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ABSTRACT

Osteoporosis is a skeletal disorder characterized by compromised bone strength that predisposes a person to increased fracture risk. Fractures are often associated with increased morbidity, higher mortality, loss of function and even psychological consequences. Pharmacotherapeutic interventions (e.g., bisphosphonates, selective estrogen receptor modulators, calcitonin, and teriparatide) in women with postmenopausal osteoporosis provide substantial reduction in fracture risk over and above risk reduction with calcium and vitamin D supplementation alone. The importance of nutritional support along with an appropriate exercise regimen, avoiding smoking and excessive alcohol use is to be emphasized along with the pharmacologic approach to osteoporosis. Despite the effectiveness of therapy with pharmacologic agents, most patients who start therapy do not remain on treatment for more than 1 year. (**Arq Bras Endocrinol Metab 2006;50/4:755-763**)

Keywords: Bone loss; Calcium and vitamin D supplementation; Bisphosphonates; Selective estrogen receptor modulators; Calcitonin; Hormonal replacement; Teriparatide

RESUMO

Atualização no Tratamento da Osteoporose.

Osteoporose é uma doença esquelética caracterizada pelo comprometimento da força óssea que predispõe ao aumento do risco de fratura na pessoa. As fraturas são sempre relacionadas com aumento da morbidade, alta mortalidade, perda funcional e mesmo consequências psicológicas. Intervenções farmacoterapêuticas (por exemplo, bisfosfonatos, moduladores seletivos dos receptores de estrogênios, calcitonina e teriparatida) na mulher com osteoporose pós-menopausa resultam numa redução substancial do risco de fratura, superior ao risco obtido com suplementação de cálcio e vitamina D somente. A importância do suporte nutricional junto com série de exercícios apropriados, o evitar o tabagismo e uso excessivo de álcool devem ser enfatizados junto com a abordagem farmacológica da osteoporose. Apesar da efetividade da terapia com agentes terapêuticos, a maioria dos pacientes que iniciam tratamento não o mantêm por mais de um ano. (**Arq Bras Endocrinol Metab 2006;50/4:755-763**)

Descritores: Perda óssea; Suplementação de cálcio e vitamina D; Bisfosfonatos; Moduladores seletivos dos receptores de estrogênio; Calcitonina; Terapia hormonal; Teriparatida

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OSTEOPOROSIS IS A DISEASE characterized by reduced bone strength and increased susceptibility to fragility fractures. The reduction in bone strength is a function of reduced bone mass and abnormal bone quality, including deteriorated microarchitecture, abnormally high bone turnover, damage accumulation, and mineralization deficits. Osteoporosis is often asymptomatic for many years until the fracture occurs. These fractures and their consequences, which include pain, disability, deformity, psychological perceptions of reduced self-worth and self-esteem, and sometimes premature death, are well recognized clinical sequelae of osteoporosis.

**WHEN TO MEASURE BMD:
GUIDELINES FROM AACE, NAMS, NOF**

The American Association of Clinical Endocrinologists (AACE), North American Menopause Society (NAMS), and National Osteoporosis Foundation (NOF) provide recommendations for the identification of patients in need of therapy (table 1) (1-3). According to AACE, all women aged ≥ 65 years, women ≥ 40 years with a history of fracture not caused by severe trauma, and younger peri- and postmenopausal women who have clinical risk factors for fractures should be assessed for osteoporosis (1).

NAMS recommends that BMD be measured in all women with medical causes of bone loss, in all patients ≥ 65 years regardless of the presence of additional risk factors, and in younger postmenopausal women with ≥ 1 risk factor. Measurement of BMD at the total hip in women ≥ 60 years may be more accurate because spinal measurements may be unreliable in older patients due to degenerative joint disease. Spine BMD testing may be more useful in younger postmenopausal women for 2 reasons: 1) There are fewer

degenerative spine changes in younger women and 2) bone loss occurs faster in the spine than in the hip and thus allows earlier detection of osteoporosis (2).

The NOF recommends BMD testing in women aged ≥ 65 years regardless of risk factors, younger postmenopausal women with ≥ 1 risk factor, and all postmenopausal women with fracture.

**WHEN TO MEASURE BMD:
GUIDELINES FROM AACE, NAMS, NOF**

The AACE guidelines identify 3 categories of women who may benefit from pharmacologic treatment: women with postmenopausal osteoporosis (e.g., those with low-trauma fracture or low BMD), women with borderline-low BMD (T-scores ≤ -1.5) if risk factors are present, and women in whom nonpharmacologic therapy has been demonstrated to be inadequate for preventing bone loss or fracture (1).

The NAMS guidelines are somewhat more conservative than the AACE guidelines in identifying patients who require treatment. Treatment is recommended in all postmenopausal women with prior vertebral or hip fracture or with total hip or spine T-scores < -2.5 and in postmenopausal women with total hip or spine T-scores from -2.0 to -2.5 and ≥ 1 additional risk factor (1,2).

According to NOF, therapy should be initiated in women with T-scores < -2.0 by hip DXA with no risk factors, those with T-scores < -1.5 and ≥ 1 risk factor, and all patients with a prior vertebral or hip fracture (3).

OVERVIEW: TREATMENT OF BONE DISEASE

Osteoporosis responds to treatment. In addition to lifestyle changes such as improved diet and increased exercise, there are a number of effective, well-tolerat-

Table 1. Guidelines for treatment of patients with postmenopausal osteoporosis.

	National Osteoporosis Foundation	North American Menopause Society	American Association of Clinical Endocrinologists
Who should receive treatment?	<ul style="list-style-type: none"> • Women with BMD T-scores < -2.0 by hip DXA with no risk factors • Women with BMD T-scores < -1.5 by hip DXA with ≥ 1 risk factor • Women with a prior vertebral or hip fracture 	<ul style="list-style-type: none"> • Postmenopausal women with total hip or spine T-scores < -2.5 • Postmenopausal women with total hip or spine T-scores from -2.0 to -2.5 and ≥ 1 risk factor for fracture • All postmenopausal women with osteoporotic vertebral fracture (no BMD needed) 	<ul style="list-style-type: none"> • Women with low-trauma fracture and low BMD • Women with BMD T-scores ≤ -2.5 • Women with borderline-low BMD (T-score ≤ -1.5) with risk factors • Women in whom nonpharmacologic measures are ineffective

Adapted from Endocr Pract. (1), Menopause (2), National Osteoporosis Foundation (3), and Am J Med (27).

ed therapies that may dramatically reduce fracture risk. In addition to reducing fracture risk, other therapeutic goals are noteworthy: stabilizing or increasing bone mass; relieving symptoms of fractures and skeletal deformity; and maximizing physical function (1). To achieve these goals, the US Surgeon General has made several recommendations (4). These are based upon adequate calcium and vitamin D intake, physical activity, and fall prevention. A second set of recommendations includes identifying and treating secondary causes of osteoporosis. A third set of recommendations includes pharmacotherapeutic interventions to improve bone density and reduce the risk of fracture.

Physical activity

Physical activity is particularly important for the accrual of optimal peak bone mass in young adulthood. It is also important in the middle and later years but for different reasons. In the older adult, weight training, for example, does not have a major impact on BMD at all sites (5). Lower impact exercises, such as walking, have an even smaller effect to increase BMD. However, exercise is always recommended because it improves mobility, muscle function, balance and, consequently, is likely to reduce the risk of falling (6).

Nutrition and calcium/vitamin D supplementation

Good nutrition and a balanced diet are important for normal growth and development. Adequate calcium intake is considered to be a most important factor that helps in the attainment and maintenance of bone mass. A double-blind, placebo-controlled study enrolled 301 healthy postmenopausal women, half of whom had a usual daily calcium intake of < 400 mg/day; the other half had an intake of 400 to 650 mg/day (8). Subjects were randomized to 2 years of therapy with placebo or calcium 500 mg/day, formulated as either calcium carbonate or calcium citrate malate. Although calcium supplementation did not affect bone loss from the spine in early postmenopausal women with low calcium intake, there were small gains in BMD at the femoral neck and radius and reductions in BMD loss at the spine among women who had been postmenopausal for ≥ 6 years and who had received calcium citrate malate. Calcium carbonate maintained BMD at the femoral neck and radius, but had no effect on spine BMD (8). A second trial, conducted in healthy postmenopausal women who received calcium or placebo for 4 years (median intake, 640 mg/day at 4 years), found sustained, significant reductions in the rate of loss of total body BMD in the calcium group

throughout the study period (9). Significantly fewer fractures occurred in the calcium group compared with the placebo group.

Vitamin D is essential for the intestinal absorption of calcium. Serum concentrations of 25-hydroxyvitamin D decline with age, necessitating supplementation in the majority of older women (7). Combining vitamin D supplementation with calcium has been shown to reduce risk of fracture. In a 3-year, double-blind study conducted in men and women aged ≥ 65 years, 389 subjects were randomized to calcium (500 mg/day) plus 700 international units (IU) of vitamin D₃ (7). Compared with placebo, combined therapy significantly increased BMD at the femoral neck and spine and over the total body. These differences were significant at 1 year; at 3 years, only total body BMD was significantly improved by calcium/vitamin D therapy. Furthermore, the incidence of nonvertebral fracture was significantly reduced among subjects who received active therapy.

The recommended dietary intake of calcium (table 2) is 1,000 mg/day for men and women aged ≤ 50 years. For those > 50 years, the recommended intake is 1,200 mg/day (10). The current recommended dietary intake for vitamin D (table 2) is 400 IU/day for men and women aged 51 to 70 years and 600 IU/day for those ≥ 71 years (11). Women at risk for deficiency due to inadequate sunlight exposure should receive up to 800 IU/day (2).

Fall prevention and bone protection

Approximately 30% of individuals aged ≥ 60 years fall at least once a year, with an increase in incidence in people aged ≥ 80 years (13). Falls have serious consequences in patients with osteoporosis or osteopenia: they can lead directly to fractures. Therefore, prevention of falls should be a priority in older patients. All patients with osteoporosis or osteopenia should be assessed for risk factors for falls. These risk factors include previous falls, fainting or loss of consciousness, muscle weakness, dizziness or balance problems, impaired vision, and certain medications (e.g., sedatives, narcotic analgesics, anticholinergics, and antihypertensives). Environmental factors, such as poor lighting, may also increase the risk of falls (2). A safety checklist to help patients eliminate common household hazards may be found on the NOF Web site (14). Hip protectors have been shown to reduce the risk of hip fracture for elderly patients who live in nursing homes; however, it remains unknown whether these findings can be generalized to lower risk populations (15).

Table 2. Recommendations for calcium and vitamin D supplementation.

	Use	Dosage
Calcium	Supplementation recommended for most men and women aged > 50 yr	Total intake 1,000 to 1,500 mg/day (adjust dosage according to dietary calcium intake)
Vitamin D	Supplementation recommended for most men and women	Age 51 to 70 yr: 400 IU/day Age ≥ 70 yr: 600 IU/day In patients at risk for deficiency because of inadequate sunlight exposure: 800 IU/day

Adapted from JAMA (12), Menopause (2), National Institutes of Health (10-12), and Am J Med (27).

Pharmacologic intervention

Bisphosphonates, selective estrogen receptor modulators (SERMs), calcitonin, teriparatide, and estrogen reduce the risk of fracture. It is important to note that the reductions in fracture afforded by these agents are in addition to the reductions obtained with calcium and vitamin D alone. In modern clinical trials with these agents, comparisons are made with “placebo” groups in which calcium and vitamin D are provided.

Bisphosphonates

Bisphosphonates are stable analogues of pyrophosphate that have a strong affinity for bone hydroxyapatite. These agents inhibit bone resorption by reducing the recruitment and activity of osteoclasts and increasing apoptosis (16-18). Bone formed while patients are receiving bisphosphonate treatment is histologically normal (19).

Alendronate

Alendronate sodium (table 3) is indicated for the prevention (5 mg daily and 35 mg weekly) and treatment (10 mg daily and 70 mg weekly) of osteoporosis in postmenopausal women (20). It has been shown to increase bone mass and reduce the incidence of fractures of the spine and hip in postmenopausal women with osteoporosis. For the prevention of osteoporosis, Alendronate should be considered in postmenopausal women who are at risk for osteoporosis and in whom maintenance of bone mass and reduction in risk of future fracture are indicated. Alendronate is also indicated to increase bone mass in men, and to treat glucocorticoid-induced osteoporosis and Paget's disease of bone in both men and women (20).

The efficacy of Alendronate 10 mg once daily in increasing bone mass has been tested in 4 double-blind, placebo-controlled clinical studies conducted in postmenopausal women with osteoporosis aged 44 to 84 years. These studies included 2 clinical 3-year trials of identical design, one of which was performed in the United States and the other multinationally (20). In these studies, significant increases in BMD relative to

baseline and placebo were observed at each measurement site; total body BMD also increased significantly. Two-year extension studies showed continued increases in BMD measured at the lumbar spine and hip trochanter, plus maintenance of BMD at the femoral neck, forearm, and total body (20).

The effect of Alendronate on fracture incidence was evaluated in the randomized, double-blind, placebo-controlled Fracture Intervention Trial (FIT) (21). Among patients with ≥ 1 baseline radiographic vertebral fracture, Alendronate significantly reduced the risk of recurrent vertebral fracture, symptomatic vertebral fracture, hip fracture, and distal radius fracture at 3 years. In a 4-year study conducted in patients with low bone mass but without a baseline radiographic vertebral fracture, Alendronate resulted in significant reductions in risk of new vertebral fracture and any symptomatic fracture (22). The risk of clinical vertebral fracture, hip fracture, or distal radius fracture was not reduced significantly in this patient population. In a combined analysis of the US and multinational 3-year studies (which included patients with or without baseline vertebral fracture), there was a statistically significant reduction in fractures among those who were treated with Alendronate and had ≥ 1 vertebral fracture (20). Among women ≥ 6 months postmenopausal, Alendronate prevented bone loss in the majority of patients at the spine, hip, and total body and reduced the rate of bone loss at the forearm by approximately 50%. Use of 70 mg Alendronate weekly has been associated with the same increases in bone density and reduction in bone turnover markers that are seen with daily 10 mg dosing.

Risedronate

Risedronate sodium (5 mg daily and 35 mg weekly) is indicated for the treatment and prevention of osteoporosis in postmenopausal women (table 3) (23). For the treatment of osteoporosis, Risedronate is indicated to increase BMD and reduce the incidence of vertebral fractures and a composite of nonvertebral osteoporosis-related fractures. For the prevention of osteoporo-

Table 3. Bisphosphonates.

	Indication	Dosage ⁺	Note for All Bisphosphonates
Alendronate*	Prevention and treatment of osteoporosis in postmenopausal women	Prevention: 5 mg/day or 35 mg/wk Treatment: 10 mg/day or 70 mg/wk	With all bisphosphonates, failure to follow dosing guidelines may result in increased risk of gastrointestinal side effects and suboptimal absorption; contraindicated in patients with swallowing abnormalities or who cannot remain upright after dosing
Ibandronate**	Prevention and treatment of osteoporosis in postmenopausal women	Prevention and treatment 150 mg/mo	
Risedronate***	Prevention and treatment of osteoporosis in postmenopausal women	Prevention and treatment: 5 mg/day or 35 mg/wk	

Adapted from manufacturer prescribing information for individual drugs (20,24), and Am J Med (27).

+ All bisphosphonates should be taken on an empty stomach, first thing in the morning, with 8 oz of water (no other liquid), \geq 30 minutes before (Ibandronate 1 hour before) eating or drinking. Patients should remain upright (sitting or standing) during this interval.

* Fosamax; Merck & Co., Inc., Whitehouse Station, NJ.

** Boniva or Bonviva; Roche Laboratories, Inc., Nutley, NJ.

*** Actonel; Aventis Pharmaceuticals, Inc., Kansas City, Mo.

sis, Risedronate is indicated to maintain bone mass and reduce risk of fracture in women at risk for osteoporosis. Risedronate is also indicated for the prevention and treatment of glucocorticoid-induced osteoporosis and for Paget's disease (23).

To date, 4 studies have assessed the effect of Risedronate on BMD. Daily Risedronate is associated with increases in BMD at the spine, hip, and distal radius as compared with placebo (23). An additional study demonstrated the therapeutic equivalence of Risedronate 35 mg once weekly in increasing BMD over 1 year (23).

The efficacy of once-daily Risedronate in reducing fracture was examined in 2 similar randomized, placebo-controlled, double-blind studies that enrolled approximately 4,000 postmenopausal women with radiographic evidence of previous vertebral fractures (23). Treatment with once-daily Risedronate resulted in significant reductions in the risk of new and worsening fractures together (33% to 49% relative risk reduction after 3 years) and new fractures alone (41% to 49% relative risk reduction after 3 years). In these trials, daily Risedronate significantly reduced the incidence of nonvertebral osteoporosis-related fractures over 3 years (39% relative risk reduction) and reduced nonvertebral fracture incidence from 16% to 11%. When the studies were combined, there was an overall

36% reduction in relative risk. In a subanalysis of these studies, patients who received Risedronate had a significantly smaller loss of height than in those who received placebo (23).

Ibandronate

Ibandronate sodium (2.5 mg once daily or 150 mg once monthly) is indicated for the prevention and treatment of osteoporosis in postmenopausal women (table 3) (24-26). In the treatment of osteoporosis, Ibandronate is indicated to reduce the incidence of vertebral fractures. Ibandronate is also indicated to maintain bone mass and reduce the risk of fracture in postmenopausal women at risk for osteoporosis (24).

The efficacy of Ibandronate in treating postmenopausal osteoporosis was assessed in a randomized, double-blind, placebo-controlled study conducted in women with osteoporosis and 1 to 4 prevalent vertebral fractures (24). Oral daily (2.5mg) or intermittent Ibandronate (between-dose interval of > 2 months), delivering a similar cumulative exposure, were evaluated in 2,946 osteoporotic women with prevalent vertebral fracture. Significant reduction in incident vertebral fracture risk by 62% and 50%, respectively, was shown after 3 years. Ibandronate significantly reduced the incidence of new vertebral fracture by compared with placebo, but it did not have an

effect on nonvertebral osteoporotic fractures. Ibandronate was shown to significantly increase BMD at the lumbar spine, total hip, femoral neck, and trochanter compared with placebo. Ibandronate 150 mg once monthly was shown not only to be comparable to the 2.5 mg daily dosage in terms of bone density gains and bone turnover reductions but actually to have significantly greater effects than daily Ibandronate after 2 year of treatment (26).

Bisphosphonate dosing

The oral bioavailability of bisphosphonates is low, ranging from 0.6 to 3% of the ingested dose. When dosing recommendations are followed, the safety profile of bisphosphonates is generally favorable. Upper gastrointestinal discomfort (e.g., heartburn, dyspepsia, and abdominal pain) is the most common adverse events. Esophagitis has been reported with Alendronate (20). A vague myalgic syndrome also occurs infrequently. Of particular concern are recent reports of osteonecrosis of the jaw among patients receiving bisphosphonates (28). However, it should be noted that the majority of these patients (87%) were receiving high-dose intravenous bisphosphonates, either Zoledronate (31%) or Pamidronate (57%) (28) for indications other than osteoporosis (e.g., breast cancer, multiple myeloma).

Bisphosphonates have unique and relatively complicated dosing requirements (table 3). In order to achieve optimum absorption and tolerability, these guidelines must be followed closely. Patients should take their pill with a full glass of plain water and avoid food and beverages for ≥ 30 minutes after morning dosing (60 minutes for Ibandronate). Importantly, patients must remain upright for ≥ 30 (Alendronate and Risedronate) or ≥ 60 (Ibandronate) minutes. Failure to follow these guidelines increases the risk of esophageal side effects and reduces absorption of the medication (20,23,24).

Both Alendronate and Risedronate are available in once-weekly formulations. Ibandronate is available as a once monthly formulation. The more intermittent dosage regimens have efficacy and tolerability similar to that of the corresponding daily formulations with regard to surrogate markers, bone mineral density and bone turnover markers (28,29). Once-weekly or once-monthly regimens may improve compliance and persistence with medication by increasing convenience, reducing pill burden, and lowering dosing frequency (32,33).

SERMS, teriparatide, calcitonin and estrogens

Raloxifene (60 mg once daily) is the only SERM currently approved for the prevention and treatment of

osteoporosis (table 4). It acts as an estrogen agonist on bone and lipid metabolism and as an estrogen antagonist in the breast and endometrium (34). Raloxifene is effective in preventing postmenopausal bone loss and reducing the risk of vertebral fractures by 30% in patients with prevalent vertebral fractures and 50% in patients without a prior vertebral fracture over 3 years (35). Reduction of nonvertebral fractures has not been demonstrated.

Raloxifene is taken daily. Its nonskeletal effects include reductions in serum lipids and, in cross sectional studies, a 76% reduction in the risk of breast cancer in women with osteoporosis ($p < 0.001$) (36). Very recent results of the STAR trial indicate that there is a significant reduction in invasive breast cancer incidence among women taking Raloxifene (see article by Diez-Perez). Raloxifene increases the risk of deep vein thrombosis and pulmonary embolism to a similar extent as hormone therapy (37).

Estrogen therapy

Although hormone therapy increases bone mass and reduces the risk of fracture in low-risk postmenopausal women, increases in the risk for breast cancer, stroke, thrombotic events, and cardiovascular disease associated with the combined use of conjugated equine estrogens and medroxyprogesterone acetate were shown in the Women's Health Initiative Trial to outweigh its skeletal benefit (table 4) (38,39). Although the effects of estrogen on fracture risk in women with osteoporosis have not been evaluated, the efficacy in an osteopenic population at lower risk argue for a positive effect on a higher risk population. Hormone therapy is not approved for the treatment of osteoporosis because the fracture data required by the US Food and Drug Administration (FDA) were never submitted.

Teriparatide

Teriparatide [PTH(1-34)] is the first 34 N-terminal amino acids of parathyroid hormone. PTH(1-34) is believed to contain in its sequence all the classical actions of the full length PTH(1-84) peptide. In a study of 1,637 postmenopausal women, a subcutaneous once-daily 20 mg dosage of the human recombinant form of teriparatide reduced the incidence of new vertebral fractures in postmenopausal women by 65% (40). Compared with placebo, teriparatide also resulted in a 53% reduction in the risk of new nonvertebral fracture after a mean of 18 months of therapy (41).

Teriparatide is approved for administration as a once-daily 20-mg subcutaneous injection for ≤ 2 years (table 4). Teriparatide is associated with only minor

Table 4. Raloxifene, teriparatide, and calcitonin.

	Indications	Dosage	Notes
Raloxifene	Prevention and treatment of postmenopausal osteoporosis	60 mg/day	<ul style="list-style-type: none"> • May reduce risk of breast cancer; improves lipids • Associated with increased risk of deep vein thrombosis and pulmonary embolism
Teriparatide*	Treatment of osteoporosis in postmenopausal women at high risk for fracture	20 µg/day (subcutaneous injection)	<ul style="list-style-type: none"> • Teriparatide given to rats for most of their lifetime caused some rats to develop a form of bone cancer • Use of the drug for > 2 years not recommended
Calcitonin	Treatment of postmenopausal osteoporosis in women who have been menopausal for ≥ 5 yr	200 IU/day intranasally; alternate nostrils daily	<ul style="list-style-type: none"> • Generally safe; patients may experience rhinitis or epistaxis
Certain estrogens	Prevention of postmenopausal osteoporosis	Various doses and regimens	<ul style="list-style-type: none"> • Increased risk of thrombosis and stroke

Adapted from National Osteoporosis Foundation (3), JAMA (36), Cancer Res Treat (37), Eli Lilly, Company (40), N Engl J Med (41), Novartis Pharmaceutical Corp. (42), and Am J Med (27).

* Forteo; Eli Lilly and Company, Indianapolis, IN.

side effects, including nausea and headache. Hypercalcemia is usually mild and transient (41). High doses of teriparatide have been shown to cause osteosarcoma in rats; however, long-term clinical studies have not demonstrated an increased frequency of tumors in bone or other tissues in humans (40).

Calcitonin

Calcitonin is a peptide produced by thyroid C cells that inhibits bone resorption by inhibiting osteoclast activity (34). Salmon calcitonin is FDA-approved for the treatment of osteoporosis in women who have been postmenopausal for ≥ 5 years. It is usually delivered as a daily intranasal spray that provides 200 IU of the drug (table 4). Although nasal calcitonin is approved for the treatment of osteoporosis, the effect of nasal calcitonin on fracture risk is not stated in its prescribing information (42). One trial (43) showed that the intranasal formulation reduced vertebral fracture by 33% to 36%, but an effect on nonvertebral or hip fracture risk was not observed (43,44). Calcitonin is generally considered safe, although some patients experience rhinitis and, rarely, epistaxis (3).

SUMMARY

Osteoporosis is a major public health problem. Fractures may have a profound impact on quality of life.

Many patients who sustain a hip fracture do not regain full mobility, often requiring nursing home care. Postmenopausal women should therefore be screened for osteoporosis risk factors and have their BMD tested, if indicated, in accordance with current guidelines. Knowledge of a patient's BMD helps physicians in diagnosing osteoporosis, making the decision to treat, and in monitoring treatment effects.

Primary care providers are ideally placed to assess their patients' risk for fracture. The data summarized in this review confirm that a variety of effective, well-tolerated treatments for osteoporosis provide fracture risk reduction over and above risk reduction with calcium and vitamin D alone. Two keys to reducing fracture rate are first to target treatment to patients who are at increased risk of fracture and then to develop strategies to improve compliance. In this latter regard, weekly and monthly dosing of bisphosphonates would appear to have advantages over daily dosing regimens.

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