Title

Screening for Osteoporosis to Prevent Fractures: US Preventive Services Task Force Recommendation Statement

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Screening for Osteoporosis to Prevent Fractures
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

IMPORTANCE By 2020, approximately 12.3 million individuals in the United States older than 50 years are expected to have osteoporosis. Osteoporotic fractures, particularly hip fractures, are associated with limitations in ambulation, chronic pain and disability, loss of independence, and decreased quality of life, and 21% to 30% of patients who experience a hip fracture die within 1 year. The prevalence of primary osteoporosis (ie, osteoporosis without underlying disease) increases with age and differs by race/ethnicity. With the aging of the US population, the potential preventable burden is likely to increase in future years.

OBJECTIVE To update the 2011 US Preventive Services Task Force (USPSTF) recommendation on screening for osteoporosis.

EVIDENCE REVIEW The USPSTF reviewed the evidence on screening for and treatment of osteoporotic fractures in men and women, as well as risk assessment tools, screening intervals, and efficacy of screening and treatment in subgroups. The screening population was postmenopausal women and older men with no known previous osteoporotic fractures and no known comorbid conditions or medication use associated with secondary osteoporosis.

FINDINGS The USPSTF found convincing evidence that bone measurement tests are accurate for detecting osteoporosis and predicting osteoporotic fractures in women and men. The USPSTF found adequate evidence that clinical risk assessment tools are moderately accurate in identifying risk of osteoporosis and osteoporotic fractures. The USPSTF found convincing evidence that drug therapies reduce subsequent fracture rates in postmenopausal women. The USPSTF found that the evidence is inadequate to assess the effectiveness of drug therapies in reducing subsequent fracture rates in men without previous fractures.

CONCLUSIONS AND RECOMMENDATION The USPSTF recommends screening for osteoporosis with bone measurement testing to prevent osteoporotic fractures in women 65 years and older. (B recommendation) The USPSTF recommends screening for osteoporosis with bone measurement testing to prevent osteoporotic fractures in postmenopausal women younger than 65 years at increased risk of osteoporosis, as determined by a formal clinical risk assessment tool. (B recommendation) The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for osteoporosis to prevent osteoporotic fractures in men. (I statement)

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The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific clinical preventive services for patients without obvious related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

Summary of Recommendations and Evidence

The USPSTF recommends screening for osteoporosis with bone measurement testing to prevent osteoporotic fractures in women 65 years and older (B recommendation) (**Figure 1**).

The USPSTF recommends screening for osteoporosis with bone measurement testing to prevent osteoporotic fractures in postmenopausal women younger than 65 years who are at increased risk of osteoporosis, as determined by a formal clinical risk assessment tool. (B recommendation)

See the Clinical Considerations section for information on risk assessment.

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for osteoporosis to prevent osteoporotic fractures in men. (I statement)

See the Clinical Considerations section for suggestions for practice regarding the I statement.

Rationale

Importance

By 2020, approximately 12.3 million individuals in the United States older than 50 years are expected to have osteoporosis.[1] Osteoporotic fractures, particularly hip fractures, are associated with limitation of ambulation, chronic pain and disability, loss of independence, and decreased quality of life, and 21% to 30% of patients who experience a hip fracture die within 1 year.[2] Seventy-one percent of osteoporotic fractures occur among women,[3] and women have higher rates of osteoporosis than men at any given age; however, men have a higher fracture-related mortality rate than women.[2,4] The prevalence of primary osteoporosis (ie, osteoporosis without underlying disease) increases with age and differs by race/ethnicity. With the aging of the US population, the potential preventable burden is likely to increase in future years.[1]

Detection

The USPSTF found convincing evidence that bone measurement tests are accurate for predicting osteoporotic fractures in women and men. The most commonly used test is central dual-energy x-ray absorptiometry (DXA) of the hip and lumbar spine. Although several bone measurement tests similarly predict risk of fracture, DXA provides measurement of bone mineral density (BMD), and most treatment guidelines use central DXA to define osteoporosis and the threshold at which to start drug therapies to prevent osteoporotic fractures. The USPSTF found adequate evidence that clinical risk assessment tools are moderately accurate in identifying risk of osteoporosis and osteoporotic fractures.

Benefits of Early Detection and Treatment

The USPSTF found 1 study that evaluated the effect of screening for osteoporosis on fracture rates; the study reported a reduction in hip fractures but did not find a reduction in other types of fractures.[4-6]

Multiple studies show that drug therapies reduce fractures in postmenopausal women with osteoporosis. For women 65 years and older, the USPSTF found convincing evidence that screening can detect osteoporosis and that treatment of women with osteoporosis can provide at least a moderate benefit in preventing fractures. For postmenopausal women younger than 65 years who are at increased risk of osteoporosis, the USPSTF found adequate evidence that screening can detect osteoporosis and that treatment provides a moderate benefit in preventing fractures.

For men, the USPSTF found inadequate evidence on the benefits and harms of treating screen-detected osteoporosis to reduce the risk of osteoporotic fractures.

Harms of Early Detection and Treatment

The USPSTF found a single study that described harms of screening for osteoporosis. It reported no increase in anxiety and no decrease in quality of life from screening.[4-6] Based on the nature of screening with bone measurement tests and the low likelihood of serious harms, the USPSTF found adequate evidence to bound these harms as no greater than small. Harms associated with screening may include radiation exposure from DXA and opportunity costs (time and effort required by patients and the health care system).

Harms of drug therapies for osteoporosis depend on the specific medication used. The USPSTF found that the risk of serious adverse events, upper gastrointestinal events, or cardiovascular events associated with the most common class of osteoporosis medication (bisphosphonates) is no greater than small. Overall, the USPSTF found adequate evidence that the harms of osteoporosis medications are small.

USPSTF Assessment

The USPSTF concludes with moderate certainty that the net benefit of screening for osteoporosis in women 65 years and older is at least moderate.

The USPSTF concludes with moderate certainty that the net benefit of screening for osteoporosis in postmenopausal women younger than 65 years who are at increased risk of osteoporosis is at least moderate.

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for osteoporosis in men.

Clinical Considerations

Patient Population Under Consideration

This recommendation applies to older adults without a history of low-trauma fractures and without conditions that may cause

Figure 1. USPSTF Grades and Levels of Certainty

What the USPSTF Grades Mean and Suggestions for Practice

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate, or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the Clinical Considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as the number, size, or quality of individual studies. inconsistency of findings across individual studies. limited generalizability of findings to routine primary care practice. lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of the limited number or size of studies. important flaws in study design or methods. inconsistency of findings across individual studies. gaps in the chain of evidence. findings not generalizable to routine primary care practice. lack of information on important health outcomes. More information may allow estimation of effects on health outcomes.
The USPSTF defines certainty as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.	

secondary osteoporosis (such as metabolic bone disease or untreated hyperthyroidism) and patients without conditions that may increase their risk of falls (**Figure 2**). This recommendation does not apply to persons who take long-term medications that may cause secondary osteoporosis (eg, glucocorticoids, aromatase inhibitors, or gonadotropin-releasing hormone agonists).

Assessment of Risk

In deciding which postmenopausal women younger than 65 years to screen with bone measurement testing, clinicians should first consider factors associated with increased risk of osteoporotic fractures. These include parental history of hip fracture, smoking, excessive alcohol consumption, and low body weight. In addition, menopausal status in women is also an important consideration because studies demonstrating treatment benefit mainly enrolled postmenopausal women. For postmenopausal women younger than 65 years who have at least 1 risk factor, a reasonable approach to determine who should be screened with bone measurement testing is to use a clinical risk assessment tool.

Several tools are available to assess osteoporosis risk: the Simple Calculated Osteoporosis Risk Estimation (SCORE; Merck), Osteoporosis Risk Assessment Instrument (ORAI), Osteoporosis Index of Risk (OSIRIS), and the Osteoporosis Self-Assessment Tool (OST). These tools seem to perform similarly and are moderately accurate at predicting osteoporosis. The FRAX tool (University of Sheffield), which assesses a person's 10-year risk of

Figure 2. Clinical Summary: Screening for Osteoporosis to Prevent Fractures

Population	Women 65 years and older	Postmenopausal women younger than 65 years at increased risk	Men
Recommendation	Screen for osteoporosis. Grade: B	Screen for osteoporosis. Grade: B	No recommendation. Grade: I (insufficient evidence)

Risk Assessment	Risk factors for osteoporotic fractures include parental history of hip fracture, smoking, excessive alcohol consumption, and low body weight. In addition, menopausal status in women is also an important consideration. For postmenopausal women younger than 65 years who have at least 1 risk factor, a reasonable approach to determine who should be screened with bone measurement testing is to use a clinical risk assessment tool. Several tools are available to assess osteoporosis risk, such as OST, ORAI, OSIRIS, SCORE, and FRAX.
Screening Tests	The most commonly used test is central dual-energy x-ray absorptiometry (DXA) of the hip and lumbar spine. Although several bone measurement tests similarly predict risk of fractures, most treatment guidelines use bone mineral density (BMD) as measured by central DXA to define osteoporosis and the treatment threshold to prevent osteoporotic fractures. Other screening tests include peripheral DXA and quantitative ultrasound (QUS).
Treatments	The US Food and Drug Administration has approved multiple drug therapies to reduce osteoporotic fractures, including bisphosphonates, parathyroid hormone, raloxifene, and estrogen. The choice of therapy should be an individual one based on the patient's clinical situation and the trade-off between benefits and harms.
Other Relevant USPSTF Recommendations	The USPSTF has made recommendations on interventions to prevent falls in community-dwelling older adults and the use of vitamin D, calcium, or combined supplementation for the primary prevention of fractures in community-dwelling adults.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to https://www.uspreventiveservicestaskforce.org.

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FRAX indicates Fracture Risk Assessment Tool; ORAI, Osteoporosis Risk Assessment Instrument; OSIRIS, Osteoporosis Index of Risk; OST, Osteoporosis Self-assessment Tool; SCORE, Simple Calculated Osteoporosis Risk Estimation Tool.

fracture, is also a commonly used tool. The FRAX tool includes questions about previous DXA results but does not require this information to estimate fracture risk. Because the benefits of treatment are greater in persons at higher risk of fracture, one approach is to perform bone measurement testing in postmenopausal women younger than 65 years who have a 10-year FRAX risk of major osteoporotic fracture (MOF) (without DXA) greater than that of a 65-year-old white woman without major risk factors. For example, in the United States, a 65-year-old white woman of mean height and weight[7] without major risk factors has a 10-year FRAX risk of MOF of 8.4%.[4,8] In comparison, a 60-year-old white woman of mean height and weight[7] with a parental history of hip fracture has a 10-year FRAX risk of MOF of 13%.[4,8]

Clinicians should note that the presence of a given risk factor or a certain age does not represent a particular risk threshold. Although the risk of osteoporosis and osteoporotic fractures generally increases with age, the presence of multiple risk factors at a younger age may indicate that the risk-benefit profile is favorable for screening with bone measurement testing.

Screening Tests

The most commonly used bone measurement test used to screen for osteoporosis is central DXA; other screening tests include peripheral DXA and quantitative ultrasound (QUS). Central DXA measures BMD at the hip and lumbar spine. Most treatment guidelines[3,4,9-11] recommend using BMD, as measured by central DXA, to define osteoporosis and the treatment threshold to prevent osteoporotic fractures.[4,12] All the osteoporosis drug therapy studies reviewed by the USPSTF used central DXA to determine eligibility for study enrollment.[4,6] Peripheral DXA measures BMD at the lower forearm and heel. Quantitative ultrasound also evaluates peripheral sites and has similar accuracy in predicting fracture risk as DXA, while avoiding the risk of radiation exposure; however, it does not measure BMD. Peripheral DXA and QUS are measured with portable devices and may be less costly and more accessible than central DXA measurement (**Table 1**).

Screening Intervals

Some observational and modeling studies have suggested screening intervals based on age, baseline BMD, and calculated projected time to transition to osteoporosis. However, limited evidence from 2 good-quality studies found no benefit in predicting fractures from repeating bone measurement testing 4 to 8 years after initial screening.[4]

Treatment

The US Food and Drug Administration (FDA) has approved multiple drug therapies to reduce osteoporotic fractures, including bisphosphonates, parathyroid hormone, raloxifene, and estrogen. The choice of therapy should be an individual one based on the patient's clinical situation and the trade-off between benefits and harms. Clinicians should educate patients on how to minimize the

Table 1. Characteristics of the Most Common Bone Measurement Screening Tests for Osteoporosis

Screening Test	Description	Other Considerations
Central DXA	Most commonly studied and used bone measurement test to screen for osteoporosis; reference to which other tests are compared; uses radiation to measure BMD at the hip and lumbar spine	Most treatment guidelines recommend using BMD, as measured by central DXA, to define osteoporosis and the treatment threshold to prevent osteoporotic fractures
Peripheral DXA	Uses radiation to measure BMD at peripheral sites, such as the lower forearm and heel; similar accuracy to that of central DXA (AUC, 0.67-0.80 in women with a mean age of 61 years [2 studies; n = 712])	Measured with portable devices, which may help increase access to screening in locations where machines that perform central DXA are not available; no treatment studies reviewed by the USPSTF used BMD measured by peripheral DXA to define treatment threshold
QUS	Uses ultrasound to evaluate peripheral bone sites (most commonly, the calcaneus); similar accuracy to that of central DXA (pooled AUC: 0.77 in women [7 studies; n = 1969] and 0.80 in men [3 studies; n = 5142])	No exposure to radiation; measured with portable devices, which may help increase access to screening in locations where machines that perform central DXA are not available; does not measure BMD, and no treatment studies use QUS measurements to define treatment threshold; cannot be routinely used to initiate treatment without further DXA measurement

Abbreviations: AUC, area under the curve; BMD, bone mineral density; DXA, central dual-energy x-ray absorptiometry; QUS, quantitative ultrasound; USPSTF, US Preventive Services Task Force.

adverse effects of drug therapies, such as reducing esophageal irritation from bisphosphonate therapy by taking the medication with a full glass of water and not lying down for at least 30 minutes afterward.

Suggestions for Practice Regarding the I Statement

When deciding whether to screen for osteoporosis to prevent osteoporotic fractures in men, clinicians should consider the following factors.

Potential Preventable Burden

The prevalence of osteoporosis in men is generally lower than in women (4.3% vs 15.4%, respectively).[1] An estimated 1 to 2 million men in the United States have osteoporosis.[5] Although men account for 29% of osteoporotic fractures in the United States, men have higher fracture-related morbidity and mortality rates than women.[3,4] Each year, about 80 000 men in the United States will have a hip fracture; 1 in 3 men who experience a hip fracture will die within a year.[13]

Older age in men is an important risk factor for osteoporotic fracture. In the absence of other risk factors, it is not until age 80 years that the prevalence of osteoporosis in white men starts to reach that of white women at age 65 years.[1] For example, in the United States, the 10-year FRAX risk of MOF is 5.0%[8] in a 65-year-old white man of mean height and weight[7] without any risk factors, and 8.4%[8] at age 80 years (vs 8.4% in a 65-year-old white woman of mean height and weight[7] without any risk factors[8]). In the presence of multiple risk factors, the 10-year FRAX risk of MOF in a 55-year-old white man can approximate the risk of a 65-year-old white woman with no risk factors; for example, the 10-year FRAX risk of MOF is 8.9% in a 55-year-old white man of mean height and weight[7] with a parental history of hip fracture who currently smokes and drinks 3 or more units of alcohol per day.[8]

Similar to women, risk factors for fractures in men include low body mass index, excessive alcohol consumption, current smoking, long-term corticosteroid use, previous fractures, and history of falls within the past year. A recent systematic review of risk factors for osteoporosis in men also found that hypogonadism, history of cerebrovascular accident, and history of diabetes are associated with an increased risk of fractures, although their clinical use in identifying men who need further bone measurement testing is unclear.[4,14]

Although clinical risk assessment tools and imaging tests to diagnose osteoporosis seem to perform as well in men as in women, evidence on the effectiveness of medications to treat osteoporosis in men is lacking.[4,6] Although some treatments have been found to be effective in preventing fractures in postmenopausal women with osteoporosis, it cannot be assumed that they will be equally effective in men because the underlying biology of bones may differ in men due to differences in testosterone and estrogen levels. The review identified limited evidence on the effect of treatment of men with osteoporosis on the prevention of fractures.[4,6] One good-quality study found a reduction in morphometric vertebral fractures but not clinical (vertebral and nonvertebral) fractures in men with osteoporosis who were treated with zoledronic acid.[15] A small study examining treatment with parathyroid hormone in men was consistent in the direction of benefit but the finding was not statistically significant.[16]

Potential Harms of Screening

The USPSTF found no studies that directly examined harms of screening in men. Potential harms of screening in men are likely to be similar to those in women. Evidence on harms of drug therapies in men is very limited.[4,6]

Current Practice

Data on how frequently men are screened for osteoporosis are limited. Several organizations have issued statements on screening in men at increased risk. Progress toward the Healthy People 2020 objectives for osteoporosis have shown little change in the number of hip fracture hospitalizations among men (464.9 vs 442.6 hospitalizations per 100 000 men in 2000 and 2010, respectively).[17]

Additional Approaches to Prevention

According to the US Centers for Disease Control and Prevention, engaging in 120 to 300 minutes of at least moderate-intensity aerobic activity each week can reduce the risk of hip fractures, and performing balance and muscle-strengthening activities each week along with moderate-intensity aerobic activity can help prevent falls in older adults.[18] The National Academy of Medicine (formerly the Institute of Medicine) has issued dietary reference intakes for calcium and vitamin D to support health; recommended daily allowances are based on age.[19)]

Table 2. Characteristics of Clinical Risk Assessment Tools for Osteoporosis[a]

Tool	Risk Factors	Scoring	Frequently Used Threshold for Increased Osteoporosis Risk
OST	Weight, kg	(kg − y) × 0.2	<2
	Age, y		
ORAI	Age, y		≥9
	≥75	15	
	65-74	9	
	55-64	5	
	45-54	0	
	Weight, kg		
	<60	9	
	60-69	3	
	≥70	0	
	No current estrogen use	2	
OSIRIS	Age, y	−0.2 × age	<1
	Weight, kg	0.2 × weight	
	Current estrogen use	2	
	Prior low-impact fracture	−2	
SCORE	Non-black race	5	≥6
	Rheumatoid arthritis	4	
	Prior rib/wrist/hip fracture	4 for each type of nontraumatic rib/wrist/hip fracture after age 45 y (max 12)	
	Never used estrogen	1	
	Age, y	3 × first digit of age	
	Weight, lb	−1 × weight divided by 10	
FRAX	Age, y	Refer to website[b]	9.3% (major osteoporotic fracture)[c]
	Sex		
	Weight, kg		
	Height, cm		
	Previous fracture		
	Parental hip fracture		
	Current smoking		
	Glucocorticoid use		
	Rheumatoid arthritis		
	Secondary osteoporosis		
	Alcohol consumption ≥3 U/d		

Abbreviations: FRAX, Fracture Risk Assessment Tool; ORAI, Osteoporosis Risk Assessment Instrument; OSIRIS, Osteoporosis Index of Risk; OST, Osteoporosis Self-Assessment Tool; SCORE, Simple Calculated Osteoporosis Risk Estimation.

[a] Table adapted from Chen SJ, et al.[42]

[b] Refer to https://www.sheffield.ac.uk/FRAX.

[c] 9.3% represents the 10-y major osteoporotic fracture risk in a 65-y-old white woman without any other risk factors in the United States, as calculated in 2011. Currently, FRAX calculates this risk to be 8.4%.

Useful Resources for Primary Care

The USPSTF recommends exercise interventions to prevent falls in community-dwelling adults 65 years and older at increased risk of falls and selectively offering multifactorial interventions based on circumstances of prior falls, presence of comorbid medical conditions, and the patient's values and preferences; it recommends against vitamin D supplementation to prevent falls.[20] In a separate recommendation, the USPSTF recommends against supplementation with 400 IU or less of vitamin D and 1000 mg or less of calcium in postmenopausal women to prevent fractures.[21] The USPSTF found insufficient evidence on supplementation with higher doses of vitamin D and calcium, alone or combined, to prevent fractures in postmenopausal women, or at any dose in men and premenopausal women.[21]

Other Considerations

Implementation

Tools that can help identify women younger than 65 years who are at increased risk of osteoporosis include SCORE, ORAI, OSIRIS, and OST.[22-26] The most commonly used thresholds to identify increased risk of osteoporosis or osteoporotic fractures are greater than or equal to 6 for SCORE, greater than or equal to 9 for ORAI, less than 1 for OSIRIS, and less than 2 for OST (**Table 2**). Additionally, the FRAX tool[8] is a computerized algorithm that calculates the 10-year probability of hip fracture and MOF using clinical risk factors. FRAX models are country specific, as they include country epidemiology. In the United States, the

risk of MOF is 8.4% in a 65-year-old white woman of mean height and weight without any other risk factors.[4,7,8]

Research Needs and Gaps

The majority of reviewed studies focused on women. Treatment trials that focus on or include men and report on fracture outcomes (rather than BMD) as well as harms are needed. More studies are also needed that evaluate the direct effect of screening for osteoporosis (either with BMD or clinical risk assessment tools) on fracture outcomes. Additional research is needed to determine whether clinical risk assessment tools alone (without BMD) could help identify patients at risk of fractures and help guide decisions to initiate medications to prevent fractures. The development of prognostic models incorporating age, baseline BMD, and hormone replacement therapy use[27,28] may also help identify optimal screening intervals.

Discussion

Burden of Disease

Osteoporosis is a skeletal disorder characterized by loss of bone mass, microarchitectural deterioration of bone tissue, and decline in bone quality leading to increased bone fragility and risk of fractures.[9,12] The World Health Organization defines osteoporosis as bone density at the hip or spine that is at least 2.5 SDs (ie, T score≤−2.5) below the mean bone density of a reference population of young healthy women, presumably at peak bone mass.[29]

In the United States, the estimated prevalence of osteoporosis among the community-dwelling population 50 years and older in 2010 was 10.3% (10.2 million adults), based on National Health and Nutrition Examination Survey data.[1] After age 50 years, the prevalence of osteoporosis is greater in women than in men (15.4% vs 4.3%, respectively).[1] The prevalence of osteoporosis varies by race/ethnicity and is highest in Mexican American (13.4%) and non-Hispanic white adults (10.2%) and lowest in non-Hispanic black adults (4.9%).[1] The prevalence of osteoporosis increases dramatically with age, from 5.1% in adults aged 50 to 59 years to 26.2% in those 80 years and older.[1] As the US population ages, it is projected that the number of persons living with osteoporosis will also increase. The number of adults 50 years and older with osteoporosis will increase from 10.2 million in 2010 to an estimated 12.3 million in 2020 and 13.6 million in 2030.[1] Based on Healthcare Effectiveness Data and Information Set data, the rate of women aged 65 to 85 years enrolled in Medicare who reported ever having a bone density test increased from 64.4% to 71.3% in 2006 and from 73.8% to 79.3% in 2016.[30]

In 2005, approximately 2 million osteoporotic fractures occurred in the United States.[3] Nearly 40% of persons who experience a fracture are unable to walk independently at 1 year, and 60% require assistance with at least 1 essential activity of daily living.[31] Hip fractures account for a large portion of the morbidity and mortality associated with osteoporotic fractures, with 21% to 30% of patients dying within 1 year of a hip fracture.[2]

Osteoporosis is usually asymptomatic until a fracture occurs; preventing osteoporotic fractures is the main goal of an osteoporosis screening strategy.

Scope of Review

The USPSTF commissioned a systematic evidence review[4,6] to search for updated evidence since the previous review in 2011 and examine newer evidence on screening for and treatment of osteoporotic fractures in men and women. The review also sought evidence on risk assessment tools, screening intervals, and efficacy of screening and treatment in subgroups. The USPSTF defined the screening population as postmenopausal women and older men with no known previous osteoporotic fractures and no known comorbid conditions or medication use associated with secondary osteoporosis. The review excluded adults younger than 40 years as well as adults with no known conditions that may increase their risk of falls.

Accuracy of Screening Tests and Clinical Risk Assessment Tools

DXA

Bone measurement testing with central DXA is the most commonly used and studied method for the diagnosis of osteoporosis. Central DXA uses radiation to measure BMD at central bone sites (hip and lumbar spine), which is the established standard for diagnosis of osteoporosis and for guiding decisions about treatment. DXA can also be used at peripheral bone sites (such as the lower forearm and heel) to identify persons with low bone mass; however, most treatment guidelines recommend follow-up with central DXA before initiating treatment for osteoporosis. Screening with peripheral DXA and other imaging techniques may help increase access to screening in geographic locations (eg, rural areas) where machines that perform central DXA may not be available. The USPSTF identified 2 studies (n = 712) that reported on the accuracy of peripheral DXA at the calcaneus to identify osteoporosis; compared with central DXA, the area under the curve (AUC) ranged from 0.67 to 0.80 in women with a mean age of 61 years.[4,32,33]

QUS

Quantitative ultrasound is another imaging technique used at peripheral bone sites (most commonly the calcaneus), and it does not require radiation exposure. Compared with central DXA, the AUC for QUS measured at the calcaneus in women ranged from 0.69 to 0.90, with a pooled estimate of 0.77 (95% CI, 0.72-0.81; 7 studies; n = 1969).[4] In men, the AUC ranged from 0.70 to 0.93, with a pooled estimate of 0.80 (95% CI, 0.67-0.94; 3 studies; n = 5142).[4] However, QUS does not measure BMD, that is the current diagnostic criteria for osteoporosis. In addition, drug therapy trials for osteoporosis treatment generally use central DXA measurement of BMD as criteria for inclusion of study populations.[4,12] Thus, before QUS results could be routinely used to initiate treatment without any further DXA measurement, a method for converting or adapting QUS results to the DXA scale needs to be developed.

Clinical Risk Assessment Tools

The USPSTF evaluated the accuracy of clinical risk assessment tools to identify risk of osteoporosis. Many of these tools can also be used to calculate risk of future fractures; however, the USPSTF focused on their accuracy to identify osteoporosis because all the treatment studies evaluated by the USPSTF enrolled patients based on

bone measurement testing, specifically central DXA measurement of BMD. The most frequently studied tools in women were the ORAI (10 studies; n = 16 780), OSIRIS (5 studies; n = 5649), OST (13 studies; n = 44 323), and SCORE (8 studies; n = 15 362). The pooled AUCs for these tools were all similar and ranged from 0.65 to 0.70. The FRAX tool (without BMD), which has been studied extensively as a clinical risk assessment tool to predict fracture risk, performs similarly in its ability to identify osteoporosis (AUC range, 0.58-0.82; 4 studies; n = 22 141).[4] These clinical risk assessment tools could be applied to postmenopausal women younger than 65 years who are at increased risk of osteoporosis to help clinicians determine who should be screened with bone measurement testing. Fewer studies are available that evaluate the performance of these tools specifically in younger women, and 1 study has suggested that FRAX is inferior to OST and SCORE in discriminating women with osteoporosis.[34] However, in the studies reviewed by the USPSTF, the range of AUCs of these tools (ORAI, OSIRIS, OST, SCORE, and FRAX) to identify osteoporosis in women younger than 65 years were similar to the pooled AUCs for women of all ages; the AUC from individual studies of clinical risk assessment tools in women younger than 65 years ranged from 0.58 to 0.85.[4] Table 2 provides more information on these clinical risk assessment tools and commonly used thresholds to determine risk of osteoporosis.

Effectiveness of Early Detection and Treatment

A single fair-quality controlled study (n = 12 483) evaluated the effect of screening for osteoporosis on fracture rates in postmenopausal women aged 70 to 85 years.[4-6] This study reported no significant difference in the primary outcome of any osteoporotic fracture in women screened with FRAX vs women receiving usual care (12.9% vs 13.5%; hazard ratio [HR], 0.94 [95% CI, 0.85-1.03]). There was also no significant difference for incidence of all clinical fractures (15.3% vs 16.0%; HR, 0.94 [95% CI, 0.86-1.03]) or mortality (8.8% vs 8.4%; HR, 1.05 [95% CI, 0.93-1.19]). However, the study reported a statistically significant reduction in hip fracture incidence (2.6% vs 3.5%; HR, 0.72 [95% CI, 0.59-0.89]).[4-6]

The USPSTF reviewed the evidence on drug therapies for the primary prevention of osteoporotic fractures. The vast majority of studies were conducted in postmenopausal women exclusively; only 2 studies were conducted in men.[4] Overall, the USPSTF found that drug therapies are effective in treating osteoporosis and reducing fractures in postmenopausal women.

Bisphosphonates

Bisphosphonates were studied most frequently; the USPSTF identified 7 studies on alendronate, 2 trials on zoledronic acid, 4 trials on risedronate, and 2 trials on etidronate.[4] All but 1 study were conducted in postmenopausal women. For women, bisphosphonates were found to significantly reduce vertebral fractures (relative risk [RR], 0.57 [95% CI, 0.41-0.78]; 5 studies; n = 5433) and nonvertebral fractures (RR, 0.84 [95% CI, 0.76-0.92]; 8 studies; n = 16 438) but not hip fractures (RR, 0.70 [95% CI, 0.44-1.11]; 3 studies; n = 8988).[4] However, most studies reporting on hip fractures may have been underpowered to detect a difference in this outcome. In the single study of men (n = 1199), zoledronic acid was found to reduce morphometric vertebral fractures (RR, 0.33 [95% CI, 0.16-0.70]) but not clinical nonvertebral fractures (RR, 0.65 [95% CI, 0.21-1.97]).[4,15]

Raloxifene

Only 1 study (n = 7705) on raloxifene met inclusion criteria for the review. The study evaluated treatment with raloxifene in postmenopausal women and found a reduction in vertebral fractures (RR, 0.64 [95% CI, 0.53-0.76]) but not nonvertebral fractures (RR, 0.93 [95% CI, 0.81-1.06]).[4]

Denosumab

The USPSTF identified 4 studies that evaluated denosumab; however, only 1 study was adequately powered to detect a difference in fractures. This study (n = 7868) evaluated treatment with denosumab in women and found a significant reduction in vertebral fractures (RR, 0.32 [95% CI, 0.26-0.41]), nonvertebral fractures (RR, 0.80 [95% CI, 0.67-0.95]), and hip fractures (RR, 0.60 [95% CI, 0.37-0.97]).[4,35]

Parathyroid Hormone

The USPSTF reviewed evidence from 2 trials on parathyroid hormone. One trial (n = 2532) conducted in women found a significant reduction in vertebral fractures (RR, 0.32 [95% CI, 0.14-0.75]) but not nonvertebral fractures (RR, 0.97 [95% CI, 0.71-1.33]).[4,36] The other trial, conducted in men, found a nonsignificant reduction in nonvertebral fractures (RR, 0.65 [95% CI, 0.11-3.83]) when comparing the FDA-approved dose of 20 µg/d vs placebo (n = 298).[4,16] However, the number of fractures in the study was small and the study was stopped early due to concerns about osteosarcoma found in animal studies.

Estrogen

Although the USPSTF did not identify any studies on estrogen for the primary prevention of fractures that met inclusion criteria, the previous review found that estrogen reduces vertebral fractures based on data from the Women's Health Initiative trial.[12]

Potential Harms of Screening and Treatment

One trial evaluated the effect of screening on anxiety and quality of life and found no difference between screened and unscreened intervention groups.[4-6] Additional potential harms of screening for osteoporosis include false-positive test results, which can lead to unnecessary treatment, and false-negative test results. The USPSTF did review several studies that reported on harms of various osteoporosis medications.[4,6] Overall, the USPSTF determined that the potential harms of osteoporosis drug therapies are small.

Bisphosphonates

Similar to the evidence on the benefits of drug therapy for the primary prevention of fractures, the most available evidence on the harms is for bisphosphonates. The USPSTF identified 16 studies on alendronate, 4 studies on zoledronic acid, 6 studies on risedronate, 2 studies on etidronate, and 7 studies on ibandronate that reported on harms. Overall, based on pooled analyses, studies on bisphosphonates showed no increased risk of discontinuation (RR, 0.99 [95% CI, 0.91-1.07]; 20 studies; n = 17 369), serious adverse events (RR, 0.98 [95% CI, 0.92-1.04]; 17 studies; n = 11 745), or upper gastrointestinal events (RR, 1.01 [95% CI, 0.98-1.05]; 13 studies; n = 20 485).[4] Evidence on bisphosphonates and cardiovascular events is more limited and generally shows no significant difference or nonsignificant increases in atrial fibrillation with bisphos-

phonate therapy. Concerns have been raised about osteonecrosis of the jaw and atypical fractures of the femur with bisphosphonate therapy. The USPSTF found only 3 studies that reported on osteonecrosis of the jaw, and none of these studies found any cases.[4] The previous review[12] noted an FDA case series that reported on osteonecrosis of the jaw with bisphosphonate use in patients with cancer. A more recent systematic review that did not meet inclusion criteria (because it included populations with a previous fracture) found higher incidence of osteonecrosis of the jaw with intravenous bisphosphonate use and with longer use. No studies that met inclusion criteria for the current review reported on atypical fractures of the femur, although some studies and systematic reviews that did not meet inclusion criteria (because of wrong study population, study design, or intervention comparator) reported an increase in atypical femur fractures with bisphosphonate use. No studies reported any cases of kidney failure, although the FDA has added a warning label noting that zoledronic acid is contraindicated in certain patients. Three trials that reported on harms of bisphosphonates included men (either combining results for men and women or including men only); results were consistent with those of women for risk of discontinuation, serious adverse events, and upper gastrointestinal events.

Raloxifene

Six trials of raloxifene therapy in women reported on various harms. Pooled analyses showed no increased risk of discontinuation due to adverse events (RR, 1.12 [95% CI, 0.98-1.28]; 6 studies; n = 6438) or increased risk of leg cramps (RR, 1.41 [95% CI, 0.92-2.14]; 3 studies; n = 6000).[4] However, analyses found a nonsignificant trend for increased risk of deep vein thrombosis (RR, 2.14 [95% CI, 0.99-4.66]; 3 studies; n = 5839), as well as an increased risk of hot flashes (RR, 1.42 [95% CI, 1.22-1.66]; 5 studies; n = 6249).[4] The previous review[12] found an increased risk of thromboembolic events with raloxifene (RR, 1.60 [95% CI, 1.15-2.23]).[4]

Denosumab

Four studies (n = 8663) reported on harms of denosumab therapy in postmenopausal women. Pooled analyses showed no significant increase in discontinuation (RR, 1.14 [95% CI, 0.85-1.52]) or serious adverse events (RR, 1.12 [95% CI, 0.88-1.44]) but found a nonsignificant increase in serious infections (RR, 1.89 [95% CI, 0.61-5.91]).[4] Three studies reported higher infection rates in women taking denosumab, and further analysis found a higher rate of cellulitis and erysipelas.[4] One study reported no occurrences of osteonecrosis of the jaw.[4]

Parathyroid Hormone

A single study of parathyroid hormone therapy in women (n = 2532) reported an increased risk of discontinuation (RR, 1.23 [95% CI, 1.08-1.40]) and other adverse events, such as nausea and headache (RR, 2.47 [95% CI, 2.02-3.03]),[4,36] whereas a single smaller study in men found no increased risk of discontinuation (RR, 1.94 [95% CI, 0.81-4.69]) or cancer (RR, 0.97 [95% CI, 0.2-4.74])[4] using the FDA-approved dose of 20 µg/d (n = 298).[4,16]

Estrogen

Similar to the evidence on the benefits of estrogen for the primary prevention of fractures, no studies met inclusion criteria for the current review. However, based on findings from the Women's Health Initiative trial, the previous review found an increased rate of gallbladder events, stroke, and venous thromboembolism with estrogen therapy, and an increased risk of urinary incontinence during 1 year of follow-up.[4,12] Women taking combined estrogen and progestin had an increased risk of invasive breast cancer, coronary heart disease, probable dementia, gallbladder events, stroke, and venous thromboembolism compared with women taking placebo, and an increased risk of urinary incontinence during 1 year of follow-up.[4,12]

Estimate of Magnitude of Net Benefit

The USPSTF found convincing evidence that bone measurement tests are accurate for detecting osteoporosis and predicting osteoporotic fractures in women and men. The USPSTF found adequate evidence that clinical risk assessment tools are moderately accurate in identifying risk of osteoporosis and osteoporotic fractures.

The USPSTF found convincing evidence that drug therapies reduce subsequent fracture rates in postmenopausal women. The benefit of treating screen-detected osteoporosis is at least moderate in women 65 years and older and in younger postmenopausal women who have similar fracture risk. The harms of treatment range from no greater than small for bisphosphonates and parathyroid hormone to small to moderate for raloxifene and estrogen. Therefore, the USPSTF concludes with moderate certainty that the net benefit of screening for osteoporosis in these groups of women is at least moderate. The single study that directly evaluated the effect of screening (with FRAX) on fracture outcomes was generally consistent with this conclusion.

The USPSTF found that the evidence is inadequate to assess the effectiveness of drug therapies in reducing subsequent fracture rates in men without previous fractures. Treatments that have been proven effective in women cannot necessarily be presumed to have similar effectiveness in men, and the direct evidence is too limited to draw definitive conclusions. Thus, the USPSTF concludes that the evidence is insufficient to assess the balance of benefits and harms of screening for osteoporosis in men.

How Does Evidence Fit With Biological Understanding?

Low bone density is a risk factor for fractures, especially in older adults. Screening for low BMD and subsequent treatment can result in increased BMD and decrease the risk of subsequent fractures and fracture-related morbidity and mortality. Most evidence supports screening for and treatment of osteoporosis in postmenopausal women; the evidence for primary prevention in men is lacking, and future research is needed. It cannot be assumed that the bones of men and women are biologically the same, especially because bone density is affected by differing levels and effects of testosterone and estrogen in men and women. Moreover, rapid bone loss occurs in women due to the loss of estrogen during menopause. Men tend to experience fractures at an older age than women, when risk of comorbid conditions and overall mortality are higher; thus, the net balance of benefits and harms of screening for and treatment of osteoporosis in men is unclear.

Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from November 7, 2017, to December 4, 2017. In response to comments, the USPSTF

added information on the accuracy of certain clinical risk assessment tools to identify osteoporosis in women younger than 65 years to the Discussion section. In addition, the USPSTF clarified that adults with certain conditions that may increase their risk of falls or those using certain medications (such as aromatase inhibitors) that may increase one's risk of fractures are excluded from this recommendation. Some comments expressed concern that the USPSTF did not recommend screening for osteoporosis in men. Although the USPSTF agrees that prevention of osteoporotic fractures in men is an important public health issue, there is currently not enough evidence demonstrating that screening for and subsequent treatment of osteoporosis in men prevents primary fractures. Studies that have evaluated screening and treatment in men have focused on populations that are out of scope for this recommendation, such as men with a history of previous fractures or men taking certain medications that may cause secondary osteoporosis. The USPSTF is calling for more research in osteoporosis screening and treatment in men, and clarified why it found the evidence insufficient to make a recommendation for or against screening in men. Last, the USPSTF updated the recommendation to include information from a recent trial that evaluated the direct effect of screening for osteoporosis on the incidence of fractures.

Update of Previous USPSTF Recommendation

This recommendation is consistent with the 2011 USPSTF recommendation on screening for osteoporosis.[37] The major change in the current recommendation is that the USPSTF expanded its consideration of evidence related to fracture risk assessment, with or without BMD testing. The USPSTF found there is still insufficient evidence on screening for osteoporosis in men.

Recommendations of Others

In 2014, the National Osteoporosis Foundation recommended BMD testing in all women 65 years and older and all men 70 years and older.[38] It also recommended BMD testing in postmenopausal women younger than 65 years and men aged 50 to 69 years based on their risk factor profile, including if they had a fracture as an adult. The International Society for Clinical Densitometry recommends BMD testing in all women 65 years and older and all men 70 years and older. It also recommends BMD testing in postmenopausal women younger than 65 years and men younger than 70 years who have risk factors for low bone mass.[39] As part of Choosing Wisely, the American Academy of Family Physicians recommends against DXA screening in women younger than 65 years and men younger than 70 years with no risk factors.[40] In 2012 (and reaffirmed in 2014), the American College of Obstetricians and Gynecologists recommended BMD testing with DXA beginning at age 65 years in all women and selective screening in postmenopausal women younger than 65 years who have osteoporosis risk factors or an adult fracture.[9] The American Association of Clinical Endocrinologists also recommends evaluating all women 50 years and older for osteoporosis risk and considering BMD testing based on clinical fracture risk profile.[10] The Endocrine Society recommends screening in men older than 70 years and adults aged 50 to 69 years with significant risk factors or fracture after age 50 years.[41]

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