PERFORMANCE OF DECISION ALGORITHMS FOR THE IDENTIFICATION OF LOW BONE MINERAL DENSITY IN PORTUGUESE POSTMENOPAUSAL WOMEN

Pedro Machado,* José António Pereira da Silva*

Abstract

Objectives: Although several algorithms have been proposed to select postmenopausal women (PMW) for dual-energy x-ray absorptiometry (DEXA) measurements, information on their utility in clinical practice is scarce. Our aim was to assess the utility and the economic repercussion of the use of five of these algorithms in Portuguese postmenopausal women.
Methods: We included 588 PMW and selected five simple algorithms: ORAI, ABONE, Body Weight Criterion, OSTA and a modified version of OSTA (OST). Sensitivities, specificities, predictive values, areas under the receiver operating characteristic curve (AUROC) and economic estimates were computed.
Results: Sensitivities ranged between 71.2%-80.8% and AUROC between 0.611-0.674. In PMW aged ≥65 years (Y), the use of any of the algorithms would cause extra costs or a residual saving. In PMW aged ≥55 and <65Y, considering total savings, ABONE had the best performance, but considering savings per preventable fracture, ORAI assumed the lead, followed by BWC. In the age group ≥40 and <55Y, the most profitable option considering total savings would be not doing DEXA to anyone; considering savings per preventable fracture, BWC figures as the most useful.
Conclusions: This study provides evidence for the validity of all the selected tools as useful algorithms to select PMW for DEXA. On the basis of our results and considering the importance of simplicity in the applicability of an algorithm, we would suggest the following strategy in Portuguese PMW: 1) Aged ≥65Y: perform DEXA irrespective of other risk factors. 2) Aged <65Y: perform DEXA if body weight <70Kg.

*Serviço de Reumatologia dos Hospitais da Universidade de Coimbra, Coimbra, Portugal

Note: This study was the winner of the "Osteoporosis Prize, Portuguese Society of Rheumatology/Merck Sharp & Dohme, 2007/2008.

Keywords: Osteoporosis; Densitometry; Postmenopausal Women; Screening; Cost-Effectiveness

Resumo

Objectivos: Apesar da validação de vários algoritmos de selecção de mulheres pós-menopáusicas (MPM) para realização de *dual-energy x-ray absorptiometry* (DEXA), a informação sobre a sua utilidade clínica é escassa. Foi nosso objectivo avaliar o desempenho e repercussão económica do uso de cinco desses algoritmos em MPM Portuguesas.
Métodos: Foram incluídas 588 MPM e considerados cinco algoritmos simples de decisão: ORAI, ABONE, Body Weight Criterion, OSTA e uma versão modificada do OSTA (OST). Calcularam-se sensibilidades, especificidades, valores preditivos, áreas da curva *under the receiver operating characteristic* (AUROC) e estimativas económicas.
Resultados: As sensibilidades variaram entre 71.2%-80.8% e a AUROC entre 0.611-0.674. Nas MPM com ≥65 anos, a utilização de qualquer um dos algoritmos traduziu-se em custos adicionais ou poupança residual. Nas MPM com ≥55 e <65 anos, considerando a poupança absoluta, o ABONE tem o melhor desempenho, mas considerando a poupança por fractura evitável, o ORAI assume a liderança, seguido pelo BWC. No grupo com ≥40 e <55 anos, a opção mais rentável em termos de poupança absoluta seria a de não realizar DEXA a ninguém. No entanto, considerando a poupança por fractura evitável, o BWC afigura-se como o mais vantajoso.
Conclusões: Este estudo fornece evidência da validade destes instrumentos como algoritmos úteis para a selecção de MPM para realização de DEXA. Considerando os resultados e a importância da simplicidade do algoritmo, sugerimos a seguinte estratégia nas MPM Portuguesas: 1) Idade ≥65 anos: realizar DEXA independentemente de outros factores de risco. 2) Idade <65 anos: realizar DEXA se peso <70Kg.

Palavras chave: Osteoporose; Densitometria; Mulheres Pós-Menopáusicas; Rastreio; Custo-Eficácia.

Introduction

Osteoporotic fractures are a major cause of morbidity and mortality, representing an enormous health care burden in developed countries.[1] At least half of all postmenopausal women will experience fractures during their lifetime.[1] Bone mineral density (BMD) is the most important independent predictor of osteoporotic fracture and each standard deviation reduction in BMD is associated with a 1.5 to 2.5-fold increase in fracture risk.[2] The importance of BMD is reinforced because it represents one of the few risk factors that can be changed leading to effective prevention of fractures.

Dual-energy X-ray absorptiometry (DEXA) is the gold-standard for the diagnosis of osteoporosis,[3] the lumbar spine and the hip being the preferred measurement sites to this purpose.[4,5] Mass screening for osteoporosis is not recommended because there is considerable overlap of BMD values between those who fracture and those who don´t.[6] Cost-effectiveness is also an issue. However, DEXA testing in high-risk groups is essential to identify appropriate candidates for preventive interventions to avoid further bone loss and fracture.[7] Thus, from the population point of view, it is essential to develop and adopt the best strategies for the selection of the population where DEXA testing achieves the highest effectiveness.[6]

A recent review of the clinical applications of bone densitometry suggests that clinicians need tools to identify patients most likely to benefit from DEXA testing.[8] A simple risk assessment tool may also have value for increasing the awareness of osteoporosis and for encouraging more efficient use of BMD measurements, that is, in patients who have a higher probability of low BMD, especially in otherwise healthy, asymptomatic patients. Several studies have examined and confirmed the ability of individual risk factors to identify postmenopausal women likely to have osteoporosis and some have proposed simple composite tools obtained by questionnaire and based on a score.[9-19] While these rules currently use a single cut point for deciding whether to test or not, it has been suggested that two cut points are preferable, as they allow the stratification of the likelihood of osteoporosis as low, moderate or high.[12-16,20] As a risk index, women at low risk would not require a BMD test, those with moderate risk would be recommended for BMD testing and those at high risk could be treated to prevent fracture without the need for BMD testing.[16,20]

The Portuguese Society of Rheumatology and the Portuguese Society of Metabolic Bone Diseases recommend the selection of women for BMD according to the presence of major and minor risk factors, or according to risk assessment tools.[21] Several guidelines/algorithms to identify high risk subjects have been published.[3,4,21-23]

However, the evidence for the utility of these rules in a clinical setting is scarce.[20,24-28] Moreover, the performance of such algorithms in identifying low bone density has never been tested in the Portuguese population. Their utility is not necessarily the same in different populations, as the contribution of different osteoporotic factors varies in different countries and areas.

In this study we evaluated and compared the performance of five simple decision algorithms for osteoporosis risk in a large sample of Portuguese postmenopausal women. The benefit of a second cut point to convert each decision rule into a risk index (low, moderate or high risk for osteoporosis) was also evaluated. We expanded the analysis beyond the usual description of sensitivity and similar qualities, to explore the impact of each algorithm on the absolute incidence of fractures and their economic burden.

Materials and methods

Population and data collection

Data collection took place in *Santo António dos Olivais* (SAOL), Coimbra, Portugal, in the years of 1998 and 1999. The methodology was previously described.[29] This county has a mixture of a rural and an urban population, representing epidemiological patterns of age and gender distribution, income and consumer habits considered to be similar to those of the general Portuguese population. It has about 25000 inhabitants. Residents were randomly selected from the 19000 registered voters following a computer-generated random number list, stratified to gender and 5 year age-groups. People were invited to participate by mail explaining the nature and purposes of the study. There were no exclusion criteria. Non-respondents were contacted a second time. We aimed at a total of at le-

ast 1600 participants. A total of 6000 invitations were sent out before this number was reached; 1100 letters bounced back due to change in address, death and other reasons. Altogether 1745 accepted to participate. From final analysis 73 participants were excluded due to incomplete data or unresolved technical difficulties in the DEXA scan. Reliable BMD of the lumbar spine and hip was available for 1672 participants: 1208 women and 464 men.

Participants responded to a comprehensive questionnaire regarding risk factors for osteoporosis in personal and family history. Height and weight were recorded. DEXA scans of the spine and proximal femur were performed, using a Hologic QDR 4500/c bone densitometer. Scans were performed and analyzed according to the manufacturer's instructions. For the purposes of this study all postmenopausal women with DEXA scans were included (study cohort=588).

Selection of the decision algorithms and calculation of their scores

Based on a critical review of the literature, with consideration of published performance indicators and simplicity, we selected 5 simple decision algorithms to test in our study cohort: the Osteoporosis Risk Assessment Instrument[13] (ORAI), the Age, Body Size, No Estrogen criterion[9] (ABONE), the Body Weight Criterion[10] (BWC), the Osteoporosis Self-Assessment Tool for Asians[12] (OSTA) and a modified version of the OSTA equation[12, 14] (OST). Their scoring methods, with previously validated selection cut-off points, are presented in Table I. All the information needed was available in the SAOL database.

Each decision algorithm was converted into a risk index to differentiate between low, moderate and high risk for osteoporosis, adopting previously validated cut-off points,[12-16,20] as follows: ORAI - low risk, a score <9, moderate risk, a score between 9 and 17, high risk, a score >17. BWC - low risk, ≥70 Kg, moderate risk, 57 to 69.9 Kg, high risk, <57 Kg. OSTA and OST - low risk, a score >1, moderate risk, a score of -3 to 1, high risk, a score <-3. Given that, to our knowledge, the ABONE has not been previously evaluated using two cut points, we chose to consider: low risk, a score ≤1, moderate risk, a score of 2, high risk, a score of 3, as these are the only possible scores in this algorithm.

All 5 decision algorithm were applied to each one of the 588 postmenopausal women belonging to our study cohort. Age was calculated to the date of the DEXA scan.

Gold standard

BMD values as assessed by DEXA were used as the gold standard for diagnosing osteoporosis. We used

Table I. Five simple decision rules for bone mineral density testing among postmenopausal women

Factor	Score
Osteoporosis Risk Assessment Instrument (ORAI), test if score ≥9	
Age 55-64 years	5
Age 65-74 years	9
Age ≥75 years	15
Weight 60-69.9 Kg	3
Weight <60 Kg	9
Not currently taking oestrogen	2
Age, Body Size, No Estrogen (ABONE), test if score ≥2	
Age >65	1
Weight <63.5 kg	1
Never used oral contraceptive or oestrogen therapy for at least 6 months	1
Body weight criterion (BWC), test if	
Weight <70 Kg	
Osteoporosis Self-assessment Tool for Asians (OSTA), test if score < 2	
0.2*body weight in Kg (truncate to yield an integer) - 0.2*age in years (truncate to yield an integer)	
Osteoporosis Self-assessment Tool (OST), test if score < 2	
0.2*(body weight in Kg - age in years), truncate to yield an integer	

the World Health Organization (WHO) thresholds to classify our patients into 3 diagnostic categories: normal (T-score ≥–1.0 SD), osteopenic (–1.0 >T-score >–2.5 SD) or osteoporotic (T-score ≤–2.5 SD). The young normal reference values used for the calculation of T-scores were NHANES III reference for the hip[30] and the HOLOGIC Caucasian reference database for the spine. In each case, the lowest BMD T-score at the lumbar spine (L1–L4), femoral neck or total hip was considered. DEXA results were available for all the 588 postmenopausal women integrating the study cohort and therefore the gold standard for osteoporosis was available for all of them. When details for only one site were available (n=1), BMD was categorized based on that single site.

Statistical analysis and evaluation of the algorithms' performance for identifying osteoporosis

Descriptive characteristics of the study population were tabulated as means and standard deviations (SD), or proportions as applicable. Differences among groups of patients were calculated by analysis of variance or chi-squared test as applicable.

In order to evaluate the performance of the five selected algorithms, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and the area under the receiver operating characteristic (AUROC) curve of each decision algorithm for selecting women with osteoporosis by BMD testing (the gold standard) were determined. In addition, the predictive values for identifying osteoporosis for each risk index of low, moderate and high risk were calculated.

Exact binomial 95% confidence intervals[31] (CI) were calculated for sensitivities, specificities and predictive values. Sensitivities, specificities and predictive values are proportions calculated according to the results obtained in our sample population. Therefore, they are point estimators in a random sample from the general PMW population. A confidence interval for the binomial parameter broadens that point estimate out, reflecting the uncertainty associated with the limited size of the sample.

Sensitivity was defined as the proportion of women with osteoporosis (DEXA T-score ≤–2.5 SD) who tested positive on the decision algorithm (indication for DEXA in the binomial classification) and specificity was defined as the proportion of women without osteoporosis (DEXA T-score >–2.5 SD) who tested normal on the decision algorithm (having index values in the range considered low risk). Positive predictive value was defined as the proportion of women with a positive algorithm score who were actual cases of osteoporosis and negative predictive value was defined as the proportion of women with a negative algorithm result who were actual non-cases of osteoporosis. The AUROC curve was used as a measure of the overall ability of each strategy to discriminate between postmenopausal women with and without osteoporosis.[32] An area of 1 represents a perfect test; an area ≤0.5 represents a worthless test.

Statistical analysis was performed using SPSS 14.0 for Windows.

Economic analysis

The analysis of the algorithms' performance for identifying osteoporosis was expanded by exploring the impact of each algorithm upon the savings in DEXA, the probability of fracture and the economic repercussions of both.

The number of lost cases of osteoporosis, preventable fractures, total savings and savings per preventable fracture were computed from the prevalence of osteoporosis in the different age groups and sensitivities. The estimated absolute risk for "any type of osteoporotic fracture" over ten years was calculated according to data published by Kanis *et al.*[33]

For economic calculations we used the present official cost of DEXA scanning for two sites within the Portuguese National Health System: 126.60€ (*Portaria 132/2003*). The hospital costs for fractures were estimated at 3000€ based on the official 2007 reimbursement table of Portuguese hospitals according to "Homogeneous Diagnostic Groups": around 4000€ per hip and humerus fractures and 1700€ for forearm fractures. For clarity, these calculations were estimated for a population of 10000, extrapolating from our data, and rounded to the nearest unit, for fractures and DEXA scans, and to the nearest hundred for costs.

Therefore, economic items (Table VII) were computed as follows (fractions rather than percentages are used in the formulas below):

a) lost cases of osteoporosis: (1-sensitivity)*fraction of women with osteoporosis within the age group*10000
b) ten-year fracture probability: mean femoral neck T-score of osteoporotic women was calculated for each age group in our cohort and ba-

sed on that mean result, the 10-year fracture probability for each age group was established according to the data published by Kanis *et al*[33] (who based his estimations on femoral neck T--score)

c) absolute excess fractures over 10 years (this is the 10-year estimation of the total number of fractures in a 10000 population, due to lost cases of osteoporosis): lost cases of osteoporosis*ten-year fracture probability, that is a*b
d) hospital costs for excess fractures (these are the direct hospital costs caused by the absolute excess of fractures over 10 years due to lost cases of osteoporosis): absolute excess fractures over 10 years*3000€, that is c*3000€
e) number of avoided DEXA scans (this is the number of DEXA scans that was not performed due to the use of a selection algorithm, compared with the "scan all" option): (1-fraction of women selected for DEXA)*10000
f) savings with DEXA scans: number of avoided DEXA scans*126.60€, that is e*126.60€
g) net balance: savings with DEXA scans *minus* hospital costs for excess fractures, that is f *minus* d
h) net balance per preventable fracture (this is the net balance adjusted to the 10-year estimation of the total number of fractures in a 10000 population): net balance÷absolute excess fractures over 10 years, that is g÷c.

Results

Our study population included 588 postmenopausal women aged 42 to 87 years, with a mean age of 60 years. Table II summarizes the descriptive characteristics of the study cohort, including age distribution, WHO criteria and T-score. A large number of participants with less than 65 years were included (72.8%).

Table III summarizes the descriptive characte-

Table II. Summary of descriptive characteristics of the postmenopausal study cohort (n=588)

Age (years, mean ± SD)	60.18 ± 8.57
Age group - n (%)	
Age ≥40 and <55 years	204 (34,7)
Age ≥55 and <65 years	224 (38,1)
Age ≥65 years	160 (27,2)
Time since menopause (years, mean ± SD)	12.30 ± 9.25
Height (cm, mean ± SD)	155.90 ± 6.24
Weight (Kg, mean ± SD)	67.18 ± 10.88
Body mass index (Kg/m2, mean ± SD)	27.68 ± 4.46
HRT use – n (%)	
Never	345 (58.7)
Past	82 (13.9)
Current	153 (26.0)
Missing	8 (1.4)
WHO diagnostic categories - n (%)	
Normal	121 (20.6)
Osteopenia	311 (52.9)
Osteoporosis	156 (26.5)
T-Score (mean ± SD)	
Lumbar spine	-1.57 ± 1.25
Femoral neck	-1.28 ± 1.02
Total hip	-0.66 ± 1.01
ORAI score (mean ± SD)	9.64 ± 6.06
ABONE score (mean ± SD)	1.43 ± 0.87
OSTA score (mean ± SD)	1.47 ± 2.86
OST score (mean ± SD)	1.19 ± 2.50

Table III. Summary of descriptive characteristics of the postmenopausal study cohort (n=588) according to the three WHO diagnostic categories†

	Normal (n=121)	Osteopenia (n=311)	Osteoporosis (n=156)	p
Age (years, mean ± SD)	56.10 ± 6.50	59.49 ± 8.33	64.71 ± 8.49	p<0.001
Age group - n (%)				p<0.001
Age ≥40 and <55 years	67 (55.4)‡	112 (36)	25 (12.3)‡	
Age ≥55 and <65 years	40 (33.1)	124 (39.9)	60 (26.8)	
Age ≥65 years	14 (11.6)‡	75 (24.1)	71 (44.4)‡	
Time since menopause (years, mean ± SD)	7.55 ± 6.66	11.73 ± 8.95	17.17 ± 9.38	p<0.001
Height (cm, mean ± SD)	158.21 ± 5.79	156.20 ± 5.90	153.51 ± 6.46	p<0.001
Weight (Kg, mean ± SD)	71.52 ± 10.15	67.4 ± 10.28	63.39 ± 11.33	p<0.001
Body mass index (Kg/m2, mean ± SD)	28.62 ± 4.19	27.69 ± 4.42	26.92 ± 4.63	p=0.007
HRT use (%)				p<0.001
Never	52 (43.0)‡	176 (56.6)	117 (75.0)‡	
Past	11 (9.1)	47 (15.1)	24 (15.4)	
Current	56 (46.3)‡	84 (27.0)	13 (8.3)‡	
Missing	2 (1.7)	4 (1.3)	2 (1.3)	
ORAI score (mean ± SD)	6.00 ± 4.69	9.14 ± 5.56	13.45 ± 5.89	p<0.001
ABONE score (mean ± SD)	0.93 ± 0.73	1.38 ± 0.81	1.94 ± 0.80	p<0.001
OSTA score (mean ± SD)	3.16 ± 2.36	1.65 ± 2.52	-0.21 ± 2.96	p<0.001
OST score (mean ± SD)	2.64 ± 2.26	1.33 ± 2.22	-0.23 ± 2.49	p<0.001

†The lowest BMD T-score at the lumbar spine, femoral neck or total hip was considered.
‡Significant adjusted standardized residuals. We used adjusted standardized residuals to identify the contribution of different cells to the significance of the chi-square test.

ristics of the study cohort stratified on the basis of the three WHO diagnostic categories.

The overall percentage of osteoporosis at lumbar spine, femoral neck or total hip was 26.5% (n=156). The percentage of osteoporosis at each measurement site was 22.6% at lumbar spine (n=133), 11.1% at femoral neck (n=65) and 3.4% at total hip (n=20). The percentage of women with osteoporosis increased with age from 12.3% among women aged ≥40 and <55 years (25/204), 26.8% among women aged ≥55 and <65 years (60/224) and 44.4% among women aged ≥65 years (n=71/160). The WHO diagnostic categories show significant differences regarding all main risk factors for osteoporosis, and also for all the risk assessment tools under scrutiny.

Table IV shows the sensitivity, specificity, predictive values and area under ROC curve of each decision rule for selecting women with osteoporosis for BMD testing in the study cohort (n=588). All screening tools, when applied with single cut-off point, showed sensitivities above 70%. Specificity was lower, ranging from 44.7% to 63.7%. Negative predictive value was also quite high in all algorithms (84.6% to 88.4%). The AUROC curve is a measure of the test accuracy[32] and in our study it ranged between 0.611 and 0.669. The AUROC curve 95% CI did not include 0.5 for any of the algorithms, confirming their capacity to distinguish between women with and without osteoporosis.

Table V summarizes the percentage of women selected for DEXA scanning as well as sensitivity, specificity, PPV and NPV for each age group. The qualities of the screening tools are different when applied to the different age groups. Overall, most of the screening tools tend to perform better, in terms of sensitivity, in the older age groups. BWC is the only exception to this observation.

Table VI shows the percentage of women with low, moderate, or high risk for osteoporosis by each decision algorithm after application of two cut-off points and corresponding negative (for low risk group) or positive predictive values (for moderate and high risk groups). The low risk group represents the postmenopausal women not selected for DEXA after applying an algorithm. The distinction between moderate and high risk groups is an attempt of stratification of the postmenopausal wo-

Table IV. Percentage of women selected for DEXA, sensitivity, specificity, predictive values and area under ROC of each decision rule for selecting women with osteoporosis† for BMD in the study cohort (n=588)

	Percentage of women selected for DEXA	Sensitivity, % (95% CI)	Specificity, % (95%CI)	PPV, % (95% CI)	NPV, % (95% CI)	AUROC (95% CI)
ORAI	56.0 (51.8-60.0)	80.8 (73.7-86.6)	53.0 (48.2-57.8)	38.3 (33.0-43.8)	88.4 (83.9-92.1)	0.669 (0.622-0.716)
ABONE	45.6 (41.5-49.7)	71.2 (63.4-78.1)	63.7 (58.9-68.2)	41.4 (35.5-47.6)	85.9 (81.6-90.0)	0.674 (0.625-0.723)
BWC	61.2 (57.2-65.2)	77.6 (70.2-83.9)	44.7 (39.9-49.5)	33.6 (28.8-38.8)	84.6 (79.3-89.1)	0.611 (0.562-0.661)
OSTA	51.0 (46.9-55.1)	75.6 (68.1-82.1)	57.9 (52.1-62.6)	39.3 (33,8-45.1)	86.8 (82.3-90.5)	0.668 (0.619-0.716)
OST	58.5 (54.4-62.5)	80.8 (73.7-86.6)	49.5 (44.7-54.4)	36.6 (31.5-42.0)	87.7 (82.9-91.6)	0.652 (0.604-0.699)

†BMD T-score ≤-2,5 by lowest value at the lumbar spine, femoral neck or total hip was considered.

men selected for DEXA after applying an algorithm. This has been suggested on the basis that it might exclude the need for DEXA in high risk individuals (who could be treated without DEXA).[13] The positive predictive values are quite low, even for the high risk groups. This means that a considerable proportion of patients would be wrongly selected for treatment if a high risk score in any algorithm was taken as direct indication for treatment without performing DEXA. The NPV associated with low risk is much more satisfactory.

Finally, Table VII shows the estimates of lost cases of osteoporosis, absolute excess fractures and cost savings as a consequence of applying each selected algorithm per age-group, as compared with the «scan all» option. For clarity, numbers were calculated for a population of 10000 and rounded to the nearest unit, for fractures and DEXA scans, and to the nearest hundred for costs.

The most restrictive algorithms result in greater savings on DEXA scans, but at the cost of larger number of ignored osteoporosis cases and subsequent fractures. Total savings may be higher but indirect costs, including suffering from fracture, will also be higher. The calculation of "savings per preventable fracture" is an attempt to bring this into account – it may be seen as the savings available to cover indirect costs of fracture, after having covered direct hospital costs. The negative values in the two last columns for those aged ≥65 years mean that savings with DEXA would not be enough to cover for direct hospital costs.

Discussion

There are three recommended steps in developing and testing tools to aid clinical decision-making: development, validation in several cohorts and impact assessment. Information on their utility in different populations is especially important in order to establish the generalizability of these approaches and to assure their validity in clinical practice as applied in different clinical and epidemiological settings.[13]

We analyzed the value of 5 simple decision algorithms for selecting individuals for bone mineral testing in 588 Portuguese postmenopausal women; mean age was 60 years and mean time since menopause was 12 years. The relevance of these decision rules could decrease in the future. There is a progressive tendency to recommend the identification of individuals for treatment based on a comprehensive fracture risk assessment rather than BMD status alone.[34] The BMD would be one among other factors to predict fracture risk. However, the importance of the WHO categories in the decision-making remains high and DEXA measurements will still be necessary in the future to incorporate BMD values into the fracture risk equations. Therefore, the performance of decision algorithms for identifying low bone density in postmenopausal women is a matter of great importance.

Compared to the majority of previous reports, this study had the virtue of not being retrospective. It was a cross-sectional study, performed in a

Table V. Percentage of women selected, sensitivity, specificity and predictive values of each decision algorithm for selecting women with osteoporosis† for BMD, according to the age groups

	Percentage of women selected for DEXA	Sensitivity, % (95% CI)	Specificity, % (95%CI)	PPV, % (95% CI)	NPV, % (95% CI)
ORAI					
≤40 and <55 years‡	26,0 (20.1-32.6)	48.0 (27.8-69.0)	77.1 (70.2-83.0)	22.6 (12.3-36.2)	91.4 (85.7-95.3)
≥55 and <65 years‡	51.8 (45.0-58.5)	71.7 (58.6-82.6)	55.5 (47.5-63.2)	37.1 (28.3-46.5)	84.3 (76.0-90.6)
<65 years‡	39.5 (34.8-44.3)	64.7 (53.6-74.8)	66.8 (61.5-71.7)	32.5 (25.6-40.2)	88.4 (83.9-92.1)
≥65 years‡	100.0 (97.7-100.0)	100.0 (94.9-100.0)	N.A.	44.4 (36.5-52.4)	N.A.
ABONE					
≥40 and <55 years‡	24.5 (18.8-31.0)	52.0 (31.3-72.2)	79.3 (72.7-85.0)	26.0 (14.6-40.3)	92.3 (86.8-95.9)
≥55 and <65 years‡	27.7 (21.9-34.0)	48.3 (35.2-61.6)	79.9 (72.9-85.7)	46.8 (34.0-59.9)	80.9 (74.0-86.6)
<65 years‡	26.2 (22.1-30.6)	49.4 (38.4-60.5)	79.6 (74.9-83.7)	37.5 (28.5-47.2)	86.4 (82.1-90.0)
≥65 years‡	97.5 (93.7-99.3)	97.2 (90.2-99.7)	2.2 (0.3-7.9)	44.2 (36.3-52.4)	50.0 (6.8-93.2)
BWC					
≥40 and <55 years‡	60.3 (53.2-67.1)	88.0 (68.8-97.5)	43.6 (36.2-51.2)	17.9 (11.6-25.8)	96.3 (89.6-99.2)
≥55 and <65 years‡	59.8 (53.1-66.3)	75.0 (62.1-85.3)	45.7 (37.9-53.7)	33.6 (25.7-42.3)	83.3 (74.0-90.4)
<65 years‡	60.0 (55.2-64.7)	78.8 (68.6-86.9)	44.6 (39.3-50.0)	26.1 (20.8-31.9)	89.5 (83.9-93.6)
≥65 years‡	64.4 (56.4-71.8)	76.1 (64.5-85.4)	44.9 (34.4-55.9)	52.4 (42.4-62.4)	70.2 (56.6-81.6)
OSTA					
≥40 and <55 years‡	23.5 (17.9-30.0)	44.0 (24.4-65.1)	79.3 (72.7-85.0)	22.9 (12.0-37.3)	91.0 (85.4-95.0)
≥55 and <65 years‡	51.3 (44.6-58.1)	68.3 (55.0-79.7)	54.9 (46.9-62.7)	35.7 (26.9-45.1)	82.6 (74.1-89.2)
<65 years‡	38.1 (33.5-42.9)	61.2 (50.0-71.6)	67.6 (62.4-72.6)	31.9 (24.8-39.7)	87.5 (83.0-91.3)
≥65 years‡	85.6 (79.2-90.7)	93.0 (84.3-97.7)	20.2 (12.5-30.1)	48.2 (39.6-56.9)	78.3 (56.3-92.5)
OST					
≥40 and <55 years‡	31.4 (25.1-38.2)	52.0 (31.3-72.2)	71.5 (64.3-78.0)	20.3 (11.3-32.2)	91.4 (85.5-95.5)
≥55 and <65 years‡	62.1 (55.4-68.4)	75.0 (62.1-85.3)	42.7 (35.0-50.6)	32.4 (24.7-40.8)	82.4 (72.6-89.8)
<65 years‡	47.4 (42.6-52.3)	68.2 (57.2-77.9)	57.7 (52.3-63.0)	28.6 (22.5-35.3)	88.0 (83.0-91.9)
≥65 years‡	88.1 (82.1-92.7)	95.8 (88.1-99.1)	18.0 (10.6-27.6)	48.2 (39.7-56.8)	84.2 (60.4-96.6)

†BMD T-score ≤-2,5 by lowest value at the lumbar spine, femoral neck or total hip was considered.
‡Percentage of women with osteoporosis: 12.3% among women aged ≥40 and <55 years (25/204), 26.8% among women aged ≥55 and <65 years (60/224), 19.9% among women aged <65 years (85/428) and 44.4% among women aged ≥65 years (71/160).
N.A.: Not applicable.

Table VI. Percentage of women with low, moderate, or high risk for osteoporosis† by each decision rule and corresponding positive predictive values

	Distribution of study sample, % (95% CI)	PPV, % (95% CI)	NPV (95% CI)
ORAI			
Low (< 9)	44.0 (40.0-48.2)	N.A.	88.4 (84.0-92.1)
Moderate (9 to 17)	45.7 (41.7-49.9)	33.8 (28.2-39.8)	N.A.
High (> 17)	10.2 (7.9-12.9)	58.3 (44.9-70.9)	N.A
ABONE			
Low (= 1)	54.4 (50.3-58.5)	N.A.	85.9 (81.6-89.6)
Moderate (= 2)	34.2 (30.4-38.2)	35.3 (28.7-42.4)	N.A.
High (= 3)	11.4 (8.9-14.1)	59.7 (47.0-71.5)	N.A.
BWC			
Low (≥ 70)	38.8 (34.8-42.9)	N.A.	84.6 (79.3-89.1)
Moderate (57 to 69.9)	44.4 (40.3-48.5)	29.1 (23.7-35.0)	N.A.
High (< 57)	16.8 (13.9-20.1)	45.5 (35.4-55.8)	N.A.
OSTA			
Low (> 1)	49.0 (44.9-53.1)	N.A.	86.8 (82.3-90.5)
Moderate (-3 to 1)	46.8 (42.7-50.9)	36.7 (31.0-42.7)	N.A.
High (< -3)	4.3 (2.8-6.2)	68.0 (46.5-85.1)	N.A.
OST			
Low (> 1)	41.5 (37.5-45.6)	N.A.	87.7 (82.9-91.6)
Moderate (-3 to 1)	55.3 (51.2-59.3)	34.8 (29.6-40.2)	N.A.
High (< -3)	3.2 (1.9-5.0)	68.4 (43.5-87.4)	N.A.

†BMD T-score < -2.5 by lowest value at the lumbar spine, femoral neck or total hip was considered. N.A. Not applicable.

non-clinical setting and in a random population. Such results are more probably generalizable than if the sample had been submitted to imprecise preselection. Because the study sample was randomly selected with no clinical exclusion criteria, we cannot be sure that all osteoporotic patients had primary osteoporosis; however, the prevalence of known secondary causes of osteoporosis in our sample was very small, and this aspect probably has very little effect on the value of our study. Our population had a wide representation in terms of age, height, weight, oestrogen use and BMD status (Table II).

An important point of this study is the high pro-

Table VII. Estimates of lost cases of osteoporosis, absolute excess fractures and cost savings as a consequence of applying each selected algorithm per age-group, as compared with the "scan all" option. Numbers extrapolated from the observed data to 10000 population.

Algorithm	Lost cases of osteoporosis	10 year fracture probability[b]	10 year absolute excess fractures[b]	Hospital costs for excess fractures	Number of avoided DEXA scans	Savings with DEXA scans	Net balance (savings minus costs)	Net balance per preventable fracture
≥65 years: 44.4% of women with osteoporosis (71/160), average femoral neck T-score -2.41								
ORAI	0	23.1%	0	0€	0	0€		
ABONE	125	23.1%	29	86,600€	250	31,700€	-55,000€	-1,900€
BWC	1063	23.1%	246	736,700€	3563	451,100€	-285,600€	-1,200€
OSTA	313	23.1%	72	216,900€	1438	182,100€	-34,900€	-500€
OST	188	23.1%	43	130,300€	1188	150,400€	20,100€	500€
Zero option[c]	4438	23.1%	1025	3,075,500€	10000	1,266,000€	-1,809,500€	-1,800€
≥55 and <65 years: 26.8% of women with osteoporosis (60/224), average femoral neck T-score -2.07								
ORAI	759	11.9%	90	271,000€	4821	610,300€	339,400€	3,800€
ABONE	1384	11.9%	165	494,100€	7232	915,600€	421,500€	2,600€
BWC	670	11.9%	80	239,200€	4018	508,700€	269,500€	3,400€
OSTA	848	11.9%	101	302,700€	4866	616,000€	313,300€	3,100€
OST	670	11.9%	80	239,200€	3795	480,400€	241,300€	3,000€
Zero option[c]	2679	11.9%	319	956,400€	10000	1,266,000€	309,600€	1,000€
≥40 and <55 years: 12.3% of women with osteoporosis (25/204), average femoral neck T-score -1.99								
ORAI	637	7.9%	50	151,000€	7402	937,100	786,100€	15,600€
ABONE	588	7.9%	46	139,400€	7549	955,700	816,300€	17,600€
BWC	147	7.9%	12	34,800€	3971	502,700	467,900€	40,300€
OSTA	686	7.9%	54	162,600€	7647	968,100	805,500€	14,900€
OST	588	7.9%	46	139,400€	6863	868,900	729,500€	15,700€
Zero option[c]	1225	7.9%	97	290,300€	10000	1,266,000	975,700€	10,100€
<65 years: 19.9% of women with osteoporosis (85/428), average femoral neck T-score -2.05								
ORAI	701	9.8%	69	206,100€	6051	766,100€	560,000€	8,200€
ABONE	1005	9.8%	98	295,500€	7383	934,700€	639,200€	6,500€
BWC	421	9.8%	41	123,800€	3995	505,800€	383,000€	9,300€
OSTA	771	9.8%	76	226,700€	6192	783,900€	557,200€	7,400€
OST	631	9.8%	62	185,500€	5257	665,500€	480,000€	7,800€
Zero option[c]	1986	9.8%	195	583,900€	10000	1,266,000€	682,100€	3,500€

[a]Derived from Kanis et al[31] for this age group, assuming the average femoral neck T-score among osteoporotic women in each age group.
[b]Absolute excess fractures: those estimated to occur over 10 years, in 10000 population due to the osteoporosis cases lost to treatment as a consequence of applying the selection algorithm.
[c]Zero option: hypothetical decision of not scanning anyone in this age group.

portion of women aged <65 years (72.8%). Indeed, this is the group where decision-aid tools are especially needed. In fact, several authorities (including Portuguese), recommend that BMD testing should be performed in all women aged ≥65 years regardless of additional risk factors.[21,23]

The representativeness of our sample is further supported by the strong relationship between WHO status and well known risk factors for osteoporosis, including age, years after menopause, height, weight, BMI and oestrogen use (Table III). The relationship with the algorithms tested here is also clear.

The choice of the best performing decision-aid tool is complex and needs to consider a variety of aspects. At a simple level one would be tempted to simply choose the test with the best sensitivity and specificity or AUROC curve. Ideally, one screening

test should be 100% sensitive and 100% specific. However, in practice this doesn't occur: sensitivity and specificity are usually inversely related: the better a test is at correctly identifying people who have the disease (sensitivity), the worse it is at correctly identifying people who are well (specificity) and vice-versa[35]. The relative importance given to one or the other of these parameters will depend on the prevalence of the condition in the target population and on the severity of the condition. The higher the prevalence and/or severity of the condition, the more one would value sensitivity and negative predictive value: the loss of cases in a highly prevalent or costly disease has a higher negative impact on the health of the population. The lower the prevalence and/or severity of the condition, the more we would require specificity and positive predictive value: applying a screening test to search for a relatively rare or not severe condition requires considerable investment for a relatively low benefit. From this perspective and as clinicians, we need to take into account that the importance of the densitometric diagnosis of osteoporosis ("severity") varies remarkably with age, as the absolute risk of fracture remains relatively small even for very low T-scores, until the age of 55, and increases sharply after that age.[33,34] Therefore, sensitivity is essential at older ages but not so crucial in younger ages, especially before the age of 55 – these patients are much less likely to suffer the consequences of their osteoporosis in the following few years.

All algorithms performed quite well in the overall cohort (Tables III and IV). They all presented good discriminatory performances (AUROC curves ranging from 0.611 to 0.674) and showed significant differences between the normal, osteopenic and osteoporotic groups, supporting their validity. The sensitivity values in the overall series (71.2% to 80.8%, Table IV) were not as satisfactory as those observed by Cadarette *et al*[20] (91.5% to 95.3%). The principal difference with that study is the lower proportion of women aged <65 years in Cadarette's study (58.5%, mean age of the cohort 62.4 years) compared to this report (72.8%, mean age of the cohort 60.2 years). This could largely explain the discordance. Emphasizing that age is an important variable in determining sensitivity and specificity we observed that sensitivity increased progressively with age, except for the BWC (Table V). This hypothesis is strengthened by the observation of lower sensitivity values (58.1% to 83.8%) by Martínez-Aguilà *et al*,[27] who analyzed an even younger cohort of postmenopausal women (95.5% of women aged <65 years, mean age of the cohort 54.2 years).

Despite the overall good performance of these tools, the impact of age supports the need to consider them according to three age groups:

1) Above 65. As osteoporosis is highly prevalent in this age-group, most authorities recommend performing DEXA scans in every person of this age group. This recommendation would render any decision algorithm as a useless intellectual exercise, but its validity needs to be tested before we adopt it. Sensitivity, i.e. how good a test is at correctly identifying people who have the disease, would be the most useful quality of a decision-aid, followed by negative predictive value, i.e. the chance that a negative result will be correct (osteoporosis is a serious and high prevalent condition at this age).
2) Below 55. The prevalence of osteoporosis and the risk associated with it are much smaller than in older age groups. Specificity, i.e. how good a test is at correctly identifying people who are well, would be the most valuable characteristic here, followed by positive predictive value, i.e the chance that a positive test result will be correct.
3) Between 55 and 65. The group with the highest need of a good decision algorithm. Ideally, for this group, the risk assessment tool would balance the qualities desired for 1) and 2), as the epidemiological background is also intermediate. Cost-effectiveness study in this group would be even more valuable.

The recommendation for universal DEXA scan after age 65 seems to perform quite well in our population: 44% of women aged ≥65 years were osteoporotic, and presented an average femoral neck T-score of -2.41, and a 23.1% 10-year probability of fracture, according to Kanis *et al*.[33] Extrapolating to a 10000 population this osteoporotic subgroup can be estimated to suffer 1025 potentially preventable osteoporotic fractures over the following 10 years (Table VII). Applying any of the algorithms to this age group would result in a net economical loss, assuming the adopted methodology. The only exception would be the OST, which would result in a net positive balance of 20100€, only 500€ per preventable fracture. It is obvious from Table VII, that the worst choice, even from the purely economical perspective would be to complete ignore the pro-

blem (zero option). This would have an excess cost of nearly 2 million Euros considering hospital costs alone. The recommendation for universal DEXA scan after age 65 is, therefore, well supported and should be adopted, without need to consider any other factors or algorithms.

Regarding the intermediate age-group (≥55 and <65 years), the choice of a preferable algorithm on the theoretical basis exposed above is difficult, as it is not possible to precisely decide which would be the best balance between the different qualities of each rule. ABONE would be the best performing tool according to the net economic balance per 10000 population (savings of 421500€, Table VII). However, it would be associated with the highest number of fractures (165), except for the zero option (319). Calculations of the net balance per preventable fracture would elect ORAI for this group with net savings of 3800€ per preventable fracture. To visualize the issue it may help if we imagine that this money could be paid as compensation for each victim of a preventable fracture. It is not a brilliant figure, but it is the best available. These calculations exclude the zero option from consideration and put BWC as second choice (3400€).

Looking now at the group aged below 55, only 12% of these women were osteoporotic, and presented an average femoral neck T-score of -1.99. This can be estimated to result in 97 osteoporotic fractures per 10000 population over the following 10 years, if left unscanned and untreated (option zero, Table VII). Comparing with the universal application of DEXA to all this population, the use of any of the alternative options would result in a significant positive net economical balance. The best choice from the purely global economical point of view would be to ignore the problem, i.e. choose the zero option (total net positive balance of nearly 1 million Euros). However this would result in a net balance per fracture victim of only 10100€ as opposed to the 40300€ per fracture estimated from the application of the BWC. Scanning every postmenopausal woman below the age of 55 is the safest option, as it would identify every single case, but it is obviously a very costly option. Applying BWC to this age group seems to offer considerable advantage.

Simplicity would advise the use of the same algorithm for both the younger groups. The choice of the best is, however, difficult, as it requires combined consideration of all four parameters. Twenty percent of women aged <65 years were osteoporotic, and presented an average femoral neck T-score of -2.05. This can be estimated to result in 195 potentially preventable osteoporotic fractures per 10000 population over the following 10 years if left totally unscanned and untreated (zero option, Table VII). Again the zero option would give the best global economical balance but at the cost of the highest number of fractures. Savings per preventable fracture would be limited to 3500€. This is far worse than what can be achieved with BWC. This algorithm would select for DEXA 60% of the population but would allow the avoidance of 80% of the potentially preventable fractures. The end result is represented by a net balance per preventable fracture of 9300€, the best of the alternatives.

These results may suggest that the two younger age groups should be treated as separate entities given that the best strategy for each is quite different. However, the advantage of using a single algorithm and the simplicity of BWC will probably have an important positive impact in the practical implementation and effectiveness of any recommendation. We would, therefore, favour the choice of this risk assessment tool as the best to use for postmenopausal women below the age of 65.

Converting the decision rules into risk indices has been suggested on the basis that it might exclude the need for DEXA on low risk individuals (who would need no treatment), as well as in high risk individuals (who could be treated without DEXA).[13] Our data on positive predictive value (true osteoporotic women within the risk category) validate previously proposed cut points (Table VI) but also preclude the approach described above. In fact, 32% to 54.5% of women included in the highest risk group by any of these algorithms did not reach the WHO criteria for osteoporosis and would be unduly treated as far as BMD goes.

In summary, this study provides evidence for the validity of the ORAI, ABONE, BWC, OSTA and OST as useful clinical aids to assist physicians in making decisions about which postmenopausal women to refer for BMD testing for the purpose of diagnosing osteoporosis. Each rule identified over 70% of women with primary osteoporosis while limiting BMD testing among those with normal BMD. The BWC seems to have a small advantage over the alternatives in our population. It performs at the highest level in both younger age-groups and is exceedingly simple.

On the basis of our results we would suggest the following strategy for selecting postmenopausal

women for DEXA scan, in the general Portuguese population:

1) Aged 65 and above: perform DEXA scan irrespective of other risk factors.
2) Aged below 65: perform DEXA scan if body weight is less than 70 Kg.

The value of clinical screening tools in young postmenopausal women has been previously evaluated in 3 studies. Gourlay *et al*,[24] in Belgium, found that the OST, ORAI, and SCORE (based on race, presence of rheumatoid arthritis, low trauma fracture, oestrogen use, age, and weight) risk assessment tools had similar discriminatory ability to identify osteoporosis at the femoral neck in a referral population of postmenopausal women aged 45–64 years (mean age of the cohort 56 years) compared to women aged ≥65 years (mean age of the cohort 70.7 years). Martínez-Aguilà *et al* [27] found that the ORAI, OST, BWC and OSIRIS (based on weight, age, oestrogen use and history of low impact fracture) were useful as screening methods to rule out the presence of osteoporosis and the need for BMD scanning in young postmenopausal women (study cohort: 95.5% of women aged <65 years, mean age 54.2 years). However, the results obtained by Rud *et al*,[25] in Denmark, question the utility of all 3 evaluated clinical decision rules (OST, ORAI, and SCORE) to select healthy perimenopausal and early postmenopausal women (mean age of the cohort 50.5 years) for DEXA.

Our results must be interpreted in the light of several limitations.

First, we did not test all decision algorithms that have been published, rather excluding more complex formulas. The decision may be arguable but the simplicity of the tool is decisive for its usefulness in clinical practice.

Second, our series is affected by historical changes; it is possible that the pattern of oestrogen use in our area has changed, as a consequence of the results of the Women's Health Initiative trial.[36, 37] This circumstance could slightly change the data concerning the ORAI and the ABONE.

Self selection of volunteers may have biased our population sample towards higher levels of education and income. However, the impact of such deviations on the evaluation of the performance of theses indices is probably minor, as they are designed for application in practice without consideration of other factors.

The practical application of these decision rules and risk indices in facilitating clinical decisions and promoting rational use of resources should be explored further, including all potential benefits as well as harms, such as those derived of labelling women at high risk for osteoporosis.[38] The use of such algorithms should not preclude due consideration of other less common but important risk factors. Women with a prior fragility fracture are at high risk for osteoporosis and recurrent fracture and should be referred for BMD testing to facilitate treatment decisions, irrespective of other consideration.[23, 39] Similarly, women with major risk factors for secondary osteoporosis should discuss bone health and BMD testing independent of these decision rules.

A larger population-based study would be valuable to assure the scientific reliability of our findings and a direct comparison with usual clinical practice would also be valuable to determine if decision rule approaches provide more optimal use of BMD testing.[40]

The major issue with this study may reside in the economical methodology employed. It certainly represents a major simplification of reality. Numerous factors, such as cost of time used for screening and for testing, cost and effectiveness of medication and its follow-up, and indirect costs of fracture have all been left out. However, the assumptions were similar to all age groups and algorithms, allowing a cross comparison under similar, although not precise, conditions. Clearly the costs and savings presented here should not be taken as a rigorous representation of reality but rather as an index for cross-comparison. We believe that this is compensated by simplicity allowing for the use of descriptors and concepts that are inspired and easily understood by the practicing clinician. Ultimately, he is the one responsible for adopting any strategy and for taking science to the benefit of individual patients and society.

Aknowledgments

This work benefited from an unrestricted educational grant by the Merk Sharp and Dohme Foundation, Lisbon, Portugal.

Correspondence to

Pedro Machado
Serviço de Reumatologia dos Hospitais
da Universidade de Coimbra
Praceta Mota Pinto
3000-075 Coimbra – Portugal
E-mail: pedrommcmachado@gmail.com

References

1. Epstein S. Postmenopausal osteoporosis: fracture consequences and treatment efficacy vary by skeletal site. Aging (Milano) 2000;12:330-341.
2. Center JR, Nguyen TV, Schneider D, Sambrook PN, Eisman JA. Mortality after all major types of osteoporotic fracture in men and women: an observational study. Lancet 1999;353:878-882.
3. Screening for osteoporosis in postmenopausal women: recommendations and rationale. Ann Intern Med 2002;137:526-528.
4. Lewiecki EM, Watts NB, McClung MR et al. Official positions of the international society for clinical densitometry. J Clin Endocrinol Metab 2004;89:3651--3655.
5. Lane NE. Epidemiology, etiology, and diagnosis of osteoporosis. Am J Obstet Gynecol 2006;194:3-11.
6. Raisz LG. Clinical practice. Screening for osteoporosis. N Engl J Med 2005;353:164-171.
7. Solomon DH, Levin E, Helfgott SM. Patterns of medication use before and after bone densitometry: factors associated with appropriate treatment. J Rheumatol 2000;27:1496-1500.
8. Bates DW, Black DM, Cummings SR. Clinical use of bone densitometry: clinical applications. Jama 2002;288:1898-1900.
9. Weinstein L, Ullery B. Identification of at-risk women for osteoporosis screening. Am J Obstet Gynecol 2000;183:547-549.
10. Michaelsson K, Bergstrom R, Mallmin H, Holmberg L, Wolk A, Ljunghall S. Screening for osteopenia and osteoporosis: selection by body composition. Osteoporos Int 1996;6:120-126.
11. Cadarette SM, Jaglal SB, Murray TM. Validation of the simple calculated osteoporosis risk estimation (SCORE) for patient selection for bone densitometry. Osteoporos Int 1999;10:85-90.
12. Koh LK, Sedrine WB, Torralba TP et al. A simple tool to identify asian women at increased risk of osteoporosis. Osteoporos Int 2001;12:699-705.
13. Cadarette SM, Jaglal SB, Kreiger N, McIsaac WJ, Darlington GA, Tu JV. Development and validation of the Osteoporosis Risk Assessment Instrument to facilitate selection of women for bone densitometry. Cmaj 2000;162:1289-1294.
14. Geusens P, Hochberg MC, van der Voort DJ et al. Performance of risk indices for identifying low bone density in postmenopausal women. Mayo Clin Proc 2002;77:629-637.
15. Lydick E, Cook K, Turpin J, Melton M, Stine R, Byrnes C. Development and validation of a simple questionnaire to facilitate identification of women likely to have low bone density. Am J Manag Care 1998;4:37--48.
16. Sedrine WB, Chevallier T, Zegels B et al. Development and assessment of the Osteoporosis Index of Risk (OSIRIS) to facilitate selection of women for bone densitometry. Gynecol Endocrinol 2002;16:245-250.
17. Salaffi F, Silveri F, Stancati A et al. An assessment tool for predicting fracture risk in postmenopausal women. Development and validation of the ORACLE score to predict risk of osteoporosis. Clin Rheumatol 2001;12:519-528.
18. Black DM, Steinbuch M, Palermo L et al. An assessment tool for predicting fracture risk in postmenopausal women. Osteoporos Int 2001;12:519--528.
19. Salaffi F, Silveri F, Stancati A, Grassi W. Development and validation of the osteoporosis prescreening risk assessment (OPERA) tool to facilitate identification of women likely to have low bone density. Clin Rheumatol 2005;24:203-211.
20. Cadarette SM, McIsaac WJ, Hawker GA et al. The validity of decision rules for selecting women with primary osteoporosis for bone mineral density testing. Osteoporos Int 2004;15:361-366.
21. Tavares V, Canhao H, Gomes JA et al. Recommendations for the diagnosis and management of osteoporosis. Acta Reumatol Port 2007;32:49-59.
22. Kanis JA, Black D, Cooper C et al. A new approach to the development of assessment guidelines for osteoporosis. Osteoporos Int 2002;13:527-536.
23. Leib ES, Binkley N, Bilezikian JP, Kendler DL, Lewiecki EM, Petak SM. Position Development Conference of the International Society for Clinical Densitometry. Vancouver, BC, July 15-17, 2005. J Rheumatol 2006;33:2319-2321.
24. Gourlay ML, Miller WC, Richy F, Garrett JM, Hanson LC, Reginster JY. Performance of osteoporosis risk assessment tools in postmenopausal women aged 45-64 years. Osteoporos Int 2005;16:921-927.
25. Rud B, Jensen JE, Mosekilde L, Nielsen SP, Hilden J, Abrahamsen B. Performance of four clinical screening tools to select peri- and early postmenopausal women for dual X-ray absorptiometry. Osteoporos Int 2005;16:764-772.
26. Chan SP, Teo CC, Ng SA, Goh N, Tan C, Deurenberg-Yap M. Validation of various osteoporosis risk indices in elderly Chinese females in Singapore. Osteoporos Int 2006;17:1182-1188.
27. Martinez-Aguila D, Gomez-Vaquero C, Rozadilla A, Romera M, Narvaez J, Nolla JM. Decision rules for selecting women for bone mineral density testing: application in postmenopausal women referred to a bone densitometry unit. J Rheumatol 2007;34:1307--1312.
28. Fujiwara S, Masunari N, Suzuki G, Ross P. Performance of osteoporosis risk indices in a Japanese population. Curr Ther Res 2001;62:586-94.
29. da Silva JAP, Carapito H, Reis P. Bone densitometry: diagnostic criteria in the Portuguese population. Acta Reumatol Port 1999;93:9-18.
30. Looker AC, Wahner HW, Dunn WL et al. Proximal femur bone mineral levels of US adults. Osteoporos Int 1995;5:389-409.
31. Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of the binomial. Biometrika 1934;26:404-13.

32. Griner PF, Mayewski RJ, Mushlin AI, Greenland P. Selection and interpretation of diagnostic tests and procedures. Principles and applications. Ann Intern Med 1981;94:557-592.
33. Kanis JA, Johnell O, Oden A, Dawson A, De Laet C, Jonsson B. Ten year probabilities of osteoporotic fractures according to BMD and diagnostic thresholds. Osteoporos Int 2001;12:989-995.
34. Kanis JA, Borgstrom F, De Laet C et al. Assessment of fracture risk. Osteoporos Int 2005;16:581-589.
35. Mausner J KS. Epidemiology. An Introductory Text. Second ed. Philadelphia: W. B. Saunders Company; 1984.
36. Rossouw JE, Anderson GL, Prentice RL et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. Jama 2002;288:321-333.
37. Hormone therapy for the prevention of chronic conditions in postmenopausal women: recommendations from the U.S. Preventive Services Task Force. Ann Intern Med 2005;142:855-860.
38. Nelson HD, Helfand M, Woolf SH, Allan JD. Screening for postmenopausal osteoporosis: a review of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med 2002;137:529-541.
39. Brown JP, Josse RG. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. Cmaj 2002;167:1-34.
40. McGinn TG, Guyatt GH, Wyer PC, Naylor CD, Stiell IG, Richardson WS. Users' guides to the medical literature: XXII: how to use articles about clinical decision rules. Evidence-Based Medicine Working Group. Jama 2000;284:79-84.

2nd European Rheumatology Conference for General Practitioners

Corinthia Hotel, Lisboa
3-5 de Outubro de 2008

2nd Mediterranean Clinical Immunology Meeting

Turquia, Antalya
4-7 de Outubro de 2008