Development and Internal Validation of the Male Osteoporosis Risk Estimation Score

Angela J. Shepherd, MD
Alvah R. Cass, MD, SM
Carol A. Carlson, BA
Laura Ray, MA
The University of Texas Medical Branch, Galveston, Tex

ABSTRACT

PURPOSE We wanted to develop and validate a clinical prediction rule to identify men at risk for osteoporosis and subsequent hip fracture who might benefit from dual-energy x-ray absorptiometry (DXA).

METHODS We used risk factor data from the National Health and Nutrition Examination Survey III to develop a best fitting multivariable logistic regression model in men aged 50 years and older randomized to either the development (n = 1,497) or validation (n = 1,498) cohorts. The best fitting model was transformed into a simplified scoring algorithm, the Male Osteoporosis Risk Estimation Score (MORES). We validated the MORES, comparing sensitivity, specificity, and area under the receiver operating characteristics (ROC) curve in the 2 cohorts and assessed clinical utility with an analysis of the number needed-to-screen (NNS) to prevent 1 additional hip fracture.

RESULTS The MORES included 3 variables—age, weight, and history of chronic obstructive pulmonary disease—and showed excellent predictive validity in the validation cohort. A score of 6 or greater yielded an overall sensitivity of 0.93 (95% CI, 0.85-0.97), a specificity of 0.59 (95% CI, 0.56-0.62), and an area under the ROC curve of 0.832 (95% CI, 0.807-0.858). The overall NNS to prevent 1 additional hip fracture was 279 in a cohort of men representative of the US population.

CONCLUSIONS Osteoporosis is a major predictor of hip fractures. Experts believe bisphosphonate treatment in men should yield results similar to that in women and reduce hip fracture rates associated with osteoporosis. In men aged 60 years and older, the MORES is a simple approach to identify men at risk for osteoporosis and refer them for confirmatory DXA scans.

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INTRODUCTION

By 2030, the number of men aged over 65 years is expected to double,1 and the incidence of hip fracture is also expected to increase.2,3 The importance of osteoporosis and hip fractures in men may be underestimated. In 2002, men accounted for about 2 million cases of osteoporosis compared with 8 million cases in women.4 The lifetime risk for hip fracture in men is about one-third of that for women (6% vs 17.5%)5,6; however, men are twice as likely to die in the hospital after a hip fracture. Furthermore, the 1-year postfracture mortality rate is 31% in men compared with 17% in women.7,8

In women early identification of osteoporosis coupled with bisphosphonate therapy has been shown to reduce hip fracture by at least 40% to 50%.9-13 Recently Orwoll et al reported a reduction in vertebral fractures in osteoporotic men and concluded that the benefit of bisphosphonate therapy in men "was very similar to those in postmenopausal women."14,15 Sato and colleagues16 found a relative risk of hip fracture of 0.19 in elderly men treated with risedronate after a stroke. These studies support the concept that early recognition and treatment of osteoporosis may reduce fractures
in men. Despite the increased mortality associated with hip fracture in men and the apparent benefit of therapy, there are no generally accepted guidelines for primary screening for osteoporosis in US men.

The purpose of this study was to develop and validate a clinical prediction rule for osteoporosis in men. A computerized random number generator assigned men to the development (n = 1,497) and validation (n = 1,498) cohorts. We excluded any variable with more than 10% missing data. We used multivariable logistic regression with backward elimination to develop the predictive model. Candidate variables for logistic regression against osteoporosis (defined by criteria stated above) were selected from bivariate analysis of the association of osteoporosis and the initial list of candidate predictive variables. Variables that were associated with osteoporosis with a 2-tailed Fisher’s exact test or Pearson χ² with P ≤ 0.20 were used in the logistic regression analysis in the development subset. Variables were retained in the model if they achieved a significance level of P ≤ 0.05. Age and weight were transformed to categorical variables and modeled with indicator variables, otherwise, candidate predictors were entered as dichotomous variables.

Next we examined subsets of the initial model to select the best fitting and most parsimonious model based on clinical utility or face validity of the variables, strength of classification based on the Hosmer-Lemeshow goodness-of-fit test, and discrimination based on the area under the receiver operating characteristic (ROC) curve. From the best fitting model, we created a simplified scoring system based on a linear combination of a simple integer transformation of the β coefficients. Both the best fitting model and the simplified scoring system were tested in the validation cohort. Before analysis of the data, we opted for a sensitivity of at least 90% for the simplified scoring system to optimize identification of men at increased risk of osteoporosis. We assessed predictive validity by comparing sensitivity, specificity, and area under the ROC curve, as well as the associated 95% confidence intervals (CI), in the validation cohort.

Analyses were performed using Statistical Analysis Software 9.1.3 program with SUDAAN 9.0.1 to adjust for design effects and weighted sampling. To determine the clinical usefulness of the Male Osteoporosis Risk Estimation Score (MORES), a scoring system, we constructed a table comparing the number needed-to-screen (NNS) to prevent 1 additional hip fracture in the next 10 years for successive age categories of men. We constructed the table following the method described by Nelson et al.

**METHODS**

**Design and Population**

This study is an analysis of 2,995 men aged 50 years and older included in the National Health and Nutrition Examination Survey (NHANES) III data set who had a valid DXA test. The NHANES III data set, which is the latest national US population sample available that contains DXA data, is based on a probability sample of 40,000 civilian noninstitutionalized individuals. The survey was conducted by the National Center for Health Statistics and Centers for Disease Control and Prevention between 1988 and 1994. Details of the sampling and data collection have been described elsewhere. The study protocol was approved by the Institutional Review Board of the University of Texas Medical Branch.

**Variables**

The initial variables considered as candidates to predict osteoporosis included the sex-neutral risk factors for osteoporosis and hip fractures in women, as reviewed and summarized by Nelson, that were also contained in the NHANES data set. Age, weight, race/ethnicity, marital status, education, alcohol use, tobacco use, physical activity, self-rated health status, chronic conditions, including diabetes mellitus, chronic obstructive pulmonary disease (COPD), and myocardial infarction, and history of maternal hip fracture formed the initial list of candidate predictors.

**Osteoporosis Definition**

Osteoporosis was defined according to the World Health Organization (WHO) criteria, using T scores derived from race/ethnicity and sex-specific bone mineral density for Hispanic, non-Hispanic white, and non-Hispanic black men aged 20 to 29 years. Bone mineral density of the total hip, measured in grams per centimeter squared, was used in accordance with the WHO recommendations. Men were characterized as osteoporotic or not osteoporotic based on measured bone mineral density of 0.681 g/cm² or less for non-Hispanic whites, 0.723 g/cm² or less for Hispanics, and 0.751 g/cm² for non-Hispanic blacks, which correspond to a T score of less than -2.5. Bone mineral density measurements were made using Hologic QDR machines and standardized with phantoms described previously by Genant et al.

**Analysis and Model Development**

We used the split-sample method to develop and validate a clinical prediction rule to identify men at increased risk for osteoporosis. A computerized random number generator assigned men to the development (n = 1,497) and validation (n = 1,498) cohorts. We excluded any variable with more than 10% missing data. We used multivariable logistic regression with backward elimination to develop the predictive model. Candidate variables for logistic regression against osteoporosis (defined by criteria stated above) were selected from bivariate analysis of the association of osteoporosis and the initial list of candidate predictive variables. Variables that were associated with osteoporosis with a 2-tailed Fisher’s exact test or Pearson χ² with P ≤ 0.20 were used in the logistic regression analysis in the development subset. Variables were retained in the model if they achieved a significance level of P ≤ 0.05. Age and weight were transformed to categorical variables and modeled with indicator variables, otherwise, candidate predictors were entered as dichotomous variables.

Next we examined subsets of the initial model to select the best fitting and most parsimonious model based on clinical utility or face validity of the variables, strength of classification based on the Hosmer-Lemeshow goodness-of-fit test, and discrimination based on the area under the receiver operating characteristic (ROC) curve. From the best fitting model, we created a simplified scoring system based on a linear combination of a simple integer transformation of the β coefficients. Both the best fitting model and the simplified scoring system were tested in the validation cohort. Before analysis of the data, we opted for a sensitivity of at least 90% for the simplified scoring system to optimize identification of men at increased risk of osteoporosis. We assessed predictive validity by comparing sensitivity, specificity, and area under the ROC curve, as well as the associated 95% confidence intervals (CI), in the validation cohort.

Analyses were performed using Statistical Analysis Software 9.1.3 program with SUDAAN 9.0.1 to adjust for design effects and weighted sampling. To determine the clinical usefulness of the Male Osteoporosis Risk Estimation Score (MORES), a scoring system, we constructed a table comparing the number needed-to-screen (NNS) to prevent 1 additional hip fracture in the next 10 years for successive age categories of men. We constructed the table following the method described by Nelson et al.
develop the US Preventive Services Task Force (USPSTF) recommendations for screening for osteoporosis in women. The 10-year age-specific hip fracture rates were obtained from Kanis et al. Age-specific prevalence of osteoporosis was derived from the NHANES III data. Assumptions were based on best available information from the medical literature and duplicated the assumption used by Nelson et al, where appropriate.

RESULTS

The weighted prevalence of osteoporosis was 4.8% in men aged 50 years and older with an interpretable DXA (N = 2,995) included in the NHANES III data set. Comparing the 1,497 men in the development cohort with the 1,498 men in the validation cohort, we found no significant differences in sociodemographic characteristics or other clinical risk factors for osteoporosis and hip fracture. Results are reported in Table 1.

Age, weight, race/ethnicity, single marital status, sedentary activity (no exercise in the previous month), past or current tobacco use, current abstinence from alcohol, self-rated health (fair/poor), less than high school education, and a history of COPD were significantly associated with osteoporosis in bivariate analysis. The results are displayed in Table 2. From these variables, age, modeled as 55 years or younger (reference category), 56 to 74 years, and 75 years or older, weight in kilograms, modeled as 70 kg or less, greater than 70 kg to 80 kg, and greater than 80 kg (reference category); single marital status; past or current tobacco use; current abstinence from alcohol; and a history of COPD were significant and retained in a logistic regression model. The initial regression model yielded a good fit to the data (Hosmer-Lemeshow test, \( \chi^2 = 6.203, df = 8, P = .624 \)) and excellent discrimination (area under the ROC curve = 0.830; 95% CI, 0.790-0.870). Based on a priori criteria of face validity, goodness-of-fit, and discrimination, we simplified the initial model to produce the final best fitting model, which contained 3 variables: age (modeled as above), weight (modeled as above), and history of COPD. The best fitting model provided a slightly better fit to the data (Hosmer-Lemeshow test, \( \chi^2 = 2.466, df = 5, P = .782 \)) and retained excellent discrimination (area under the ROC curve = 0.830; 95% CI, 0.790-0.870).

Table 1. Comparison of Sociodemographic and Clinical Characteristics of Men in Development and Validation Cohorts

| Univariate Factors | Development Cohort (n = 1,497) | Validation Cohort (n = 1,498) |
|--------------------|-------------------------------|-------------------------------|
| Mean age, y (SD)   | 63.8 (9.4)                    | 64.2 (9.7)                    |
| Mean weight, kg (SD)| 83.1 (15.1)                   | 82.9 (14.8)                   |
| Race/ethnicity     |                               |                               |
| Non-Hispanic white | 88.9                          | 88.5                          |
| Non-Hispanic black | 8.1                           | 8.5                           |
| Hispanic           | 3.0                           | 3.0                           |
| Osteoporosis, %    | 5.2                           | 4.4                           |
| Marital status – unmarried, % | 19.4 | 20.3 |
| Less than high school education, % | 36.4 | 36.4 |
| Maternal hip fracture, % | 9.7  | 8.0  |
| Currently abstains from alcohol, % | 52.6 | 54.9 |
| Ever smoked tobacco, % | 81.5 | 82.1 |
| Sedentary activity, % | 12.1 | 13.6 |
| Self-rated health, fair/poor, % | 24.5 | 22.9 |
| Diagnosis of diabetes mellitus, % | 10.4 | 11.0 |
| Diagnosis of COPD, % | 12.0 | 10.0 |
| Diagnosis of CAD (MI), % | 12.8 | 11.4 |

CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; MI = myocardial infarction.

Note: Adjusted and reported using sampling and design weights from National Health and Nutrition Examination Survey III.

Table 2. Bivariate Analysis of Available Risk Factors and Osteoporosis in the Development Cohort (n = 1,497)

| Risk Factor for Osteoporosis | Odds Ratio (95%CI) | P Value |
|------------------------------|--------------------|---------|
| Age                          |                    | <.001   |
| ≤55 years                    | 1.0*               |         |
| 56-74 years                  | 5.6 (1.47-21.1)    |         |
| ≥75 years                    | 15.1 (3.9-59.0)    |         |
| Weight                       |                    | <.001   |
| ≤70 kg                       | 27.3 (10.2-72.9)   |         |
| >70-80 kg                    | 7.0 (2.2-22.5)     |         |
| >80 kg                       | 1.0*               |         |
| Race/ethnicity               |                    | .007    |
| Non-Hispanic white           | 1.0*               |         |
| Non-Hispanic black           | 1.9 (1.1-3.4)      |         |
| Hispanic                     | 0.5 (0.2-1.3)      |         |
| Marital status, unmarried    | 3.1 (1.5-6.2)      | .017    |
| Less than high school education | 1.9 (1.1-3.2)   | .034    |
| Currently abstains from alcohol | 2.3 (1.2-4.3)  | .009    |
| Ever smoked tobacco          | 3.1 (1.5-6.3)      | .002    |
| Sedentary activity           | 3.3 (1.7-6.6)      | .026    |
| Self-rated health, poor/fair | 2.6 (1.5-4.6)      | .012    |
| Diagnosis of diabetes mellitus | 1.2 (0.5-3.0)    | .756    |
| Diagnosis of COPD            | 4.5 (2.5-8.3)      | .003    |
| Diagnosis of myocardial infarction | 2.0 (1.0-4.2) | .162    |
| Family history of maternal hip fracture | 2.4 (0.6-9.3) | .117    |

Note: Adjusted and reported using sampling and design weights from NHANES III.

COPD = chronic obstructive pulmonary disease.

* Reference category.
MALE OSTEOPOROSIS RISK ESTIMATION SCORE

From the best fitting model, we created a simplified scoring algorithm, the Male Osteoporosis Risk Estimate Score (MORES), derived from a linear combination of whole integers based on a transformation of the β coefficients, which is shown in Table 4. We selected a cut-point of 6 or more, which produced a sensitivity greater than 0.90. In the development cohort, a MORES value of 6 or more points produced a sensitivity of 0.91 (95% CI, 0.80-0.97), a specificity of 0.58 (95% CI, 0.53-0.64), and an area under the ROC curve of 0.822 (95% CI, 0.782-0.863). In the validation cohort, a MORES value of 6 or more points produced a sensitivity of 0.95 (95% CI, 0.81-0.99), a specificity of 0.61 (95% CI, 0.57-0.64), and an area under the ROC curve of 0.842 (95% CI, 0.811-0.873). Combining the development and validation cohorts, a MORES value of 6 or more points produced a sensitivity of 0.95 (95% CI, 0.81-0.99), a specificity of 0.61 (95% CI, 0.57-0.64), and an area under the ROC curve of 0.832 (95% CI, 0.807-0.858). In addition, testing the MORES algorithm across the non-Hispanic white, non-Hispanic black, and Hispanic racial/ethnic groups, showed similar values for sensitivity and specificity, except that specificity was slightly higher in non-Hispanic whites.

To evaluate the clinical impact of the MORES, we conducted an analysis of the NNS to prevent 1 additional hip fracture in a cohort of 10,000 men aged 50 years and older. In this simulation, men aged 50 years and older would complete the MORES questionnaire, and anyone scoring 6 or more points would be referred for a DXA scan. If the DXA scan confirmed osteoporosis, bisphosphonate therapy would be prescribed. We used assumptions for the male simulation cohort similar to those described by Nelson et al18 to develop a NNS table for the USPSTF recommendations for osteoporosis screening for women. Overall, in a cohort of men aged 50 years and older, representative of the US population, use of the MORES results in 279 men referred for DXA screening to prevent 1 additional hip fracture.

Table 3. Multiple Logistic Regression Models for Initial and Best-Fitting Models: Development Cohort (n = 1,454)

| Variable | β Coefficient | Standard Error (β) | Wald Statistic | P Value | Odds Ratio 95% CI |
|----------|---------------|--------------------|---------------|---------|------------------|
| Initial model: 6 variables | | | | | |
| Intercept | -7.83 | 1.00 | − | − | − | − | − | − |
| Age ≤55 years | 0.00 | − | − | − | 1.00 | − | − | − |
| 56-74 years | 1.18 | 0.73 | − | − | 3.26 | 0.77-13.73 | − | − | − |
| ≥75 years | 1.70 | 0.71 | − | − | 5.50 | 1.33-22.71 | − | − | − |
| Weight ≤70 kg | 3.01 | 0.48 | − | − | 20.20 | 7.79-52.35 | − | − | − |
| >70-80 kg | 1.81 | 0.56 | − | − | 6.12 | 2.01-18.59 | − | − | − |
| >80 kg | 0.00 | − | − | − | 1.00 | − | − | − |
| Marital status, unmarried | 0.86 | 0.35 | 6.10 | .015 | 2.37 | 1.18-4.73 | − | − | − |
| Currently abstains from alcohol | 0.85 | 0.033 | 6.53 | .012 | 2.34 | 1.21-4.52 | − | − | − |
| Ever smoked tobacco | 1.18 | 0.39 | 8.93 | .004 | 3.25 | 1.49-7.12 | − | − | − |
| Diagnosis of COPD | 1.18 | 0.36 | 10.99 | .001 | 3.26 | 1.61-6.60 | − | − | − |
| Best fitting model: 3 variables | | | | | |
| Intercept | -6.28 | 0.87 | − | − | − | − | − |
| Age ≤55 years | 0.00 | − | − | − | 1.00 | − | − | − |
| 56-74 years | 1.29 | 0.71 | − | − | 3.64 | 0.89-14.81 | − | − | − |
| ≥75 years | 2.03 | 0.68 | − | − | 7.58 | 1.95-29.90 | − | − | − |
| Weight ≤70 kg | 3.07 | 0.48 | − | − | 21.52 | 8.27-55.97 | − | − | − |
| >70-80 kg | 1.86 | 0.57 | − | − | 6.44 | 2.08-19.90 | − | − | − |
| >80 kg | 0.00 | − | − | − | 1.00 | − | − | − |
| Diagnosis of COPD | 1.32 | 0.37 | 12.67 | .001 | 3.76 | 1.80-7.85 | − | − | − |

CI = confidence interval; COPD = chronic obstructive pulmonary disease.
Note: Forty-three cases excluded from analysis due to a missing value for at least 1 variable. Data adjusted and reported using sampling and design weights from NHANES III.

Table 4. Male Osteoporosis Risk Estimation Score (MORES)

| Risk Factor | Logistic Regression β Coefficient | MORES Points* |
|-------------|-----------------------------------|--------------|
| Age ≤55 years | 0.00 | 0 |
| 56-74 years | 1.29 | 3 |
| ≥75 years | 2.03 | 4 |
| Weight ≤70 kg (≤154 lb) | 3.07 | 6 |
| >70-80 kg (>154-176 lb) | 1.86 | 4 |
| >80 kg (>176 lb) | 0.00 | 0 |
| COPD | 1.32 | 3 |

COPD = chronic obstructive pulmonary disease.
* Screening threshold is 6 points or greater.
† Reference category.
DISCUSSION

We developed and validated a clinical prediction rule, MORES, to stratify the risk of asymptomatic osteoporosis based on age and weight categories and a history of COPD. In a sample representative of the US male population aged 50 years and older, 44% of men would have positive screening results with the MORES and would be referred for a confirmatory DXA scan. The MORES correctly identified 93% of the men with osteoporosis in this nationally representative sample and showed excellent predictive validity in the validation cohort.

Low weight was the strongest predictor of osteoporosis, and the MORES supports DXA testing in all men aged 50 years and older who weigh 70 kg (154 lb) or less. We chose to model weight as opposed to body mass index because it is easier to obtain and more reliably available in most clinical settings. Men aged 56 years and older with a history of COPD also met DXA screening thresholds. Age alone was not a criterion for screening with a DXA scan. Only those men in the oldest age-group (aged 75 years and older) who have a weight of greater than 80 kg (176 lb) and/or a history of COPD would meet screening thresholds. The MORES does not assume a linear relationship between increasing weight and lower risk of osteoporosis. Similar to data for women, the weight and osteoporosis data for men show a plateau in the protective effect of increased weight. For men, the protection afforded by weight plateaus at 80 kg (176 lb). Clinical guidelines that model the protective effect of weight without consideration of a ceiling effect may underestimate the risk of osteoporosis.

In developing the best fitting model, we eliminated history of smoking, single marital status, and abstinence from alcohol. History of COPD and smoking probably represent similar risk factors for osteoporosis, however, smoking is probably less specific and was excluded. Although single marital status has been associated with hip fracture in women and men, it is probably a surrogate for other factors and was excluded for lack of face validity. Excluding abstinence from alcohol had no effect on the model. Knowledge of these and other minor risk factors may raise the level of awareness of clinicians for osteoporosis in men but are of marginal value in deciding on who should be referred for DXA scans.

### Table 5. Simulated Screening for Osteoporosis in 10,000 Men Aged 50 Years and Older: 10-Year Hip Fracture Outcomes

| Variables | 50-54 | 55-59 | 60-64 | 65-69 | 70-74 | 75-79 | 80-84 | 85-89 | Overall |
|-----------|-------|-------|-------|-------|-------|-------|-------|-------|---------|
| Base/case assumptions* | | | | | | | | | |
| Fracture risk \(^{27}\) | 0.034 | 0.037 | 0.091 | 0.133 | 0.215 | 0.328 | 0.362 | 0.333 | 0.135 |
| Osteoporosis prevalence (NHANES III) | 0.007 | 0.034 | 0.036 | 0.049 | 0.051 | 0.094 | 0.119 | 0.257 | 0.048 |
| Relative risk for hip fracture with treatment \(^{18}\) | 0.63 | 0.63 | 0.63 | 0.63 | 0.63 | 0.63 | 0.63 | 0.63 | 0.63 |
| Adherence to treatment, proportion \(^{18}\) | 0.70 | 0.70 | 0.70 | 0.70 | 0.70 | 0.70 | 0.70 | 0.70 | 0.70 |
| Results per 10,000 men | | | | | | | | | |
| Predicted cases of osteoporosis, n | 70 | 340 | 360 | 490 | 940 | 1,190 | 2,570 | 480 |
| MORES screen: true positive | 65 | 316 | 335 | 456 | 474 | 874 | 1,107 | 2,390 | 446 |
| MORES screen: false negative | 5 | 24 | 25 | 34 | 36 | 66 | 83 | 180 | 34 |
| MORES screen: true negative | 5,859 | 5,699 | 5,688 | 5,611 | 5,599 | 5,345 | 5,198 | 4,384 | 5,617 |
| MORES screen: false positive | 4,071 | 3,961 | 3,952 | 3,899 | 3,891 | 3,715 | 3,612 | 2,046 | 3,903 |
| Referred for DXA (TP + FP), n | 4,136 | 4,277 | 4,287 | 4,355 | 4,365 | 4,589 | 4,719 | 5,436 | 4,350 |
| Predicted hip fractures: screened MORES:DXA | | | | | | | | | |
| Predicted hip fractures: true positive | 1.64 | 13.36 | 22.58 | 44.91 | 75.56 | 212.47 | 296.86 | 589.76 | 44.72 |
| Predicted hip fractures: false negative | 0.17 | 1.36 | 2.29 | 4.56 | 7.68 | 21.58 | 30.15 | 59.91 | 4.54 |
| Predicted hip fractures: total | 1.81 | 14.71 | 24.87 | 49.47 | 83.24 | 234.05 | 327.02 | 649.67 | 49.26 |
| Predicted hip fractures: unscreened | 2.38 | 19.38 | 32.76 | 65.17 | 109.65 | 308.32 | 430.78 | 855.81 | 64.90 |
| NNS MORES:DXA | 7,216 | 917 | 544 | 278 | 166 | 62 | 46 | 45 | 595 |

* Formulas used in calculations are available upon request from the authors.

DXA = dual energy x-ray absorptiometry; FP = false positive; MORES = Male Osteoporosis Risk Estimate Score; NHANES = National Health and Nutrition Examination Survey; NNS = number needed to screen; RX = diagnosis of osteoporosis and treatment with bisphosphonate therapy; no RX = diagnosis of osteoporosis and no treatment; TP = true positive.
The performance of the MORES compares favorably with other clinical guidelines to determine which men should be referred for DXA. The Osteoporosis Self-assessment Tool (OST)\textsuperscript{30,31} is based on a complex calculation using self-reported age and weight. Adler et al tested the OST in men attending pulmonary or rheumatology clinics.\textsuperscript{30} After eliminating men with known osteoporosis, the modified OST achieved a sensitivity of 93% and specificity of 66% in this highly selected population presumed to be at greater risk for osteoporosis than the general population. In addition to cumbersome calculations, the lack of uniformity in values selected as screening thresholds at which DXA is recommended is confusing.\textsuperscript{30-32}

Broussard and Magnus\textsuperscript{33} also examined data from NHANES III and found low body mass index (less than 22 kg/m\textsuperscript{2}), current cigarette smoking, and low physical activity to be independent risk factors for osteoporosis. The presence of 1 or more risk factors was predictive of osteoporosis. Their analysis, however, was limited to modifiable risk factors. We found similar results with respect to weight as a parallel to body mass index, smoking, and sedentary lifestyle; however, sedentary lifestyle did not remain significant in multivariable logistic regression when other factors were considered. Sedentary lifestyle is likely associated with advancing age, which was not modeled by Broussard and Magnus and is a more important predictor of risk for osteoporosis. Given the efficacy of bisphosphonates and the excess mortality in men who sustain a hip fracture, all risk factors should be considered when determining a need for DXA testing, not just modifiable indicators.

The 2002 Canadian guidelines\textsuperscript{34} recommend DXA testing on all men aged 65 years and older. Restricting testing to men aged 65 years and older would miss a significant number of men younger than 65 years who have lower body weight or a history of COPD; it would also refer a substantial number of men aged 65 years and older for DXA scans who are not at significantly increased risk for osteoporosis. This recommendation, when tested in the NHANES III subset of men aged 50 years, yielded a sensitivity of 0.72 and a specificity of 0.55.

The clinical utility of the MORES, as measured by the NNS to prevent 1 additional hip fracture, compares favorably with the USPSTF findings for women. USPSTF recommended universal DXA testing for women aged 65 years with a NNS of 731 to prevent 1 additional hip fracture. The MORES, with similar assumptions of subsequent treatment, adherence, and fracture reduction in those diagnosed with osteoporosis, results in a NNS to prevent 1 additional hip fracture of 544 in men aged 60 to 64 years. The NNS is lower in older age-groups, which suggests that the MORES could be used in men aged 60 years and older to identify those who would benefit from a DXA. Even in men aged 55 to 59 years, the NNS is 917 using the MORES. Considering the excess mortality of hip fractures in men compared with women, the MORES may improve patient outcomes in this age-group of men as well.

Our study has several limitations. The MORES was developed and validated in the same population sample. Ideally, it should be evaluated in other independent samples, including populations outside the United States. We chose the split-sample method to develop and validate the MORES. Even though the split-sample technique is widely used and accepted, we recognize the limitations, especially the reduction in sample size associated with splitting the sample. Other methods, such as bootstrap and recursive partitioning, also known as classification and regression tree analysis, could have been used; however, these methods are less familiar to most clinicians and less intuitive.

Another limitation is the lack of vertebral bone mineral density measurements in the NHANES III data set. As a result, the current study does not consider vertebral osteoporosis. Newer data from NHANES (1999-2004) include vertebral bone mineral density values and should be examined as they become available. Our study was aimed at risk assessment in asymptomatic men and does not apply to men with preexisting fractures, new fractures, or secondary causes of osteoporosis.

Finally, the NNS analysis is based on indirect evidence and several general assumptions regarding adherence to treatment and treatment response. To the extent possible we used the best available data from the medical literature and stayed within the assumption used by the Nelson et al\textsuperscript{18} in preparing the USPSTF recommendations for women. Ultimately, we need a large prospective study to directly investigate the effect of clinical risk assessment and selective use of confirmatory DXA scan vs usual care to determine whether early recognition and treatment of osteoporosis in men will result in a reduction in hip and other osteoporosis fractures and the associated morbidity and mortality.

According to the US Census Bureau, the number of men older than 65 years is expected to double by the year 2030.\textsuperscript{1} The overall incidence of osteoporosis and resulting fractures is therefore expected to increase markedly in the ensuing decades. Recognition and treatment of osteoporosis before the occurrence of a fracture have the potential to reduce morbidity and mortality related to osteoporotic fractures in men. The MORES appears to perform better than currently available risk assessment guidelines for men. The MORES is simpler to calculate than the OST, includes important nonmodifiable risks not included in the Broussard and Magnus recommendations, and yields greater sensitivity and specificity than the Canadian guidelines. The MORES...
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