

# Screening for Osteoporosis to Prevent Fractures

## US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

**IMPORTANCE** Osteoporotic fractures are associated with psychological distress, subsequent fractures, loss of independence, reduced ability to perform activities of daily living, and death.

**OBJECTIVE** The US Preventive Services Task Force (USPSTF) commissioned a systematic review to evaluate the evidence on the benefits and harms of screening for osteoporosis to prevent fractures in adults 40 years or older with no known diagnosis of osteoporosis or history of fragility fracture.

**POPULATION** Adults 40 years or older without known osteoporosis or history of fragility fractures.

**EVIDENCE ASSESSMENT** The USPSTF concludes with moderate certainty that screening for osteoporosis to prevent osteoporotic fractures in women 65 years or older has moderate net benefit. The USPSTF concludes with moderate certainty that screening for osteoporosis to prevent osteoporotic fractures in postmenopausal women younger than 65 years at increased risk has moderate net benefit. The USPSTF concludes that the evidence is insufficient and the balance of benefits and harms for screening for osteoporosis to prevent osteoporotic fractures in men cannot be determined.

**RECOMMENDATION** The USPSTF recommends screening for osteoporosis to prevent osteoporotic fractures in women 65 years or older. (B recommendation) The USPSTF recommends screening for osteoporosis to prevent osteoporotic fractures in postmenopausal women younger than 65 years who are at increased risk for an osteoporotic fracture as estimated by clinical risk assessment. (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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**Group Information:** The US Preventive Services Task Force (USPSTF) members appear listed at the end of this article.

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## Summary of Recommendations

See the Summary of Recommendations figure.

## Preamble

The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms to improve the health of people nationwide.

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.

The USPSTF is committed to mitigating the health inequities that prevent many people from fully benefiting from preventive services. Systemic or structural racism results in policies and practices, including health care delivery, that can lead to inequities in health. The USPSTF recognizes that race, ethnicity, and gender are all social rather than biological constructs. However, they are also often important predictors of health risk. The USPSTF is committed to helping reverse the negative impacts of systemic and structural racism, gender-based discrimination, bias, and other sources of health inequities, and their effects on health, throughout its work.

Population	Recommendation	Grade
Women 65 years or older	The USPSTF recommends screening for osteoporosis to prevent osteoporotic fractures in women 65 years or older. See the Practice Considerations section for more information on screening tests.	B
Postmenopausal women younger than 65 years with 1 or more risk factors for osteoporosis	The USPSTF recommends screening for osteoporosis to prevent osteoporotic fractures in postmenopausal women younger than 65 years who are at increased risk for an osteoporotic fracture as estimated by clinical risk assessment. See the Practice Considerations section for more information on risk assessment and screening tests.	B
Men	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. See the Practice Considerations section for suggestions for practice regarding the I statement.	I

USPSTF indicates US Preventive Services Task Force.

#### Pathway to Benefit

To achieve the benefit of screening to reduce morbidity and mortality from fractures, women found to have osteoporosis should be further evaluated, counseled, and, if appropriate, receive evidence-based management.

See **Table 1** for more information on the USPSTF recommendation rationale and assessment and the eFigure in the Supplement for information on the recommendation grade. See the **Figure** for a summary of the recommendation for clinicians. For more details on the methods the USPSTF uses to determine the net benefit, see the USPSTF Procedure Manual.<sup>5</sup>

## Importance

Osteoporosis is a skeletal disorder characterized by decreased bone mass leading to increased bone fragility and fracture risk. Osteoporotic fractures are associated with psychological distress, subsequent fractures, loss of independence, reduced ability to perform activities of daily living, and death. Morbidity from fragility fractures at central skeletal sites, particularly the hip, is much greater than morbidity from fragility fractures at other sites.<sup>1</sup> Evidence shows that only 40% to 60% of persons experiencing a hip fracture recover their prefracture level of mobility and ability to perform activities of daily living.<sup>2</sup>

The age-adjusted prevalence of osteoporosis is 12.6% among community-dwelling US residents 50 years or older. Prevalence of osteoporosis is higher among persons 65 years or older (27.1% in women and 5.7% in men), in women compared with men,<sup>3</sup> and among Asian, Hispanic, and White persons.<sup>4</sup>

## USPSTF Assessment of Magnitude of Net Benefit

The US Preventive Services Task Force (USPSTF) concludes with moderate certainty that screening for osteoporosis to prevent osteoporotic fractures in women 65 years or older has **moderate net benefit**.

The USPSTF concludes with moderate certainty that screening for osteoporosis to prevent osteoporotic fractures in postmenopausal women younger than 65 years at increased risk has **moderate net benefit**.

The USPSTF concludes that the evidence is insufficient and the balance of benefits and harms for screening for osteoporosis to prevent osteoporotic fractures in men **cannot be determined**.

## Practice Considerations

### Patient Population Under Consideration

This recommendation applies to adults 40 years or older without known osteoporosis or history of fragility fractures. It does not apply to persons with secondary osteoporosis due to an underlying medical condition (eg, cancer, metabolic bone diseases, or hyperthyroidism) or chronic use of a medication (eg, glucocorticoids) associated with bone loss.

In this recommendation statement, the recommendations are stratified by "men" and "women," although the net benefit estimates are driven by sex as assigned at birth (ie, male/female) rather than gender identity. In describing the evidence, sex terms are reported as used by study authors, which are typically "men" and "women." Transgender men and transgender women who have not undergone any hormonal treatment associated with transitioning likely have the same risks as persons assigned female and male sex at birth; however, they should consult with their clinician to determine which recommendation best applies to them.

### Definitions

In 1994, the World Health Organization defined osteoporosis in postmenopausal White women as bone density at the hip or lumbar spine that is 2.5 standard deviations or lower (T score  $\leq -2.5$ ) than the mean bone mineral density (BMD) measured at that site for a reference population of young healthy White women.<sup>5</sup> This ultimately became the reference standard for persons of all racial and ethnic groups, and for males and females.<sup>7</sup>

Fragility fractures (also known as "low-energy" or "low-trauma" fractures) are fractures sustained from a fall from standing height or lower that would not cause a fracture in most healthy persons.<sup>8</sup>

Table 1. Summary of USPSTF Rationale

Rationale	Assessment
Detection	<ul style="list-style-type: none"> <li>The USPSTF found adequate evidence that centrally measured DXA BMD can accurately predict osteoporotic fractures in women.</li> <li>The USPSTF found adequate evidence that clinical risk assessment tools have sufficient accuracy to identify osteoporosis in women and predict certain osteoporotic fractures, particularly hip fractures, in women and men.</li> </ul>
Benefits of early detection and intervention and treatment	<ul style="list-style-type: none"> <li>The USPSTF found adequate direct evidence that screening for fracture risk in women 65 years or older provides a moderate benefit in preventing fractures.</li> <li>The USPSTF found convincing evidence that treatment of women 65 years or older with osteoporosis provides a moderate benefit in preventing fractures.</li> <li>For postmenopausal women younger than 65 years with risk factors for osteoporosis, the USPSTF found adequate evidence that screening can detect osteoporosis and fracture risk and convincing evidence that treatment provides a moderate benefit in preventing fractures.</li> <li>The USPSTF found inadequate evidence on the benefits of screening for and treatment of osteoporosis to reduce the risk of osteoporotic fractures in men.</li> </ul>
Harms of early detection and intervention and treatment	<ul style="list-style-type: none"> <li>Based on the nature of screening and the low likelihood of serious harms, the USPSTF found adequate evidence to bound the harms of screening for osteoporosis as no greater than small.</li> <li>The USPSTF found adequate evidence that the harms of treatment of osteoporosis are small in women.</li> <li>The USPSTF found inadequate evidence on the harms of screening for or treatment of osteoporosis to prevent fractures in men.</li> </ul>
USPSTF assessment	<ul style="list-style-type: none"> <li>The USPSTF concludes with moderate certainty that screening for osteoporosis to prevent osteoporotic fractures in women 65 years or older has moderate net benefit.</li> <li>The USPSTF concludes with moderate certainty that screening for osteoporosis to prevent osteoporotic fractures in postmenopausal women younger than 65 years at increased risk has moderate net benefit.</li> <li>Due to a lack of available data, the USPSTF concludes that the evidence is insufficient, and the balance of benefits and harms for screening for osteoporosis to prevent osteoporotic fractures in men cannot be determined.</li> </ul>

Abbreviations: BMD, bone mineral density; DXA, dual-energy x-ray absorptiometry; USPSTF, US Preventive Services Task Force.

Major osteoporotic fracture (MOF) is defined as a fracture of the hip, spine, wrist, or shoulder.

### Assessment of Risk

Although bone density is an important risk factor for fragility fractures, advancing age is a stronger determinant.<sup>9</sup> Older adults have much higher fracture rates than younger adults with the same BMD because of concurrent increasing risk from declining bone quality and an increasing risk of falling.<sup>10</sup>

When deciding which postmenopausal women younger than 65 years to screen, the USPSTF suggests a 2-step approach. Clinicians can first determine the presence of risk factors for osteoporosis and fracture. These include menopausal status, low body weight, parental history of hip fracture, cigarette smoking, and excess alcohol consumption.<sup>11,12</sup> For postmenopausal women younger than 65 years with 1 or more risk factors (in addition to postmenopausal status), the USPSTF then recommends using a clinical risk assessment tool (ie, a tool designed to identify osteoporosis or predict fracture risk) to estimate risk and help decide whether screening is warranted. More details about risk assessment tools and increased risk are provided in the Screening Tests and Screening Strategies section.

Other medical conditions and medications (eg, corticosteroids or diabetes treated with insulin) may also increase risk of osteoporosis and, subsequently, fragility fractures. The prevalence of osteoporosis and incidence of osteoporotic fractures differs among racial and ethnic groups. Studies show lower fracture incidence in Asian, Black, and Hispanic populations compared with White populations among both men and women.<sup>13,14</sup> Differences in BMD alone are not sufficient to explain racial and ethnic differences in fracture incidence. For example, Asian women have been found to have lower BMD than White women but lower fracture risk.<sup>15-17</sup> Although the underlying causes for the differences in fracture incidence among racial and ethnic groups remain uncertain, they are likely due in part to social and environmental factors or differences in clinical risks.<sup>1</sup>

### Screening Tests and Screening Strategies

The most commonly used bone measurement test to screen for osteoporosis is dual-energy x-ray absorptiometry (DXA) at a central site (eg, total hip, femoral neck, or lumbar spine). Centrally measured DXA correlates with bone strength and clinical fracture outcomes and uses low doses of radiation.<sup>18</sup> Fracture risk at a specific site is best predicted if bone density is measured at that site.<sup>19</sup>

Some evidence suggests that BMD alone may not be the most useful predictor of fracture risk, especially in younger populations.<sup>20</sup> Several risk assessment tools that incorporate age and sex, with or without other risk factors, have been developed to either identify probability of osteoporosis or predict fracture risk. It is important to note that some of the risk assessment tools were developed on small cohorts of homogeneous populations or have limited published evidence.

Risk assessment tools designed to estimate future fracture risk that can be used with or without BMD as a risk factor input include FRAX,<sup>8</sup> the Fracture Risk Calculator (FRC),<sup>21</sup> and the Garvan Fracture Risk Calculator.<sup>22,23</sup> Of note, the predictive accuracy of these tools often improves when BMD is included in the risk assessment calculation.<sup>1</sup> Risk assessment tools designed to identify osteoporosis (eg, the Osteoporosis Risk Assessment Instrument [ORAI] and the Osteoporosis Self-assessment Tool [OST]) generally require fewer risk inputs than tools designed to predict fracture risk.<sup>1</sup>

FRAX is the most studied fracture risk assessment tool. Country-specific versions of FRAX are available that have been calibrated using country-specific fracture incidence and mortality data, which are part of the FRAX risk calculation.<sup>24</sup> As of 2016, FRAX was incorporated into 120 guidelines worldwide and added into DXA software following regulatory approval by the US Food and Drug Administration and has been incorporated into clinical decision support tools within electronic health record systems.<sup>25</sup> FRAX predicts the 10-year probability of hip fracture or MOF for persons aged 40 to 90 years by using demographic and clinical factors alone or in combination with BMD

**Figure. Clinician Summary: Screening for Osteoporosis to Prevent Fractures**

What does the USPSTF recommend?	<b>Women 65 years or older:</b> Screen for osteoporosis to prevent osteoporotic fractures. <b>Grade: B</b>
	<b>Postmenopausal women younger than 65 years with 1 or more risk factors for osteoporosis:</b> Screen for osteoporosis to prevent osteoporotic fractures. <b>Grade: B</b>
	<b>Men:</b> The current evidence is insufficient to assess the balance of benefits and harms of screening for osteoporosis to prevent osteoporotic fractures in men. <b>Grade: I statement</b>
To whom do these recommendations apply?	These recommendations apply to adults 40 years or older without known osteoporosis or history of fragility fractures. They do not apply to persons with secondary osteoporosis due to an underlying medical condition (eg, cancer, metabolic bone diseases, or hyperthyroidism) or chronic use of a medication (eg, glucocorticoids) associated with bone loss.
What's new?	<ul style="list-style-type: none"> <li>For the current recommendation, the USPSTF has noted that screening includes dual energy x-ray absorptiometry (DXA) bone mineral density (BMD), with or without fracture risk assessment.</li> <li>This recommendation is otherwise consistent with the 2018 USPSTF recommendation on screening for osteoporosis.</li> </ul>
How to implement this recommendation?	<ul style="list-style-type: none"> <li>Screen women 65 years or older with DXA BMD, with or without fracture risk assessment.</li> <li>For postmenopausal women younger than 65 years, the USPSTF suggests first assessing for the presence of 1 or more risk factors for osteoporosis. For women who have 1 or more risk factors, assess for increased risk using a clinical risk assessment tool. For women assessed to be at increased risk, screen for osteoporosis with DXA BMD, with or without fracture risk assessment.</li> <li>To achieve the benefit of screening to reduce morbidity and mortality from fractures, women found to have osteoporosis should be further evaluated, counseled, and, if appropriate, receive evidence-based care management.</li> <li>There is insufficient evidence to recommend for or against screening for osteoporosis in men.</li> <li>Clinicians should use their clinical judgment regarding whether to screen for osteoporosis in men.</li> </ul>
Why is this recommendation and topic important?	<ul style="list-style-type: none"> <li>Osteoporotic fractures are associated with psychological distress, subsequent fractures, loss of independence, reduced ability to perform activities of daily living, and death. Evidence shows that only 40% to 60% of persons experiencing a hip fracture recover their prefracture level of mobility and ability to perform activities of daily living.</li> <li>The age-adjusted prevalence of osteoporosis is 12.6% among community-dwelling US residents 50 years or older. Prevalence of osteoporosis is higher among persons 65 years or older (27.1% in women and 5.7% in men) and in women compared with men.</li> </ul>
What are other relevant USPSTF recommendations?	The USPSTF has issued recommendations on interventions to prevent falls in community-dwelling older adults and on the use of vitamin D and calcium to prevent fractures and falls in community-dwelling adults.
What are additional tools and resources?	<ul style="list-style-type: none"> <li>The National Institutes of Health has information on osteoporosis (<a href="https://www.niams.nih.gov/health-topics/osteoporosis">https://www.niams.nih.gov/health-topics/osteoporosis</a>, <a href="https://www.niams.nih.gov/health-topics/osteoporosis/diagnosis-treatment-and-steps-to-take">https://www.niams.nih.gov/health-topics/osteoporosis/diagnosis-treatment-and-steps-to-take</a>, and <a href="https://www.nia.nih.gov/health/osteoporosis/osteoporosis">https://www.nia.nih.gov/health/osteoporosis/osteoporosis</a>).</li> </ul>
Where to read the full recommendation statement?	Visit the USPSTF website ( <a href="https://www.uspreventiveservicestaskforce.org/">https://www.uspreventiveservicestaskforce.org/</a> ) or the JAMA website ( <a href="https://jamanetwork.com/collections/44068/united-states-preventive-services-task-force">https://jamanetwork.com/collections/44068/united-states-preventive-services-task-force</a> ) to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others

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.

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measured at the femoral neck.<sup>24,26</sup> Risks predicted by FRAX alone and by BMD alone are similar, but both are less accurate than risks predicted by FRAX plus BMD.<sup>27</sup> In the US, 4 different versions of FRAX calibrated using racial- and ethnic-specific fracture incidence data are available, including unique versions for Hispanic, non-Hispanic Asian, non-Hispanic Black, and non-Hispanic White persons.<sup>25</sup> Concerns exist regarding the validity of race-specific FRAX calculators. Because hip fracture incidence in the US is lower in most non-White racial and ethnic groups, predicted fracture risk estimates for Asian, Black, and Hispanic persons will always be lower than for White persons of the same age, sex, weight, BMD, and clinical

risk factors in the FRAX model,<sup>28,29</sup> which could lead to racial and ethnic differences in who is offered treatment among persons of otherwise identical age, BMD, and clinical risk profile. It is also unclear which version of FRAX to use for persons who are multiracial, or immigrants from other countries who are now living in the US.<sup>30</sup> Other limitations of the FRAX instrument include use of binary exposure to glucocorticoids and alcohol use (yes/no vs quantified dose exposure), lack of use of lumbar spine BMD or trabecular bone score, lack of information collected about history of falls or frailty, use of cohort studies that are 30 to 40 years old to estimate race-specific fracture incidence, use of mortality estimates that have not been

updated since 2004, and lack of inclusion of medical conditions such as diabetes that may portend an increased risk.<sup>25,31,32</sup>

Screening for osteoporosis to prevent fractures consists of a central DXA BMD, with or without fracture risk assessment. Because most fragility fractures occur in persons without osteoporosis (ie, with DXA T scores >-2.5), some screening strategies focus on identifying those at risk for fracture and not just those with osteoporosis.<sup>25</sup> Results from randomized clinical trials (RCTs) are now available that evaluated screening strategies using some combination of the FRAX risk calculation and BMD; no published studies have been designed to evaluate a treatment strategy based on fracture risk (ie, FRAX) alone. Centrally measured DXA was the test used to determine eligibility for participants enrolled in nearly all trials of bone-conserving pharmacotherapies.<sup>1</sup> Thus, screening can entail DXA with or without fracture risk assessment.

Similarly, approaches to determining whom to screen among postmenopausal women younger than 65 years who have 1 or more risk factors (ie, determining who is at increased risk) could reasonably focus on assessment of fracture risk or risk of osteoporosis, using 1 of several risk assessment tools. Table 2 includes examples of risk assessment tools that have been reported to have reasonable accuracy for identifying osteoporosis (OST or ORAI) or predicting hip fracture (FRAX) in women younger than 65 years.<sup>1</sup> The risk assessment tools for identifying osteoporosis (OST or ORAI)<sup>34,35</sup> have commonly used thresholds for defining increased risk at which further screening with DXA is suggested (Table 2). For FRAX, there is no such threshold defined with respect to its use in screening. However, to provide context, a 65-year-old White female with a body mass index (BMI) of 25 (calculated as weight in kilograms divided by square of height in meters) and no risk factors has a 10-year risk of hip fracture of 1.3% and a 10-year risk of MOF of 9.3% based on FRAX without BMD input. The USPSTF does not intend that these 10-year risk levels (in the example given) be used as mechanistic thresholds for determining who should receive further screening with DXA. Rather, it is suggested that the results of risk assessment be used to help inform decisions about further screening with DXA.

### Screening Intervals

Cohort studies evaluating screening intervals suggest that repeating BMD testing at an interval of 4 to 8 years does not result in additional accuracy in predicting fractures.<sup>1</sup> Other studies attempted to identify appropriate screening intervals based on the time in which it takes individuals to transition to osteoporosis or a certain fracture risk threshold. The screening intervals varied across studies, but generally, transition to osteoporosis occurred over shorter intervals for individuals with lower baseline T scores and older age (eg, almost 17 years for 10% of women with normal BMD at baseline to develop osteoporosis vs about 5 years for women with a baseline T score in the -1.50 to -1.99 range).<sup>36</sup>

### Treatment

The US Food and Drug Administration has approved several drug therapies for the treatment or prevention of osteoporosis, including bisphosphonates, denosumab, romosozumab, parathyroid hormone, raloxifene, calcitonin, and estrogen (with or without progesterone).

Clinicians should be aware that treatment recommendations that are based on risk assessment tools with race-specific calcula-

**Table 2. Characteristics of Selected Risk Assessment Tools for Osteoporosis or Fracture Risk<sup>a</sup>**

Risk factors	Scoring
<b>OST (&lt;2 frequently used as threshold to define increased osteoporosis risk)</b>	
Weight, kg	(kg - y) × 0.2
Age, y	
<b>ORAI (≥9 frequently used as threshold to define increased osteoporosis risk)</b>	
Age, y	
≥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
<b>FRAX (no specific threshold to define increased osteoporosis risk)<sup>b</sup></b>	
Age, y	Refer to website <sup>c</sup>
Sex	
Weight, kg	
Height, cm	
Previous fracture	
Parental hip fracture	
Current smoking	
Glucocorticoid use	
Rheumatoid arthritis	
Secondary osteoporosis	
Alcohol consumption ≥3 U/d	

Abbreviations: BMI, body mass index; FRAX, Fracture Risk Assessment Tool; MOF, major osteoporotic fracture; OST, Osteoporosis Self-Assessment Tool; ORAI, Osteoporosis Risk Assessment Instrument.

<sup>a</sup> Table adapted from FRAX Fracture Risk Assessment Tool<sup>24</sup> and Chen et al.<sup>33</sup>

<sup>b</sup> FRAX was designed to predict fracture risk. For context only: A 65-year-old White female with a BMI of 25 and no risk factors has a 10-year risk of hip fracture of 1.3% and 10-year risk of MOF of 9.3%.

<sup>c</sup> Refer to website (<https://frax.shef.ac.uk/FRAX/index.aspx>).

tors (eg, FRAX) but that use fixed fracture risk treatment thresholds not specific to race and ethnicity may be less likely to identify Asian, Black, and Hispanic persons as high risk and, subsequently, may be less likely to offer treatment compared with White persons of the same age, BMD, and clinical risk profile. Similarly, prediction models that do not include conditions that are associated with increased fracture risk and that disproportionately affect certain racial and ethnic groups (eg, diabetes) may result in biased underestimates of risk. For these reasons, it may be reasonable to avoid strict application of risk assessment tool treatment thresholds at the individual level to account for additional risks (eg, fall risk) not considered in risk assessment tools like FRAX.<sup>37,38</sup>

### 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

Based on National Health and Nutrition Examination Survey data from 2017 to 2018, age-adjusted prevalence of osteoporosis is 12.6% among US residents 50 years or older. Prevalence is higher in women (19.6%) compared with men (4.4%) and among persons 65 years or older (27.1% in women and 5.7% in men) compared with persons aged 50 to 64 years (13.1% in women and 3.3% in men).<sup>3</sup>

Morbidity and mortality resulting from a fragility fracture are the primary concerns from having osteoporosis. Based on Medicare data, approximately 1.8 million beneficiaries experienced a new osteoporotic fracture in 2016.<sup>39</sup> Although osteoporosis and fragility fractures are more common in women than men, excess mortality related to osteoporosis and fragility fractures is greater in men.<sup>40,41</sup>

Men have similar risk factors associated with fragility fractures as women, including increasing age, low BMI, excessive alcohol intake, current smoking, chronic corticosteroid use, history of prior fractures, history of falls within the past year, hypogonadism, history of cerebrovascular accident, and history of diabetes.<sup>42</sup>

### Potential Harms

Potential harms of screening in men may be similar to those in women. Evidence on harms of drug therapies in men is limited.<sup>1</sup>

### Current Practice

Data on how frequently men are screened for osteoporosis are limited. Guidelines developed by various organizations and specialty societies vary. Some organizations recommend screening for osteoporosis in men older than 70 years. Other organizations do not specify for or against screening in men or recommend against it.<sup>1</sup>

### Additional Tools and Resources

The National Institutes of Health has information on osteoporosis (<https://www.niams.nih.gov/health-topics/osteoporosis>, <https://www.niams.nih.gov/health-topics/osteoporosis/diagnosis-treatment-and-steps-to-take>, and <https://www.nia.nih.gov/health/osteoporosis/osteoporosis>).

### Other Related USPSTF Recommendations

The USPSTF recommends exercise interventions to prevent falls in community-dwelling adults 65 years or 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.<sup>43</sup> In its 2018 recommendation statement, the USPSTF recommended against supplementation with 400 IU or less of vitamin D and 1000 mg or less of calcium in postmenopausal women to prevent fractures. 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.<sup>44</sup> This recommendation is in the process of being updated; in the current draft recommendation, the USPSTF recommends against supplementation with vitamin D with or without calcium for the primary prevention of fractures in community-dwelling postmenopausal women and men 60 years or older, and against supplementation with vitamin D for the prevention of falls in community-dwelling postmenopausal women and men 60 years or older.

## Update of Previous USPSTF Recommendation

This recommendation updates the 2018 USPSTF recommendation on screening for osteoporosis. In 2018, the USPSTF recommended screening for osteoporosis with bone measurement testing to prevent osteoporotic fractures in women 65 years or older and in postmenopausal women younger than 65 years who are at increased risk of osteoporosis, as determined by a formal clinical risk assessment tool.<sup>45</sup> For the current recommendation, the USPSTF has noted that screening can include DXA BMD, with or without fracture risk assessment. The current recommendation is otherwise generally consistent with the 2018 recommendation.

## Supporting Evidence

### Scope of Review

The USPSTF commissioned a systematic review to evaluate the benefits and harms of screening for osteoporosis to prevent fractures in adults 40 years or older with no known diagnosis of osteoporosis or history of fragility fracture.<sup>1,46</sup> This review presents data to update the USPSTF's 2018 recommendation. The previous recommendation evaluated multiple imaging modalities (eg, peripheral DXA and quantitative ultrasound); however, this review only reports evidence for central DXA—the bone measurement test most commonly used to screen for osteoporosis.

### Accuracy of Screening Tests and Risk Assessment

#### BMD

Central DXA measures BMD at central bone sites (hip and lumbar spine) and is the established standard for the diagnosis of osteoporosis. Additionally, centrally measured DXA was the test used for determining T scores and determining eligibility among participants enrolled in nearly all trials of bone-conserving pharmacotherapies. Still, given that screening trials enrolled participants based on fracture risk, and that the goal of treating osteoporosis is to prevent fracture, the USPSTF reviewed studies that reported on the accuracy of centrally measured BMD for predicting fracture. The USPSTF found 13 unique cohorts that reported on the discrimination of BMD alone (as a continuous variable) for predicting MOF. These studies reported areas under the receiver operating characteristic curve (AUCs) ranging from 0.60 to 0.80. Twelve cohorts reported AUCs for predicting hip fracture; they were somewhat more accurate than MOF outcomes, with AUCs ranging from 0.64 to 0.86.<sup>1,46</sup>

Fewer studies reported on the predictive accuracy of BMD in women younger than 65 years. One study of women aged 45 to 54 years in the United Kingdom reported an AUC for predictive accuracy of BMD at the femoral neck of 0.64 (95% CI, 0.63-0.66) over a follow-up of 3 to 12 years.<sup>47</sup> One retrospective study exclusively in men 65 years or older reported an AUC for BMD over a follow-up of 15.8 years of 0.76 (95% CI, 0.71-0.80) for the prediction of MOF and 0.76 (95% CI, 0.72-0.81) for the prediction of hip fracture.<sup>48</sup>

#### Accuracy of Risk Assessment Instruments to Identify Osteoporosis

Forty-three unique cohorts reported on diagnostic accuracy of 15 risk assessment instruments for identifying osteoporosis. More than one-half of the cohorts included populations with a mean age between



### Harms of Screening and Treatment

Evidence on the harms of screening for osteoporosis is limited.<sup>1,46</sup> The SCOOP trial reported no difference in anxiety between participants in the screening and control groups.<sup>55</sup>

Several trials reported on the harms of treatment of bisphosphonates. A pooled analysis of 21 RCTs found no significant difference in serious adverse events. One trial reported a statistically significant increase in gastrointestinal adverse events in the treatment group compared with placebo<sup>61</sup>; however, a pooled analysis of 26 RCTs (representing 27 comparisons) found no significantly increased risk of gastrointestinal adverse events in participants taking bisphosphonates compared with those taking placebo. Six RCTs that reported on the incidence of atrial fibrillation found no statistically significant increased risk. Three RCTs reporting on incidence of myocardial infarction had very imprecise RR estimates with wide CIs because of small sample sizes and rare events.<sup>1,46</sup>

Although 1 study of zoledronic acid in men reported a statistically significant increase in incident myocardial infarction (RR, 4.68 [95% CI, 1.02-21.5]), this outcome was not statistically significant in 2 other RCTs. Relative risk estimates were imprecise and CIs were wide in all these studies.<sup>1,46</sup> One cohort study of zoledronic acid users found no statistically significant differences in atrial fibrillation (adjusted hazard ratio [aHR], 1.18 [95% CI, 0.99-1.40]), myocardial infarction (aHR, 0.92 [95% CI, 0.64-1.31]), or cardiovascular mortality (aHR, 0.97 [95% CI, 0.81-1.15]) but did find a statistically significant increased risk for heart failure (aHR, 1.32 [95% CI, 1.08-1.61]), although it did not control for known confounders of heart failure such as BMI, smoking and alcohol exposure, or hypertension.<sup>62</sup>

Osteonecrosis of the jaw and atypical fractures of the femur are potential rare harms of bisphosphonates. Five trials of bisphosphonates reported no cases of osteonecrosis of the jaw, and no trials reported on atypical femur fractures.<sup>1,46</sup> A cohort study of new users of zoledronic acid reported an increased risk of atypical femur fractures (aHR, 2.46 [95% CI, 1.17-5.15]),<sup>62</sup> and a cohort study of new bisphosphonate users reported an increased risk of atypical femur fractures with bisphosphonate use (aHR, 1.53 [95% CI, 1.36-1.73]) over a mean follow-up of 1 year,<sup>63</sup> although both studies may have been subject to residual confounding. One systematic review that did not meet inclusion criteria for the current review because no comparator group of nonusers was included reported incidence estimates for osteonecrosis of the jaw in individuals using bisphosphonates ranging from 0.01% to 0.06%.<sup>64</sup>

For denosumab, pooled analyses found no significant increase in serious adverse events (5 RCTs) or upper gastrointestinal tract adverse events (4 trials), although the CIs were wide for that outcome. Two trials reported no significant increase in cardiovascular events, although the estimate was imprecise in 1 of these trials. Three trials reported no cases of osteonecrosis of the jaw, and 2 trials reported no cases of atypical femur fracture.<sup>1,46</sup>

### Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from June 11 to July 8, 2024. Some comments requested that the USPSTF recommend screening for osteoporosis in men. The USPSTF agrees that osteoporosis can be a significant source of morbidity and mortality in men. However, there are no studies on the benefits and harms of screening for osteoporosis or fracture risk in men, and evidence on the ben-

efits and harms of treatment is very limited. The USPSTF wants to clarify that the I statement is not a recommendation against screening; it indicates that the evidence is insufficient to assess the balance of benefits and harms and is a call for more research. In the absence of evidence, clinicians and their patients should decide together whether to be screened. The USPSTF also wants to reiterate that this recommendation does not apply to individuals, including men, who have medical conditions or are taking medications associated with bone loss.

Some comments requested that this recommendation statement include other modalities in addition to DXA BMD. This recommendation statement focuses on DXA for several reasons, including that DXA is the most commonly used bone density measurement test to screen for osteoporosis, it correlates with bone strength and clinical fracture outcomes, it uses a low dose of radiation, and it was the test used for determining T scores and eligibility among participants in nearly all trials of bone-conserving pharmacotherapies. Some comments requested that the USPSTF specify a screening interval. In response, the USPSTF notes that the evidence related to screening intervals for osteoporosis is limited; what is known that could be helpful is discussed in the Practice Considerations section, and the USPSTF calls for more research to help inform appropriate screening intervals.

In response to public comment, the USPSTF clarified that screening can include DXA with or without fracture risk assessment, that it suggests using a 2-step approach for postmenopausal women younger than 65 years, and that Table 2 is intended to provide examples of tools that can be used to predict fracture risk or identify osteoporosis but is not intended to be a comprehensive list. Last, the USPSTF agrees with comments that more research is needed on bone density in transgender persons and has specified this as a research need (see the online version of Table 3 [[https://www.uspreventiveservicestaskforce.org/home/getfilebytoken/kHT3WGUaG2wTz2pF\\_ke7bn](https://www.uspreventiveservicestaskforce.org/home/getfilebytoken/kHT3WGUaG2wTz2pF_ke7bn)]).

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### Research Needs and Gaps

See Table 3 for research needs and gaps related to screening for osteoporosis to prevent fractures.

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### Recommendations of Others

Several organizations have put forth osteoporosis and fracture risk screening guidelines that vary based on age, sex, menopausal status, and other characteristics. Some organizations recommend a combination of fracture risk assessment and DXA screening. In 2023, the Canadian Task Force on Preventive Health Care recommended screening women 65 years or older for fracture risk with the Canadian FRAX tool to facilitate shared decision-making about pharmacotherapy. If pharmacotherapy is considered, it then recommends ordering DXA testing to reestimate fracture risk with BMD input to the FRAX. It recommended against screening men 40 years or older and women younger than 65 years.<sup>65</sup> The 2020 American Association of Clinical Endocrinologists guideline recommends evaluating all women 50 years or older for fracture risk and considering BMD measurement based on clinical fracture risk profile.<sup>66</sup>



**Table 3. Research Needs and Gaps in Screening for Osteoporosis to Prevent Fractures**

To fulfill its mission to improve health by making evidence-based recommendations for preventive services, the USPSTF routinely highlights the most critical evidence gaps for creating actionable preventive services recommendations. The USPSTF often needs additional evidence to create the strongest recommendations for everyone, especially those with the greatest burden of disease. In some cases, clinical preventive services have been well studied, but there are important evidence gaps that prevent the USPSTF from making recommendations for specific populations. In this table, the USPSTF summarizes the gaps in the evidence for screening for osteoporosis to prevent fractures that need to be addressed to advance the health of the nation. For additional information and detail on research needed to address these evidence gaps, see the Research Gaps Taxonomy table on the USPSTF website ([https://www.uspreventiveservicestaskforce.org/home/getfilebytoken/kHT3WGUaG2wTz2pF\\_ke7bn](https://www.uspreventiveservicestaskforce.org/home/getfilebytoken/kHT3WGUaG2wTz2pF_ke7bn)).

**Screening for osteoporosis to prevent fractures**

More research is needed on the benefits and harms of screening, and of different screening strategies.

- Studies are needed on the benefits and harms of screening for osteoporosis or fracture risk to prevent osteoporotic fractures and related morbidity and mortality in men.
- Research is needed on the benefits and harms of screening using BMD alone vs fracture risk assessment tools alone vs the combination of BMD and fracture risk assessment in postmenopausal women.

Research is needed to develop and validate new primary care-feasible risk assessment tools that accurately predict risk of hip and nonhip major osteoporotic fractures in women and men. This research should include populations broadly representative of the US population and sufficient numbers of postmenopausal women younger than 65 years and men to be able to report on accuracy in these groups.

Research is needed to develop and validate new primary care-feasible risk assessment tools that accurately identify osteoporosis in women and men. This research should include populations broadly representative of the US population and sufficient numbers of postmenopausal women younger than 65 years and men to be able to report on accuracy in these groups.

Decision analysis studies are needed to help inform the optimal start and stop ages and screening interval in women. (KQ2d, CQ1)

Research is needed on the benefits and harms of pharmacotherapy to prevent fractures in men with primary osteoporosis and without a history of fragility fractures. (KQ4)

Abbreviations: BMD, bone mineral density; CQ, contextual question; KQ, key question; USPSTF, US Preventive Services Task Force.

Other guidelines focus on osteoporosis screening via DXA measurement of BMD in older adults. The 2021 American College of Obstetricians and Gynecologists guidelines recommend BMD screening with DXA beginning at age 65 years in all women and selective screening with BMD in women younger than 65 years who have an

elevated risk of osteoporosis based on a formal clinical risk assessment tool.<sup>67</sup> The American Academy of Family Physicians follows the USPSTF's 2018 recommendation; however, it specifically recommends against DXA screening in women younger than 65 years and in men younger than 70 years with no risk factors.<sup>68,69</sup>

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