

Evaluation of Decision Rules for Referring Women for Bone Densitometry by Dual-Energy X-ray Absorptiometry

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THE IDENTIFICATION OF WOMEN at risk for osteoporotic fractures by measurement of low bone mineral density (BMD) is an important strategy to reduce the burden of fracture-related morbidity associated with this disease.^{1,2} Dual-energy x-ray absorptiometry (DXA) is accepted as the most accurate clinical method for identifying those with low BMD.^{2,3} Suggestions concerning who should be tested are quite broad. The National Osteoporosis Foundation (NOF) 1998 practice guidelines (revised in 1999)⁴ recommend BMD testing in women considering treatment who are aged 65 years or older, and in younger postmenopausal women considering treatment who have 1 or more risk factors for osteoporotic fracture other than menopause. The recommendation to select perimenopausal women on the basis of “other risk factors” is echoed in a number of other guidelines.^{2,5-9} However, given that many postmenopausal women have at least 1 of these factors,¹⁰ the question may not be whom to test, but rather whom not to test.

Context Identification of women with low bone mineral density (BMD) is an important strategy in reducing the incidence of osteoporotic fractures. However, screening all women is not recommended.

Objectives To assess the diagnostic properties of 4 decision rules—Simple Calculated Osteoporosis Risk Estimation (SCORE), Osteoporosis Risk Assessment Instrument (ORAI), Age, Body Size, No Estrogen (ABONE), and body weight less than 70 kg (weight criterion)—for selecting women for dual-energy x-ray absorptiometry (DXA) testing and to compare results with recommendations made in the National Osteoporosis Foundation (NOF) practice guidelines.

Design and Setting Analysis of data from the Canadian Multicentre Osteoporosis Study, a population-based community sample, collected from 9 study centers across Canada between February 1996 and September 1997.

Participants Postmenopausal women aged 45 years or older (N=2365) without bone disease who had DXA data for the femoral neck, data to apply selection criteria, and who were not currently taking estrogens or who had been taking hormone replacement therapy for 5 or more years.

Main Outcome Measures Sensitivity, specificity, and area under the receiver operating characteristic (AUROC) curve of each of the 4 decision rules and the NOF guidelines for identifying women with a BMD T score of less than -1.0 SD, less than -2.0 SD, and no more than -2.5 SD at the femoral neck, and percentages of women recommended for testing, stratified by BMD level and age.

Results The percent of women with a BMD T score less than -1 , less than -2 , and no more than -2.5 were 68.3%, 25.4%, and 10.0%, respectively. The AUROC curves were greatest using SCORE and ORAI. The sensitivity for identifying women with a BMD T score of less than -2.0 was 93.7% (95% confidence interval [CI], 91.8%-95.6%) using the NOF guidelines and was 97.5% (95% CI, 96.3%-98.8%), 94.2% (95% CI, 92.3%-96.1%), 79.1% (95% CI, 75.9%-82.3%), and 79.6% (95% CI, 76.4%-82.8%), respectively, using the SCORE, ORAI, ABONE, and weight criterion. However, the NOF guidelines also resulted in 74.4% (95% CI, 71.3%-77.6%) of women with a normal BMD (T score of -1.0 or higher) being tested compared with 69.2% (95% CI, 65.9%-72.5%), 56.3% (95% CI, 52.7%-59.8%), 35.8% (95% CI, 32.4%-39.2%), and 38.1% (95% CI, 34.6%-41.6%), respectively, using the 4 decision rules. Assessments suggest that ABONE and weight criterion are not useful case-finding approaches.

Conclusion The SCORE and ORAI decision rules are better than the NOF guidelines at targeting BMD testing in high-risk patients. The acceptability of these rules in clinical practice merits further investigation given their potential effect on the use of densitometry services.

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Clinical decision rules are evidence-based tools that can help reduce uncertainty in medical practice by implementing clear criteria for the use of major clinical findings.^{11,12} Several decision rules based on clinical criteria have been developed to guide decisions for BMD referrals.¹³⁻¹⁶ They range from the very simple, being based on weight alone,¹³ to more complex selection schemes requiring the assessment of many risk factors.¹⁴ The purpose of this study was to assess the diagnostic properties of the NOF recommendations and 4 decision rules.^{4,13-16}

METHODS

Study Sample

The Canadian Multicentre Osteoporosis Study (CaMos) is a population-based 5-year cohort study evaluating the relationship between risk factors for osteoporosis, measures of BMD, and osteoporotic fracture.¹⁷ In brief, an age-, sex-, and region-stratified random sample of the Canadian population was selected using a telephone-based sampling frame. This included noninstitutionalized residents aged 25 years or older within 50 km of 9 study centers across Canada. CaMos participants were fluent in English or French, or in the case of Toronto and Vancouver, English, French, or Chinese. Baseline data collection began February 1996, and ended September 1997. Eligible subjects were invited to meet with a trained interviewer to complete a standardized questionnaire about risk factors for osteoporosis and to visit the center for DXA testing. The present study included data from 6 sites: Calgary, Halifax, Québec City, Saskatoon, St John's, and Vancouver. Given that the Osteoporosis Risk Assessment Instrument (ORAI) was developed using CaMos Ontario data (Hamilton, Kingston, and Toronto),¹⁵ these sites were excluded from the current analyses. Menopausal women aged 45 years or older with DXA data at the femoral neck were eligible for this study. Participants with physician-diagnosed bone disease, taking bone sparing medication other than

ovarian hormones, or missing data for any of the risk factors required by the decision rules or NOF guidelines were excluded.

The NOF guidelines⁴ and the decision rules each provide guidance to clinicians in making referrals for BMD testing. The recommendations are made to help identify the average woman at risk for primary osteoporosis. Identification of women at high risk for secondary osteoporosis would be independent of respective recommendations for testing. Therefore, women at high risk for secondary osteoporosis were excluded from this study. The NOF guidelines recommend BMD testing only among women considering treatment, ie, when there is a decision to be made. For the purposes of this study it was assumed that all women would consider treatment depending on DXA results. Although women currently taking hormone replacement therapy (HRT) would not be eligible for testing (no decision to be made regarding treatment), the NOF physician's guide recommends testing in those taking HRT for prolonged periods. As a result, whereas women taking HRT for less than 5 years were excluded, those taking HRT for 5 years or more were included in the study.

Inclusion of Decision Rules for Referring Women for Bone Densitometry

We conducted a MEDLINE search to identify articles published in English providing decision rules based on simple criteria to identify menopausal community-dwelling women for BMD testing. Decision aids based on regression models¹⁸ or involving detailed questionnaires¹⁹ were excluded from this analysis. Our search identified 4 decision rules for BMD testing.¹³⁻¹⁶

Application of NOF Guidelines and Decision Rules

TABLE 1 summarizes the criteria that clinicians are recommended to use in deciding which women should undergo bone densitometry under the NOF guidelines and the 4 decision rules.

Each strategy was applied to the cohort using individual responses to the CaMos questionnaire. Among women 65 years or younger, selection criteria were limited to the 4 major risk factors highlighted in the NOF physician's guide, ie, weight less than 57.6 kg, personal history of fracture as an adult, history of fracture in a first-degree relative, and current smoker. These 4 criteria were chosen by the NOF²⁰ because they are key determinants of hip fracture risk among white women.²¹ The NOF guideline specifies family history to include maternal or paternal wrist, hip, or spine fracture after the age of 50 years. These specific data were not collected by CaMos. Therefore, any parental minimal trauma fracture was used as a proxy. The CaMos questionnaire grouped fractures of the forearm and wrist. Minimal trauma fractures of the forearm/wrist were included as a history of wrist fracture in Simple Calculated Osteoporosis Risk Estimation (SCORE) derivation. Finally, weight was recorded in kilograms by CaMos.

Outcome Measure

Bone mineral density was measured using the following DXA machines: Hologic QDR 4500 (in Calgary), Hologic QDR 2000 (in Halifax and Québec), Hologic QDR 1000 (in Saskatoon and Vancouver) (Hologic Inc, Waltham, Mass), and Lunar DPX (in St John's), (Lunar Corporation, Madison, Wis). T scores were calculated from cross-calibrated Hologic BMD equivalents²² using Canadian young adult normal values at the femoral neck.²³ Although a recent update from the International Osteoporosis Foundation³ suggests that the Third National Health and Nutrition Examination Survey (NHANES III) reference data be used to derive T scores, there is increasing evidence supporting local reference standards.²⁴ As well, the Canadian young adult normal reference at the femoral neck (mean [SD], 0.857 [0.125] g/cm²)²³ is similar to that reported by NHANES III for non-Hispanic white Americans (mean [SD], 0.858 [0.120] g/cm²).²⁵

Low BMD at either the hip or lumbar spine is clinically relevant for deciding about prophylactic treatment to prevent osteoporosis and fragility fractures.⁵ However, given that the NOF guidelines⁴ were derived from assessments at the hip and the increasing questions regarding the application of the World Health Organization criteria to sites other than the hip,³ BMD outcomes in this study were assessed as being present at the femoral neck.

Osteoporosis treatment guidelines⁴⁻⁷ suggest pharmacological interventions among those with osteoporosis (T score ≤ -2.5 SDs) and no intervention among women with normal BMD (ie, T score ≥ -1.0). While most guidelines^{2,5-7} suggest that treatment be considered for those with osteopenia (T score of -1.0 to -2.5), the NOF guidelines provide more specific recommendations; suggesting treatment to reduce fracture risk among menopausal women with a BMD T score below -1.5 if other risk factors are present, or below -2.0 in the absence of risk factors.⁴ For the purposes of this analysis, a T score of less than -2.0 was taken as the suggested threshold to initiate pharmacological therapy to reduce fracture incidence in menopausal women, hereafter referred to as the *treatment threshold*.

Statistical Analysis

Demographic and other characteristics of the study population were tabulated as means and SDs, or proportions as applicable. The area under the receiver operating characteristic (AUROC) curve was used as a measure of the overall ability of each strategy to discriminate between women with varying degrees of low BMD. Three BMD outcomes were examined for each strategy: a BMD T score of less than -1.0 (complement of normal BMD⁴⁻⁷), less than -2.0 (below treatment threshold), and no more than -2.5 (osteoporosis⁴⁻⁷). The AUROC curves were calculated and compared with applying methods for correlated AUROC curves.²⁶ The AUROC curves for identifying osteoporosis were plotted.

The decision rules are scoring systems amenable to AUROC curve analysis. Although the NOF recommendations are not presented as a scoring system, the guide states that the more risk factors a woman has, the greater the risk for fracture.⁴ The status report²⁰ summarizing evidence-based recommendations suggested that physicians use a counting method of risk factors among menopausal women aged 65 years or younger, giving 1 point for history of fracture, weight, and smoking. We thus derived "NOF points" by giving 1 point to each factor.

The number of points recommended by the developers of respective decision rules was used to select women for testing, ie, SCORE points of 6 or more, ORAI points of 9 or more, Age, Body Size, No Estrogen (ABONE) points of 2 or more, body weight of less than 70 kg (weight

criterion), and NOF points of 1 or more. Given the discrepancy between the text and scoring in the ABONE article, we contacted the author who confirmed that patients with an ABONE score of 2 or more are recommended for testing (L. Weinstein, written communication, February 2001).¹⁶ Sensitivity, specificity, and corresponding 95% confidence intervals (CIs) were calculated at the recommended cut-point for each method. Finally, given that 2 of the selection methods (NOF and ORAI) recommend all women aged 65 years or older for testing, the proportion of women selected by each tool was stratified by age as 45 to 64 years old and 65 years or older, and presented by level of BMD as: normal BMD (T score ≥ -1 SD), mild osteopenia (T score -1.0 to no less than -2.0), moderate osteopenia (T score -2.0 to -2.5), and osteoporosis (T score ≤ -2.5).

Table 1. Selection Criteria Suggested From the National Osteoporosis Foundation Practice Guidelines and 4 Clinical Decision Rules for Bone Mineral Density Testing Among Postmenopausal Women Considering Treatment*

| Guideline/Rule | Selection Cut Point | Scoring System |
|--|---------------------|---|
| National Osteoporosis Foundation (NOF) ⁴ | Score ≥ 1 | One point each for† Age ≥ 65 y Weight < 57.6 kg Personal history of fracture: minimal trauma fracture > 40 y Family history of fracture‡ Current cigarette smoking |
| Simple Calculated Osteoporosis Risk Estimation (SCORE) ¹⁴ | Score ≥ 6 | Points are given for Race: 5 if not black Rheumatoid arthritis: 4 if applicable History of minimal trauma fracture after age 45 y: 4 for each fracture of the wrist§, hip, or rib, to a maximum of 12 Age: 3 times first digit of age in years Estrogen therapy: 1 if never used Weight: -1 times weight in lb divided by 10 and truncated to integer |
| Osteoporosis Risk Assessment Instrument (ORAI) ¹⁵ | Score ≥ 9 | Points are given for Age: 15 if 75 y or older, 9 if 65-74 y, 5 if 55-64 y Weight: 9 if < 60 kg, 3 if 60.0-69.9 kg Estrogen use: 2 if not currently taking estrogen |
| Age, Body Size, No Estrogen (ABONE) ¹⁶ | Score ≥ 2 | Points are given for Age: 1 if > 65 y Weight: 1 if < 63.5 kg Estrogen use: 1 if never used oral contraceptives or estrogen therapy for at least 6 mo |
| Body weight criterion ¹³ | | Weight < 70 kg |

*ORAI is also applicable for use in premenopausal women aged 45 years or older.

†For the purpose of the area under the receiver operating characteristic (AUROC) curve analysis, each factor was given 1 point. All those with at least 1 "NOF point" were identified for testing.

‡NOF guidelines stipulate maternal/paternal history of hip, wrist, or spine fracture when the parent was 50 years or older. These specific data was not collected in CaMos.

§Forearm/wrist were included as a history of wrist fracture.

Table 2. Summary of Demographics, Risk Factors for Osteoporosis, and Bone Mineral Density (BMD) Status in the Study Cohort (N = 2365)

| Characteristics | No. (%) |
|--|-------------|
| Demographics | |
| Age, y | |
| 45-54 | 220 (9.3) |
| 55-64 | 758 (32.1) |
| 65-74 | 962 (40.7) |
| ≥75 | 425 (18.0) |
| Weight, kg | |
| <50 | 114 (4.8) |
| 50-59 | 460 (19.5) |
| 60-69 | 760 (32.1) |
| 70-79 | 569 (24.1) |
| ≥80 | 462 (19.5) |
| Race | |
| White | 2285 (96.6) |
| Asian | 42 (1.8) |
| Black | 8 (0.3) |
| Other | 30 (1.3) |
| Factors Influencing Osteoporosis Risk | |
| Minimal trauma fractures | |
| Rib, hip, or forearm/wrist since age 45 y | 194 (8.2) |
| Any site since age 40 y | 500 (21.1) |
| Estrogen therapy | |
| Current use (for ≥5 y) | 412 (17.4) |
| Past use | 526 (22.2) |
| Estrogen | |
| Never used* | 922 (39.0) |
| Other risk factors | |
| Rheumatoid arthritis | 155 (6.6) |
| Current smoker | 316 (13.4) |
| Parental history of fracture | 743 (31.4) |
| Bone Mineral Density | |
| BMD status | |
| Normal BMD | 755 (31.7) |
| Osteopenia | 1390 (58.3) |
| Osteoporosis | 239 (10.0) |
| BMD T score† | |
| <-1.0 SD‡ | 1629 (68.3) |
| <-2.0 SD§ | 605 (25.4) |
| ≤-2.5 SD | 239 (10.0) |

*Oral contraceptives or estrogen replacement.

†Not mutually exclusive categories.

‡Complement of normal BMD.

§Below treatment threshold.

||Osteoporosis.

RESULTS

A total of 3288 menopausal women aged at least 45 years had DXA data at the femoral neck. Among these, a total of 402 were excluded with either a diagnosis of osteoporosis (382) or taking bone sparing medications such as calcitonin or bisphosphonates (20). A further 158 were excluded with potential causes for secondary osteoporosis. In addition, 69 were missing data to calculate decision rules, and 294 currently using HRT for less than 5 years were excluded, leaving a total sample size of 2365 women.

The mean age and weight of the study cohort was 66.4 (SD, 8.8) years and 69.0 (13.3) kg, respectively. TABLE 2 provides a summary of demographics, osteoporosis risk factors, and the distribution of BMD in the study cohort. The population under investigation was largely composed of white women (96.6%). Among those younger than 65 years (n=978), 43.5% had normal BMD, 52.1% had osteopenia (26.1% of whom fell below the treatment threshold), and 4.7% had osteoporosis.

The sensitivity and specificity at the developers' recommended cut-point and the AUROC curve for each approach to select women with any clinically significant decrease in BMD (T score <-1.0), below the treatment threshold (T score <-2.0), and with osteoporosis (T score ≤-2.5) are presented in TABLE 3. The AUROC curves for identifying women with osteoporosis are plotted in the FIGURE. The SCORE and the ORAI had the best discriminatory performance at all BMD thresholds evaluated. When restricted to osteoporosis, SCORE, ORAI, and weight criterion were equivalent, with an AUROC curve of 0.80, 0.79, and 0.79, respectively.

The NOF, SCORE, and ORAI selection criteria resulted in more than 94% of women below the treatment threshold and more than 96% of women with osteoporosis for initial testing, with SCORE being the most sensitive. However, NOF and SCORE would also recommend 74.4% (95% CI, 71.3%-77.6%) and 69.2% (95% CI, 65.9%-72.5%) of women with normal BMD for testing, compared with 56.3% (95% CI, 52.7%-59.8%) with the ORAI. The other decision rules would miss from 13% to 17% of women with osteoporosis but result in less than 40% of women with normal BMD recommended for testing; 35.8% (95% CI, 32.4%-39.2%) with ABONE and 38.2% (95% CI, 34.6%-41.6%) using the weight criterion.

The overall proportion of women selected by each method ranged from 55% to 84% (TABLE 4). The NOF and SCORE would each result in 84% of women aged 45 years or older being recommended to undergo DXA testing. The correspond-

ing figures for the other decision rules were 75% of women for ORAI and 55% and 56% for ABONE and weight criterion, respectively. When looking at results by age, the SCORE selected 95% of women aged 65 years or older, coming close to the recommendations made by the NOF and ORAI that include women aged 65 years or older as part of their selection criteria. However, the SCORE also selected a higher proportion of younger women (69%), particularly in comparison to the ORAI (39%) and the ABONE (22%). This translates into 55% of women aged 45 to 64 years with normal BMD being selected by SCORE (comparable to the NOF), compared with 23% and 12% using the ORAI and ABONE, respectively. The weight criterion selected 53% of younger vs 59% of older women, the closest proportion by age compared with any other method. However, the weight criterion only captured 83% of younger women and 79% of older women below the treatment threshold. Although ABONE selected 88% of older women below the treatment threshold, more than half of younger women with moderate osteopenia and osteoporosis were missed.

COMMENT

In recent years, the availability of new pharmacological treatments for osteoporosis²⁷ have put new pressures on primary care physicians to screen patients at risk for fragility fracture with BMD testing. The clinical challenge is to identify those at greatest risk for fracture,¹ while limiting unnecessary testing in those with normal BMD who have a low risk for fracture.^{1,6} Current guidelines^{2,5-9} providing lists of indications for BMD testing may be difficult to translate into a clinical case-finding strategy for practice.^{12,28} Decision rules using a more limited, but specific set of clinical factors provide an alternative approach to guide decisions for BMD testing.

Two of the decision rules (SCORE and ORAI) as well as the NOF guidelines selected 94% or more women below the treatment threshold and more than 96% of women with osteoporosis. However, the specificity of the ORAI was signifi-

cantly better, selecting 56% of women with normal BMD compared with 69% and 74% with the SCORE and NOF, respectively. Although the ABONE and weight criterion would result in even fewer tests (<40%) among women with normal BMD, 20% of women below the treatment threshold would not be selected for DXA testing.

Overall, the NOF guidelines and SCORE each selected 84% of the study population. The ORAI selected significantly fewer women (75%), yet recommended just as many women aged 45 to 64 years with moderate osteopenia (67%), and more women with osteoporosis (87% vs 80%) compared with the NOF guidelines. Therefore, the ORAI, similar to the NOF in selecting all women aged 65 years or older, is clearly superior to the NOF guidelines, providing more specific recommendations to limit unnecessary testing among women younger than 65 years. Similarly, given that the tools have comparable performance, the simplicity of the ORAI vs the SCORE suggests that it might be more readily adopted in clinical practice,¹² and thus may have a better impact on identifying women for initial BMD testing vs the SCORE. An impact assessment¹¹ of the 2 rules is warranted to assess the effectiveness of these decision rules applied in practice. Future research should evaluate the SCORE and ORAI critically from the perspective of both physicians and health planners/policy advisors. Clinicians may not favor using a rule that limits testing in women who may be appropriately selected for treatment on the basis of BMD results, preferring instead to use clinical judgment, or to opt for universal screening. However, a policy for screening all menopausal women has been widely rejected, and it may be difficult for clinicians to assign appropriate weight to multiple risk factors in each patient individually. Decision rules may therefore be more productive in terms of useful decision making.¹¹ Decision rules are not meant to replace diagnostic tests, but rather complement them by helping to identify higher risk populations that are more likely to benefit from testing.¹¹ Clinical

Table 3. Sensitivity, Specificity, and Area Under the Receiver Operating Characteristic (AUROC) Curve for Strategies to Identify Postmenopausal Women Aged 45 Years or Older Below Various Bone Mineral Density (BMD) T Scores at the Femoral Neck (N = 2365)*

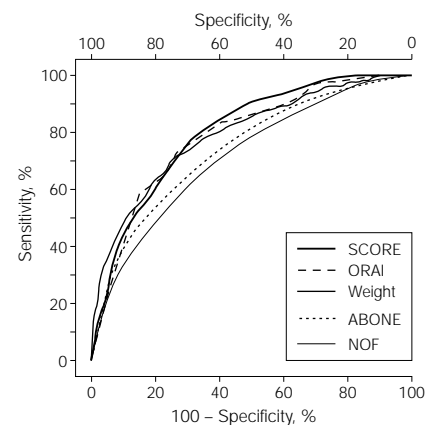
| | % (95% CI) | | AUROC Curve (SE) |
|--------------------------------|------------------|------------------|------------------|
| | Sensitivity | Specificity | |
| BMD T score <-1.0 SD | | | |
| NOF | 87.9 (86.3-89.4) | 25.6 (22.4-28.7) | 0.64 (0.01) |
| SCORE | 90.6 (89.2-92.0) | 30.8 (27.5-34.1) | 0.72 (0.01) |
| ORAI | 83.2 (81.4-85.0) | 43.7 (40.2-47.3) | 0.71 (0.01) |
| ABONE | 64.4 (62.1-66.8) | 64.2 (60.8-67.6) | 0.67 (0.01) |
| Weight criterion | 64.1 (61.7-66.4) | 61.9 (58.4-65.4) | 0.68 (0.01) |
| BMD T score <-2.0 SD | | | |
| NOF | 93.7 (91.8-95.6) | 19.8 (17.9-21.7) | 0.67 (0.01) |
| SCORE | 97.5 (96.3-98.8) | 20.8 (18.9-22.7) | 0.77 (0.01) |
| ORAI | 94.2 (92.3-96.1) | 31.9 (29.7-34.1) | 0.76 (0.01) |
| ABONE | 79.1 (75.9-82.3) | 52.7 (50.3-55.0) | 0.71 (0.01) |
| Weight criterion | 79.6 (76.4-82.8) | 52.2 (49.9-54.5) | 0.74 (0.01) |
| BMD T score ≤-2.5 SD | | | |
| NOF | 96.2 (93.8-98.6) | 17.8 (16.2-19.4) | 0.70 (0.02) |
| SCORE | 99.6 (98.8-100) | 17.9 (16.2-19.5) | 0.80 (0.01) |
| ORAI | 97.5 (95.5-99.5) | 27.8 (25.9-29.7) | 0.79 (0.01) |
| ABONE | 83.3 (78.5-88.0) | 47.7 (45.6-49.8) | 0.72 (0.02) |
| Weight criterion | 87.0 (82.8-91.3) | 47.6 (45.5-49.7) | 0.79 (0.02) |

*NOF indicates National Osteoporosis Foundation guidelines (selection at cut-point of 1); SCORE, Simple Calculated Osteoporosis Risk Estimation (selection at cut-point of 6); ORAI, Osteoporosis Risk Assessment Instrument (selection at cut-point of 9); ABONE, Age, Body Size, No Estrogen (selection at cut-point of 2); Weight criterion, selection of women who weigh less than 70 kg; and CI, confidence interval.

decisions for treatment should be based on actual DXA bone density values and the patient risk profile, rather than relying on the decision rule results.

Targeting high-risk populations is important for achieving cost-effective interventions.²⁹ Selection of women aged 65 years or older makes intuitive sense, because women at this age are entering the highest period of risk for hip fractures,³⁰ and supports the view that screening should likely be aimed at women aged 65 years or older.³¹ Both the ORAI and the NOF practice guidelines suggest BMD testing in all women aged at least 65 years who are considering treatment, regardless of risk profile. At the recommended cut-point of 6, the SCORE also selected 95% of women in this age group. However, other researchers have begun to explore specific selection criteria aside from age among older groups. Currently, this is limited to regression models³² that would not be easy to implement in a clinical setting.¹² Others argue that there is an upper age limit beyond which DXA testing is not necessary (>80 years,³³ >70 years⁴), supporting treatment

Figure. The Area Under the Receiver Operating Characteristic (AUROC) Curves for Osteoporosis



SCORE indicates Simple Calculated Osteoporosis Risk Estimation; ORAI, Osteoporosis Risk Assessment Instrument; ABONE indicates Age, Body Size, No Estrogen; and NOF, National Osteoporosis Foundation guidelines.

among these oldest age groups in the presence of multiple risk factors without DXA. Further research is warranted, however, to identify the effectiveness of treatment without BMD results. A recent randomized con-

trolled clinical trial identified the importance of BMD testing in making decisions for drug therapy, finding that risedronate reduced fracture incidence among elderly women with low BMD, but no protection was observed among those selected based on clinical factors other than BMD status.³⁴

Data in this study provide information based on DXA results at one point in time. The purpose of initial DXA testing is to identify those who would benefit from treatment or prophylaxis to reduce the risk of fragility fracture based on low BMD. As such, the ultimate out-

come of interest is fracture, and future studies should evaluate the proportion of missed cases that eventually fracture. Such longitudinal evaluation may also provide information regarding the repeated use of decision rules to select women for initial DXA testing. Furthermore, in addition to BMD results, the best predictor of fracture is prevalent fracture. The NOF recommendations include prevalent fracture as an indication for BMD testing. Although the SCORE includes a variant of this (gives points for previous fracture), it would not select all of these patients. Like-

wise, minimal trauma fractures were associated with low BMD in development of the ORAI, but fracture history was excluded from the decision rule to simplify the instrument.¹⁵ Similar to the separate identification of women at high risk for secondary osteoporosis, it is important in practice to suggest absolute BMD testing among those with prevalent fragility fracture if they are considering treatment. The simple screening and treatment of individuals with fragility fracture are often neglected in practice.³⁵⁻³⁷

Given that CaMos oversampled older age groups, our study sample had proportionately more women older than 65 years as compared to the actual distribution of menopausal women in Canada. This may have affected the overall specificity of each selection method and overestimated the total proportion selected by each tool. Given that we did not have specific data regarding age or site of fractures in parents, by including any parental minimal trauma fracture, we may have overselected women for testing based on NOF. In addition, rheumatoid arthritis is a known cause of secondary osteoporosis.⁴ Given the inclusion of rheumatoid arthritis in SCORE derivation, we included subjects with this condition. Inclusion of women with rheumatoid arthritis may have increased the sensitivity of the SCORE, but decreased the sensitivity of the other selection methods that target women at risk for primary osteoporosis. Finally, among initial contacts providing basic demographic data, the response rate for women aged 45 years or older among the 6 CaMos sites included in this study was 62.1%. Proportions agreeing to participate decreased with increasing age, from 75.7% among those aged 45 to 54 years to 35.7% among those older than 84 years. This may indicate a healthy cohort effect, where healthier women participated in the study, and thus an underrepresentation of frail and sick individuals at older ages. Alternatively, given the nature of the study, which evaluates risk factors for osteoporosis, perhaps a different self-selection bias occurred, where

Table 4. Selection of Women by Age Group and Bone Mineral Density (BMD) Outcomes in the Study Cohort Using Recommended Cut-Points*

| | No. (%) | | |
|--|---------------------------|--------------------------|------------------------|
| | Ages 45-64 y (n = 978) | Ages ≥65 y (n = 1387) | All Ages (N = 2365) |
| National Osteoporosis Foundation (NOF) | | | |
| Normal BMD† | 232 (55.0) | 321 (100.0) | 553 (74.4) |
| Mild osteopenia‡ | 264 (62.4) | 596 (100.0) | 860 (84.4) |
| Moderate osteopenia§ | 58 (66.7) | 277 (100.0) | 335 (92.0) |
| Osteoporosis | 37 (80.4) | 193 (100.0) | 230 (96.2) |
| Total selected | 591 (60.4) | 1387 (100.0) | 1978 (83.6) |
| Simple Calculated Osteoporosis Risk Estimation (SCORE) | | | |
| Normal BMD† | 231 (54.7) | 283 (88.2) | 514 (69.2) |
| Mild osteopenia‡ | 319 (75.4) | 563 (94.5) | 882 (86.6) |
| Moderate osteopenia§ | 75 (86.2) | 275 (99.3) | 350 (96.2) |
| Osteoporosis | 45 (97.8) | 193 (100.0) | 238 (99.6) |
| Total selected | 670 (68.5) | 1314 (94.7) | 1984 (83.9) |
| Osteoporosis Risk Assessment Instrument (ORAI) | | | |
| Normal BMD† | 97 (23.0) | 321 (100.0) | 418 (56.3) |
| Mild osteopenia‡ | 186 (44.0) | 596 (100.0) | 782 (76.7) |
| Moderate osteopenia§ | 58 (66.7) | 277 (100.0) | 335 (92.0) |
| Osteoporosis | 40 (87.0) | 193 (100.0) | 233 (97.5) |
| Total selected | 381 (39.0) | 1387 (100.0) | 1768 (74.8) |
| Age, Body Size, No Estrogen (ABONE) | | | |
| Normal BMD† | 52 (12.3) | 214 (66.7) | 266 (35.8) |
| Mild osteopenia‡ | 102 (24.1) | 466 (78.2) | 568 (55.7) |
| Moderate osteopenia§ | 42 (48.3) | 236 (85.2) | 278 (76.4) |
| Osteoporosis | 23 (50.0) | 176 (91.2) | 199 (83.3) |
| Total selected | 219 (22.4) | 1092 (78.7) | 1311 (55.4) |
| Weight criterion | | | |
| Normal BMD† | 163 (38.6) | 121 (37.7) | 284 (38.2) |
| Mild osteopenia‡ | 239 (56.5) | 330 (55.4) | 569 (55.8) |
| Moderate osteopenia§ | 70 (80.5) | 202 (72.9) | 272 (74.7) |
| Osteoporosis | 41 (89.1) | 168 (87.0) | 209 (87.4) |
| Total selected | 513 (52.5) | 821 (59.2) | 1334 (56.4) |

*Cut-points for selection: NOF (1), SCORE (6), ORAI (9), ABONE (2), Weight criterion (<70 kg). Moderate osteopenia

+ osteoporosis = amount below treatment threshold.

†BMD T score ≥ -1.0 SD.

‡-1.0 SD > BMD T score ≥ -2.0 SD.

§-2.0 SD > BMD T score > -2.5 SD.

||BMD T Score ≤ -2.5 SD.

those at higher risk or with a family history were more likely to participate in the study. Further evaluations in other populations are important to access the generalizability of these findings.

DXA testing is important for evaluating the severity of bone loss and making treatment decisions. The ABONE and weight criterion decision rules miss 13% to 17% of women with osteoporosis and are thus not useful case-finding approaches for DXA testing. The SCORE and the ORAI, however, are better than the NOF guidelines, targeting testing on women at high-risk for low BMD. The acceptability of these rules in clinical practice merits further investigation. Future research should include a cost-effectiveness analysis to identify acceptable sensitivity and specificity, and an impact assessment to evaluate the utility of these decision rules in clinical practice.

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REFERENCES

- McClung MR. Therapy for fracture prevention. *JAMA*. 1999;282:687-689.
- Genant HK, Cooper C, Poor G, et al. Interim report and recommendations of the World Health Organization task-force for osteoporosis. *Osteoporos Int*. 1999;10:259-264.
- Kanis JA, Glüer C-C. An update on the diagnosis and assessment of osteoporosis with densitometry. *Osteoporos Int*. 2000;11:192-202.
- National Osteoporosis Foundation. *Physician's Guide to Prevention and Treatment of Osteoporosis*. Belle Mead, NJ: Excerpta Medica Inc; 1999.
- Scientific Advisory Board, Osteoporosis Society of Canada. Clinical practice guidelines for the diagnosis and management of osteoporosis. *CMAJ*. 1996;155:1113-1133.
- Kanis JA, Delmas P, Burckhardt P, Cooper C, Torgerson D. The European Foundation for Osteoporosis and Bone Disease, for guidelines for diagnosis and management of osteoporosis. *Osteoporos Int*. 1997;7:390-406.
- The prevention and management of osteoporosis: consensus statement. Australian National Consensus Conference 1996. *Med J Aust*. 1997;167(suppl):S1-S15.
- Joseph P, Hughes D. Osteoporosis: guidelines for general practitioners. *Aust Fam Physician*. 1997;26:1181-1196.
- Baran DT, Faulkner KG, Genant HK, Miller PD, Pacifici R. Diagnosis and management of osteoporosis: guidelines for the utilization of bone densitometry. *Calcif Tissue Int*. 1997;61:433-440.
- Kanis JA, Torgerson D, Cooper C. Comparison of the European and USA practice guidelines for osteoporosis. *Trends Endocr Metab*. 2000;11:28-32.
- McGinn TG, Guyatt GH, Wyer PC, et al. Users' guides to the medical literature, XXII: how to use articles about clinical decision rules. *JAMA*. 2000;284:79-84.
- Laupacis A, Sekar N, Stiell IG. Clinical prediction rules: a review and suggested modifications of methodological standards. *JAMA*. 1997;277:488-494.
- Michaëlsson K, Bergström R, Mallmin H, Holmberg L, Wolk A, Ljunghall S. Screening for osteopenia and osteoporosis: selection by body composition. *Osteoporos Int*. 1996;6:120-126.
- 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.
- 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.
- Weinstein L, Ullery B. Identification of at-risk women for osteoporosis screening. *Am J Obstet Gynecol*. 2000;183:547-549.

17. Kreiger N, Tenenhouse A, Joseph L, et al. Research notes: the Canadian Multicentre Osteoporosis Study (CaMos): background, rationale, methods. *Can J Aging*. 1999;18:376-387.

18. Carroll J, Testa MA, Erat K, LeBoff MS, Fuleihan GE-H. Modeling fracture risk using bone density, age, and years since menopause. *Am J Prev Med*. 1997;13:447-452.

19. Goemaere S, Zegels B, Toye K, et al. Limited clinical utility of a self-evaluating risk assessment scale for postmenopausal osteoporosis: lack of predictive value of lifestyle-related factors. *Calcif Tissue Int*. 1999;65:354-358.

20. Osteoporosis: review of the evidence for prevention, diagnosis and treatment and cost-effectiveness analysis. *Osteoporos Int*. 1998;8(suppl 4):S7-S80.

21. Cummings SR, Nevitt MC, Browner WS, et al. Risk factors for hip fracture in white women. *N Engl J Med*. 1995;332:767-773.

22. Genant HK, Grampp S, Glüer CC, et al. Universal standardization for dual x-ray absorptiometry: patient and phantom cross-calibration results. *J Bone Miner Res*. 1994;9:1503-1514.

23. Tenenhouse A, Joseph L, Kreiger N, et al. Estimation of the prevalence of low bone density in Canadian women and men using a population-specific DXA reference standard: the Canadian Multicentre Osteoporosis Study (CaMos). *Osteoporos Int*. 2000;11:897-904.

24. Gürelek A, Bayraktar M, Ariyürek M. Inappropriate reference range for peak bone mineral density in dual-energy x-ray absorptiometry: implications for the interpretation of t-scores. *Osteoporos Int*. 2000;11:809-813.

25. Looker AC, Wahner HW, Dunn WL, et al. Updated data on proximal femur bone mineral levels of US adults. *Osteoporos Int*. 1998;8:468-489.

26. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics*. 1988;44:837-845.

27. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. *JAMA*. 2001;285:785-795.

28. Wasson JH, Sox HC, Neff RK, Goldman L. Clinical prediction rules: application and methodological standards. *N Engl J Med*. 1985;313:793-799.

29. Jonsson B, Christiansen C, Johnell O, Hedbrandt J, Karlsson G. Cost-effectiveness of fracture prevention in established osteoporosis. *Scand J Rheumatol*. 1996;25:30-38.

30. Black DM. Screening and treatment in the elderly to reduce osteoporotic fracture risk. *Br J Obstet Gynaecol*. 1996;103:2-8.

31. Torgerson DJ. Is there a future for non-menopausal screening strategies for osteoporosis prevention? *Osteoporos Int*. 1998;8(suppl 1):S57-S61.

32. Ballard PA, Purdie DW, Langton CM, Steel SA, Mussurakis S. Prevalence of osteoporosis and related risk factors in UK women in the seventh decade: osteoporosis case finding by clinical referral criteria or predictive model? *Osteoporos Int*. 1998;8:535-539.

33. Fogelman I. Screening for osteoporosis. *BMJ*. 1999;319:1148-1149.

34. McClung MR, Geusens P, Miller PD, et al. Effect of risedronate on the risk of hip fracture in elderly women. *N Engl J Med*. 2001;344:333-340.

35. Hajcsar EE, Hawker G, Bogoch ER. Investigation and treatment of osteoporosis in patients with fragility fractures. *CMAJ*. 2000;163:819-822.

36. Torgerson DJ, Dolan P. Prescribing by general practitioners after an osteoporotic fracture. *Ann Rheum Dis*. 1998;57:378-379.

37. Kamel HK, Hussain MS, Tariq S, Perry HM III, Morley JE. Failure to diagnose and treat osteoporosis in elderly patients hospitalized with hip fracture. *Am J Med*. 2000;109:326-328.