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ORIGINAL ARTICLE

Sensitivity of osteoporosis screening guidelines for eventual hip fracture in older male veterans

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This study sought to determine whether guideline-recommended clinical criteria to select men for osteoporosis screening provide significantly better sensitivity than the osteoporotic screening tool (OST) among men who later went on to have a hip fracture, and whether the sensitivity differs by race. This retrospective observational study uses data from the Department of Veterans Affairs Austin Automation Center. We identified 825 male veterans with hip fractures from 2007 to 2009. Clinical risk factors used as screening selection criteria were abstracted from five accepted guidelines. Outpatient encounters were examined for each subject to determine whether they would have met screening selection criteria for each guideline in the 5 years before their hip fracture event. Sensitivities for each guideline were compared with the OST, using McNemar's exact test. Sensitivities of Veterans Affairs Health Service Research and Development Services (VA HSR&D) and National Osteoporosis Foundation (NOF) guidelines were 77% and 82%, respectively, and were significantly better than the OST sensitivity of 72% ($P<0.05$). Sensitivities of American College of Physicians (ACP; 68%), VA Secretary's Letters (45%) and Center for Medicare and Medicaid Services (13%) were significantly worse than the OST sensitivity ($P<0.001$). The sensitivities of the VA HSR&D, ACP and NOF were significantly higher in Whites compared with non-Whites (76% vs 65%, $P<0.01$; 70% vs 58%, $P<0.01$; and 84% vs 70%, $P<0.001$, respectively). Only VA HSR&D and NOF clinical screening criteria are more sensitive than OST in identifying veterans who subsequently experience hip fractures, and these sensitivities vary by race.

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Introduction

Hip fractures are of particular concern in men because of their significant morbidity and mortality, resulting in substantial disease burden and health-care costs.[1,2] The 1-year mortality rate after hip fracture in men is twice that in women.[3] The inpatient mortality rates for Veterans after sustaining a hip fracture are more than double that of the general population, making this a particularly vulnerable group.[4] Hip fractures are also associated with loss of independence,[5] and men 65 years of age or older who survive a hip fracture will likely achieve a lower level of post-fracture function compared with a woman in a similar circumstance.[6] Therefore, identifying men at high risk for hip fracture and implementing prevention plans is an important clinical goal.

Although bone mineral density (BMD) measurement with dual-energy X-ray absorptiometry (DXA) identifies patients at high risk for fracture likely to benefit from osteoporosis treatment, a recent cost-effectiveness analysis found that universal screening with DXA may not be cost-effective in men.[7] Several evidence-based health organizations have therefore proposed using clinical risk factors to select the subgroup of men most likely to benefit from a strategy of DXA screening and treatment. These organizations include the Veterans Affairs (both the Health Service Research and Development Service (VA HSR&D), and the VA Under Secretary's Letter guidelines), the American College of Physicians (ACP) and the National Osteoporosis Foundation (NOF). In addition, the Centers for Medicare and Medicaid Services (CMS) have established required clinical criteria for DXA reimbursement in men. However, there are important differences between these guidelines in terms of risk factors to use to select men for osteoporosis screening, or indeed whether screening is indicated in men at all.[8] Furthermore, there may be important racial differences in clinical risk factors that predict osteoporotic fracture among older men.[9]

The osteoporosis screening tool (OST) has also been suggested as a clinical tool to select men for DXA screening.[10,11] The OST is a simple formula that incorporates age and weight

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into a screening calculation to develop a risk score for osteoporosis. The OST can be easily applied to electronic medical records for automated identification of high-risk individuals who should receive DXA screening. However, its ability to identify those who will subsequently experience hip fracture has not previously been studied.

Hip fracture rates are also known to vary by race. Among older US Black and Hispanic men, rates of hip fracture are considerably lower, and risk factors associated with fracture are different than among White men.[9,12–14] These differences may affect the ability of screening selection criteria to identify non-Whites who go on to have hip fractures, but this has not been previously examined. With respect to screening using the OST, there are no race differences (White vs non White) in the performance of OST screening in identifying DXA-determined osteoporosis.[11] However, race differences in sensitivity of OST screening in identifying men who subsequently have fracture have not be studied previously, and will be examined here.

The purpose of this study was to compare the sensitivity of various screening selection guidelines in identifying male veterans who will ultimately suffer a hip fracture. We compared each guideline's sensitivity with the OST, which uses the smallest number of clinical risk factors (age and weight) to target high-risk individuals who should go on to receive DXA screening. A secondary objective was to determine whether these sensitivities differed by race.

Results

A total of 825 men were identified as having an incident hip fracture between 2007 and 2009 who met the study criteria. **Table 1** shows participant characteristics for all subjects in the study population as well as for White and non-White subjects only. Mean age at qualifying hip fracture was 77 years, 81% were White, and average body mass index (BMI) was 26 kg m^{-2}. The sample had several comorbidities with high prevalence, including 37% with diabetes, 19% with a prior hip fracture and 15% with gastrectomy.

Sensitivities of guidelines for DXA screening compared with use of OST

Only VA HSR&D and NOF screening selection criteria had a higher sensitivity in identifying those who would go on to develop a hip fracture than the OST sensitivity (77% and 82%, respectively vs 72% ($P<0.05$)). The VA Secretary's Letter, ACP and CMS coverage criteria sensitivity were 45%, 68% and 13%, respectively, and were significantly lower than the OST sensitivity ($P<0.0001$).

The sensitivities of the VA HSR&D, ACP and NOF screening selection criteria varied by race. A significantly higher sensitivity was observed in Whites compared with non-Whites for the VA HSR&D (76% vs 65%, $P<0.01$), the ACP guidelines (70% vs 58%, $P<0.01$) and the NOF guidelines (84% vs 70%, $P<0.001$).

Reasons for meeting prescreening selection criteria per guidelines

We examined the risk factors that were the most frequent triggers for participants to meet prescreening selection criteria for each guideline. The most frequent risk factors triggers identified were weight loss $>10\%$ (67%), diabetes (37%), prior fracture (19%), gastrectomy (15%) and anticonvulsant use (14%).

Discussion

The primary goal of using risk factors to select men for osteoporosis screening is to identify those who will go on to develop fracture so that prevention strategies can be implemented, while avoiding unnecessary testing and intervention on those who will not. Our study examined the sensitivity of current screening selection criteria in identifying those who will develop hip fracture, the most clinically devastating fracture type. We found that certain guideline-based screening selection criteria and the OST have good sensitivity for identifying men who will go on to have a hip fracture. Only the VA HSR&D and the NOF guidelines performed significantly better than the OST, whereas the CMS reimbursement criteria had the lowest sensitivity. We also identified clinically important race differences in the sensitivities of current screening selection criteria, with poor sensitivity in non-White, primarily African American men. As many Veterans use non-VA hospitals for acute problems such as hip fractures, we were not able to confidently identify a non-hip fracture group, and therefore could not calculate the specificity of the guidelines.

Although many prior studies have examined which individual risk factors are predictive of low BMD scores or fractures, these studies have not examined which clusters of risk factors have the greatest sensitivity to select men for osteoporosis screening.[15,16] Therefore, the sensitivity or specificity of the screening selection criteria proposed by clinical practice guidelines are not clearly known from existing literature, where relative risk, hazard ratios or odds ratios of individual risk factors are generally reported. Positive predictive values of individual risk factors and screening selection criteria have been reported, but vary substantially with the prevalence of osteoporosis in the population and are therefore not easily generalizable.[17] Of note, the World Health Organization fracture risk algorithm (FRAX, University of Sheffield, Sheffield, UK) is a tool that incorporates clinical risk factors, as well as BMI or BMD at the femoral neck, to estimate 10-year probability of fracture risk.[18] As operationalized in the United States, FRAX is not intended to select men for osteoporosis screening but rather to identify who should receive pharmacotherapy. As the purpose of our study was to examine the ability of guideline-recommended screening selection criteria and the OST to identify men who should go on to get DXA screening, we did not estimate FRAX + BMI for our cohort. In other settings such as the United Kingdom, FRAX + BMI is used to identify men at intermediate risk to go on for additional risk stratification with DXA;[19] therefore, it may be useful to include FRAX + BMI in further studies of screening selection test sensitivity and specificity.

No other studies have examined sensitivity of OST for identifying men who will go on to have a hip fracture, whereas OST sensitivity to identify DXA-determined osteoporosis has previously been reported. Specifically, in a US Veteran male population, the OST (with a score less than 3) has a sensitivity of 93% for DXA-determined osteoporosis.[11] In a meta-analysis, Liu *et al.*[15] evaluated the performance of the OST and found that it has a sensitivity of 81% to identify DXA-determined osteoporosis in women and men. Other studies found that the sensitivity of the OST to identify DXA-determined osteoporosis

Table 1 Characteristics of male veteran study population

Characteristics	*All races* (n = *825*)	*White*[a] (n = *668*)	*Non-White*[a] (n = *107*)
Age at fracture, mean (s.d.)	76.7 (10.1)	77.0 (10.0)	73.7 (10.6)
Average weight (lbs)[b], mean (s.d.)	177.3 (34.9)	177.6 (34.5)	173.4 (35.9)
Average height (inches)[c], mean (s.d.)	69.0 (3.0)	69.0 (3.0)	69.4 (3.2)
BMI, mean (s.d.)	26.1 (4.7)	26.2 (4.5)	25.3 (5.0)
Weight loss >10%[d]	553 (67.0)[e]	439 (65.7)	81 (75.7)
Health conditions			
Anorexia	0 (0.0)	0 (0.0)	0 (0.0)
Bilateral orchiectomy	0 (0.0)	0 (0.0)	0 (0.0)
Diabetes (combined type 1 and type 2)	307 (37.2)	243 (36.4)	45 (42.1)
Gastrectomy	124 (15)	105 (15.7)	11 (10.3)
Hyperparathyroidism	6 (0.7)	4 (0.6)	2 (1.9)
Hyperthyroidism	13 (1.5)	11 (1.7)	1 (0.9)
Pernicious anemia	15 (1.8)	14 (2.1)	1 (0.9)
Rheumatoid arthritis	21 (2.6)	16 (2.4)	4 (3.7)
Medication use			
Glucocorticoid use	55 (6.7)	43 (6.4)	9 (8.4)
Anticonvulsant use	116 (14.1)	91 (13.6)	15 (14.0)
Androgen deprivation use	12 (1.5)	9 (1.4)	3 (2.8)
Other risk factors			
Prior fractures	154 (18.7)	128 (19.2)	12 (11.2)
Family history	0 (0.0)	0 (0.0)	0 (0.0)

Abbreviation: BMI, body mass index.
[a]For race designation, 30 participants were excluded owing to 'mixed race' and 20 were excluded owing to missing race variable. [b]Average of all weights for first fiscal year represented in study period. [c]Average of all heights during study period. [d]Weight loss percentage was calculated as follows, [(Max weight) − (Min weight)]/(Max weight) × 100, where the Max weight must come before the Min weight. [e]Unless otherwise noted, # (%) with condition are shown.

was 70–90% in Asian and Caucasian populations,[10,20,21] and 83–87% in moderate and high-risk African American males.[22] In addition to performing moderately well in identifying DXA-determined osteoporosis, we found that the OST performs similarly well in identifying patients who would go on to fracture a hip. The OST sensitivity of 72% suggests that OST alone may be sufficient in clinical practice, as it performed better than several guideline screening selection criteria, including the VA Secretary's Letter, ACP and CMS reimbursement criteria. It is possible that these guideline screening selection criteria are either missing clinically important criteria that predict future fracture or that some of their criteria cannot be reliably captured from the medical record, which may explain their lower sensitivities.

We identified clinically important race differences in sensitivity of screening selection criteria that have not been previously well described. Specifically, some of the screening selection guidelines were substantially less sensitive in identifying non-White men with subsequent hip fracture, which has critical clinical implications. Current clinical guidelines may not identify non-White men at high risk for hip fracture as well as White men, leading to underscreening and therefore undertreatment in this population. This may in turn lead to a higher burden of preventable fractures in the non-White population. Differences in risk factors for osteoporosis by race may partially explain the varying sensitivities of screening selection criteria. Prior cohort studies have examined which risk factors are most associated with osteoporosis and low BMD in African American and other non-White populations. Broussard *et al.*[23] found that low BMI, low calcium intake, current cigarette smoking and physical inactivity were the strongest independent risk factors in these populations. However, not all current guidelines include these risk factors in their screening selection criteria, which may account in part for the lower sensitivity in the non-White population. Of note, our study was unable to capture physical inactivity, low calcium intake or current smoking in administrative data, and thus may underestimate guideline sensitivities in the non-White male population. However, guideline screening selection criteria that included low BMI, such as VA HSR&D and ACP, had sensitivities that were lower in non-White compared with White men. This is an important finding, as despite offering race-adjusted risk estimates the FRAX tool may also underestimate fracture risk in non-White men.[24] As noted, it is possible that differences in the distribution of risk factors for osteoporosis by race may partially explain the lower ability of screening selection criteria and the FRAX to estimate fracture risk in a non-White population. These findings suggest that fracture risk factors differ between White and non-White populations, and well-designed cohort studies of non-White subjects with fracture outcomes are needed to inform screening guidelines. Importantly, the OST sensitivity for identifying fracture-determined osteoporosis in non-White men was 71% and similar to White men in our study.

Our findings have several clinical implications. First, our data support the use of risk factor-based guidelines in identifying men who should go on to get DXA screening based on their high sensitivity in identifying those who will develop hip fracture and may benefit from further evaluation and treatment strategies. However, additional studies are needed to determine the balance of sensitivity and specificity, and the resulting benefits and harms of screening for individual patients. Second, we identified most of the risk factors using readily available

Table 2 Sensitivity of osteoporosis screening selection guidelines and sensitivity differences by race

Guideline, screening selection criteria	*All subjects (n = 825) Sensitivity[a] (95% CI)*	*White (n = 668) Sensitivity[a] (95% CI)*	*Non-White (n = 107) Sensitivity[a] (95%CI)*
Osteoporosis screening tool (OST)[11] Score calculation = (weight (kg) − age) × 0.2 OST positive score: using <3 score threshold	0.72 (0.69–0.75)	0.73 (0.69–0.76)	0.71 (0.620.80)
Veterans affairs (VA) HSR&D[28] Age > 70 and One or more risk factors (1) Weight loss >20% (2) Low BMI < 25 kg m^{-2} (3) Diabetes (type 1 or 2) (4) Anorexia (5) Pernicious anemia (6) Family history (7) Gastrectomy (8) Anticonvulsant therapy (>3 months) (9) Hyperthyroidism (10) Hyperparathyroidism (11) Rheumatoid arthritis (12) Physical inactivity[d] (13) Current smoking[d] (14) Low calcium intake[d] or Age > 50 and One or more risk factors (1) Glucocorticoid use (2) Prior fracture	0.77 (0.74–0.79)[b]	0.76 (0.74–0.80)	0.65 (0.56–0.74)[c]
Veterans affairs (VA) under Secretary Letter[e] Age > 50 and One or more risk factors (1) Glucocorticoid use (2) Prior fracture (3) Gastrectomy (4) Bilateral orchiectomy (5) Androgen deprivation therapy (6) Anticonvulsant therapy (7) Rheumatoid arthritis (8) Osteopenia on X-ray[d] (9) Malabsorption[d] (10) Celiac disease[d] (11) Bariatric surgery[d] (12) Excess alcohol consumption[d] (13) Current smoking[d] (14) Mobility disorders [d] (15) Organ transplantation[d]	0.45 (0.41–0.48)[b]	0.45 (0.41–0.49)	0.38 (0.29–0.48)
American College of Physicians (ACP)[29] Age > 70 and One or more risk factors (1) BMI < 25 kg m^{-2} (2) >10% weight loss (3) Bilateral orchiectomy (4) Androgen deprivation therapy (5) Physical inactivity[d] or Age > 50 and One or more risk factors (1) Glucocorticoid use (2) Prior fracture	0.68 (0.65–0.72)[b]	0.70 (0.67–0.74)	0.58 (0.49–0.67)[c]
National Osteoporosis Foundation (NOF)[30,31] One or more risk factor in an older man (1) All men over age 70 (2) Prior fracture (3) Glucocorticoid use (4) Rheumatoid arthritis	0.82 (0.80–0.85)[b]	0.84 (0.81–0.87)	0.70 (0.61–0.79)[c]

Table 2 (Continued)

Guideline, screening selection criteria	*All subjects (n = 825) Sensitivity[a] (95% CI)*	*White (n = 668) Sensitivity[a] (95% CI)*	*Non-White (n = 107) Sensitivity[a] (95%CI)*
Center for Medicaid and Medicare Services (CMS)[32] One or more risk factor in an older man (1) Vertebral fracture (2) Glucocorticoid use (3) Osteoporosis drug use (4) Hyperparathyroidism	0.13 (0.11–0.15)[b]	0.13 (0.11–0.16)	0.11 (0.05–0.17)

Abbreviations: BMI, body mass index; HSR&D, Health Service Research and Development Services.
[a]Veterans were identified as meeting prescreening selection criteria for each guideline if they met at least one of the guideline's criteria, otherwise they were coded as not meeting prescreening criteria. [b]Guideline sensitivities under all subjects were compared with OST as the reference, significance expressed as $P < 0.05$. [c]Within guideline sensitivity difference by race, uses White as reference, comparisons are performed within each guideline, significance expressed as $P < 0.05$. [d]Not reliably available from administrative data and not included in calculated sensitivity. [e]VA Under Secretary Letter. (2011) Screening, diagnosis, evaluation and treatment of male osteoporosis algorithm.

administrative data; health systems with electronic medical records could develop automated searches to identify and flag those who meet screening criteria.[25] Such system-wide interventions may be particularly attractive in capitated health systems or accountable care organizations. Third, we found that the OST, a simple clinical tool to select men for DXA screening, has comparable ability to identify those who will subsequently have fracture as compared with recommended screening selection criteria, which incorporate a larger number of clinical risk factors in their guidelines. The OST also has the potential to be easily applied to automated searches through the electronic medical record. Finally, clinicians caring for non-White men should be aware that the sensitivity of current screening selection guidelines is limited, and consider the use of alternative risk factors for these populations. Future guidelines may need to develop distinct screening criteria for non-White men if other risk factor groups are found to have better sensitivity and specificity.

The strengths and limitations of our study should be considered. The VA database provided access to a large and ethnically diverse population of US males, as well as to a large repository of pharmacy, laboratory, inpatient and outpatient administrative health data. However, administrative data are not able to identify all the factors included in the guidelines, such as family history or physical activity. As such, it is possible that the sensitivity of some of these screening selection guidelines could be higher with inclusion of all clinical risk factors. The items that were not easily picked up in our study data (that is, smoking, physical activity and calcium intake) are unlikely to be readily available in other health system administrative data portals. Therefore, we do not expect that this would affect the utility of our findings. The accuracy of International Classification of Disease (ICD-9) diagnosis codes in medical records is also variable. A previous study found the error frequency of clinical diagnoses and procedure coding to be $\sim$22%.[26] Studies report a higher reliability in inpatient hip fracture coding, with 85% agreement between and abstractor reading only the medical chart and an investigator reading the operative note for partial and total hip arthroplasty.[27] However, as electronic medical record use increases, health systems may consider using automated risk factor identification to select men for screening, and thus our study that uses hospital medical record data provides clinically meaningful information. Finally, as noted above we could not calculate specificity from our data set; this is an important issue that requires further study. The purpose of our study, however, was not to describe the test characteristics of these screening selection criteria or of the OST, but rather to compare their ability with correctly identify men who go on to develop a hip fracture, and whether their sensitivity varies by race. Given the high morbidity and mortality associated with hip fractures, sensitivity of guideline-recommended screening selection criteria and of the OST still provides valuable and clinically important information.

In conclusion, several guideline-recommended screening selection criteria and the OST have excellent sensitivity for hip fracture in White men, whereas several other guidelines and Medicare reimbursement criteria have poor sensitivity. Administrative data can be used to identify most risk factors, and in an era of electronic health records has the potential for use by health systems to identify men for osteoporosis screening. There is a need for further studies to determine the specificity of screening selection criteria, and to develop improved screening criteria for non-White men.

Materials and Methods

Data from the Department of Veterans Affairs Austin Automation Center, a central repository for clinical patient data in the Veterans Health Administration, from VISNs 6–8 (southeastern United States) were used for this study.

Patient selection and data collection

This retrospective cohort study included male Veterans, over the age of 50 years, with an incident hip fracture that occurred between 2007 and 2009 identified using inpatient ICD-9 codes. Veterans needed at least two primary care clinic stops at a VA health-care facility in a single year before their index hip fracture in fiscal years 2003–2008 in order to identify the population receiving longitudinal care in the VA system, which would allow for ascertainment of comorbidity information and other clinical risk factors. Veterans also needed at least one measurement for weight within the study period, as the OST could not be calculated without this variable.

Definitions of screening selection criteria variables

Clinical variables recommended by the five different clinical practice guidelines are listed in **Table 2**. We used outpatient and

inpatient ICD-9 codes using the VA outpatient clinical files and the national drug file to determine whether each subject met the clinical criteria. Clinical risk factors were operationalized as follows:

Medication use (glucocorticoid, anticonvulsant and androgen deprivation therapy) was defined as prescription of any agent, regardless of dose, for at least 3 months within the 5-year study period (fiscal year 2003–2008).

Medical conditions (diabetes mellitus type 1 and 2, anorexia nervosa, gastrectomy, pernicious anemia, bilateral orchiectomy, family history of osteoporosis, primary hyperparathyroidism, prior osteoporotic fracture, hyperthyroidism, rheumatoid arthritis and vertebral fracture) were defined by presence of relevant ICD-9 codes during any outpatient visit in any study year before their index hip fracture (fiscal years 2003–2008). The age at which prior osteoporotic fracture is considered a risk factor remains unclear. As per usual clinical practice, in our study it was operationalized as presence of prior osteoporotic fracture among those over age 50 years.

Height and weight measurement. For weight, we used the average of all weights for the first fiscal year represented in study period. For height, we used the average of all heights during the study period. Weight loss percentage was calculated as follows, [(Max weight) − (Min weight)]/(Max weight) × 100, where the Max weight must come before the Min weight.

Veterans were identified as meeting prescreening selection criteria for each guideline if they met at least one of the guideline's criteria, otherwise they were coded as not meeting prescreening criteria. Several guidelines included criteria for which no ICD-9 code was available, including physical inactivity and mobility disorders, and these criteria were omitted. Guideline screening criteria for which ICD-9 coding was considered unreliable or rare in our data were also omitted from the analysis, including family history of osteoporosis, current smoking, low calcium intake, osteopenia on X-ray, malabsorption, celiac disease, bariatric surgery, excess alcohol consumption and organ transplantation.

The OST score calculation was determined as follows, [(weight (kg) − age) × 0.2]. A score range of less than 3 indicates moderate to high risk.[11] In our study, those with a score in this range were considered to screen positive as this is a score where additional osteoporosis testing is generally recommended.

Statistical analysis

Patient demographics and clinical variables were evaluated with counts and percentages, or with means and s.d. Sensitivity was calculated as the proportion of men with hip fracture who did meet criteria for osteoporosis screening. The sensitivity was calculated individually for each of the guidelines and for the OST score. The sensitivity of each candidate guideline was compared with the OST using McNemar's exact test. The McNemar exact test is a nonparametric test for comparing two correlated proportions. In a prespecified subgroup analysis, the sensitivities by race (White vs non-White) were evaluated using χ^2-analyses. As veterans frequently use outside facilities for acute problems such as hip fracture, we were unable to reliably identify a population that did not have hip fracture. Therefore, specificity was not calculated for this study. SAS v9.3 was used for all analyses (SAS Institute, Cary, NC, USA).

Conflict of Interest

CC-E has received grants from and consults for Amgen, consults for Novartis and received grants from the Department of Defense. In addition, CC-E has a patent pending and is co-owner of Biscardia Inc., a company pursing cardiovascular indications for bisphosphonates. The remaining authors declare no conflict of interest.

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