### CLINICAL GUIDELINES



# Screening for Osteoporosis in Men: A Clinical Practice Guideline from the American College of Physicians

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**Description:** The American College of Physicians developed this guideline to present the available evidence on risk factors and screening tests for osteoporosis in men.

**Methods:** Published literature on this topic was identified by using MEDLINE (1990 to July 2007). Reference mining was done on the retrieved articles, references of previous reviews, and solicited articles from experts. The inclusion criteria for the studies were measuring risk factors for low bone mineral density or osteoporotic fracture in men or comparing 2 different methods of assessment for the presence of osteoporosis in men. This guideline grades the evidence and recommendations by using the American College of Physicians' clinical practice guidelines grading system.

**Recommendation 1:** The American College of Physicians recommends that clinicians periodically perform individualized assessment

of risk factors for osteoporosis in older men (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 2:** The American College of Physicians recommends that clinicians obtain dual-energy x-ray absorptiometry for men who are at increased risk for osteoporosis and are candidates for drug therapy (Grade: strong recommendation; moderate-quality evidence).

**Recommendation 3:** The American College of Physicians recommends further research to evaluate osteoporosis screening tests in men.

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Osteoporosis in men is an important public health problem. Osteoporosis in men is substantially underdiagnosed, undertreated, and underreported and inadequately researched (1, 2). Although osteoporosis is often viewed as a disease of women, studies show that osteoporotic fractures also result in substantial morbidity, mortality, and financial expenses in men (3–7). The prevalence of osteoporosis is estimated to be 7% in white men, 5% in black men, and 3% in Hispanic men. Data on prevalence in Asian-American men and other ethnic groups are lacking (2). With the aging of the population, rates of osteoporosis in men are expected to increase nearly 50% in the next 15 years, and hip fractures rates are projected to double or triple by 2040 (2).

This guideline presents the available evidence on risk fac-

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tors and screening tests for osteoporosis in men. The target audience for this guideline is all clinicians, and the target patient population is all adult men older than age 50 years. These recommendations are based on the systematic evidence review by Liu and colleagues (8) in this issue and the Agency for Healthcare Research and Quality-sponsored Southern California Evidence-based Practice Center evidence report (9).

### **METHODS**

The literature search was done by Liu and colleagues and included studies from MEDLINE from 1990 to July 2007. In addition, the authors did reference mining of retrieved articles, references of previous reviews, and solicited articles from experts. Four researchers (2 pairs of an endocrinologist and a general internist trained in health services research) reviewed the list of titles and selected articles for further review. This guideline is based on an evaluation of 389 articles, of which 176 addressed risk factors for osteoporosis and 27 addressed diagnostic tools for osteoporosis. All of the included studies measured risk factors for osteoporosis or fracture in men or compared a non-dual-energy x-ray absorptiometry (DXA) index screening test with a gold standard reference test (either DXA-defined osteoporosis [T-score threshold of -2.5] or the occurrence of an osteoporotic fracture). The back-

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ground article in this issue (8) provides details about the methods used for the systematic evidence review.

This guideline grades the evidence and recommendations by using the American College of Physicians' clinical practice guidelines grading system adopted from the classification developed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) workgroup (**Table**). In addition, to assess the internal validity of diagnostic studies, Liu and colleagues (8) used the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) evaluation tool.

Our main interest is to determine the risk factors for osteoporotic fracture that are mediated through low bone mineral density (BMD) and thus define men who would be more likely to benefit from DXA. However, in the interest of brevity, for the remainder of the article we simplify this to "risk factors for osteoporosis." The objective of this guideline is to synthesize the evidence for the following questions:

1. What are the risk factors for osteoporosis in men?

2. Are there any validated tools (other than central BMD) to screen for osteoporosis in men?

3. What are the risk factors for low BMD-mediated fracture?

### CLINICAL DIAGNOSIS OF OSTEOPOROSIS

The clinical diagnosis of osteoporosis is made in 2 ways: occurrence of an osteoporotic fracture and the World Health Organization's (WHO) bone density criteria. Fragility fractures are an important characteristic of osteoporotic bone disease and typically occur after a prolonged decrease in BMD and quality. Fragility fracture is defined by the WHO as a fracture from low-level trauma, meaning a fall from a standing height or lower. The bones most commonly fractured are the distal radius, proximal humerus, hip, and vertebral body. In 1994, the WHO defined osteoporosis as a BMD greater than 2.5 SDs (T-score, -2.5) below that of a young, healthy population as measured by DXA.

The standard for measuring BMD and diagnosing osteoporosis in men (and women) is DXA (10, 11). However, DXA is not universally available, is not portable, and is an imperfect predictor of future fractures. In addition, screening with DXA may not be cost-effective in all groups (expenses per quality-adjusted life-year varied from \$30 000 to \$248 000, depending on age) (10–14). Therefore, it is important to evaluate non-DXA osteoporosis tests that are sensitive, inexpensive, and easily implemented.

### **RISK FACTORS FOR OSTEOPOROSIS**

A high-quality meta-analysis showed that the most important risk factors for osteoporosis in men are age (>70 years), low body weight (body mass index <20 to 25 kg/m<sup>2</sup> or lower), weight loss (>10% [compared with the

# *Table.* The American College of Physicians' Guideline Grading System\*

Quality of Evidence	Strength of Recommendation		
	Benefits Clearly Outweigh Risks and Burden OR Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced with Risks and Burden	
High	Strong	Weak	
Moderate	Strong	Weak	
Low	Strong	Weak	
Insufficient evidence to determine net benefits or risks	I-recommendation		

\* Adopted from the classification developed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) workgroup.

usual young or adult weight or weight loss in recent years]), physical inactivity (participates in no physical activity on a regular basis [walking, climbing stairs, carrying weights, housework, or gardening]), use of oral corticosteroids, and previous fragility fracture (15). Most of the studies in this systematic review included participants older than age 50 years from the United States or Europe; thus the findings are limited in their generalizability to other populations.

The authors also reviewed evidence for other potential risk factors. Alcohol use results in an increased probability of fracture but has not been associated with decreased BMD in the available studies (16-21). Androgen deprivation therapy (pharmacologic and orchiectomy) is a strong predictor of both osteoporosis and fracture (22-33). Cigarette smoking and low dietary intake of calcium are moderate predictors of an increased risk for low bone mass; they are probably also risk factors for fracture, but the supporting evidence is less clear. Spinal cord injury is a moderate predictor of both low BMD and osteoporotic fracture in men. Data are insufficient in men to determine whether the presence of respiratory disease (independent of steroid use), type 2 diabetes, dietary intake of vitamin D, thyroid disease and thyroid replacement therapy, gastrointestinal malabsorption, rheumatoid arthritis, and hyperparathyroidism increase the risk for low BMD-mediated fracture. All of these possible risk factors have plausible physiologic rationales, and some have data supporting an association with osteoporosis and fracture in women, but data in men are lacking.

### SCREENING TESTS FOR OSTEOPOROSIS

The diagnosis of osteoporosis is based on reduced BMD as measured by DXA (10, 11). However, DXA is expensive, and it is not portable or available everywhere (10-14). Therefore, it is important to identify and evaluate the efficacy of non-DXA screening tests. When calcaneal ultrasonography was evaluated in women, it was not suffi-

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ciently sensitive or specific to serve as a screening test for diagnosis of osteoporosis (34).

The studies evaluating osteoporosis screening tests in this guideline can be broadly divided into 2 categories: those that assess a test against a BMD measurement (DXA) and those that assess a test against a fracture occurrence.

### Calcaneal Ultrasonography versus DXA-Measured BMD

Calcaneal ultrasonography is a diagnostic tool in which an ultrasonography probe is placed on either heel to measure BMD. It has many advantages, including portability, low cost, and the absence of ionizing radiation. However, there is no accepted threshold for a positive T-score of the quantitative ultrasonography index, and the thresholds used in the evaluated studies varied from 0 to -2.5.

Evidence showed that a calcaneal ultrasonography Tscore of -1.0 had a sensitivity of 75% and a specificity of 66% to diagnose BMD-determined osteoporosis (central DXA T-score <-2.5) (34–38). When the calcaneal ultrasonography T-score was decreased to -1.5, the specificity increased to 78% but sensitivity decreased to 47%.

# Osteoporosis Self-assessment Screening Tool versus DXA-Measured BMD

The osteoporosis self-assessment screening tool (OST) is a simple test used to develop a risk score for osteoporosis by using a person's age and weight (risk score = [weight in kilograms – age in years]  $\times$  0.2). No accepted threshold for a positive OST risk score exists, and thresholds used have varied from -1 to 3 in various studies.

Evidence from 2 studies that evaluated Asian men showed that an OST risk score of -1 had a sensitivity of 70% to 90% and a specificity of 70% to diagnose BMDdetermined osteoporosis (37, 39). In a study of U.S veterans, an OST threshold of 3 was associated with a sensitivity of 93% and specificity of 66% (40). However, when the OST threshold was decreased to 1, the sensitivity decreased to 75% and specificity increased to 80%.

### Calcaneal Ultrasonography versus Fracture Occurrence

Evidence from 10 studies showed that calcaneal ultrasonography moderately predicts fragility fractures in men (41-48). Several studies showed that each additional SD reduction in a calcaneal ultrasonography measurement resulted in an increased risk for hip fracture and nonspinal fracture (46, 48), and ultrasonography stiffness parameters were strongly associated with previous fragility fracture (42).

# Combination of Calcaneal Ultrasonography and DXA-Measured BMD

Some researchers have suggested the use of calcaneal ultrasonography to identify patients who should have a confirmatory DXA testing. The evidence is less clear on the benefit of combining calcaneal ultrasonography and DXA BMD measurements compared with either test alone to predict fractures. One study showed a strong association of fragility fractures with BMD at the hip (odds ratio, 3.4) and calcaneal ultrasonography (odds ratio, 3.2). When both tests were used, the odds ratio increased to 6.1 (42). However, analysis of receiver-operating characteristic curves from another study showed that the combination was not superior to either test alone in predicting hip fractures (area under the curve for ultrasonography alone, 0.84; for BMD alone, 0.85; and for the combination, 0.85) (48).

#### **SUMMARY**

High-quality evidence shows that age, low body weight, physical inactivity, and weight loss are strong predictors of an increased risk for osteoporosis in men. There is also moderate-quality evidence that previous fragility fracture, systemic corticosteroid therapy, androgen deprivation therapy, and spinal cord injury are predictors of an increased risk for osteoporosis in men. Cigarette smoking and low dietary intake of calcium predict low bone mass.

Some studies suggest that OST may have higher sensitivity and specificity than calcaneal ultrasonography does in diagnosing DXA-determined osteoporosis (37, 39, 40). However, the primary outcome in the studies was not fractures, so this result should be viewed with caution because the clinical outcome of fracture is of most interest to patients and clinicians. In addition, moderate-quality evidence showed that calcaneal ultrasonography is an independent predictor of fractures in men even though its ability to diagnose DXA-determined osteoporosis is limited. Whether the combination of DXA BMD measurements and calcaneal ultrasonography to assess for fractures is better than either test alone remains uncertain.

#### **R**ECOMMENDATIONS

Recommendation 1: The American College of Physicians recommends that clinicians periodically perform individualized assessment of risk factors for osteoporosis in older men (Grade: strong recommendation; moderate-quality evidence).

A careful assessment of risk for osteoporosis in men is important. The appropriate age to start risk assessment is uncertain. However, by age 65 years, at least 6% of men have DXA-determined osteoporosis (49), therefore, assessment of risk factors before this age is reasonable. Factors that increase the risk for osteoporosis in men include age (>70 years), low body weight (body mass index <20 to 25 kg/m<sup>2</sup>), weight loss (>10% [compared with the usual young or adult weight or weight loss in recent years]), physical inactivity (participates in no physical activities on a regular basis [walking, climbing stairs, carrying weights, housework, or gardening]), corticosteroid use, androgen deprivation therapy, and previous fragility fracture. Risk assessments should be updated periodically for men who choose not to be screened.

Recommendation 2: The American College of Physicians

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recommends that clinicians obtain DXA for men who are at increased risk for osteoporosis and are candidates for drug therapy (Grade: strong recommendation; moderate-quality evidence).

Bone density measurement with DXA is the accepted reference standard for diagnosing osteoporosis in men (10, 11). Men who are at increased risk for osteoporosis are candidates for DXA. Little evidence about alternatives to DXA exists. The 2 most studied methods are quantitative ultrasonography (usually of the calcaneus) and the OST. Available evidence indicates that neither alternative is sufficiently sensitive or specific at predicting DXA-determined bone mass to be recommended as a substitute for DXA. Although 1 study has demonstrated a strong relationship between calcaneal ultrasonography and subsequent fracture, until treatment trials establish the effectiveness of therapy for osteoporosis diagnosed by ultrasonography rather than DXA, the role of ultrasonography in initiating therapy remains uncertain. No studies have evaluated the optimal intervals for repeated screening by using BMD measurement with DXA.

The evidence review showed that calcaneal ultrasonography predicts DXA-determined osteoporosis only modestly well. However, more important, it was a strong predictor of fracture in men. This may be because ultrasonography identifies other bone properties, such as bone quality, which may not be identified on DXA. Because treatment trials have not measured the effectiveness of therapy for osteoporosis diagnosed by ultrasonography rather than DXA, the role of ultrasonography in diagnosis remains uncertain.

Recommendation 3: The American College of Physicians recommends further research to evaluate osteoporosis screening tests in men.

A major limitation of existing osteoporosis screening studies is the use of BMD measurement (DXA) as the primary outcome rather than fracture occurrence. Although there is a large body of evidence about risk factors for osteoporosis in women, more research is needed to understand whether these risk factors also apply to men. Therapy should be evaluated in terms of fracture occurrence because of the significant disability, morbidity, mortality, and expenses that are associated with osteoporotic fractures. Furthermore, the harms of screening in this age group, such as radiation exposure and false-positive results, should also be studied. In addition, more research is needed in evaluating other screening tests, such as quantitative computed tomography, other types of questionnaires, or peripheral BMD measurements, which might also be useful as screening tests in men. Further research should explore whether acceptable substitutes for DXA exist (in terms of establishing the need for pharmacologic therapy). Research that explores the age at which men should begin to consider screening for osteoporosis and effective prevention measures for osteoporosis in men is also needed.

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**Note:** Clinical practice guidelines are "guides" only and may not apply to all patients and all clinical situations. Thus, they are not intended to override clinicians' judgment. All ACP clinical practice guidelines are considered automatically withdrawn or invalid 5 years after publication, or once an update has been issued.

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