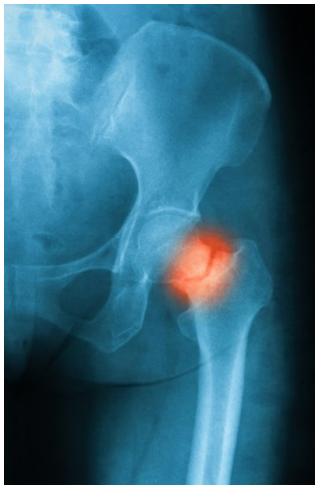
10 novembre 2017

Screening Osteoporosi:

l'Us Preventive Services Task Force

aggiorna le linee guida



articoli correlati

04-07-2018 | Screening osteoporosi, aggiornate le raccomandazioni Usa. Il quadro della situazione

28-06-2018 | Screening dell'osteoporosi, aggiornate indicazioni Usa per prevenire fratture

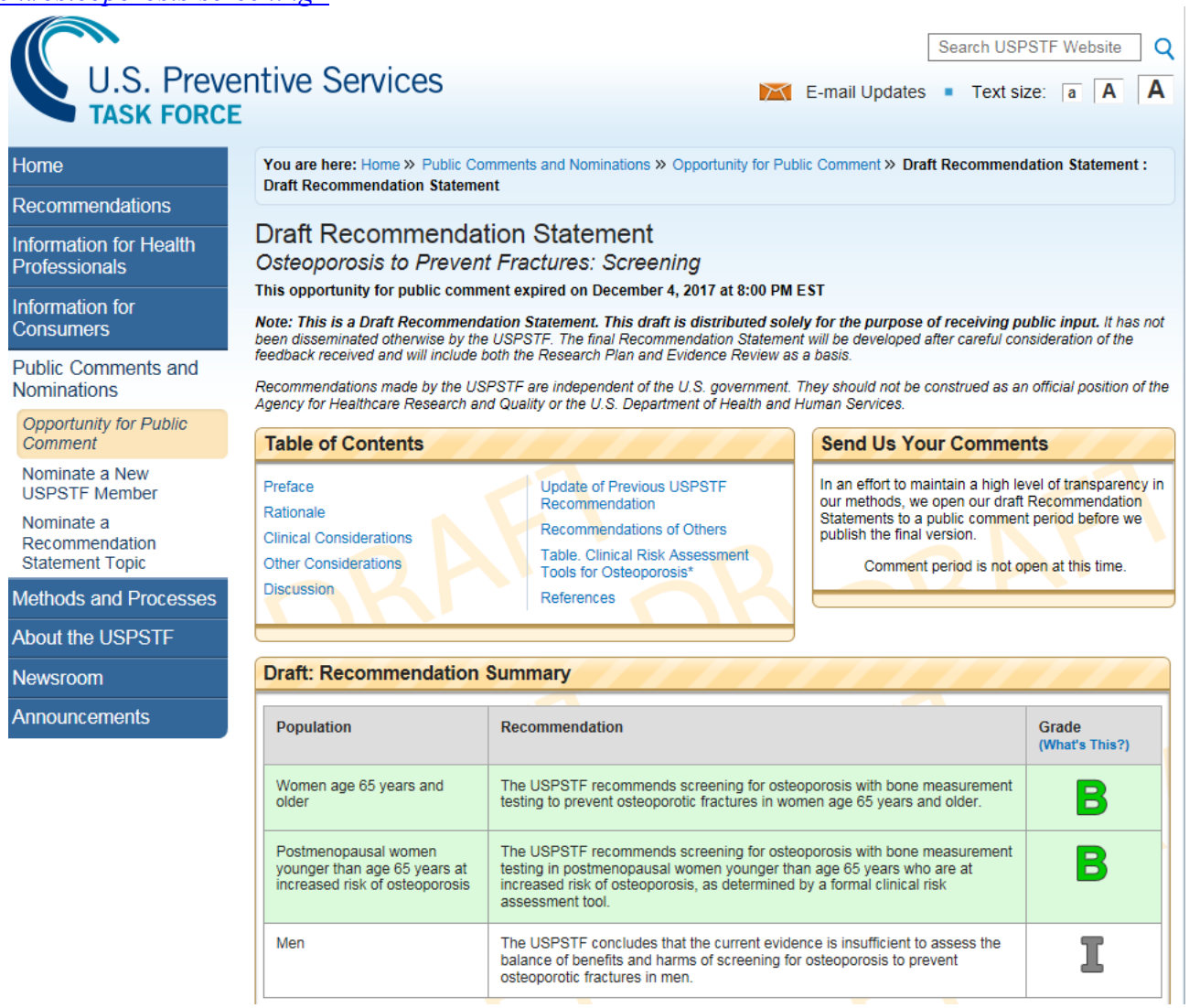
27-06-2017 | Osteoporosi e fratture da fragilità, nuove linee guida condivise da otto società scientifiche

La Us Preventive Services Task Force (Uspstf) ha pubblicato in bozza l'aggiornamento delle linee guida 2011 sullo screening dell'osteoporosi per prevenire le fratture. Il documento è simile al precedente, a eccezione di una leggera modifica del valore di cut-off del Fracture Risk Assessment Tool (Frax), un algoritmo approvato dall'Organizzazione mondiale della sanità che stima le probabilità di incorrere in una frattura osteoporotica nell'arco dei 10 anni successivi basandosi sulla presenza o meno dei principali fattori di rischio. «Questa modifica permette di identificare le donne fra 50 e 65 anni da sottoporre a screening» spiega **Alex Krist**, coautore del documento nonché professore di medicina di famiglia alla Virginia Commonwealth University di Richmond e co direttore della Virginia Ambulatory Care Outcomes Research Network. In sintesi, le nuove linee guida propongono lo screening di routine per le donne di 65 anni e oltre, mentre per quelle in post-menopausa di età compresa fra 50 e 65 anni consiglia di ricorrere allo screening solo in presenza di un rischio fratturativo nei 10 anni successivi almeno dell'8,4%.

«Questa percentuale è considerata equivalente al livello di rischio di una donna caucasica di 65 anni senza i principali fattori di rischio» puntualizza l'autore, aggiungendo che, come già specificato nel documento del 2011, il vantaggio dello screening per l'osteoporosi nel genere maschile

non è ancora chiaramente dimostrato, data anche la prevalenza significativamente più bassa (4,3%) rispetto alle donne (15,4%). Più evidente, invece, il vantaggio della diagnosi precoce nel genere femminile. «Senza di essa la maggior parte delle donne non saprà di avere l'osteoporosi fino a quando non si fratturerà» afferma Krist. E conclude: «Da questo documento emerge con chiarezza che nelle donne in post-menopausa lo screening per l'osteoporosi consente di scoprire e curare in anticipo la malattia, migliorando la prevenzione delle fratture».

Uspstf - Draft Recommendation Statement
https://www.uspreventiveservicestaskforce.org/Page/Document/draft-recommendation-statement/osteoporosis-screening1



Draft: Preface

The U.S. 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.

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Draft: Rationale

Importance

By 2020, approximately 12.3 million Americans older than age 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 die within 1 year of a hip fracture.[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 (i.e., osteoporosis without underlying disease) increases with age and differs by race/ethnicity. With the aging of the U.S. population, the potential preventable burden is likely to increase in future years.

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. While several bone measurement tests similarly predict risk of fracture, DXA directly measures bone mineral density (BMD), and most treatment guidelines use central DXA to define osteoporosis and the treatment threshold 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 no studies that evaluated the effect of screening for osteoporosis on fracture rates or fracture-related morbidity or mortality.

Studies show that drug therapies reduce fractures in postmenopausal women with osteoporosis. 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 in women age 65 years and older. The USPSTF found adequate evidence that screening can detect osteoporosis and that treatment provides a moderate benefit in preventing fractures in postmenopausal women younger than age 65 years who are at increased risk of osteoporosis.

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

Harms of Early Detection and Treatment

The USPSTF found no studies that described harms of screening for osteoporosis in men or women. 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 medications are small.

USPSTF Assessment

The USPSTF concludes with moderate certainty that the net benefit of screening for osteoporosis in women age 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 age 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.

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Draft: Clinical Considerations

Patient Population Under Consideration

This recommendation applies to older adults without a history of low-trauma fracture and without conditions that may cause secondary osteoporosis, such as metabolic bone disease or untreated hyperthyroidism. This recommendation does not apply to persons who take long-term medications that may cause secondary osteoporosis (e.g., glucocorticoids).

Assessment of Risk

In deciding which postmenopausal women younger than age 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, excess alcohol consumption, and low body weight. In addition, menopausal status in women may also be an important consideration, because studies demonstrating treatment benefit mainly enrolled postmenopausal women. For postmenopausal women younger than age 65 years who have at least one risk factor, a reasonable approach to determine who should undergo screening with bone measurement testing is to use a clinical risk assessment tool.

One commonly used tool is the FRAX® tool (University of Sheffield, UK), which assesses a person's 10-year risk of fracture. 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, it is reasonable to perform bone measurement testing in postmenopausal women younger than age 65 years who have a FRAX risk of major osteoporotic fracture (MOF) (without DXA) greater than 8.4% (i.e., the risk level of a 65-year-old white woman with no major risk factors). For example, a 60-year-old white woman with a parental history of hip fracture has a 10-year FRAX risk of MOF of 13%. Other tools that have similar accuracy to assess osteoporosis risk as FRAX include the Simple Calculated Osteoporosis Risk Estimation (SCORE™) (Merck, Inc.), Osteoporosis Risk Assessment Instrument (ORAI), Osteoporosis Index of Risk (OSIRIS), and the Osteoporosis Self-Assessment Tool (OST). Pooled results for the area under the curve (AUC) of the accuracy of FRAX, SCORE, ORAI, OSIRIS, and OST to identify osteoporosis risk are similar and range from 0.60 to 0.70.

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

Common bone measurement tests used to screen for osteoporosis include DXA and quantitative ultrasound (QUS). DXA measures BMD at central sites (hip and lumbar spine) or peripheral sites (such as wrist, forearm, and calcaneus). QUS evaluates peripheral sites and has similar accuracy in predicting fracture risk as DXA, while avoiding the risk of radiation exposure, but does not measure BMD. Most treatment guidelines recommend using BMD, as measured by central DXA, to define osteoporosis and the treatment threshold to prevent osteoporotic fractures; all the osteoporosis drug therapy studies reviewed by the USPSTF used central DXA to determine study enrollment. Peripheral DXA and QUS are measured with portable devices and may be less costly and more accessible than central DXA measurement.

Screening Intervals

Limited evidence suggests no benefit from repeating bone measurement testing between 4 and 8 years after initial screening.[4]

Treatment

Multiple drug therapies are approved by the U.S. Food and Drug Administration (FDA) to reduce 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 tradeoff between benefits and harms. Clinicians should provide patient education on how to use drug therapies to minimize adverse effects, 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; of these, 1 in 3 men will die within a year.[5]

Advancing age in men is an important risk factor. The 10-year risk of MOF in a 65-year-old white man without any risk factors is 4.9% (vs. 8.4% in a 65-year-old white woman without any risk factors).[4] 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.[4] Based on the FRAX tool, if multiple risk factors are present (parental history of hip fracture, current smoking, and drinking 3 or more units of alcohol per day), the 10-year 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.

Similar to women, risk factors for fracture in men include low body mass index, excess 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 utility in identifying men who need further bone measurement testing is unclear.[4, 6]

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. While some treatments have been found to be effective in preventing fractures in postmenopausal women with osteoporosis, it cannot be assumed that they will be as equally effective in men, because the underlying biology of bones may be different 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. One good-quality study found a reduction in vertebral and nonvertebral fractures in men with osteoporosis who received zoledronic acid.[7] A small study examining parathyroid hormone in men was consistent in the direction of benefit but was not statistically significant.[8]

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 treatment harms in men is very limited.[4]

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).[9]

Additional Approaches to Prevention

According to the Centers for Disease Control and Prevention, engaging in 150 minutes of moderate-intensity aerobic activity each week and performing muscle-strengthening activities at least 2 days per week can help strengthen bones and muscles and prevent falls in older adults.[10] 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.[11]

Useful Resources for Primary Care

The USPSTF is in the process of updating its 2012 recommendation statement on interventions to prevent falls in community-dwelling older adults and its 2013 recommendation statement on vitamin D, calcium, or combined supplementation to prevent fractures. In its draft recommendation, the USPSTF recommends exercise to prevent falls in community-dwelling adults age 65 years and older at increased risk of falls and recommends against the use of vitamin D supplementation to prevent falls. For the same population, the USPSTF also recommends selectively offering multifactorial interventions based on circumstances of prior falls, presence of comorbid medical conditions, and the patient's values and preferences. In a separate recommendation, the USPSTF recommends against supplementation with 400 IU or less of vitamin D and 1,000 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.

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Draft: Other Considerations

Implementation

The FRAX tool[12] is a computerized algorithm that calculates the 10-year probability of hip fracture and MOF using clinical risk factors. FRAX models are country specific to include country epidemiology. In the United States, the risk of MOF in a 65-year-old white woman without any other risk factors is 8.4%.[4] Other tools that could be used to help identify women younger than age 65 years who are at increased risk of osteoporosis include SCORE, ORAI, OSIRIS, and OST.[13-17] The most commonly used thresholds to identify persons at 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).

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. 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[18, 19] may also help identify optimal screening intervals.

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Draft: 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.[20, 21] The World Health Organization defines osteoporosis as bone density at the hip or spine that is 2.5 standard deviations or lower (i.e., T-score ≤ -2.5) than the mean bone density of a reference population of young, healthy women, presumably at peak bone mass.[22]

In the United States, the estimated prevalence of osteoporosis among the community-dwelling population age 50 years and older in 2010 was 10.3% (10.2 million persons), 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 Americans (13.4%) and non-Hispanic whites (10.2%) and lowest in non-Hispanic blacks (4.9%).[1] The prevalence of osteoporosis increases dramatically with age from 5.1% in adults ages 50 to 59 years to 26.2% in those age 80 years and older.[1] As the U.S. population ages, it is projected that the number of persons living with osteoporosis will also increase. The number of persons age 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 the Healthcare Effectiveness Data and Information Set, the rate of women ages 65 to 85 years enrolled in Medicare who reported ever having a bone density test increased from 64.4%–71.3% in 2006 to 73.8%–79.3% in 2015.[23]

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 one essential activity of daily living.[24] 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 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 age 40 years.

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 wrist, forearm, and calcaneus) to identify persons with low bone mass; however, most treatment guidelines recommend followup 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 (e.g., rural areas) where machines that perform central DXA may not be available. The USPSTF identified two studies (n=1,212) that reported on the accuracy of peripheral DXA at the calcaneus to identify osteoporosis; compared with central DXA, the AUC ranged from 0.67 to 0.803 in women with a mean age of 61 years.[25, 26]

QUS

QUS 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% confidence interval [CI], 0.72 to 0.81; k=7; n=1,969).[4] In men, the AUC ranged from 0.70 to 0.93, with a pooled estimate of 0.80 (95% CI, 0.67 to 0.94; k=3; n=5,142).[4] However, QUS does not measure BMD, which is the current diagnostic criteria for osteoporosis. In addition, all drug therapy trials for osteoporosis use central DXA measurement of BMD as inclusion criteria. 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 (k=10; n=16,680), OSIRIS (k=5; n=5,649), OST (k=10; n=24,739), and SCORE (k=8; n=15,262). The pooled AUC 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, 0.60 [95% CI, 0.56 to 0.63]; k=1; n=2,857). These clinical risk assessment tools could be applied to postmenopausal women younger than age 65 years who are at increased risk of osteoporosis to help clinicians determine who should be screened with bone measurement testing. The Table provides more information on these clinical risk assessment tools and commonly used thresholds to determine risk of osteoporosis.

Effectiveness of Early Detection and Treatment

No controlled studies have evaluated the effect of screening for osteoporosis on fracture rates or fracture-related morbidity or mortality in either women or men. The USPSTF reviewed the evidence on drug therapies for the primary prevention of osteoporotic fractures. The vast majority of studies were conducted in women exclusively; only two studies were conducted in men.[4] Overall, the USPSTF found that pharmacotherapy is effective in treating osteoporosis and reducing fractures in postmenopausal women.

Bisphosphonates

Bisphosphonates were studied most frequently; the USPSTF identified seven studies on alendronate, two trials on zoledronic acid, four trials on risedronate, and two trials on etidronate. All but one 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 to 0.78]; k=5; n=5,433) and nonvertebral fractures (RR, 0.84 [95% CI, 0.76 to 0.92]; k=8; n=16,438) but not hip fractures (RR, 0.70 [95% CI, 0.44 to 1.11]; k=3; n=8,988).[4] In the single study of men (n=1,199), zoledronic acid was found to reduce morphometric vertebral fractures (RR, 0.33 [95% CI, 0.16 to 0.70]) but not nonvertebral fractures (RR, 0.65 [95% CI, 0.21 to 1.97]).[4, 7]

Raloxifene

Only one study (n=7,705) on raloxifene met inclusion criteria for the review. It evaluated raloxifene in postmenopausal women and reported a reduction in vertebral fractures (RR, 0.64 [95% CI, 0.53 to 0.76]) but not nonvertebral fractures (RR, 0.93 [95% CI, 0.81 to 1.06]).[4]

Denosumab

The USPSTF identified three studies that evaluated denosumab; however, only one study was adequately powered to assess fractures. This study (n=7,868) evaluated denosumab in women and found a significant reduction in vertebral fractures (RR, 0.32 [95% CI, 0.26 to 0.41]), nonvertebral fractures (RR, 0.80 [95% CI, 0.67 to 0.95]), and hip fractures (RR, 0.60 [95% CI, 0.37 to 0.97]).[4, 27]

Parathyroid Hormone

The USPSTF reviewed evidence from two trials on parathyroid hormone. One trial (n=2,532) was conducted in women and reported a significant reduction in vertebral fractures (RR, 0.32 [95% CI, 0.14 to 0.75]) but not nonvertebral fractures (RR, 0.97 [95% CI, 0.71 to 1.33]).[4, 28] The other trial was conducted in men and reported a nonsignificant reduction in nonvertebral fractures (RR, 0.65 [95% CI, 0.11 to 3.83]) when comparing the FDA-approved dose of 20 µg per day vs. placebo (n=298).[8] 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.

Potential Harms of Screening and Treatment

Potential harms of screening for osteoporosis include false-positive test results, which can lead to unnecessary treatment; false-negative test results; and patient anxiety about positive test results. The USPSTF found no studies that addressed the potential harms of screening. The USPSTF did review several studies that reported on harms of various medications. Overall, the USPSTF determined the potential harms of pharmacotherapy to be small.

Bisphosphonates

Similar to the evidence on the benefits of pharmacotherapy for the primary prevention of fractures, the most available evidence on the harms of pharmacotherapy is for bisphosphonates. The USPSTF identified 16 studies on alendronate, five studies on zoledronic acid, six studies on risedronate, two studies on etidronate, and seven 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 to 1.07]; k=20; n=17,369), serious adverse events (RR, 0.98 [95% CI, 0.92 to 1.04]; k=17; n=11,745), or upper gastrointestinal events (RR, 1.01 [95% CI, 0.98 to 1.05]; k=13; 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 bisphosphonate therapy. Concerns have been raised about osteonecrosis of the jaw and atypical fractures of the femur with bisphosphonate therapy. The USPSTF found only three studies that reported on osteonecrosis of the jaw, and none of these studies found any cases.[4] The previous review noted a case series published by the FDA that reported on osteonecrosis of the jaw with bisphosphonate use in cancer patients. 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 greater duration of 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. 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 to 1.28]; k=6; n=6,438) or increased risk of leg cramping (RR, 1.41 [95% CI, 0.92 to 2.14]; k=3; n=6,000).[4] However, analyses found a nonsignificant trend for increased risk of deep vein thrombosis (RR, 2.14 [95% CI, 0.99 to 4.66]; k=3; n=5,839), as well as an increased risk of hot flashes (RR, 1.42 [95% CI, 1.22 to 1.66]; k=5; n=6,249).[4] The previous review found an increased risk of thromboembolic events with raloxifene (RR, 1.60 [95% CI, 1.15 to 2.23]).[4]

Denosumab

Three studies (n=8,451) reported on harms of denosumab therapy in postmenopausal women. Pooled analyses showed no significant increase in discontinuation (RR, 1.16 [95% CI, 0.88 to 1.54]) or serious adverse events (RR, 1.23 [95% CI, 0.78 to 1.93]) but found a nonsignificant increase in serious infections (RR, 1.89 [95% CI, 0.61 to 5.91]).[4] All three studies reported higher infection rates in women taking denosumab, and further analysis found a higher rate of cellulitis and erysipelas.[4]

Parathyroid Hormone

A single study of parathyroid hormone therapy in women (n=2,532) reported a higher risk of discontinuation (RR, 1.22 [95% CI, 1.08 to 1.40]) and other adverse events, such as nausea and headache (RR, 2.47 [95% CI, 2.02 to 3.03]),[4, 28] while a single, smaller study in men found no increased risk of discontinuation (RR, 1.94 [95% CI, 0.81 to 4.69]) or cancer (RR, 0.97 [95% CI, 0.2 to 4.74])[4] using the FDA-approved dose of 20 µg per day (n=298).[8]

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 a higher rate of gallbladder events, stroke, and venous thromboembolism with estrogen therapy, and an increased risk of urinary incontinence during 1 year of followup.[4] Women taking combined estrogen and progestin had a higher 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 followup.[4]

Estimate of Magnitude of Net Benefit

The USPSTF found no studies that evaluated the effect of screening for osteoporosis on fracture rates or fracture-related morbidity or mortality.

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 screening-detected osteoporosis is at least moderate in women age 65 years and older and 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 USPSTF concludes 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 could not 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 elderly persons. Screening and treating low BMD detected through screening can result in increased BMD and decrease the risk of subsequent fractures and fracture-related morbidity and mortality. Most evidence supports screening and treatment of osteoporosis in postmenopausal women; the evidence for primary prevention in men is lacking, and future research is needed. One cannot assume 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. Although women have a higher risk of osteoporosis at an earlier age than men, likely due to loss of estrogen during menopause, it raises the question of whether the benefits of treatment observed in trials in women can be directly extrapolated to men.

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Draft: Update of Previous USPSTF Recommendation

This recommendation is consistent with the 2011 USPSTF recommendation on screening for osteoporosis.[29] 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.

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Draft: Recommendations of Others

In 2014, the National Osteoporosis Foundation recommended BMD testing in all women age 65 years and older and all men age 70 years and older.[30] It also recommended BMD testing in postmenopausal women younger than age 65 years and men ages 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 age 65 years and older and all men age 70 years and older. It also recommends BMD testing in postmenopausal women younger than age 65 years and men younger than age 70 years who have risk factors for low bone mass.[31] The American Academy of Family Physicians recommends screening in women age 65 years and older and younger women whose fracture risk is equal to or greater than that of a 65-year-old white woman.[32] In 2012 (and reaffirmed in 2014) the American College of Obstetricians and Gynecologists recommended BMD screening with DXA beginning at age 65 years in all women and selective screening in postmenopausal women younger than age 65 years who have osteoporosis risk factors or an adult fracture.[21] The American Association of Clinical Endocrinologists also recommends evaluating all women age 50 years and older for osteoporosis risk and consider BMD testing based on clinical fracture risk profile.[33] The Endocrine Society recommends screening in men older than age 70 years and adults ages 50 to 69 years with significant risk factors or fracture after age 50 years.[34]

Draft: Table. Clinical Risk Assessment Tools for Osteoporosis

Tool	Risk Factors	Scoring	Frequently Used Threshold for Increased Osteoporosis Risk
FRAX	Age (years) Sex Weight (kg) Height (cm) Previous fracture Parental hip fracture Current smoking Glucocorticoid use Rheumatoid arthritis Secondary osteoporosis Alcohol consumption ≥3 units/day	†	8.4% (MOF)‡
OST	Weight (kg) Age (years)	(kg-years) × 0.2	<2
ORAI	Age ≥75 years Age 65–74 years Age 55–64 years Age 45–54 years Weight <60 kg Weight 60–69 kg Weight >70 kg No current estrogen use	+15 +9 +5 +0 +9 +3 +0 +2	≥9
OSIRIS	Age (years) Weight (kg) Current estrogen use Prior low-impact fracture	-0.2 × age +0.2 × weight +2 -2	<1
SCORE	Nonblack race Rheumatoid arthritis Prior rib/wrist/hip fracture Never used estrogen Age (years) Weight (lb)	+5 +4 +4 for each type of nontraumatic rib/wrist/hip fracture after age 45 years (max +12) +1 +3 × first digit of age -1 × weight divided by 10	≥6

* Table adapted from Chen SJ et al.[35]

† Refer to https://www.sheffield.ac.uk/FRAX/tool.jsp.

‡ 8.4% represents the 10-year MOF risk in a 65-year-old white woman without any other risk factors in the United States, as calculated in 2011. Currently, FRAX calculates this risk to be 9.3%.

Abbreviations: MOF=major osteoporotic fracture; ORAI=Osteoporosis Risk Assessment Instrument; OSIRIS=Osteoporosis Index of Risk; OST=Osteoporosis Self-Assessment Tool; SCORE=Simple Calculated Osteoporosis Risk Estimation.

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