Quality Indicators for the Management of Osteoporosis in Vulnerable Elders

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Osteoporosis is a systemic skeletal disease characterized by low bone mass, microarchitectural deterioration of bone tissue, and a consequent increase in bone fragility and susceptibility to fracture (1). Approximately 10 million people in the United States, 80% of whom are women, have osteoporosis, and another 18 million (83% women) have low bone mass (2). Osteoporosis is a major cause of morbidity and death in older persons. The clinical complications of osteoporosis include fractures, most commonly vertebral, hip, and forearm; disability; deformity; and chronic pain. For women who are 50 years of age, the estimated lifetime risk for osteoporotic fracture is 54% (3). For white men who are 50 years of age, the lifetime risk for hip fracture is an estimated 5% to 6% (2). Studies suggest that the prevalence of vertebral fractures is similar for men and women (4, 5). Approximately 4% of patients older than 50 years of age who experience a hip fracture will die while in the hospital, and 24% will die within 1 year of experiencing hip fracture (6). In the United States in 1995, osteoporotic fractures cost an estimated $13.8 billion (7).

METHODS

The methods for developing the ACOVE quality indicators for the management of osteoporosis, including the literature review and expert panel consideration, are detailed elsewhere in this supplement (8). A structured literature review found 2960 titles on osteoporosis, from which abstracts and articles were identified that were relevant to this report. Based on the literature and the authors’ expertise, 24 potential quality indicators were proposed. The search terms and results of the literature review can be accessed at www.acponline.org/sci-policy/.

RESULTS

Of the 24 potential quality indicators, 9 were judged to be valid by the expert panel process (see the quality indicators on pp 653-667), 3 additional indicators were accepted and merged into the indicators presented in this paper, and 12 were not accepted (www.acponline.org/sci-policy/). We summarize the literature supporting each of the indicators judged to be valid by the expert panel process.

Quality Indicators 1 and 2
Prevention of Osteoporosis

ALL female vulnerable elders should be counseled at least once regarding intake of dietary calcium and vitamin D and weight-bearing exercises,

ALL female vulnerable elders who smoke should be counseled annually about smoking cessation

BECAUSE such measures may prevent osteoporosis and decrease risk for fractures.

Supporting Evidence. The literature review did not identify any clinical trials of preventive counseling for osteoporosis. Numerous risk factors, both modifiable and nonmodifiable, have been identified for osteoporosis. Modifiable risk factors—which include poor dietary calcium intake, sedentary lifestyle, smoking, and low serum levels of vitamin D (9–12)—warrant patient education on the potential benefits of changes in diet and lifestyle. The evidence for increasing intake of calcium and vitamin D and adopting an exercise program as a means to prevent bone loss is reviewed in indicators 5 and 6. Current smoking has been associated with lower bone mineral density (BMD) and increased risk for fracture after minimal trauma in most studies (2). In the Study of Osteoporotic Fractures (2), the relative risk for fracture after adjustment for age and BMD was 1.5 for current smokers compared with nonsmokers. Five guidelines recommend preventive counseling (13–17). Two additional guidelines recommend counseling for women at risk because of nonmodifiable factors, such as ethnicity and family history (1, 18).
Quality Indicator 3
Educating Patients about Hormone Replacement Therapy

All female vulnerable elders should be counseled about estrogen replacement therapy at least once because estrogen replacement therapy improves BMD and decreases the risk for fracture.

Supporting Evidence. The literature search did not identify any trials that specifically included counseling about hormone replacement therapy (HRT). However, numerous studies have demonstrated the benefits of HRT on BMD and fracture risk. A meta-analysis of HRT studies estimated a pooled relative risk for hip fracture of 0.75 (95% CI, 0.68 to 0.84) for persons who had ever used HRT compared with women who had never received estrogen (19). This may have been a low effect estimate because the authors noted that discontinuation of estrogen use produced an accelerated rate of bone loss, in which BMD could return to near-baseline levels. This meta-analysis calculated that HRT would increase life expectancy by 1 year among women at increased risk for hip fracture.

One small, randomized, placebo-controlled trial of secondary prevention demonstrated a relative risk of 0.39 (CI, 0.16 to 0.95) for repeated vertebral fracture among women with osteoporosis receiving estrogen replacement compared with women receiving placebo (20). Other randomized clinical trials of estrogen replacement therapy did not report fracture data, and the most likely reasons were brief duration and relatively small sample sizes.

Seven randomized clinical trials with BMD as the outcome measure demonstrated a statistically significant increase in BMD in the treatment group relative to that of the placebo group (21–27). Numerous other studies with various designs demonstrated the effects of HRT on BMD and/or fracture risk. These effects, which are detailed in the Table, include decreased rate of bone loss (28); increased BMD (29, 30); and decreased risk for fracture of the spine (31), hip (32, 34), and wrist (32, 38). Three sets of guidelines (16, 45, 46) include recommendations that all perimenopausal and postmenopausal women be counseled about the risks and benefits of HRT.

Quality Indicator 4
Identification of Secondary Osteoporosis

If a vulnerable elder has a new diagnosis of osteoporosis, then during the initial evaluation period, an underlying cause of osteoporosis should be sought by checking medication use and current alcohol use because osteoporosis may be caused by an underlying modifiable condition.

Supporting Evidence. No clinical trials have evaluated the effectiveness of screening for medication and alcohol use in patients with newly diagnosed osteoporosis. Medications that are associated with an increased risk for osteoporosis include anticonvulsants, cytotoxic drugs, thyroid hormone replacement, corticosteroids, heparin, and lithium (13). The amount of alcohol required to adversely affect osteoporosis has not been established. In a study of men with osteoporosis, 12% of the cases were attributable to alcoholism and 12% to corticosteroid use (47). As these are potentially modifiable risk factors, the National Osteoporosis Foundation (13), the American Medical Directors Association (15), and the Osteoporosis Society of Canada (18) have recommended taking a patient history of medication and alcohol use. The American Association of Clinical Endocrinologists recommends assessment of particular medications and of alcohol intake as part of the risk-factor assessment (16), and a similar investigation is recommended by the American College of Rheumatology (48).

Quality Indicator 5
Exercise Therapy for Patients with a New Osteoporotic Fracture

If an ambulatory vulnerable elder has an osteoporotic fracture diagnosed, then physical therapy or an exercise program should be offered within 3 months because exercise will decrease the risk for falls, may decrease fracture risk and pain, and may increase BMD.

Supporting Evidence. Two randomized, controlled trials of exercise therapy for osteoporosis were identified (49, 50). One trial of 92 postmenopausal women with back pain who received no concomitant therapy for osteoporosis found that exercise stabilized BMD and improved pain (49). Approximately one third of these participants had osteoporosis-related fractures at baseline. The second randomized trial in healthy postmenopausal women demonstrated the slowest decline in BMD among the participants who adhered most to a prescribed exercise program (50). A nonrandomized clinical trial of healthy postmenopausal women found that the
effects of exercise on spinal BMD were additive to the effects of HRT (51).

A case–control study demonstrated a significantly reduced risk for hip fracture for persons who were physically active in the past (odds ratio, 0.54 to 0.66) (52). The prospective Study of Osteoporotic Fractures found that exercise was associated with a 30% reduction in risk for fractures (risk ratio, 0.7 [95% CI, 0.5 to 0.9]) (11). In a follow-up multivariate analysis of the Study of Osteoporotic Fractures, axial BMD was positively associated with physical activity (53). Also, a 4-year prospective study of exercise in osteoporotic patients reported

that exercise could improve quality of life by decreasing pain (54).

Numerous guidelines support the use of weight-bearing exercise for the prevention and treatment of osteoporosis (1, 13, 15, 16, 45, 46, 48, 55).

**Quality Indicator 6**

**Calcium and Vitamin D Supplementation**

IF a vulnerable elder has osteoporosis, THEN use of calcium and vitamin D supplements should be recommended at least once BECAUSE this will retard bone loss and possibly prevent fractures.
Supporting Evidence. Two randomized, controlled trials compared the effect of calcium supplementation versus placebo on bone loss in postmenopausal women (56, 57). One study demonstrated that BMD declined less rapidly in the treatment group ($P \leq 0.04$) (56). Four-year follow-up data from this study showed that fewer fractures occurred in the calcium supplementation group ($P = 0.037$) (58). The second study found that daily calcium supplementation (500 mg/d) was beneficial for prevention of bone loss at the radius, but not at other sites, for women who were postmenopausal for more than 6 years (57). Supplementation also decreased bone loss at the spine, femoral neck, and radius ($P < 0.05$) in women with dietary calcium intake less than 400 mg/d. One systematic review of 14 randomized, controlled trials and quasi-controlled trials of supplementation with vitamin D and its analogues with fracture as an outcome (59) concluded that the effect of vitamin D supplementation on risk for fracture was inconsistent and that further randomized, controlled trials were needed before a general recommendation for vitamin D supplementation can be made. Two large trials (60, 61) included in the review showed limited evidence of reducing the incidence of hip and other peripheral fractures, while limited evidence from four small trials (62–65) and one large trial (60) suggested efficacy in reducing vertebral fractures.

Of the five randomized, controlled trials identified by the search of vitamin D supplementation studies with or without calcium that measured BMD of the spine (66–70), all but one (67) reported improved BMD in the treatment group versus the control group. Only two identified trials included vulnerable elders. One randomized, controlled trial (61) of calcium and vitamin D supplementation of nursing home residents demonstrated a decreased rate of peripheral fractures associated with vitamin D supplementation. However, a randomized, controlled trial (71) that included older adults residing in assisted-living facilities found no difference in fracture rates between treatment and placebo groups.

Nine of the guidelines identified in the search recommended the use of calcium supplementation for the prevention or treatment of osteoporosis if dietary intake of calcium is inadequate (definition of adequate intake varied from 800 mg/d to 1800 mg/d) (1, 13, 15, 45, 72–75), whereas six guidelines recommended vitamin D supplementation for older adults, for individuals who avoid sun exposure, or for those with inadequate intake (recommended intake varied from 400 IU/d to 800 IU/d) (13, 15, 16, 73–75).

Quality Indicator 7
Calcium and Vitamin D Supplementation with Corticosteroid Use

IF a vulnerable elder is taking corticosteroids for more than 1 month, THEN the patient should be offered calcium and vitamin D BECAUSE this will retard the rate of bone loss and decrease the risk for fracture among individuals on long-term steroid therapy.

Supporting Evidence. The search identified one systematic review of the effects of calcium and vitamin D supplementation for patients receiving corticosteroids (76). The systematic review included five clinical trials (four of which were randomized) and found that supplementation had a beneficial effect on the BMD of the lumbar spine and radius but not on the femoral neck. The small amount of data on fractures from these trials suggested a small but not significant protective effect. This review suggested that while the efficacy of vitamin D and calcium supplementation is modest, physicians should consider offering this relatively benign intervention for patients receiving corticosteroids.

The American College of Rheumatology Task Force on Osteoporosis Guidelines recommends calcium and vitamin D supplementation as a first-line preventive measure for patients using corticosteroids (48).

Quality Indicator 8
Treatment of Osteoporosis

IF a female vulnerable elder is newly diagnosed with osteoporosis, THEN the patient should be offered treatment with HRT or bisphosphonates or calcitonin within 3 months of diagnosis BECAUSE these treatments improve BMD, reduce the rate of bone loss, and decrease the risk for fracture.

Supporting Evidence. With the approval of bisphosphonates, calcitonin, and selective estrogen-receptor modulators, the treatment of osteoporosis has become more varied and complex. For many years, estrogens were the only option approved by the Food and Drug Administration. The data supporting the use of estrogen for osteoporosis are provided in indicator 3. In addition, numerous guidelines support HRT as the treatment of
choice (1, 16, 17). However, these guidelines preceded reports from the Heart and Estrogen/progestin Replacement Study (HERS) trial (77), a study of postmenopausal women with established coronary artery disease who were randomly assigned to receive either HRT or placebo and were followed for an average of 4.1 years. This study found that HRT did not reduce the rate of ischemic heart disease events and in fact may have increased the risk for such events early in treatment. In addition, recent reports further implicate HRT as a risk factor for breast cancer (78, 79). These studies may influence the choice of HRT as the first-line treatment for osteoporosis. The most recent guidelines from the American Association of Clinical Endocrinologists (80) and the National Osteoporosis Foundation (81) do not recommend HRT over other forms of treatment.

Most of the many randomized trials of bisphosphonates demonstrated a significant improvement in BMD associated with the medication. Therefore, this review focused on trials reporting fracture data. A meta-analysis of five randomized, placebo-controlled trials of alendronate therapy for at least 2 years in postmenopausal women with osteoporosis (82), all of whom had a BMD T score of $-2.0$ or lower, found that the relative risk for a nonvertebral fracture for the alendronate group relative to placebo was 0.71 (CI, 0.5 to 0.99; $P = 0.048$). Three additional reports of two alendronate trials not included in the meta-analysis were identified. In one study, the alendronate-treated group achieved statistically significant increases in BMD at multiple sites compared with the placebo group (83). However, no significant difference was found in nonvertebral fractures between the two groups. The Fracture Intervention Trial (84) was a study with two groups; one group contained women with existing vertebral fractures and the other group had women with no history of vertebral fractures. After 2 years of treatment with alendronate or placebo, the alendronate-treated women with prior vertebral fractures experienced a decrease in radiographically apparent vertebral fractures (relative risk, 0.53 [CI, 0.41 to 0.68]) as well as clinically apparent vertebral fractures (relative hazard, 0.45 [CI, 0.27 to 0.72]) relative to the placebo group (84). The treatment group also experienced a decrease in nonvertebral fractures (relative hazard, 0.80 [CI, 0.63 to 1.01]), including hip fractures (relative hazard, 0.49 [CI, 0.23 to 0.99]). After 3 years of treatment, subgroup analyses of the cohort with existing vertebral fractures demonstrated that the 47% risk reduction in new vertebral fractures experienced by the entire cohort was consistent across age groups, baseline BMD, and number of preexisting vertebral fractures (85). To prevent one new vertebral fracture, eight women at least 75 years of age must receive treatment for 5 years. In the second arm of the study (women without a history of vertebral fractures), BMD increased at all sites, but the reduction in fractures was statistically significant only among women with a T score at the femoral neck of $-2.5$ or lower (86).

The search identified five randomized, placebo-controlled trials that examined the efficacy of etidronate in the treatment of osteoporosis and reported fracture data (87–91). While all trials demonstrated improvements in BMD with etidronate in the treatment of osteoporosis and reported fracture data (87–91). While all trials demonstrated improvements in BMD with etidronate use compared with placebo, only three demonstrated a significant reduction in vertebral fracture risk (87, 88, 91), and none demonstrated any benefit for nonvertebral fractures.

Calcitonin also has been used in the treatment of osteoporosis. A meta-analysis of randomized clinical trials of calcitonin and etidronate in postmenopausal women demonstrated for both calcitonin and etidronate a positive pooled difference between mean vertebral spine BMD between the treatment and the control groups (93). There were 59.2 vertebral fractures per 1000 patients-years for the calcitonin group compared with 28.3 for the etidronate group. The authors concluded that the evidence was insufficient to recommend one therapy over the other.

The search also identified two reviews of the effects of calcitonin. One study concluded that calcitonin may prevent bone loss but found little evidence for fracture prevention (94), whereas the other review cited several randomized clinical trials that demonstrated an increase in BMD with calcitonin use but stated that no published randomized prospective trials have demonstrated any efficacy for fracture prevention (95). Since the expert panel meeting, one randomized, double-blind, placebo-controlled trial has suggested that nasal calcitonin decreases the risk for new vertebral fractures (96).
Selective estrogen receptor modulators are a class of medications with tissue-specific estrogen agonist and antagonist functions. One randomized, placebo-controlled trial found that treatment with raloxifene, a selective estrogen receptor modulator, significantly improved BMD without causing adverse effects on the uterine lining (97). A 3-year randomized, controlled trial of raloxifene therapy in postmenopausal women with osteoporosis demonstrated reduced risk for vertebral fracture (for 120 mg/d, relative risk, 0.5 [CI, 0.4 to 0.7]) but no change in the risk for nonvertebral fracture (98).

Quality Indicator 9
Testosterone Therapy for Male Osteoporosis

If a male vulnerable elder has osteoporosis and is hypogonadal, THEN he should be offered testosterone treatment BECAUSE testosterone therapy has been shown to improve bone density and therefore may decrease fracture risk.

Supporting Evidence. Hypogonadal men, who for the purposes of this indicator are defined as those with low testosterone levels (which can be determined by free testosterone or total testosterone with sex hormone–binding globulin), may be at increased risk for osteoporosis. No direct evidence showed that treatment with testosterone would improve BMD or reduce fracture risk among elderly hypogonadal men with osteoporosis. However, a chain of indirect evidence supports this indicator. First, testosterone deficiency is present in approximately 30% of men with osteoporosis (99). Second, serum testosterone levels correlate with BMD in men in some, but not all, studies (100). Third, two small studies were identified that demonstrated the benefit of testosterone therapy among osteoporotic men with normal testosterone levels. An open-label, prospective study (101) of 23 men with primary osteoporosis demonstrated that intramuscular testosterone injections significantly improved BMD of the lumbar spine. A 1-year randomized, controlled crossover study of 15 asthmatic, glucocorticoid-treated men (mean age, 61 years) found that bone density of the lumbar spine improved by 5% during the treatment phase but not the control phase \( (P = 0.05) \) (102). Fourth, in a convenience sample of 72 men with low serum testosterone levels, testosterone replacement maintained BMD in the normal range and resulted in the greatest increases for participants with the lowest BMD at initiation of therapy (103). The American College of Rheumatology guidelines for the treatment of men with glucocorticoid-induced osteoporosis recommend testosterone therapy for men with a T score less than $-1$ if serum testosterone is low (48).

Subsequent to the meeting of the expert panel, a 36-month randomized, placebo-controlled trial (104) of testosterone replacement for BMD in 108 men aged 65 years and older with low serum testosterone reported no difference in the change in lumbar spine BMD between the treatment and control groups. However, for those with a pretreatment serum testosterone level less than 6.94 nmol/L (<200 ng/dL), the increase in BMD was significantly greater for testosterone recipients than for placebo recipients.

DISCUSSION

Osteoporosis is associated with significant morbidity and death in vulnerable elders. Improvement in the quality of care that these patients receive may result in improved outcomes. The ACOVE project identified nine process measures believed to be valid indicators for use in quality-of-care measurement. These indicators can potentially serve as a basis to compare the care provided by various health care delivery systems and to track the change in care over time.

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