



## OSTEOPOROSIS CASE STUDY

### Postmenopausal Osteoporosis: 60-Year-Old Postmenopausal Caucasian Woman

A 60-year-old postmenopausal Caucasian woman is seeing you for her annual checkup. She has been in good general health for the past several years.

## Case Study 2

She experienced menopause in her early 50s and initiated hormone therapy (HT) with estrogen/progestin to relieve menopausal symptoms; she has been on HT primarily for the prevention of osteoporosis. She has no other chronic conditions.

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Older postmenopausal women who have been on long term hormone therapy since menopause to prevent osteoporosis are faced with the decision of changing their therapy in light of the results of the Women's Health Initiative trial and new professional guidelines. Their risk factors for osteoporosis and fracture need to be evaluated together with their bone mineral density. Effective treatment options are available for the prevention of bone loss and the treatment of osteoporosis.

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Address questions about the content of this CME Program to:

R. Mark Evans, PhD  
American Medical Association  
515 North State Street  
Chicago, IL 60610  
[mark\\_evans@ama-assn.org](mailto:mark_evans@ama-assn.org)

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American Medical Association  
515 North State Street  
Chicago, IL 60610  
[cmeorders@ama-assn.org](mailto:cmeorders@ama-assn.org)

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### CME Needs Assessment

A recent report, Bone Health and Osteoporosis, from the US Department of Health and Human Services' Surgeon General, stressed that despite the tremendous potential that we now have in a new era of bone health, the bone health status of America continues to be in jeopardy.<sup>1</sup> An estimated 30 million American women have osteoporosis or low bone mass, and this number is expected to increase dramatically as the population ages. Each year, approximately 1.5 million fractures are attributed to osteoporosis, with the lifetime risk of fracture increasing with age.

Results from the National Osteoporosis Risk Assessment (NORA) study suggest that a significant number of women in the US have undetected low bone mineral density (BMD). This longitudinal study evaluated more than 200,000 postmenopausal women with no prior osteoporosis diagnosis. Data on these women were retrieved from more than 4000 primary care practices in 34 states. According to the World Health Organization criteria, nearly 40% of NORA participants had low bone mass and 7% had osteoporosis. Increasing age was most highly correlated with low BMD.<sup>2</sup> In another study, data from the National Ambulatory Care Survey from 1993 to 1997 were analyzed in an effort to find evidence of osteoporosis and to assess primary care physicians' diagnosis of osteoporosis and vertebral fracture and their treatment. During the 5 years of the study, fewer than 2% of primary care physicians (family physicians, general practitioners, internists, obstetricians and gynecologists) diagnosed osteoporosis or vertebral fracture. Further analysis revealed that appropriate drug therapy was offered to only 36% of patients diagnosed with osteoporosis.<sup>3</sup>

This program reviews the criteria for initiating treatment in postmenopausal women, as well as pharmacologic and nonpharmacologic management options. Studies show that many physicians continue to fail to diagnose and treat postmenopausal osteoporosis—even in older patients who have suffered a fracture.<sup>2,3</sup> And even when therapy is suggested, evidence-based recommendations may not be followed. To help bridge this gap between current knowledge and its application in patient care, this continuing medical education module presents the current state of postmenopausal osteoporosis management for primary care physicians that is based on professional guidelines and evidence from clinical trials.

### Intended Audience

This continuing medical education program is intended for primary care physicians and those physicians who treat osteoporosis.

### Educational Objectives

After completion of this program, physicians should be able to:

- Describe the considerations in altering the management of a postmenopausal woman who has been receiving hormone therapy.
- Explain nonpharmacologic measures to reduce fracture risk and bone loss.
- Describe pharmacologic options when switching therapy

## OSTEOPOROSIS CASE STUDY

Postmenopausal Osteoporosis: 60-Year-Old Postmenopausal Caucasian Woman

### Patient History

A 60-year-old postmenopausal Caucasian woman is seeing you for her annual checkup. She has been in good general health for the past several years. She experienced menopause in her early 50s and initiated hormone therapy (HT) with estrogen/progestin for her menopausal symptoms; she has remained on HT primarily for prevention of osteoporosis. She is currently not on any chronic medications other than HT.

Although the patient has no personal history of fractures, her older sister experienced a hip fracture. She is 5'7" and weighs 112 lbs. She smokes cigarettes, drinks several cups of coffee a day, and rarely exercises. Her height has remained stable over the past 4 years.

Given the publicity surrounding the results of the Women's Health Initiative (WHI) on estrogen/progestin and estrogen alone, she expresses concern about the risk/benefit of her continued use of HT.

### Future Fracture Risk

#### What is this patient's risk of a future fracture?

Although she does not have a personal history of fracture, she does have other risk factors for osteoporotic fracture. Advancing

age itself is a significant risk factor for fracture and in addition to, her risk profile includes female gender, Caucasian race, lack of exercise, current cigarette smoking, and low body weight (5'7", 112 lbs). Her family history of an older sister with hip fracture

**Table 1. Major Risk Factors for Osteoporosis and Related Fractures in Caucasian and Postmenopausal Women**

- Personal history of fracture as an adult
- History of fragility fracture in a first-degree relative
- Low body weight (< about 127 lbs)
- Current smoking
- Use of oral corticosteroid therapy for more than 3 months

#### **Additional Risk Factors**

- Impaired vision
- Estrogen deficiency at an early age (<45 years)
- Dementia
- Poor health/frailty
- Recent falls
- Low calcium intake (lifelong)
- Low physical activity
- Alcohol in amounts >2 drinks/day

Reprinted with permission from the National Osteoporosis Foundation Physician's Guide to Prevention and Treatment, 2003.

**Table 2. Recommendations for Measuring BMD in Women for Assessing Risk of Fracture**

#### **National Osteoporosis Foundation**

- All women aged 65 and older regardless of risk factors
- Younger postmenopausal women with 1 or more risk factors, other than being white, postmenopausal, and female
- Postmenopausal women who present with fractures (to confirm diagnosis and determine disease severity)

#### **US Preventive Services Task Force**

- All women 65 years of age and older should be screened routinely for osteoporosis.
- Routine screening beginning at 60 years of age for women at increased risk for osteoporotic fractures.

The USPSTF makes no recommendation for or against routine osteoporosis screening in postmenopausal women who are younger than 60 years of age or in women 60 to 64 years of age who are not at increased risk for osteoporotic fractures.

#### **International Society for Clinical Densitometry\***

- Women 65 years of age and older
- Postmenopausal women under 65 years of age with risk factors
- Men aged 70 years and older
- Adults with a fragility fracture
- Adults with a disease or condition associated with low bone mass or bone loss
- Adults taking medications associated with low bone mass or bone loss
- Anyone being considered for pharmacologic therapy
- Anyone being treated, to monitor treatment effect
- Anyone not receiving therapy in whom evidence of bone loss would lead to treatment

†The decision to test for BMD should be based on an individual's risk profile, and testing is never indicated unless the results are likely to influence a treatment decision.

\*Risk factors include parental history of hip fracture, current cigarette smoking, a body weight <127 lbs., use of (or plans to use) oral glucocorticoids longer than 3 months, or serious long-term conditions thought to increase fracture risk, such as hyperthyroidism or malabsorption.

Sources: Physician's Guide to Prevention and Treatment of Osteoporosis. 2nd ed. Washington, DC: National Osteoporosis Foundation; 2003. and Position statement: executive summary. The Writing Group for the International Society for Clinical Densitometry (ISCD) Position Development Conference. *J Clin Densitom.* 2004;7:7-12. and Screening for osteoporosis in postmenopausal women: recommendations and rationale. *Ann Intern Med.* 2002;137:526-528.

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also increases this patient's risk of osteoporotic fracture. These are risk factors for osteoporosis, identified by the NOF as key factors in determining the risk of hip fracture—independent of BMD (Table 1).<sup>4</sup>

### Clinical Evaluation

#### How should this patient be evaluated?

A physical exam was performed, with no abnormalities noted. Measurement of the patient showed no loss of height over the last several years. Assessment of her caloric, vitamin D and calcium intake is consistent. Given the patient's age, risk factor profile for fractures, and her willingness to consider treatment for osteoporosis, it would be appropriate to obtain a BMD measurement. Most expert guidelines recommend BMD testing in all postmenopausal women under age 65 who have one or more additional risk factors for osteoporotic fracture (Table 2).

#### BMD Testing Results

A BMD test performed on this patient revealed a left hip T-score of -1.5. A hip T-score of -1.5 is considered borderline-low, and therefore, should prompt consideration of other medical conditions that may be contributing to her bone loss, since this patient has been on HT for several years. Laboratory results revealed normal CBC and serum chemistries, with a slightly elevated urinary calcium excretion. Serum thyrotropin, serum 25-hydroxyvitamin D, and urinary-free cortisol values were all within the normal reference range. Based on the lab results, no secondary causes for low BMD were identified.

This patient has low BMD or osteopenia; her additional risk factors increase her risk for future osteoporotic fracture.

### Preventive Strategies

#### What preventive strategies should be recommended for this patient?

This woman should be encouraged to quit smoking, since cigarette smoking is associated with increased catabolism of endogenous estrogen. Women smokers are typically more thin, undergo earlier menopause, and experience more fractures. The age-related bone loss that occurs in both men and women in the fifth decade of life and thereafter also appear to be accelerated among smokers.<sup>8-10</sup> She should remain cognizant of the recommended daily intake of 1200 mg/d to 1500 mg/d of calcium and 400 IU of vitamin D. There are a variety of food sources of calcium (Table 3). The NOF has developed a useful guide to assist in estimating calcium intake (Table 4).

**Table 3. Selected Food Sources of Calcium**

Food	Amount (mg)	Percent DV
Yogurt, plain, low fat, 8 oz	415	42%
Yogurt, fruit, low fat, 8 oz.	245-384	25%-38%
Sardines, canned in oil, with bones, 3 oz.	324	32%
Cheddar cheese, 1 ½ oz shredded	306	31%
Milk, non-fat, 8 fl oz.	302	30%
Milk, reduced fat (2% milk fat), no solids, 8 fl oz.	297	30%
Milk, whole (3.25% milk fat), 8 fl oz	291	29%
Milk, buttermilk, 8 fl oz.	285	29%
Milk, lactose reduced, 8 fl oz.**	285-302	29-30%
Mozzarella, part skim 1 ½ oz.	275	28%
Tofu, firm, made w/calcium sulfate, ½ cup***	204	20%
Orange juice, calcium fortified, 6 fl oz.	200-260	20-26%
Salmon, pink, canned, solids with bone, 3 oz.	181	18%
Pudding, chocolate, instant, made w/ 2% milk, ½ cup	153	15%
Cottage cheese, 1% milk fat, 1 cup unpacked	138	14%
Tofu, soft, made w/calcium sulfate, ½ cup***	138	14%
Spinach, cooked, ½ cup	120	12%
Instant breakfast drink, various flavors and brands, powder prepared with water, 8 fl oz.	105-250	10-25%
Frozen yogurt, vanilla, soft serve, ½ cup	103	10%
Ready to eat cereal, calcium fortified, 1 cup	100-1000	10%-100%
Turnip greens, boiled, ½ cup	99	10%
Kale, cooked, 1 cup	94	9%
Kale, raw, 1 cup	90	9%
Ice cream, vanilla, ½ cup	85	8.5%
Soy beverage, calcium fortified, 8 fl oz.	80-500	8-50%
Chinese cabbage, raw, 1 cup	74	7%
Tortilla, corn, ready to bake/fry, 1 medium	42	4%
Tortilla, flour, ready to bake/fry, one 6" diameter	37	4%
Sour cream, reduced fat, cultured, 2 Tbsp	32	3%
Bread, white, 1 oz	31	3%
Broccoli, raw, ½ cup	21	2%
Bread, whole wheat, 1 slice	20	2%
Cheese, cream, regular, 1 Tbsp	12	1%

\*DV=Daily Value

\*\*Content varies slightly according to fat content; average =300 mg calcium

\*\*\* Calcium values are only for tofu processed with a calcium salt.

Tofu processed with a non-calcium salt will not contain significant amounts of calcium.

Daily Values (DV) were developed to help consumers determine if a typical serving of a food contains a lot or a little of a specific nutrient. The DV for calcium is based on 1000 mg.

Understanding Osteoporosis. Chicago, IL: American Medical Association; 2000.

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### Calcium Supplements

Calcium supplements (Table 5) are another option for ensuring adequate daily requirements. These supplements (especially calcium carbonate) should be taken with food if possible, because the acid load of the meal enhances absorption. However, calcium citrate is absorbed reasonably well on an empty stomach.<sup>11</sup> Refined preparations are preferred, since these contain low levels of lead and other contaminants. A dose of calcium before bedtime may help reduce PTH levels at night; however, controlled clinical trials comparing calcium at bedtime to calcium during waking hours have not been done. If more than 500 mg/d is used, the dosage should be split to increase absorption. Calcium preparations should be taken in divided doses, since only about 500 mg of calcium can be absorbed at a time.

### Vitamin D Supplementation

The generally recommended daily dose of vitamin D is 400 IU to 800 IU. Although vitamin D is present in fortified milk, the actual amount may be quite variable. Food sources of vitamin D are provided in Table 6.

Fish oils, like cod liver oil, contain vitamin D, but are not generally recommended and may provide toxic levels of vitamin A if taken in large quantity. For elderly women, 800 IU/d is recommended and

can be taken twice daily in 400 IU doses. Sunlight may provide reasonable amounts of vitamin D in southern latitudes, but the amount absorbed is highly variable depending on the season, latitude, and use of sunscreens. While this patient is not vitamin D deficient, it should be kept in mind that patients who are either vitamin D insufficient or deficient require treatment with higher doses of vitamin D. Severe cases of vitamin D deficiency can lead to osteomalacia or rickets. Patients can be treated with 50,000 IU once a week for up to 3 months with follow-up blood tests of vitamin D, calcium and PTH levels; some patients may require longer courses of treatment.<sup>12</sup> Over-the-counter preparations of vitamin D are in the form of vitamin D<sub>2</sub> (ergocalciferol) and D<sub>3</sub> (cholecalciferol). The potent active metabolite produced by the kidney, calcitriol (1,25-dihydroxyvitamin D) is available as a prescription product and has FDA-approved indications for the management of hypocalcemia and metabolic bone disease in patients undergoing chronic renal dialysis or with hyperparathyroidism. Calcitriol has also been used to treat secondary osteoporosis. Because it has been associated with hypercalcemia and hypercalciuria, calcitriol is not routinely used for postmenopausal osteoporosis.

### Weight-bearing Exercise

The importance of a regular weight bearing exercise program cannot be overemphasized. Adequate physical activity can

**Table 4. Estimating Daily Dietary Calcium Intake**

Step 1: Estimate calcium intake from calcium rich foods*			
Product	No. of Servings/Day	Calcium Content per Serving, mg	Calcium, mg
Milk (8 oz)	_____ X	300	= _____
Yogurt (8 oz)	_____ X	400	= _____
Cheese (1 oz)	_____ X	200	= _____
Fortified foods or juices	_____ X	80 – 1000**	= _____
Step 2: Total from above +250 mg from nondairy sources = total dietary calcium			

\*About 75% to 80% of the calcium consumed in American diets is from dairy products.

\*\*Calcium content of fortified foods varies

Permission from the National Osteoporosis Foundation. Physician's Guide to Prevention and Treatment of Osteoporosis. 2nd ed. Belle Meade, NJ: Excerpta Medica Inc.;2003. <sup>5</sup>

**Table 5. Some Commonly Used Calcium Supplements**

Type	Brand Name	Strength per Tab (mgs)	Elemental Calcium
Calcium Carbonate	Alka Mints	850	340
	Caltrate	1600	600
	OsCal	625 or 1250	250 or 500
	Titralac	420	168
	Titralac Liquid	1000	400
	Tums/Tums E-X	500 or 750	200 or 300
	Tums Ultra/Tums 500	1000 or 1250	400 or 500
Calcium Citrate	Citrical Liquitabs	2376 mg/tab	500
	Citrical	950 mg/tab	200
	Citrical Caplets, +D	1500	315 + 200 IU vitamin D

Source: NIH Office of Dietary Supplements. Facts About Dietary Supplements - Vitamin D. *NIH Clinical Center* [Web site]. August 7, 2001. Available at: <http://www.cc.nih.gov/cc/supplements/vitd.html#food>. Accessed December 6, 2002.

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help reduce the risk of falls in older patients by increasing muscle balance and tone. Tai chi and other muscle toning exercises have been studied in the prevention and treatment of osteoporosis and may have value in preventing fractures related to falls. Swimming is a healthy exercise choice, but is not weight-bearing—the key factor in maintenance of bone density. Women with particularly low BMD may do water aerobics to improve strength without increasing their risk of fracture. Measures to prevent falls should be discussed with this patient.

### Fall Prevention

Given the patient's age, low BMD, and other risk factors for osteoporotic fracture, it is important to discuss approaches to reduce her risk of falling. The value of assessing the risk of falling, and intervening in those at high risk (e.g., those with pre-existing fragility fractures), is supported by randomized clinical trials in elderly patients.<sup>13</sup> In those with a pre-existing fragility fracture, fall prevention measures are useful. Over 90% of hip and wrist fractures are thought to be the result of a fall.<sup>14</sup> Elderly patients may be at risk for falling for a variety of reasons, including frailty and associated deconditioning, poor visual acuity, impaired hearing, and use of medications with neurologic effects that compromise protective neuromuscular reflexes (e.g., long-acting benzodiazepines).<sup>15</sup>

### Measures to Reduce Fall Risk

Review everyday environmental hazards and suggest measures to eliminate these potential causes of falls. The American Association of Clinical Endocrinologists recommends the following steps:<sup>15</sup>

- Minimize risk of falls with gait and balance training
- Adjust dosage of drugs with sedative effects, which could slow reflexes, decrease coordination, and impair the patient's ability to break the impact of a fall
- Anchor rugs
- Minimize clutter
- Remove loose wires
- Use nonskid mats
- Install handrails in bathrooms, halls, and along stairways
- Light hallways, stairwells, and entrances
- Encourage patient to wear sturdy, low-heeled shoes
- Hip protectors (in patients predisposed to falling)

## Treatment Options

### What treatment options can be offered?

This patient meets the criteria for pharmacological treatment.<sup>4,15</sup> This patient has been on HT since menopause to prevent osteo-

**Table 6. Selected Food Sources of Vitamin D**

Food	Amount (IU)	Percent DV
Cod liver oil, 1 Tbsp	1360	340
Salmon, 3 ½ oz cooked	360	90
Mackerel, 3 ½ oz cooked	345	90
Tuna fish, canned in oil, 3 oz	200	50
Sardines, canned in oil, drained, 1¼ oz	250	70
Milk, nonfat, reduced fat, and whole, vitamin D fortified, 1 cup	98	25
Margarine, fortified, 1 Tbsp	60	15
Pudding, prepared from mix and made with vitamin D fortified milk, ½ cup	60	15
Ready-to-eat cereals fortified with 10% of the DV for vitamin D, ¾ cup to 1 cup servings (servings vary according to the brand)	40	10
Egg, 1 whole (vitamin D is found in egg yolk)	20	6
Liver, beef, cooked, 3½ oz	15	4
Cheese, Swiss, 1 oz	15	4

\*DV = Daily Value. DVs are reference numbers developed by the Food and Drug Administration (FDA) to help consumers determine if a food contains a lot or a little of a specific nutrient. The DV for vitamin D is 400 IU (10 µg) for adults. Most food labels do not list vitamin D content unless a food has been fortified with this nutrient. The percent DV (%DV) listed on the table above tells you the percent of the DV provided in one serving. A food providing 5% of the DV or less is a low source while a food that provides 10-19% of the DV is a good source and a food that provides 20% or more of the DV is high in that nutrient. It is important to remember that foods that provide lower percentages of the DV also contribute to a healthful diet. Source: National Institutes of Health.

porosis. Her therapeutic options include continued HT, discontinuation of HT and initiation of a bisphosphonate, raloxifene, or intranasal calcitonin. Because there was no baseline BMD measurement performed at the initiation of her HT eight years ago, assessment of her current therapy could not be adequately evaluated. However, since she had indicated concern about remaining on HT, the risks and benefits of continuing HT and the significance of the results of the WHI trial should be discussed.

### Hormone Therapy

While randomized controlled studies and meta-analyses have demonstrated the effect of hormone therapy on BMD,<sup>16-18</sup> the Women's Health Initiative (WHI) confirmed for the first time the effects of combined continuous hormone therapy on osteoporotic fracture reduction at several sites, including the hip.<sup>19,20</sup> Hip and vertebral fractures decreased by at least one-third in both of the trials and total fractures decreased by 24%-30%. However, the clear fracture benefits of postmenopausal hormone therapy (HT) with conjugated equine estrogen (CEE)/ medroxyprogesterone acetate (MPA) or CEE alone are offset by the adverse effects (e.g., increased risk of stroke, cognitive impairment, and deep vein thrombosis) encountered in the women taking HT.<sup>21-23</sup> The WHI trials also found that HT provided no cardioprotective benefit, and increased the risk of breast cancer.

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### Recommendations on HT in Postmenopausal Women

This patient should be informed that there are a number of recommendations from a variety of professional and governmental organization on the use of HT in postmenopausal women. Medical professional groups include the American Association for Clinical Endocrinology and the American College of Obstetricians and Gynecologists. Governmental organizations include the FDA, the US Surgeon General, and the United States Preventive Services Task Force.

### USPSTF, Surgeon General and FDA Recommendations for Hormone Therapy

- After reviewing the most current risk/benefit data on HRT in postmenopausal women, the USPSTF recommended against the routine use of estrogen and progestin for the prevention of chronic conditions in this patient group.<sup>24</sup>
- The 2004 Surgeon General's report stated that any decision to use HT must take into consideration its impact on overall health outcomes, including not only its potential to reduce the risk of fractures, but also its potential to increase the risk of other health problems.<sup>1</sup>
- The FDA has advised that postmenopausal women who use or are considering using estrogen or estrogen with progestin discuss its benefits (e.g., relief from moderate to severe hot flashes and symptoms of vulvar and vaginal atrophy) and risks with their physicians.<sup>25</sup> Although HT is effective for the prevention of postmenopausal osteoporosis, it should only be considered for women at significant risk of osteoporosis who cannot take non-estrogen medications.

### American College of Obstetricians and Gynecologists Guidelines for Hormone Therapy

Recently, American College of Obstetricians and Gynecologists (ACOG) issued a state-of-the-art guide to hormone therapy<sup>26</sup> which reaffirmed many of its earlier recommendations issued following the WHI trials.

### ACOG Recommendations

- Combined hormone therapy should not be used for the prevention of diseases such as cardiovascular disease, due to the small but significant increased risk of conditions such as breast cancer, heart attack, stroke and blood clots;
- Estrogen-alone therapy, used for women who have had a hysterectomy, should also not be used for prevention of diseases, due to increased risks of blood clots and stroke. Although estrogen therapy carries fewer risks than combined HT, women with a uterus should not use estrogen alone due to their increased risk of uterine cancer;
- Hormone therapies are appropriate for the relief of vasomotor symptoms, so long as a woman has weighed the risks and benefits with her doctor;

- Women on combined hormone therapy or estrogen therapy should take the smallest effective dose for the shortest time possible and annually review the decision to take hormones.

The ACOG report noted that while hormone therapies should not be used solely for disease prevention, there are instances where disease prevention is appropriate as a secondary benefit for women already taking hormones for vasomotor symptoms, including its use in the prevention of osteoporosis.

### American Association of Clinical Endocrinologists Guidelines for Hormone Therapy

Finally, the updated 2003 American Association of Clinical Endocrinologists (AAACE) Guidelines state the following: "AAACE recommends against prescribing menopausal hormonal therapy to asymptomatic women to prevent or treat osteoporosis or for prevention of heart disease or other chronic medical problems."<sup>15</sup>

### Consideration of Low-dose Estrogen HT

It is not yet known if a short course of low-dose estrogen will provide long-term benefits for bone health will reducing the cardiovascular risks found in the WHI trial. Lower doses of estrogen (e.g., 0.3 mg CEE per day or even lower 14 mcg/d by transdermal patch) or combination hormones can help to preserve bone density in the short term in postmenopausal women.<sup>17,27</sup> Unfortunately, at this point, the long-term effects of lower doses, formulations (including estrogens or progesterone), and modes of administration (e.g., transdermal administration) on bone and other tissues have not been studied.

### Other treatment options that can be offered?

Because of her concern for the potential risks of HT, she elects to discontinue this course of therapy. Her decision to discontinue HT places her at risk for an increased rate of bone loss. Previous studies have shown that discontinuation of HRT in this age group can be associated with significant bone loss of up to 4% in the first year and continued accelerated bone loss.<sup>28</sup> Therefore, she should begin a proven alternative therapy to prevent bone loss and fractures, especially with her low BMD while on HT and her other risk factors for osteoporotic fracture.

Careful consideration should be given to other therapeutic options (Table 7) proven to prevent fractures, while weighing the risks and benefits of each. Antiresorptive therapy with a bisphosphonate, raloxifene, or intranasal calcitonin can be offered, in addition to vitamin D and calcium supplementation. Clinical trial data supports the enhancement of BMD and the antifracture benefit of these agents. A meta-analysis of all clinical trials of antiresorptive agents and calcium and vitamin D by the Osteoporosis Research Advisory Group (ORAG) showed that all these agents, including vitamin D (in those deficient), reduced the risk of vertebral fractures.<sup>29</sup>

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**Table 7. Labeled Indications and Dosage for Antiresorptive Therapies for the Prevention and Treatment of Osteoporosis**

Antiresorptive Therapy	Labeled Indication	Dose	Evidence for Vertebral Fracture Reduction	Evidence for Nonvertebral Fracture Reduction
<b>Bisphosphonates</b>				
Alendronate	<b>Prevention</b> Postmenopausal osteoporosis	5 mg/d or 35 mg weekly		
	<b>Treatment</b> Postmenopausal osteoporosis	10 mg/d or 70 mg weekly	Yes	Yes
	Men with osteoporosis	10 mg/d or 70 mg weekly		
	Glucocorticoid-induced osteoporosis in men and women	5 mg/d, 10 mg/d in postmenopausal women not receiving estrogen		
Ibandronate*	<b>Prevention</b> Postmenopausal osteoporosis	2.5 mg/d		
	<b>Treatment</b> Postmenopausal osteoporosis	2.5 mg/d	Yes	No
Risedronate	<b>Prevention</b> Postmenopausal osteoporosis	5 mg/d or 35 mg weekly		
	Glucocorticoid-induced osteoporosis in men and women	5 mg/d		
	<b>Treatment</b> Postmenopausal osteoporosis	5 mg/d or 35 mg weekly	Yes	Yes
	Glucocorticoid-induced osteoporosis in men and women	5 mg/d		
	<b>Calcitonin</b>			
	<b>Treatment</b> Postmenopausal osteoporosis (women >5 years postmenopausal)	Intranasal: 1 spray per day (200 IU/d) Injectable: SC or IM 100 IU/d	Yes	No
<b>Estrogen</b>				
Low Dose Transdermal	<b>Prevention</b> Postmenopausal osteoporosis in women at significant risk for osteoporosis	14 mcg/d	No	No
<b>SERMS</b>				
Raloxifene	Prevention Postmenopausal osteoporosis	60 mg/d		
	Treatment Postmenopausal osteoporosis	60 mg/d	Yes	No

\*FDA-approved, but not commercially available

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Bisphosphonate therapy (on the strength of prospective controlled clinical trials) has a broad spectrum of antifracture benefit and is a good choice to replace HT. Alendronate, risedronate, and ibandronate have an FDA-approved indication for the treatment and prevention of osteoporosis in postmenopausal women; however, ibandronate is not yet clinically available and is undergoing additional studies for a less frequent dosing schedule.

Raloxifene is also a reasonable choice of treatment. At this time, it has not been determined if these combinations of these agents reduce fracture risk greater than single-agent therapy. Combination therapy is generally reserved for patients who have experienced a fracture while on therapy with a single drug, those who start out with a very low BMD and a history of multiple fractures, and those with very low BMD who lose more bone mass on therapy with a single drug.<sup>1</sup>

This patient is not yet a candidate for anabolic therapy with teriparatide. Teriparatide or human recombinant parathyroid hormone (PTH 1-34) has FDA-approved labeling for the treatment of osteoporosis in postmenopausal women who are at high risk for fracture. These include women with a history of osteoporotic fracture, who have multiple risk factors for fracture, or who have failed or are intolerant to previous osteoporosis therapy. Unlike antiresorptive agents, teriparatide therapy stimulates new bone formation.<sup>30</sup>

Regardless what therapy is chosen, it is advisable that a follow-up BMD test be performed in 2 years after therapy is initiated to evaluate the effectiveness of treatment.

### Summary

The results of the WHI trial have influenced a postmenopausal patient with low BMD and risk factors for osteoporotic fractures to discontinue HT that she has been on for 8 years. Given the higher risk for venous thrombosis, myocardial infarction, stroke, or breast cancer over a 5-year period compared to the benefit of reduced fracture risk in this patient, professional guidelines would suggest other therapeutic options to reduce the risk of osteoporosis and fracture. Antiresorptive therapy with bisphosphonates or the selective estrogen receptor modulator raloxifene are reasonable alternatives, together with adequate daily calcium and vitamin D and an appropriate weight-bearing exercise program.

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