in bone mass or with a greater prevalence of breakages in epidemiological studies. However, there are no validation studies for many of the proposed criteria.

This study assessed the AETIM guide and related the results to the ones that would have been obtained by using NOF, ICOCG and WHO guides in the same population. The study was carried out on a sample population where the only limitation was age. This was applied as an exclusion criterion due to the low prevalence of densitometry indication in people<46 years old obtained in previous studies and the study was performed with the same indication criteria for the technique; this exclusion criterion was also chosen for the low

### Table 5

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
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<tr>
<td>T&lt;−1</td>
<td>T≤−2.5</td>
<td>T&lt;−1</td>
<td>T≤−2.5</td>
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<td>Pre-menopausal females 45-65 years old (n=46)</td>
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<tr>
<td>AETIM</td>
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<td>71.79 (58.79-84.80)</td>
<td>71.11 (58.01-84.21)</td>
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<tr>
<td>NOF</td>
<td>57.14 (42.85-71.44)</td>
<td>64.10 (50.24-77.97)</td>
<td>62.22 (48.21-76.23)</td>
</tr>
<tr>
<td>NOF 2010</td>
<td>28.57 (15.52-41.63)</td>
<td>82.05 (70.96-93.14)</td>
<td>80.00 (68.44-91.56)</td>
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<tr>
<td>WHO</td>
<td>71.43 (58.37-84.48)</td>
<td>58.97 (44.76-73.19)</td>
<td>55.56 (41.20-69.91)</td>
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<tr>
<td>WHO 2003</td>
<td>57.14 (42.84-71.44)</td>
<td>76.92 (64.75-89.10)</td>
<td>73.33 (68.14-83.37)</td>
</tr>
<tr>
<td>ICOCG</td>
<td>42.86 (28.56-57.16)</td>
<td>76.92 (64.75-89.10)</td>
<td>75.56 (63.14-89.97)</td>
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<td>Post-menopausal females 45-65 years old (n=103)</td>
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<td>37.04 (27.71-46.36)</td>
<td>52.94 (43.30-62.58)</td>
<td>73.47 (64.94-80.00)</td>
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<td>87.04 (80.55-93.52)</td>
<td>30.61 (21.71-39.51)</td>
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<tr>
<td>WHO 2003</td>
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<td>0</td>
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<td>ICOCG</td>
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<td>82.35 (74.99-89.72)</td>
<td>51.66 (41.51-60.82)</td>
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</tr>
<tr>
<td>WHO 2003</td>
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<td>0</td>
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</tr>
<tr>
<td>ICOCG</td>
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<td>WHO 2003</td>
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<td>55.56 (42.88-68.24)</td>
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<tr>
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<td>66.67</td>
<td>75.00</td>
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<tr>
<td>NOF 2010</td>
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<td>100</td>
<td>100</td>
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<td>WHO</td>
<td>91.24-100</td>
<td>52.41-80.92</td>
<td>61.90-88.30</td>
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<tr>
<td>WHO 2003</td>
<td>83.33</td>
<td>83.33</td>
<td>5.40-27.94</td>
</tr>
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</table>

AETIM indicates Agency for Health Technology Assessment and Research; ICOCG, International Committee for Osteoporosis Clinical Guidelines; NPV, negative predictive value; PPV, positive predictive value; T, T-score; WHO, World Health Organisation.
prevalence of bone mass and osteoporotic fractures in this age group observed during epidemiological studies. The sample was divided into subgroups to include representation of the population of both sexes and at any age above 45 years old. This differentiates it from other studies, mainly centred in post-menopausal women, or that exclude individuals that have any diseases that can influence bone.6,27 The distribution in subgroups, which although it does not reflect the general population structure or that going to medical consultations, allows us to understand the capability of the different guides in identifying, in a stratified manner, patients who would benefit from determining bone mass.

The age interval and inclusion of males and females constitute a study limitation, as they oblige us to reduce sample size. However, they allow us to better define the sensitivity and specificity of each guide in each group.

The study population came from medical consultations from primary care and rheumatology. This fact could make us think of a different distribution in the risk factors. However, a previous study on risk factor prevalence did not show such distribution differences in the most important risk factors.20,21

The clinical guides are designed to be used with the general population, but they are usually applied only to a population with access to health service. The population that visits a health service centre comes from the general population, although it makes up a subgroup that probably has a greater number of risk factors of low bone mass or fracture. Applying guides designed for the general population to this subgroup should make it possible to identify individuals with a risk of having lower bone mass more often than if they were directly applied to the general population. For this reason, a low performance in this population subgroup makes us think that its use in the general population would be low.

Only if the health system is sufficiently large to be able to periodically review all its population would the general population then correspond to the population to which the guide is applied. This circumstance only occurs if the population is very small or when the health system is disproportionally very important. Although the sample study does not exactly correspond to the general population, more than 90% of the people > 65 years old consult the doctor at some stage during the year in our environment, which is why the bias is probably small in this age group. In other groups, there is an attendance bias.

The authors are unaware of any studies that exist that analyse the use of these guides in identifying males with low bone mass, despite some guides not restricting them to just female use. This study allows us to compare the behaviour of these guides in both genders. The AETIM guide has low sensitivity but high specificity in identifying males less than 66 years old with low bone mass and is not very useful above this age. The WHO and NOF 2010 guides have even worse results. In all cases, the NPV is high for osteoporosis.

The results indicate that the criteria analysed are not sufficient to discriminate between patients with normal BMI, osteopenia or osteoporosis from clinical risk factors. It is not possible to predict the state of bone mass in an individual patient with sufficient reliability, except in extreme situations (absence of risk factors or presence of multiple factors), which are not very significant in the population. The criteria that require various risk factors to indicate bone densitometry, such as those of AETIM, are restrictive (high specificity but low sensitivity in detecting osteoporosis). In contrast, those that require only one risk factor are not very specific, although more sensitive. It can therefore be suggested that patients who do not comply with the AETIM densitometry indication criteria do not require a bone densitometry.

It was necessary to define more precisely some of the risk factors included in the guides when designing this study. For example, the AETIM defines age>70-80 years old or the body mass index < 20-25 as a high risk factor. In the WHO criteria, kyphosis is an indication criterion (without making the degree clear), as well as low calcium intake. This lack of definition gives an assessment at the time of application that could be different from one clinician to another, giving rise to differing results.

To conclude, the AETIM criteria, the same as other criteria assessed, are useful to select patients for whom it would not be necessary to perform a densitometry. The sensitivity of the AETIM criteria in identifying patients with low body mass (index T<-1) or osteoporosis is low, except for the group of post-menopausal women > 65 years old, where all the criteria are sensitive, although with low specificity.

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Conflict of interest

The authors declare no conflict of interest.

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