



Complete Summary

GUIDELINE TITLE

Management of postmenopausal osteoporosis: position statement of The North American Menopause Society.

BIBLIOGRAPHIC SOURCE(S)

Management of postmenopausal osteoporosis: position statement of the North American Menopause Society. Menopause 2002 Mar-Apr; 9(2): 84-101. [129 references] [PubMed](#)

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

- Postmenopausal osteoporosis
- Postmenopausal osteoporotic fracture

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Diagnosis
Evaluation
Management
Prevention
Risk Assessment
Screening

CLINICAL SPECIALTY

Endocrinology
Family Practice
Geriatrics
Internal Medicine
Nutrition
Obstetrics and Gynecology
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Health Plans
Managed Care Organizations
Nurses
Pharmacists
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To present an evidence-based position statement regarding the management of postmenopausal osteoporosis
- To define the current standards of clinical practice as they apply to diagnosis, prevention, and treatment of osteoporosis in the postmenopausal woman

TARGET POPULATION

Postmenopausal women in North America

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis; Risk Factor Assessment

1. Assessment for risk factors associated with osteoporosis and fractures, including a history, physical examination, and diagnostic tests
2. Bone mineral density measurement, as indicated; Dual-energy x-ray absorptiometry (DXA) is the technical standard
3. Interpretation and clinical application of T scores
4. Evaluation for secondary causes of osteoporosis
 - a. Routine tests, including complete blood cell count and serum levels of calcium, alkaline phosphatase, thyroid-stimulating hormone, albumin, urinary calcium excretion
 - b. Special tests, as indicated, including measurement of serum protein electrophoresis, parathyroid hormone, and 25-hydroxyvitamin D.

Prevention/Management/Treatment

1. Lifestyle approaches to prevent bone loss and fractures

- a. Nutrition, including adequate intakes of calcium, vitamin D, magnesium
 - b. Isoflavones
 - c. Exercise
 - d. Smoking cessation
 - e. Alcohol avoidance
 - f. Measures to prevent falls
2. Pharmacologic approaches for the prevention and/or treatment of osteoporosis
 - a. Estrogen replacement therapy (ERT)/hormone replacement therapy (HRT)
 - b. Bisphosphonates (alendronate, risedronate, etidronate)
 - c. Selective estrogen-receptor modulators (SERMs), such as raloxifene
 - d. Calcitonin
 - e. Other therapies (parathyroid hormone, tibolone, statins, thiazide)
 - f. Combination therapies (estrogen replacement therapy/hormone replacement therapy with other osteoporosis therapies in postmenopausal women)

MAJOR OUTCOMES CONSIDERED

- Incidence of postmenopausal osteoporosis and osteoporotic fracture
- Risk of postmenopausal osteoporosis and osteoporotic fracture
- Morbidity and mortality associated with osteoporotic fracture
- Effect of osteoporosis therapy on bone loss and risk for fracture

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
 Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The North American Menopause Society (NAMS) conducted a search of the medical literature on postmenopausal osteoporosis using the database MEDLINE, as well as a search of references in the published literature. Priority was given to evidence from randomized, controlled clinical trials and meta-analyses of such trials, followed by evidence from controlled observational studies, using criteria described elsewhere. Conclusions from other evidence-based guidelines also were reviewed.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

An editorial board composed of experts from both clinical practice and research institutions was enlisted to review the published data supporting statements and conclusions. If the evidence was contradictory or inadequate to form a conclusion, a consensus-based opinion was made.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Clinicians and researchers acknowledged to be experts in the field of osteoporosis were enlisted to review the evidence and to prepare recommendations for the North American Menopause Society (NAMS) Board of Trustees. The document that was prepared was edited, modified, and subsequently approved by the NAMS Board of Trustees in November 2001.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This position statement was reviewed by the Board of Trustees of The North American Menopause Society. It was edited, modified, and subsequently approved by The North American Menopause Society in November 2001.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Excerpted by the National Guideline Clearinghouse (NGC)

Evaluation

All postmenopausal women should be assessed for risk factors associated with osteoporosis. This assessment requires a medical history, physical examination, and diagnostic tests. The goals of this evaluation are to identify the woman's risk of fracture, establish whether the woman has osteoporosis, assess the severity of the woman's osteoporosis, rule out secondary causes in a woman with osteoporosis, and identify modifiable risk factors for falls and injuries.

The history-taking and physical examination for a postmenopausal woman should focus on the detection of risk factors for osteoporosis and fractures. Most of these risks can be uncovered with a simple questionnaire along with the standard physical measurements. Potentially modifiable risk factors should be noted. Risk factors may help explain contributing causes of osteoporosis or help guide therapeutic recommendations, but they cannot be used to diagnose osteoporosis.

Physical Signs of Osteoporosis

Loss of height may be a sign of vertebral fracture in postmenopausal women. After achieving maximum height, most midlife women (and men) will lose 1.0 to 1.5 inches of height as part of their normal aging process, primarily as a result of shrinkage of intervertebral disks. In otherwise asymptomatic women, height loss greater than 1.5 inches may be associated with vertebral compression fractures that are indicative of osteoporosis. Height should be measured using an accurate and precise method, such as a stadiometer.

Acute or chronic back pain should raise suspicion of vertebral fractures. These fractures typically cause chronic back pain and fatigue, especially in the middle back. The mid-back vertebrae T12 and L1 are the most common fracture sites, followed by T6 through T9. Ultimately, multiple vertebral compression fractures result in the most obvious sign of osteoporosis, kyphosis (abnormal curvature of the thoracic spine). Because back pain, height loss, and kyphosis may occur without osteoporosis, vertebral fractures should be confirmed by radiography. Similarly, height loss without back pain requires radiologic evaluation for spine fractures, which can be asymptomatic in two-thirds of the cases. Also, women with a vertebral fracture are at high risk for subsequent fracture, making identification of even greater clinical importance. Wrist fracture, which tends to occur at an earlier age than vertebral or hip fracture, may also be an early clinical expression of osteoporosis.

Bone Mineral Density Measurement

Bone mineral density testing is the preferred method to diagnose osteoporosis. Bone mineral density is a strong predictor of fracture risk because bone mass accounts for 75% to 85% of the variation in bone strength. Testing of bone

mineral density should be performed based on a woman's risk profile. Testing is not indicated unless the results will influence a treatment or management decision.

Although not all experts agree, The North American Menopause Society (NAMS) recommends that bone mineral density be measured in all women with medical causes of bone loss and in those who are at least 65 years of age, regardless of additional risk factors. Testing is also indicated for all postmenopausal women younger than age 65 with one or more of the following risk factors for fracture: a nonvertebral fracture after menopause, low body weight (<127 lbs), or a history of a first-degree relative who has experienced a hip or vertebral fracture. For elderly women who have experienced an osteoporotic vertebral fracture, treatment may be given without bone mineral density measurement, although baseline bone mineral density testing may be useful to follow the effects of therapy. A nonvertebral fracture in the absence of low bone mineral density is not an indication for treatment. Testing of bone mineral density in early postmenopause may be valuable in helping women make a decision about preventive therapy.

Healthy premenopausal women do not require bone mineral density testing because of the low prevalence of osteoporosis in this population. Bone mineral density testing is indicated only in premenopausal women who experience a low-trauma fracture or who have known secondary causes of osteoporosis.

Analyses performed by the National Osteoporosis Foundation show that bone mineral density testing is cost-effective for postmenopausal women aged 50 to 60 years with risk factors or for those beyond the age of 60 to 65 with or without risk factors. Several tests to measure bone mineral density are available, either radiation-based or radiation-free. Dual-energy x-ray absorptiometry (DXA) is the technical standard for measuring bone mineral density. All the recent large, randomized, controlled clinical trials have used dual-energy x-ray absorptiometry of the hip and spine to determine therapeutic efficacy. Dual-energy x-ray absorptiometry is the preferred technique because it measures bone mineral density at the important sites of osteoporotic fractures, especially the hip.

The total hip is the preferred site for bone mineral density testing, especially in women older than age 60, primarily because of the high prevalence of extraosseous ossification that makes spinal measurements unreliable. The spine, however, is a useful site for bone mineral density measurement in early postmenopausal women, because they tend to lose bone faster in the spine than in the hip. Although tests at peripheral sites (e.g., wrist, calcaneus) can identify women with low bone mass, they may not be as useful as central-site tests (e.g., hip, spine) because the results are not as precise. Peripheral site measurements should be limited to the assessment of fracture risk when dual-energy x-ray absorptiometry is not available. They should not be used to diagnose osteoporosis or to follow response to therapy.

To standardize values from different bone densitometry tests, results are reported as standard deviations, either as a Z score or a T score. A Z score is based on the standard deviation (SD) from the mean bone mineral density of a reference population of the same sex, ethnicity, and age. A T score is based on the mean peak bone mineral density of a normal, young adult population and is expressed

in terms of standard deviations from the average value of this reference population.

In general, lower bone mineral density T scores indicate more severe osteoporosis and higher risk of fracture. Every decrease of one standard deviation from age-adjusted bone density represents approximately a 10% to 12% change in bone mineral density and an increase in the risk of fracture by a factor of approximately 1.5.

Repeat dual-energy x-ray absorptiometry testing in untreated postmenopausal women typically is not useful until 3 to 5 years have passed. In general, postmenopausal women lose about 0.5 in standard deviations from the mean in both T and Z scores every 5 years.

For women receiving osteoporosis therapy, bone mineral density monitoring before 2 years of therapy are completed may not provide clinically useful information. Not observing an increase in bone mineral density is not evidence of treatment failure. In one study, most women who appeared to have lost more than 4% of bone mineral density during the first year of treatment (with either alendronate or raloxifene) showed substantial gains the second year while remaining on the same therapy. The decrease in bone mineral density could be due to imprecision in the dual-energy x-ray absorptiometry measurement. However, an apparent decrease in vertebral bone mineral density greater than 4% to 5% would indicate a need to evaluate compliance with therapy and dosing instructions as well as to search for secondary causes of bone loss.

In 1994, the World Health Organization (WHO) defined osteoporosis as a bone mineral density T score below -2.5 SD based on measurements of any skeletal site. A revised World Health Organization report published in 2000 (Kanis JA, Gluer C-C. An update on the diagnosis and assessment of osteoporosis with densitometry. Committee of Scientific Advisors, International Osteoporosis Foundation. *Osteoporos Int* 2000; 11: 192-202) stated that a measurement at either the total hip or femoral neck is preferred, but that posterior-anterior (not lateral) vertebral bone mineral density can be used to make the diagnosis (refer to Table 2 titled "Definition of Osteoporosis Based on BMD of Total Hip" in the original guideline document). The current industry standard for hip bone mineral density is the total hip, and the accepted reference populations used by all dual-energy x-ray absorptiometry densitometers come from the Third National Health and Nutrition Examination Survey (NHANES III). The North American Menopause Society (NAMS) supports the use of the revised World Health Organization guidelines.

Interpretation and clinical application of T scores are made after all other pertinent data are evaluated, particularly the age and fracture history of the woman. For example, at the same T score of -2.5, a 75-year-old woman has about 8 to 10 times the 10-year hip fracture risk of a 45-year-old woman.

The fracture risk, however, depends on other factors, such as frailty, falls, and previous fractures. For example, a woman who has had a vertebral fracture has a 5-fold increased risk of sustaining another vertebral fracture during the first year after the fracture and twice the risk of a hip fracture as a woman with the same bone mineral density T score who has not had a fracture.

Biochemical Markers

Biochemical markers of bone turnover cannot diagnose osteoporosis, predict bone density, or predict fracture risk. However, these tests have been studied as a means of assessment that could be used earlier in the course of therapy to show therapeutic response. Bone turnover changes can provide evidence of osteoporosis therapy efficacy much earlier than bone mineral density changes (sometimes within weeks). The value of such markers in routine clinical practice, however, has not been established.

Tests for Secondary Causes of Osteoporosis

Once osteoporosis is diagnosed, any secondary causes of osteoporosis should be identified. Various laboratory tests can help identify secondary causes of osteoporosis (refer to Table 3 titled "Routine Laboratory Tests for Osteoporosis Evaluation" in the original guideline document). Tests that should be performed routinely include a complete blood cell count and serum levels of calcium, alkaline phosphatase, thyroid-stimulating hormone, and albumin, as well as urinary calcium excretion to identify calcium malabsorption or renal calcium leak. Special tests may be appropriate, including measurement of serum protein electrophoresis, parathyroid hormone, and 25-hydroxyvitamin D.

Lifestyle Approaches

All postmenopausal women, regardless of their osteoporosis risk factors, should be encouraged to engage in steps to prevent bone loss and fractures, such as eating a balanced diet (including adequate intakes of calcium and vitamin D), participating in appropriate exercise, not smoking, avoiding excessive alcohol consumption, and instituting measures to prevent falls. Some of these steps, such as smoking cessation and exercising, offer health benefits beyond their effects on osteoporosis.

Nutrition

A balanced diet is important for bone development as well as for general health. Some women, such as elderly women with reduced appetites or women who diet frequently or have eating disorders, may not consume adequate vitamins and minerals to maintain optimal bone mass. In general, women should be advised to eat more fruits and vegetables and minimize consumption of fats.

For women 75 years of age and older, observational research suggests that adequate protein intakes may help minimize bone loss. Protein supplements (20 g/day) in elderly patients (mean age 82) who have sustained a hip fracture have been shown to significantly shorten the hospital stay (median stay 69 days versus 102 days for placebo recipients) after the hip fracture and improve the clinical outcomes while in the hospital. Protein recipients also had significantly lower rates of complications and mortality than the controls 7 months after their hip fracture.

An adequate intake of both calcium and vitamin D is recognized as an essential component of any osteoporosis prescription drug regimen. For example, a review of 31 clinical trials evaluating estrogen and calcium supplements found annual

bone mineral density gains at the hip were significantly greater for the 20 trials testing estrogen plus calcium (2.4%) compared with the 11 trials evaluating estrogen alone (0.9%).

Calcium

Evidence has clearly established the importance of adequate calcium intake in programs focused on bone. Calcium requirements rise after midlife, particularly in postmenopausal women, owing in large part to estrogen-related shifts in intestinal calcium absorption and renal conservation. The primary factor influencing the amount of calcium absorbed is the amount of calcium ingested.

Most experts support the published recommendations for daily calcium consumption from either the U.S. National Institutes of Health (revised in 1994) or the U.S. National Academy of Sciences (revised in 1997). Recommendations related to perimenopausal and postmenopausal women are presented in Table 4 titled "Recommended Daily Elemental Calcium Intakes in Peri- and Postmenopausal Women" in the original guideline document.

The recommended calcium intakes are based on the total calcium content of various foods. To achieve maximum calcium absorption, food selection decisions should reflect the food's calcium bioavailability and the presence in the meal of other foods that may inhibit calcium absorption (e.g., oxalic acid-containing foods, such as spinach, and phytate-rich grains, such as wheat bran). Calcium requirements should optimally be met by food sources, with a calcium supplement added only if needed.

The side effect profile from recommended levels of calcium intake is insignificant. No calcium intervention trials have reported any serious side effects associated with these intakes. Nevertheless, some women have difficulty tolerating some calcium supplements, requiring a switch to a different type of supplement.

Higher than recommended calcium intakes produce no currently recognized health benefits to women, and side effects can occur. Intakes greater than 2,500 mg/day (the upper limit for healthy adults set by the U.S. National Academy of Sciences) can increase the risk for hypercalciuria and, possibly, hypercalcemia, which, in extreme cases, can lead to kidney damage.

No single laboratory test can accurately detect calcium deficiency. In general, postmenopausal women in the United States and Canada have dietary calcium intakes that are low, with median intakes of approximately 600 mg/day. Specific populations of postmenopausal women at increased risk for inadequate calcium intake include women who are elderly, lactose intolerant, follow a vegetarian diet, or have poor eating habits.

Dietary sources should be the primary source of calcium intake because there are other essential nutrients found in high-calcium food. Dairy products are among the best sources of calcium based on their high elemental calcium content, high absorption rate, and low cost relative to total nutritional value. Supplements and fortified foods are an alternative source for women not able to consume enough dietary calcium; most women need an additional 600 to 900 mg/day (2 to 3 dairy portions) over their daily dietary intake to reach the recommended levels.

However, a level of caution may be needed to avoid consuming more than 2,500 mg/day.

Calcium intakes of up to 1,500 mg/day do not appear to increase the risk of developing renal calculi and may actually reduce the risk. For perimenopausal and postmenopausal women at high risk for developing renal calculi, foods may be the best sources of calcium. If calcium supplementation is needed, each dose should be taken with meals. Calcium supplements should be considered contraindicated in a woman with a calcium-containing renal calculus until her urinary biochemical profile has been assessed.

Vitamin D

The nutrient vitamin D is essential for the intestinal absorption of calcium. Ensuring sufficient vitamin D intake is fundamental to all prevention and treatment programs for postmenopausal osteoporosis.

The current recommended dietary intake for vitamin D is 400 IU/day for women aged 51 to 70 years and 600 IU/day for women older than age 70. The National Osteoporosis Foundation recommends intakes of up to 800 IU/day for women at risk of deficiency because of inadequate sunlight exposure, such as elderly, chronically ill, housebound, institutionalized women, or those who live in northern latitudes. The safe upper limit of vitamin D is 2,000 IU/day. Higher doses may introduce risks such as hypercalciuria and hypercalcemia and should be avoided.

Sources of vitamin D include sunlight, vitamin D-fortified dairy products, fatty fish, and supplements. Daily requirements can usually be met with a multivitamin supplement (typically containing 400 IU vitamin D) plus moderate sun exposure. Many women over the age of 65 who have little or no sun exposure and rely on multivitamins alone for vitamin D intake may have suboptimal vitamin D levels. Currently, there is no worldwide consensus on criteria for acceptable serum 25-hydroxyvitamin D values, but if minimization of parathyroid hormone concentration is used, as some suggest, the lower end of the normal 25-hydroxyvitamin D concentration would be in the range of 28 to 32 ng/ml (70 to 80 nmol/L). Vitamin D is very long-acting, and thus, taking vitamin D at the same time as a calcium supplement is not necessary, although it can be a convenient way to obtain adequate levels of both nutrients.

It is well established that supplemental calcium can reduce the rate of postmenopausal bone loss, especially 5 or more years after menopause, and can reduce the risk of fracture, particularly in the elderly. However, calcium, either alone or with vitamin D, is not as effective as are estrogen replacement therapy (ERT), hormone replacement therapy with estrogen plus progestogen (HRT), selective estrogen-receptor modulators (SERMs), or bisphosphonates. Nevertheless, calcium and vitamin D are both essential components of osteoporosis therapy in combination with all antiresorptive agents.

Magnesium

Another nutrient, magnesium, is sometimes mentioned as a necessary supplement for the protection of bone health and/or for absorption of calcium. Although magnesium is a necessary nutrient for the metabolic activity of all cells,

in most trials focused on bone mineral density or osteoporotic fracture, benefits of calcium were observed without magnesium supplementation. Moreover, a study with calcium absorption as the endpoint found that 789 to 826 mg/day of magnesium, more than double the daily average magnesium intake (280 mg) for postmenopausal women, had no effect on calcium absorption.

Two studies that did report an increase in bone mineral density in postmenopausal women who received magnesium-containing supplements were small and not well controlled, and they do not present persuasive evidence of a beneficial effect from magnesium. However, in frail elderly women and women with gastrointestinal disease, magnesium supplements may be needed.

Isoflavones

Studies to date do not support the use of isoflavones to prevent or treat osteoporosis. Although some data suggest that isoflavones (a class of phytoestrogens found in rich supply in soybeans and soy products as well as in red clover) may favorably affect bone health, few randomized, controlled clinical studies with humans have been conducted, and all involved small numbers of subjects in trials of short duration. Ipriflavone, a synthetic isoflavone available without a prescription in the United States, has not demonstrated a positive effect on bone density, bone turnover markers, or fracture risk in osteoporotic women.

Exercise

Physical activity plays an important role in reducing the risk of falls in elderly women with osteoporosis. Exercise programs for the elderly reduce their risk of falling by 10%, and programs that include training for balance reduce the risk by nearly 20%. Exercise for women with established osteoporosis should not include heavy weight bearing or activity so vigorous that it may trigger a fracture.

Exercise is also important for early postmenopausal women. For bone benefits, they should be advised to add muscle strength training to their exercise program.

Postmenopausal women who do not use either estrogen replacement therapy or hormone replacement therapy often lose bone mass. Some evidence shows that strength training may curb bone loss in these women. For women who do use estrogen replacement therapy/hormone replacement therapy, strength training provides additional benefits, allowing them to increase bone mass rather than just maintain it with estrogen replacement therapy/hormone replacement therapy alone. Strength training can be performed as little as twice a week and need not involve special equipment other than simple weights or elastic bands.

Smoking Cessation

Because smoking can lead not only to lower bone mineral density but also to a wide range of health problems and increased fracture risk, smoking cessation should be encouraged for all women who are smokers. A wide array of smoking cessation aids are available, including prescription products (with and without nicotine) and behavior-modification smoking cessation programs.

Alcohol Avoidance

The level of alcohol consumption associated with an increased risk of falls is more than seven drinks a week, as established by the Framingham Study. Postmenopausal women who drink should be advised to drink moderately and not to exceed seven drinks a week. One drink is considered to be one beer, 4 oz of wine, or 1 oz of liquor.

Fall Prevention

In the United States, about 30% of people over age 60 fall at least once a year. The incidence of falls increases with age, rising to a 50% annual rate in people over 80 years of age. Elderly women have a significantly higher risk for falls than do men of the same age. As a result, prevention of falls that can cause fractures should be an aspect of routine care for all elderly women.

After menopause, a woman's risk for falls should be assessed at least annually. Clinical factors related to an increased risk for falls include a history of falls, fainting, or loss of consciousness; muscle weakness, dizziness, or balance problems; problems with muscle coordination; and impaired vision. Medications that affect balance and coordination (e.g., sedatives, narcotic analgesics, anticholinergics, and antihypertensives) are also risk factors. Safety hazards in the home and work environment, such as obstacles and poor lighting, also contribute to the risk of falls.

Pharmacologic Approaches

A management strategy focused on lifestyle approaches may be all that is needed for women who are at low risk for osteoporotic fracture. The North American Menopause Society (NAMS) recommends considering osteoporosis therapy in the following populations (these recommendations represent a change from previous NAMS recommendations based on additional published data regarding fracture efficacy):

- All postmenopausal women with total hip or spine T scores worse than -2.5.
- All postmenopausal women with total hip or spine T scores from -2.0 to -2.5 and at least one additional risk factor for fracture.
- All postmenopausal women with an osteoporotic, vertebral fracture (no bone mineral density is needed).

Several pharmacologic options are available for the prevention and treatment of osteoporosis, including estrogen replacement therapy/hormone replacement therapy, bisphosphonates, selective estrogen-receptor modulators (SERMs), and calcitonin. Refer to the original guideline document for a detailed discussion of these pharmacologic options.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The position statement was supported by evidence from randomized, controlled clinical trials and meta-analyses of such trials, controlled observational studies, conclusions from other evidence-based guidelines. If the evidence was contradictory or inadequate to form a conclusion, a consensus-based opinion was made.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of postmenopausal osteoporosis may help prevent fractures by slowing or preventing bone loss, maintaining bone strength, and minimizing or eliminating factors that may contribute to falls.

Specific Potential Benefits

- Exercise. Exercise programs for the elderly reduce their risk of falling by 10%, and programs that include training for balance reduce the risk by nearly 20%.
- Estrogen Replacement Therapy (ERT)/Hormone Replacement Therapy (HRT). The positive bone mineral density effects of systemic estrogen (oral or transdermal), with or without a progestogen, are well established. More than 50 randomized, placebo-controlled clinical trials have demonstrated that estrogen replacement therapy/hormone replacement therapy initially increases spine bone mineral density 4% to 6% and hip bone mineral density 2% to 3%, and maintains those increases after 3 years of treatment. Regarding fracture prevention, observational studies have indicated a significant reduction in hip fracture risk in women who use systemic estrogen replacement therapy/hormone replacement therapy. A meta-analysis of studies published up to 1992 yielded evidence of a 25% reduction in the risk of hip fracture for postmenopausal women who had ever used estrogen replacement therapy/hormone replacement therapy. A more recent meta-analysis found that estrogen replacement therapy/hormone replacement therapy use for at least 1 year significantly reduced the risk of nonvertebral fracture (relative risk 0.73), although the effect was somewhat reduced in women beginning therapy when they were older than 60 years. A large prospective, cohort study of elderly women, the Study of Osteoporotic Fractures, found a significant fracture risk reduction of 34% for nonspine fractures in current long-term users of estrogen replacement therapy/hormone replacement therapy compared with never users. The investigators also found that estrogen replacement therapy/hormone replacement therapy is more effective in reducing fracture risk if started within 5 years of menopause and if used longer than 10 years. In the Heart and Estrogen/Progestin Replacement Study (HERS), a randomized, controlled trial of 2,763 postmenopausal women, no reduction in fracture risk was observed after 4 years of hormone replacement therapy (0.625 mg/day conjugated equine estrogens (CEE) plus 2.5 mg/day medroxyprogesterone acetate).

These women did not have osteoporosis and were at relatively low risk for fracture. In the Swedish Hip Fracture Study, a large, population-based, case-control study of women aged 50 to 81 with hip fractures, only recent use of estrogen replacement therapy/hormone replacement therapy was associated with optimal fracture protection. However, this study suggested that therapy can be beneficial even if started several years after menopause. The overall fracture risk appeared to decrease with duration of estrogen use and addition of a progestogen.

- Bisphosphonates. Clinical trials have demonstrated that these agents increase bone mineral density at the spine and hip in a dose-dependent manner; they also reduce the risk of vertebral and nonvertebral fracture by 30% to 50%.

Alendronate. For women in early menopause, 2 to 4 years of treatment with alendronate (5 mg or more daily) increased bone mineral density at the spine and hip from 1% to 4% from baseline while placebo recipients had decreases of 2% to 4% during that time, a statistically significant between-group difference. In a 7-year trial, alendronate was associated with bone mineral density increases from baseline of 5% to 10% at the spine and hip in postmenopausal women who had low bone mineral density or established osteoporosis.

The efficacy of alendronate in decreasing fracture risk has been demonstrated only in postmenopausal women with osteoporosis, defined as having either an existing vertebral fracture or a T score worse than -2.5. In the Fracture Intervention Trial, 3 years of alendronate therapy significantly reduced the risk of nonspine fracture by 27% and new spine fracture by 50% in women with osteoporosis; however, it had no statistically significant effect in women without osteoporosis.

Risedronate. In a trial of early postmenopausal women (range 40-60 years) with normal bone mass, doses of 5 mg/day for 2 years produced significant bone mineral density increases of 5.7% in the lumbar spine and 5.4% in the hip compared with placebo. In older postmenopausal women (mean age approximately 69 years), 3 years of risedronate therapy significantly increased bone mineral density compared with placebo in the spine (4.3%) and femoral neck (2.8%).

Several studies have found fracture risk reductions with risedronate. In two studies of postmenopausal women with established osteoporosis, 1 to 3 years of treatment with 5 mg/day risedronate significantly reduced the risk of vertebral fracture compared with placebo. After 1 year of therapy, the relative risk of vertebral fracture was reduced by 61% to 65%. After 3 years of therapy, vertebral fracture risk reductions were still statistically significant relative to placebo. In one of these studies, the risk of nonvertebral fracture was significantly reduced by 39%.

In the Hip Intervention Program Study Group, risedronate significantly reduced the relative risk for hip fracture by 40% among elderly women (70-79 years old) with confirmed osteoporosis; however, it did not significantly lower the risk in elderly women (≥ 80 years) with risk factors for falling but who did not have osteoporosis confirmed by bone mineral density.

Etidronate. A meta-analysis of 13 trials investigating intermittent cyclic etidronate therapy (14 days every 3 months) for postmenopausal osteoporosis found that, relative to control groups, 1 to 3 years of therapy (400 mg/day) increased BMD by 4.1% in the lumbar spine and 2.3% in the femoral neck. This analysis concluded that etidronate significantly reduced the risk for vertebral fracture (by 37%) but not the risk for nonvertebral fracture.

- Selective Estrogen-Receptor Modulators (SERM). Raloxifene has been shown to significantly reduce serum and urinary markers of bone turnover in postmenopausal women compared with controls. At 2 years, it produces significant bone mineral density increases of 2.4% for both the spine and hip relative to placebo. Over 3 years, raloxifene reduces the risk of vertebral fracture in postmenopausal women with osteoporosis by 35% to 50%, although a reduction in fracture risk at other sites was not demonstrated.
- Calcitonin. Calcitonin therapy has produced positive spinal bone mineral density effects, but at the hip, its efficacy is less clear.

In the Prevent Recurrence of Osteoporotic Fractures study (PROOF), a large randomized, double-blind, placebo-controlled study of intranasal calcitonin, doses of 200 IU/day for 5 years significantly reduced the risk of new vertebral fracture by 33% compared with placebo in postmenopausal women with established osteoporosis. However, at either 100 IU/day or 400 IU/day, statistically significant reductions were not observed. After 5 years, a significant spinal bone mineral density increase compared with placebo was seen only for the 400-mg dose recipients. No significant effect on hip bone mineral density occurred at any dose. The absence of a dose response as well as a 60% dropout rate has led some experts to doubt the reliability of these data. Calcitonin also has been found to reduce bone pain from osteoporotic vertebral compression fractures.

POTENTIAL HARMS

Side effects and adverse reactions

- Estrogen replacement therapy/hormone replacement therapy. Despite the potential advantages, an estimated 50% to 75% of women who begin estrogen replacement therapy/hormone replacement therapy discontinue within 6 months; often cited among the reasons for discontinuance are concerns about the link between estrogen and an increased risk of breast cancer. The magnitude of the link, however, remains unresolved. Estrogen replacement therapy/hormone replacement therapy also carries a 3-fold increased risk of venous thromboembolic events. Furthermore, the hormone replacement therapy-induced uterine bleeding is unacceptable to some women.
- Bisphosphonates. Bisphosphonates may cause upper gastrointestinal (GI) disorders, and are contraindicated in those with esophageal abnormalities that delay esophageal emptying or who are unable to stand or sit upright for at least 30 minutes after ingestion. Also, as less than 1% of a bisphosphonate dose is normally absorbed, and food or drink further decreases absorption, the agent must be taken when the stomach is empty. Food or drink must be avoided for at least 30 minutes after dosing.

- Raloxifene. Hot flashes are the most common side effect of raloxifene, so the medication cannot be used to treat vasomotor symptoms associated with menopause and might even exacerbate the symptoms. Raloxifene carries the same risk as estrogen replacement therapy/hormone replacement therapy of venous thromboembolic events, such as deep vein thrombosis. Therefore, like estrogen replacement therapy/hormone replacement therapy, raloxifene should not be given during periods of prolonged immobilization.
- Calcium. The side effect profile from recommended levels of calcium intake is insignificant. No calcium intervention trials have reported any serious side effects associated with these intakes. Nevertheless, some women have difficulty tolerating some calcium supplements, requiring a switch to a different type of supplement. Intakes greater than 2,500 mg/day (the upper limit for healthy adults set by the U.S. National Academy of Sciences) can increase the risk for hypercalciuria, and possibly, hypercalcemia, which, in extreme cases, can lead to kidney damage.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Bisphosphonates are contraindicated in women with esophageal abnormalities that delay esophageal emptying or who are unable to stand or sit upright for at least 30 minutes after ingestion.
- Calcium supplements should be considered contraindicated in a woman with a calcium-containing renal calculus until her urinary biochemical profile has been assessed.

QUALIFYING STATEMENTS

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- Because standards of care and available treatment options differ throughout the world, the focus is limited to therapies available in North America.
- Adequate randomized trials evaluating the effectiveness of estrogen therapy on reducing fracture risk in women with osteoporosis have not been undertaken.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Management of postmenopausal osteoporosis: position statement of the North American Menopause Society. Menopause 2002 Mar-Apr;9(2):84-101. [129 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE DEVELOPER(S)

The North American Menopause Society - Private Nonprofit Organization

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GUIDELINE COMMITTEE

Expert Consensus Committee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from [The North American Menopause Society \(NAMS\) Web site](#).

Print copies: Available from NAMS, P.O. Box 94527, Cleveland, OH 44101, USA
Order forms are available at The North American Menopause Society [NAMS] Web site, www.menopause.org

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Boggs PP, Utian WH. The North American Menopause Society develops consensus opinions. *Menopause* 1998 Summer; 5(2): 67-8.

Electronic copies: Available from [The North American Menopause Society \(NAMS\) Web site](#).

Print copies: Available from NAMS, P.O. Box 94527, Cleveland, OH 44101, USA
Order forms are available at The North American Menopause Society [NAMS] Web site, www.menopause.org.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on July 19, 2002. The information was verified by the guideline developer on August 7, 2002.

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