

Osteoporosis Prevention: Strategies Applicable for General Population Groups

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Osteoporosis is a common condition of the elderly population that entails considerable morbidity and mortality. Although prevention recommendations often focus on perimenopausal women, the condition begins well before the age of menopause and also affects men. Prevention techniques include hormonal replacement therapy, optimization of calcium intake and absorption, weight-bearing exercise, cessation of tobacco and alcohol abuse, fall prevention, and management of predisposing medical conditions. All of these techniques are analyzed by commonly accepted criteria. Recommendations for osteoporosis prevention that are applicable to general population groups are presented.

As the number of elderly people in the United States increases, osteoporosis has become a focus of attention in the lay and scientific press as well as in the advertising media. Health consequences of osteoporosis are considerable and largely mediated through falls. Falls are the leading cause of accidental death in persons 65 years old or older.^{1,2} Treatment of the established syndrome is of limited effect, so techniques of prevention are important to consider. Recently published comprehensive recommendations for adult health maintenance have not included osteoporosis prevention^{3,4} or have limited recommendations to women at the time of menopause.⁵ Considering the high prevalence of osteoporosis and its occurrence in men as well as women, consideration of more vigorous prevention strategies is warranted. Such strategies include promotion of maximum peak bone density in the fourth decade of life as well as minimization of the subsequent decline in bone density, which occurs in the second half of life.

At Group Health Cooperative of Puget Sound, there were 132 hospitalizations for hip fracture in persons 45 years old or older in 1983 alone. Based on the magnitude and importance of the osteoporosis problem, the Group Health Medical Staff Committee on Prevention (MSCP) performed a comprehensive analysis of various modalities

for prevention with the intent of arriving at a prudent strategy that could be widely recommended to enrollees. The MSCP was established in 1978 to serve as a forum for discussion and development of practice and program recommendations in primary and secondary prevention.⁶ Specific, widely recognized criteria for evaluating screening and preventive strategies are used.^{5,7,8} The present report is the result of deliberations and practical recommendations for prevention employing this approach.

REVIEW BY SPECIFIC CRITERIA

1. *The condition must have a significant effect on the quality or quantity of life.* Osteoporosis is a decrease in bone density to such a degree that fractures occur from trauma normally not expected to result in fracture. Annual costs of osteoporosis-related fractures in the United States have been estimated as \$6.1 billion.⁹ The most common osteoporosis-related fractures are of the proximal femur, vertebral body, distal forearm, proximal humerus, and ribs. Of these sites the proximal femur fracture, or "hip fracture," affects quality and quantity of life to the greatest extent. Fracture-related mortality is 12 to 20 percent and occurs mostly in the first four months following fracture.¹⁰ Among those who were living at home at the time of fracture, about one half have a deterioration in social function over a 2½-year follow-up period.¹¹

2. *The incidence of the condition must be sufficient to justify the cost of screening.* Osteoporosis-related fractures are predominantly seen in postmenopausal women and

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TABLE 1. RISK FACTORS FOR OSTEOPOROSIS

Modifiable Factors	Nonmodifiable
Estrogen deficiency	Small, thin body habitus
Calcium deficiency	Female
Immobilization/inactivity	Nonblack race
Alcoholism	
Smoking	
Certain co-existing medical conditions (see Table 2)	

men aged over 65 years. In the United States in 1984, there were 28.5 million women aged over 55 years and 11.3 million men aged over 65 years, and this population at risk is predicted to increase at least through the year 2000.¹² Falls are common in the elderly population and are often a co-factor with osteoporosis in fractures. Twenty-five to 40 percent of individuals aged 65 years or older experience at least one fall per year with a resultant fracture 6 to 8 percent of the time.^{2,13}

Osteoporosis has been estimated to be a factor in 70 percent of fractures among white women aged over 40 years and in 15 percent of white men of similar age.¹⁴ Hip fracture incidence is about 1 percent per year in women enrolled in Medicare, with a cumulative incidence by 90 years of age of 32 percent for women and 17 percent for men.^{10,15} The hip fracture rate in black women, one half that of white women, is also substantial. Spinal compression fractures have occurred in 25 percent of white women by the age of 65 years, while humeral and distal forearm fractures each have an incidence of about 0.6 percent per year among women aged 60 to 74 years. Thus the late form of the syndrome characterized by fractures is extremely common. The incidence of earlier stages of osteoporosis is unknown, largely because of lack of diagnostic criteria.

3. *The condition must have an asymptomatic period during which detection and treatment significantly reduce morbidity or mortality.* Osteoporosis is a disease of insidious onset involving a long presymptomatic phase. Bone mass (or density) is the factor usually used to quantify osteoporosis, although other factors are also associated with bone fragility.^{16,17} Peak bone mass occurs at about 35 years. From that chronologic milestone onward, women may lose 45 percent of their vertebral bone mass and 55 percent of the proximal femur mass over their lifetime. Men start at about 30 percent higher peak mass, and lose at a lower rate. The loss of bone in men is linear at a rate of about 0.3 percent per year. In women a more complex pattern is seen, with losses of up to 2 percent per year occurring for about five years immediately after menopause, and a more gradual loss (0.2 to 0.7 percent) before and after that accelerated phase.¹⁸⁻²⁰ Two general strategies for preventing osteoporosis, then, are (1) to in-

crease the peak bone mass early in life, and (2) to decrease the rate of decline later in life.

Detection and treatment of osteoporosis prior to the symptomatic phase are important for two reasons. First, symptomatic manifestations (fractures) entail considerable effects on the quality and duration of life. Second, because, with the possible exception of exercise, commonly employed preventive measures merely decrease or halt the rate of bone loss, not restore lost density; the earlier such measures are initiated, the more effective they will be.

4. *Tests that are acceptable to patients must be available at reasonable cost to detect the condition in the asymptomatic period.* Efforts at early detection of osteoporosis are comparable to efforts at early detection of atherosclerosis. In each disease a long asymptomatic phase precedes clinical manifestations, with a gradual progression of pathologic correlates of disease (decreased bone density or atheromatous plaques). While pathologic findings can be measured for each process, early recognition is most practical in a clinical setting by risk-factor identification.

Risk factors for osteoporosis can be classified as modifiable (where intervention is a plausible means of osteoporosis prevention) and nonmodifiable (but useful to alert the clinician to increased risk) (Table 1). A family history of osteoporosis and few pregnancies are sometimes listed as risk factors, but supportive data are not convincing.

In general, the risk factors listed are easily determined by history or physical examination. Estrogen deficiency occurs in women after menopause or oophorectomy and in those amenorrheic because of athletic training or elevated prolactin levels.^{21,22} All of these factors have been associated with osteoporosis, and the risk increases with the number of years since cessation of menses. Insufficient calcium intake is widespread. In the United States more than three quarters of all women have daily intakes below the recommended daily allowance (RDA) guidelines of 0.8 g.²³ Premenopausal women and women on estrogen replacement therapy have been found to require 1.0 g of calcium daily to maintain calcium balance, while postmenopausal women require 1.5 g.²⁴ Checklists are commonly available through local dairy councils to aid in the assessment of calcium intake. Decreased absorption of calcium can also lead to deficiency and may occur in malabsorption syndromes, in lactase deficiency, and with vitamin D deficiency. Activity level is clearly important and is measured on a continuum, with bedrest as the greatest risk for bone thinning. Among ambulatory people bone density correlates well with the amount of weight-bearing activity.²⁵ Alcoholics are at increased risk for osteoporosis even if they remain productive in their careers.²⁶ Similarly, smokers have decreased bone density.^{27,28} Blacks, both male and female, have higher bone density than whites

of the same sex and twofold lower fracture rates.²⁹ Little is known about risk in other races. Fracture risks vary among geographic regions and among different racial groups in a given region, but how much of the effect is on the basis of race is unknown. Numerous medical conditions and therapies have been associated with osteoporosis and are listed in Table 2.

Unfortunately, at the present time, quantification of relative and attributable risk for individual osteoporosis risk factors and combinations is not possible. Similarly, the discriminatory ability of risk factors is unknown. Nevertheless, from a practical standpoint risk factors can both indicate which patients are at relatively higher risk and point to areas of intervention.

A wide variety of radiologic approaches to osteoporosis detection have been studied. Quantitative computerized tomography and single and dual photon absorptiometry have been employed widely in studies of treatment efficacy. None, however, has yet shown sufficient discriminatory power to be applicable for general screening purposes.³⁰

In summary, screening for osteoporosis should be limited to risk factor identification. The cost of risk factor determination in the context of a preventive care visit is negligible and entails no patient discomfort. It is not known which risk factors or combinations thereof are the best predictors of disease, but risk factor modification is a reasonable course given present knowledge.

5. *Acceptable methods of treatment must be available.*

6. *Treatment in the asymptomatic phase must yield a therapeutic result superior to that obtained by delaying treatment until symptoms appear.* Because of the large number of treatment options to consider, factors 5 and 6 are considered jointly for each option. The justification for attempting treatment in the asymptomatic phase has been discussed above, so evidence of treatment efficacy and treatment acceptability will be the present focus. Studies of efficacy commonly report bone density rather than fracture rate as the outcome indicator. Bone density is not an ideal predictor of fractures,¹⁷ but is currently the most practical object of study.

Hormonal Replacement Therapy

Several prospective controlled studies in perimenopausal women, with two years or more of follow-up of bone density, have shown significant benefit from estrogen replacement therapy.^{20,31-34} Whether bone density remains relatively stable or increases with estrogen therapy is controversial, though small but significant increases in density with estrogen have been reported.^{20,31,35} Some workers have classified recently postmenopausal women into rapid and slow loser subgroups. Estrogens have been found effective in both groups.³⁶

TABLE 2. MEDICAL CONDITIONS ASSOCIATED WITH INCREASED RISK OF OSTEOPOROSIS*

Endocrine Disorders	Medications
Hyperparathyroidism	Corticosteroids
Hyperthyroidism	Heparin
Hyperadrenalcorticalism	Thyroid hormone
Premature menopause (including surgical) and amenorrhea	Aluminum-containing antacids
	Furosemide
	Anticonvulsants
Congenital Disorders	Immobilizing Disorders
Turner's syndrome	Parkinsonism
Klinefelter's syndrome	Rheumatoid arthritis
Homocystinuria	Bed rest
Testicular feminization	Paralysis from any cause
Adrenogenital syndrome	
Gastrointestinal Disorders	
Peptic ulcer disease	
Malabsorption syndrome	
Lactase deficiency	
Postgastrectomy	

* In addition, conditions that make one prone to falls or that are treated with medications that cause gait instability (neuroleptics, vasodilators, diuretics) increase the risk of fractures as a manifestation of osteoporosis

Studies of fracture rates with estrogen are more limited but consistent with bone density studies. Case-control studies of hip fractures have found relative risks of 0.4 to 0.7 among estrogen users.³⁷⁻⁴⁰ In each study, the risk decreased the longer estrogen was continued or increased with increased time since cessation of estrogen. In a prospective study of secondary prevention of vertebral fractures, Riggs et al⁴¹ reported an almost threefold reduction among those receiving estrogens.

Estrogens appear effective in doses equivalent to 0.625 mg of conjugated estrogen if started from two months to six years after cessation of menses.^{31,34,42} It is not known how much later they can be started and still be effective. A lower dose of estrogen (0.3 mg) combined with calcium may be as effective but has not been extensively studied.⁴³ Optimal duration of therapy is unknown, though continuation after the age of 70 years is not generally recommended. After cessation of estrogen therapy, bone density begins to decline in a fashion similar to that at normal menopause.³⁵

A major risk of estrogen therapy is endometrial cancer. The reported magnitude of the relative risk has varied from 1.7 to 20 times.^{44,45} While estrogens are most strongly related to localized endometrial cancer, the risk of invasive and extrauterine forms is also increased.^{45,46} Overall mortality has not been found to be increased in estrogen users, perhaps because of concomitant beneficial effects.⁴⁷ Estrogen therapy has also been associated with a 2.5-fold relative risk of surgically treatable gallbladder disease.⁴⁸

Beneficial effects of estrogens include decreased hot flashes and reversal of vaginal atrophy. Two recent cohort studies reached opposite conclusions regarding a beneficial or detrimental effect of estrogen on coronary artery disease.^{49,50} Concurrent cyclic administration of progesterone and estrogen has been suggested to decrease risk of endometrial cancer.⁵¹ Progestones, however, including medroxyprogesterone acetate, may have adverse effects on serum lipids,^{52,53} and many women find the resumption of menses associated with cyclic progesterone therapy unacceptable.⁵⁴ Nevertheless, the weight of evidence currently favors the use of progesterone for women receiving estrogen replacement therapy, unless the uterus is surgically absent.

In summary, strong evidence supports a beneficial effect of estrogen replacement therapy in preventing osteoporosis; however, adverse effects of estrogen or progesterone limit somewhat the general applicability. Estrogen replacement therapy is most clearly indicated for women with premature surgical menopause. Other women at high risk for osteoporosis are candidates for hormonal replacement therapy after risks and benefits are thoroughly discussed. Younger women with diet- or exercise-related amenorrhea should be considered candidates for hormonal therapy unless return of menses is anticipated shortly.

Calcium and Vitamin D

Evidence for a role of calcium intake in prevention of osteoporosis is not so strong as that for estrogens, but the associated risks are less for calcium. Epidemiologic studies suggest that lifelong adequate calcium intake, including during the growth and consolidation phases (up to 35 years), is important for preserving bone density later in life.^{55,56} Some, but not all, prospective placebo-controlled studies in healthy postmenopausal women have found calcium supplementation to be helpful in slowing the rate of bone density decline.^{32,33} Two recent studies of early postmenopausal women suggest that calcium supplements may have relatively little effect on postmenopausal bone density loss. In this group of women the benefits appear to be considerably less than those of estrogens and may be limited to cortical bone.^{43,57} However, in a group of women with a history of osteoporotic vertebral fractures, Riggs and co-workers⁴¹ found calcium supplementation effective in reducing by one half the rate of vertebral body (trabecular bone) fractures, suggesting benefit in manifest osteoporotic disease.

Premenopausal women and women on hormonal replacement therapy have been found to require 1.0 g of calcium daily to maintain calcium balance, whereas postmenopausal women not on therapy require 1.5 g.²⁴ A

recent prospective study of normal women in early menopause brings these values into question.⁵⁸ Women were classified into three groups with calcium intakes of 1.0 to 2.0 g daily, and no differences in rate of bone density decline were observed. However, the median calcium intake among US women postmenopausally, 500 mg,⁵⁹ is considerably below any of the groups studied. Men and children have not been studied so intensively from an osteoporosis standpoint. The RDA guidelines seem a reasonable recommendation for these groups.

Vitamin D is required for optimal calcium absorption. Persons with decreased renal function and those with little exposure to sunlight are at risk for deficiency. Fortified dairy products are the main dietary sources. No controlled studies have demonstrated a benefit from vitamin D supplementation, but 400 to 800 IU daily is a prudent precaution for those at risk.

Risks of calcium supplementation occur mainly in the overzealous. Calcium intakes in excess of those recommended above have caused milk-alkali syndrome, especially when the carbonate form is used as a supplement. Kidney stones are said to seldom result from modest calcium supplementation,⁶⁰ but formal trials in general population groups have not been reported. Patients with diseases that predispose to hypercalcemia (sarcoidosis, hyperparathyroidism, certain malignancies) should not be given supplemental calcium.

In summary, the importance of calcium intake in osteoporosis prevention is uncertain. The beneficial effects may be limited to particular skeletal sites. While most studies have included only perimenopausal women, the benefits of calcium may be greatest with lifelong adequate intake, supplementation in those aged over 65 years, and those with known osteoporosis. Benefits in men are unproven. Although calcium supplementation alone should not be considered adequate prevention in high-risk individuals, it is a safe and probably effective component of a comprehensive prevention program.

Exercise

Several prospective, controlled studies have shown a beneficial effect of weight-bearing exercise on bone density in postmenopausal women of varying age and health status.⁶¹⁻⁶³ The duration of exercise studied varied from one half to one hour three times a week. No controlled studies of exercise and fracture rate have been reported. Epidemiologic studies showing increased bone density in weight-bearing portions of athlete's skeletons support a similar role of exercise earlier in life and in men.¹⁶ Exercises to promote cardiovascular fitness would also be likely to promote bone health so long as they are of a weight-bearing type, such as dancing, walking, or calisthenics. Risks

of such exercise have not been completely quantified, although obviously the program advised must take into consideration the physical limitations of each patient to avoid causing injuries.⁶⁴

Alcoholism, Smoking

Both alcoholism and smoking have been found to be associated with osteoporosis, but no studies of intervention in these habits for osteoporosis prevention have been reported. Considering the other health effects of these habits, it would appear prudent to incorporate cessation advice in an osteoporosis prevention program.

Other Medical Conditions

Numerous medical conditions (Table 2) have been associated with osteoporosis. Interventions aimed at correcting endocrinopathies and malabsorption states and minimizing immobilization and medications associated with osteoporosis would appear sensible, but there is no empirical support of efficacy. Falls often precipitate fractures in osteoporotic individuals. A fall in an elderly individual, even when no injury occurs, must be taken as a serious warning sign to consider fall prevention. Ambulation assists, such as walkers and environmental modifications, including no-slip treads and handrails, and minimization of psychotropic⁶⁵ and hypotensive medications are reasonable strategies to help prevent the manifestations of osteoporosis. Wandering has been found to be a major risk factor for hip fracture among demented patients.⁶⁶

CONCLUSIONS

Osteoporosis is a problem of considerable impact. Early detection is imprecise, and no clinically applicable screening tests exist at present. A large number of risk factors have been identified, however, and modification of these factors appears warranted in many cases. Such intervention should be considered in the second or third decade of life to promote maximum peak bone density. Among preventive techniques, evidence of efficacy is strongest for estrogen replacement therapy, but risks are also highest. Estrogen should be considered for high-risk women at the time of cessation of menses, especially if cessation is premature. Adequate calcium intake is a prudent recommendation for all age groups, although evidence of efficacy is not definitive. Weight-bearing exercise is beneficial to bone and may have additional health benefits. Elimination of other risk factors is prudent where

Estrogen replacement	Recommended for high-risk women from cessation of menses to 70 years. Given as 0.625 mg conjugated estrogen (or equivalent) daily 25 days each month For women with intact uteri, add medroxyprogesterone acetate 10 mg daily on days 16 through 25
Calcium intake	Assure adequate intake in all age groups. Recommended daily intake (add 400 mg for pregnancy or lactation)— Children: 800 mg Teenagers: 1,200 mg Men: 800 mg Premenopausal women, women taking estrogen: 1,000 mg Postmenopausal women not taking estrogen: 1,500 mg
Exercise	Advisable for all age groups; should be weight bearing, at least 30 minutes three times weekly
Habit modification	Assist with discontinuing smoking and excess alcohol intake
Management of co-existing diseases	Limit use of medicines associated with bone thinning and falls. Correct endocrinopathies; minimize immobilization. Suggest environmental changes to minimize falls in the disabled or elderly

practical, although of unproven benefit in promoting bone health.

A summary of preventive recommendations arrived at in discussions in the Group Health Cooperative of Puget Sound Medical Staff Committee on Prevention appears in Table 3. There is need for further research that will delineate in a quantitative fashion the relative risks, attributable risks, and discriminate power of osteoporosis risk factors, individually and in combination.

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