

The Relationship and Impact of Osteoporosis and Breast Cancer in Post-Menopausal Women

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Summary

Osteoporosis and breast cancer are two diseases that affect a large number of women. Because of the effects of estrogen on each, there are medications that can be used to treat osteoporosis and prevent breast cancer. Selecting which women would benefit the most from an agent for both diseases is not yet well defined.

Key Points

- There are effective medications to treat osteoporosis that have advantages and disadvantages.
- Biphosphonates, with the exception of ibandronate, have the best evidence for preventing fractures.
- Because of effects in bone and breast tissue, raloxifene should be considered for treatment of osteoporosis in women who have osteoporosis and are at high risk for breast cancer.
- Various levels of risk for breast cancer are not well defined.

OSTEOPOROSIS IS A SYSTEMIC SKELETAL disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. Bone strength reflects the integration of two main features: bone density and bone quality. Bone quality refers to architecture, turnover, damage accumulation (e.g., microfractures), and mineralization. The clinical outcome of concern is the increased risk of fracture.

Normal bone looks like a slice of Swiss cheese (Exhibit 1). Although there are holes in it, there is more cheese than holes. With osteoporosis, there are gaping holes; pieces seem to be missing altogether and others hang by only a thread. This leaves an architecturally weakened structure with significantly reduced mass. The World Health Organization defines osteoporosis as a bone mineral density (BMD)

For an American woman at age 50, the risk of suffering an osteoporotic fracture in her remaining lifetime has been estimated at 40 percent with 2/3 of the fractures occurring after age 75.²

at the hip or spine that is less than or equal to 2.5 standard deviations below the young normal mean reference population.¹

Osteoporosis is the most common bone disorder affecting humans.² Although osteoporosis can affect any bone, the hip, spine, and wrist are most likely to be affected. Osteoporosis affects an estimated 10 to 44 million Americans.^{3,4} Another 34 million Americans are estimated to have low bone mass, meaning that they are at an increased risk for osteoporosis and fractures.⁴

Of postmenopausal white women in the United States, approximately 21 percent have osteoporosis.² About one out of every two Caucasian women will experience an osteoporosis-related fracture at some point in her lifetime, as will approximately one in five men.² Although osteoporosis is less frequent in African Americans, those with osteoporosis have the same elevated fracture risk as Caucasians.

Unfortunately, it is estimated that less than one third of osteoporosis cases have been diagnosed.² Of the women who have been diagnosed, only one in seven receive treatment. Because of the aging population, 50 percent of Americans over age 50 will be at risk of fracture by 2020 if nothing is done.²

Exhibit 1



Bone constantly undergoes remodeling (Exhibit 2). Osteoclasts resorb damaged areas of bone creating resorption cavities. These cavities are filled with new bone (formation) by osteoblasts. This new bone is then mineralized by osteocytes. Thus, osteoporosis is a disorder of the remodeling process in which resorption significantly exceeds formation.

Men and women experience a protracted slow phase bone loss with aging. This process begins at around age 35 at a rate of 0.5 to 1 percent per year.² This slow phase of bone loss with aging is caused by decreased osteoblastic activity. Osteoclasts create resorption cavities of normal depth; however, the osteoblasts fail to refill them completely. Another contributor to this phase of bone loss is decreased gastrointestinal absorption of calcium with aging.

Women experience additional bone loss during a transient accelerated phase during the perimenopausal and menopausal phase of life. Bone loss begins to accelerate about two to three years before the last menses and begins to slow three to four years after menopause. During the accelerated phase, women can lose 2 percent of bone annually. Afterward, bone loss slows to 1 to 1.5 percent per year.

Normal bone mass is considered to be 90 to 100 percent of peak bone mass. Osteopenia, which is marked by thinning bone but intact microarchitecture, is 75 to 90 percent of peak bone mass. Patients with osteopenia have a slightly higher risk of fracture than someone with normal bone mass. Osteoporosis is less than 75 percent of peak bone mass. Patients with osteoporosis have a high risk of fracture.

The three most common sites of osteoporosis-related fractures are wrist, vertebra, and hip.³ More than 250,000 wrist fractures occur annually. Many times, these fractures are the result of a patient trying to break a fall. A wrist fracture is a warning of cortical bone loss. Vertebral fractures are most likely to occur between 50 and 70 years of age. Greater

Exhibit 2: Postmenopausal Osteoporosis Treatment Guidelines

- **North American Menopause Society**
– Menopause. 2006;13:340-367.
- **American College of Physicians**
– Ann Intern Med. 2008;149:404-15.
- **American Association of Clinical Endocrinologists**
– 2003, Endocrine Practice. 2003;9:544-64.
- **National Osteoporosis Foundation**
– 2008, www.nof.org.

Reference: 2,4,7,8

than 700,000 vertebral fractures occur annually and are associated with significant pain and deformity. Two or more vertebral fractures are likely to disable a woman or limit her physical activities for greater than 30 days per year.

Hip fractures, more accurately fractures of the proximal femur, have an annual incidence of more than 250,000.⁵ They are the primary cause of morbidity, mortality and cost related to osteoporotic fractures. The median age of first-time hip fracture is 82 years of age. A woman's lifetime risk of fracturing her hip is equal to her risk of breast, ovarian, and uterine cancers combined. About 20 percent of patients who have a hip fracture do not survive one year, 20 percent do not regain the ability to walk without assistance, and 30 percent require long-term care.⁵ Other skeletal sites are not immune to bone loss, thus can fracture. An estimated 300,000 of these other sites are fractured annually.⁵

Osteoporosis-related fractures create a heavy economic burden, causing more than 432,000 hospital admissions, almost 2.5 million medical office visits and about 180,000 nursing home admissions annually in the United States.⁶ The cost to the health care system associated with osteoporosis-related fractures has been estimated at \$17 billion for 2005; hip fractures account for 14 percent of incident fractures and 72 percent of fracture costs.⁶ Due to the aging population, the Surgeon General estimates that the number of hip fractures and their associated costs could double or triple by the year 2040.²

There are effective pharmacologic agents for preventing and treating osteoporosis. The focus of this discussion is treatment of postmenopausal osteoporosis. Several national organizations have published evidence-based guidelines on managing postmenopausal disease (Exhibit 2).^{2,4,7,8}

According to the National Osteoporosis Foundation (NOF) guidelines, postmenopausal women and

Exhibit 3: Fracture Risk Reduction

	Vertebral Fractures	Non-spine Fractures	Hip Fractures
Alendronate	↓,strong evidence	↓,strong evidence	↓,strong evidence
Ibandronate	↓,strong evidence	↔,strong evidence	Not studied
Risedronate	↓,strong evidence	↓,strong evidence	↓,strong evidence
Zoledronic acid	↓,strong evidence	↓,strong evidence	↓,strong evidence
Calcitonin	↓,fair evidence	↔,strong evidence	Not studied
Raloxifene	↓,strong evidence	↔,strong evidence	↔,strong evidence
Teriparatide	↓,strong evidence	↓,fair evidence	↔,weak evidence

Decrease: ↓
No effect: ↔

Reference: 4

men age 50 and older presenting with a hip or vertebral fracture, T score of -2.5 at the femoral neck or spine after appropriate evaluation to exclude secondary causes, or low bone mass (T-score between -1.0 and -2.5 at the femoral neck or spine) and a 10-year probability of a hip fracture of 3 percent or a 10-year probability of a major osteoporosis-related fracture of 20 percent based on the U.S.-adapted WHO algorithm should be considered for treatment.³ Unfortunately, waiting until a fracture occurs to treat means a patient has already lost a significant amount of bone. Appropriate screening using BMD testing should be used to identify those patients with osteoporosis or osteopenia.

All patients with osteoporosis should receive adequate calcium and vitamin D. For patients to get maximum benefit from the prescription medications, which will be discussed later, they should be getting at least 1200 mg of elemental calcium daily and 800 to 1,000 IU vitamin D daily.³ Because calcium and vitamin D supplements are typically available over the counter, it may be difficult for a managed care plan to determine if patients are achieving this goal.

Although calcium and vitamin D are necessary for bone health, supplementation by itself is insufficient therapy to prevent osteoporosis-related fractures. This was demonstrated in a seven-year study, which was part of the Women's Health Initiative. In 36,282 postmenopausal women, aged 50 to 79, 1000mg calcium carbonate with 400 IU vitamin D daily resulted in small but significant increases in bone min-

eral density but did not significantly reduce risk of hip fracture.⁹

The prescription medications for treating osteoporosis are divided into two categories: formation stimulating agents and antiresorptive agents. Formation stimulating agents primarily affect osteoblasts and increase bone formation. Newly formed bone either overfills resorption cavities or is laid down on surfaces not previously resorbed. The one currently available agent, teriparatide (Forteo[®]), is a synthetic form of parathyroid hormone (PTH).

Teriparatide is typically reserved for women and men with the severest disease or who have failed or are intolerant of previous osteoporosis therapy. This agent is reserved for those with the most severe disease because of the potential adverse effect of osteosarcoma, the requirement for daily self-injection, and cost. Although no cases of osteosarcoma have been reported in humans, the medication carries a black box warning about this potential and the treatment period is limited to two years.

Antiresorptive agents' major actions are to suppress bone resorption preventing further bone loss, decrease the number or depth of resorptive sites, stop further architectural loss, and slow bone turnover to allow better mineralization. These agents can increase BMD by 2 to 8 percent, but the resulting increase in BMD appears to be due to more complete mineralization rather than increased synthesis of bone. Because older adults generally lose 0.5-1 percent of their BMD per year, these medications are preventing this loss. Antiresorptive agents,

Exhibit 4

	Administration	Major adverse effects	Estimated retail cost for 30 day supply*
Alendronate	Oral, daily or weekly, available as solution and in combination with vitamin D	esophageal irritation or erosion; bone, joint and/or muscle pain; hypocalcemia; osteonecrosis	\$81.85 (4 x 70 mg)
Ibandronate	Oral, daily or monthly; IV, quarterly		\$104 (30 x 2.5 mg)
Risedronate	Oral, weekly combo with calcium		\$104 (1 x 150 mg)
Zoledronic acid	Once yearly infusion	bone, joint and/or muscle pain; hypocalcemia; osteonecrosis	\$108 (\$1,300 per infusion)
Calcitonin	Daily nasal spray	rhinitis; nasal crusts, sores, bleeding; arthralgia	\$102 – 131 (per bottle)
Raloxifene	Oral, daily	hot flashes, venous thrombo-embolic events (PE, DVT)	\$112 (30 x 60 mg)
Teriparatide	Daily subcutaneous injection	leg cramps, dizziness, ?osteosarcoma	\$900 (1 syringe)

PE, pulmonary embolism; DVT, deep vein thrombosis

*Based on the dosage strength and number of units shown. Generic product used where available.

Pricing data from www.blueshieldca.com and www.drugstore.com

which are FDA approved for treatment of osteoporosis include the bisphosphonates (alendronate [Fosamax[®], generic], ibandronate [Boniva[®]], risedronate [Actonel[®]], zoledronic acid [Reclast[®]]), salmon-calcitonin [Fortical[®], Miacalcin[®]], and raloxifene [Evista[®]]. Hormone replacement therapy (HRT) with estrogen or the combination of estrogen and progesterone is another antiresorptive therapy but is only indicated for prevention of osteoporosis. Because the demonstrated risks appear to exceed the benefits, hormone replacement therapy is not indicated for treatment and preventive use should be carefully considered.¹⁰

Estrogen does play a role in bone health. It acts on both osteoclasts and osteoblasts to inhibit bone breakdown at all stages of life and also may stimulate bone formation. The Woman's Health Initiative (WHI) study found that five years of HRT reduced the risk of clinical vertebral fractures and hip fractures by 34 percent, and other osteoporotic fractures by 23 percent.¹¹ This study reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein phlebitis during five years of treatment with combined conjugated equine estrogen and medroxyprogesterone (Prempro[®]). Subsequent analysis of these data showed no increase in cardiovascular disease in

women starting treatment within 10 years of menopause.¹² In the estrogen only arm of WHI, no increase in breast cancer incidence was noted over 7.1 years of treatment.¹¹

In selecting pharmacologic therapy for osteoporosis treatment, there are differences among the available agents. Selection of therapy depends on efficacy data, side effect profile, risk versus benefit assessment, confounding diseases, cost, patient preference, and individual characteristics such as magnitude of fracture risk, over-all health, and age.

Exhibit 3 summarizes the efficacy data for the various agents for treatment of osteoporosis.⁴ In general, the strongest efficacy data are available for the bisphosphonates (ibandronate is the exception). Good-quality evidence has shown they decrease the risk of vertebral, hip, and non-vertebral fracture. Ibandronate has not been shown to reduce non-vertebral fractures. Raloxifene has been shown to reduce vertebral fractures but has no effect on non-vertebral and hip fractures. Good-quality evidence shows that teriparatide prevents vertebral fractures. The evidence related to teriparatide preventing non-vertebral fractures is mixed. Fair-quality evidence shows that calcitonin reduces vertebral fractures. Good-quality evidence indicates that calcitonin does not reduce non-vertebral fractures.

Exhibit 5: A woman's chance of being diagnosed with breast cancer

- **Age 30-39:** 0.43 percent (often expressed as 1 in 233)
- **Age 40-49:** 1.44 percent (1 in 69)
- **Age 50-59:** 2.63 percent (1 in 38)
- **Age 60-69:** 3.65 percent (1 in 27)

- **Lifetime Risk:** 12.03 percent (1 in 8)

Reference: 15

Another difference in these agents is their administration (Exhibit 4). They are available as oral tablets for daily, weekly, and monthly oral dosing, subcutaneous daily self-injection, nasal spray, quarterly intravenous infusion, and yearly intravenous infusion. The intravenous infusions may be used in patients with adherence problems to assure administration. For some patients self-injection or nasal sprays may be difficult.

Each agent also has a unique adverse event profile (Exhibit 4). The potential adverse effects may make one agent a better choice for a particular patient. For example, the oral bisphosphonates can cause significant esophageal irritation and ulcers. They are not appropriate agents for patients who cannot sit or stand for at least 30 minutes after taking. They also are not appropriate for a patient with swallowing difficulties, except the liquid form of alendronate. Patients with a history of thromboembolism should not receive raloxifene.

Another piece of the selection criteria is cost (Exhibit 4). The estimated retail price a patient without prescription coverage would pay for a 30-day supply is similar for all the agents except teraparotide. Depending on pricing structure, a managed care plan may have preferred agents or tiered co-pays. Because zoledronic acid and ibandronate are given as intravenous infusions, a managed care plan should ensure that their reimbursement structure is not shifting use to these agents over oral agents inappropriately. For some plans, infusions are paid from medical benefits and oral medications are covered under pharmacy benefits.

A cost effectiveness analysis using annual U.S. age specific incidence of clinical hip, spine, forearm, shoulder, rib, pelvis, and lower leg fractures, costs (2005 U.S. dollars), and quality-adjusted life years, found that osteoporosis treatment, at \$600 per year medication cost for five years with 35 percent fracture reduction, was cost-effective when the 10-year hip fracture probability reached approximately three percent.¹³ Depending on contract pricing, osteoporosis medications may or may not be priced at this cost-effective level.

Treatment guidelines also can be useful in helping

select therapy, particularly when developing managed care formularies. The ACP osteoporosis guidelines suggest that bisphosphonates are reasonable options to consider as first-line therapy, particularly for patients who have a high risk for hip fracture.⁴ These guidelines note that evidence from head-to-head trials is insufficient to demonstrate the superiority of one bisphosphonate over another, but that alendronate and risedronate have been studied more than other bisphosphonates. A recent systematic review by Catherine MacLean and colleagues found that data are insufficient to determine the relative efficacy or safety of all the agents for treating osteoporosis.¹⁴

One area, which none of the treatment guidelines addresses, is concomitant breast cancer risk. Many women who have osteoporosis also are at high risk for developing breast cancer. The National Cancer Institute estimates, based on current rates, 12 percent of women born today will be diagnosed with breast cancer at some time in their lives (Exhibit 5).¹⁵ Breast cancer is the 2nd leading cause of cancer death in American women. During 2008, an estimated 182,460 new cases and over 40,000 deaths due to breast cancer will occur in the United States. Over \$8 billion is spent in the United States each year on treatment of breast cancer.¹⁵

Invasive ductal carcinoma and invasive lobular carcinoma are the most common types of breast malignancies. Invasive breast cancer has started to extend beyond the basement membrane of the ducts or lobules into the surrounding normal breast tissue. The American Cancer Society estimates that approximately three out of four new breast cancer cases are invasive breast cancer.¹⁶ Noninvasive breast cancers include ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS).

Because lifetime cumulative exposure to estrogen appears to be a risk factor for breast cancer, agents that block the effects of estrogen in breast tissue have been studied for cancer prevention. The selective estrogen receptor modulators (SERMs) – tamoxifen and raloxifene – are one class of agents that can be used to prevent breast cancer. Because tamoxifen is not FDA approved for osteoporosis treatment, only raloxifene's effects will be discussed. SERMs are mixed estrogen agonists/antagonists with selective ability to act like estrogen in some tissues and not in others. Raloxifene has estrogen activity in bone and cardiovascular tissue while blocking estrogenic effects in the breast and uterus.

Three clinical trials in more than 15,000 postmenopausal women comparing raloxifene to placebo have demonstrated that raloxifene reduces the risk of invasive breast cancer by 44 to 72 percent.¹⁷⁻

19 A fourth clinical trial in 19,747 postmenopausal women at high risk for developing breast cancer compared raloxifene to tamoxifen.²⁰ In this trial, the risk of developing invasive breast cancer was similar for the two treatments.

MORE was an osteoporosis treatment trial over four years in 7,705 postmenopausal women with low to normal risk for breast cancer.¹⁷ The three treatment groups were raloxifene 60 mg/day, raloxifene 120 mg/day, or placebo. During the trial, 39 cases of breast cancer were detected in the placebo group and 22 in the pooled raloxifene group. This was a 72 percent reduction (relative risk = 0.28; 95 percent CI = 0.17–0.46). The risk of estrogen receptor (ER)-positive invasive breast cancer decreased by 84 percent, but there was no effect on ER-negative breast cancer. Using data from this study, 93 osteoporotic women would need to be treated with raloxifene for four years to prevent one case of invasive breast cancer.

The CORE trial was a continuation of MORE.¹⁸ In this trial, raloxifene 60 mg/day or placebo was given to 4,011 postmenopausal women for an additional four years. The four-year incidences of invasive breast cancer and ER-positive breast cancer were reduced by 59 percent (HR = 0.41; 95 percent CI = 0.24 to 0.71) and 66 percent (HR = 0.34; 95 percent CI = 0.18 to 0.66), respectively. There was no difference between the two groups in incidence of ER-negative invasive breast cancer during CORE (p = .86). Over the eight years of both trials (CORE and MORE), the incidences of invasive breast cancer and ER-positive invasive breast cancer were reduced by 66 percent (HR = 0.34; 95 percent CI = 0.22 to 0.50) and 76 percent (HR = 0.24; 95 percent CI = 0.15 to 0.40), respectively, in the raloxifene group compared with the placebo group. During the CORE trial, the relative risk of thromboembolism in the raloxifene group compared with that in the placebo group was 2.17 (95 percent CI = 0.83 to 5.70). This increased risk, also observed in the MORE trial, persisted over the eight years of both trials.

In the Raloxifene Use for the Heart (RUTH) study, 10,101 postmenopausal women (mean age, 67.5 years) with coronary heart disease (CHD) or multiple risk factors for CHD received either 60 mg of raloxifene or placebo for a median of 5.6 years.¹⁹ There was a reduced risk of invasive breast cancer (40 versus 70 events; hazard ratio, 0.56; CI, 0.38 to 0.83). The absolute risk reduction was 1.2 invasive breast cancers per 1000 women treated for one year. Compared with placebo, raloxifene had no significant effect on the risk of primary coronary events (533 versus 553 events; hazard ratio, 0.95; 95 percent confidence interval, 0.84 to 1.07). There was an in-

Exhibit 6: Risk Factors for Breast Cancer

- Advancing age
- Family history of invasive breast cancer (first-degree relative)*
- History of atypical hyperplasia or lobular carcinoma in situ*
- Previous or abnormal breast biopsy
- BRCA1, BRCA2 genes
- Advanced age at first live birth (or nulliparity)
- Female gender
- Early age at menarche
- ERT/HRT
- Race
- Ionizing radiation
- Obesity (post-menopause)
- Alcohol

*Strongest risk factors

BRCA, breast cancer, ERT, estrogen replacement therapy, HRT, hormone replacement therapy

Reference: 15,16

creased risk of fatal stroke (59 versus 39 events; hazard ratio, 1.49; 95 percent confidence interval, 1.00 to 2.24; absolute risk increase, 0.7 per 1000 woman-years) and venous thromboembolism (103 versus 71 events; hazard ratio, 1.44; 95 percent confidence interval, 1.06 to 1.95; absolute risk increase, 1.2 per 1000 woman-years) in the raloxifene treatment group.

The study of tamoxifen and raloxifene (STAR) included 19,747 postmenopausal women 35 years of age or older with a five year predicted risk for breast cancer greater than or equal to 1.66 percent (mean 4.03 percent).²⁰ In this National Cancer Institute study, the participants received 60 mg of raloxifene or 20 mg of tamoxifen daily for five years. One hundred and sixty eight breast cancers developed in 9,745 women on raloxifene with 163 cases in 9,726 on tamoxifen [NS]. There was a 36 percent decrease in uterine cancers in women on raloxifene compared with tamoxifen and 30 percent fewer DVTs and PEs in raloxifene group [NS]. While the reduction in endometrial cancer did not achieve statistical significance, other studies have not shown an increase in endometrial cancers with raloxifene, which does occur with tamoxifen. Notably, about 50 percent of women screened for STAR did not meet entry criteria and 80 percent of eligible women declined participation. The median treatment duration in this study was approximately three years, and the nonadherence rate was about 30 percent.

Based on the results of the trials discussed here, the FDA approved indications for raloxifene were expanded. In addition to treatment and prevention of osteoporosis in postmenopausal women, raloxifene is now indicated for reduction in risk of invasive breast

cancer in postmenopausal women with osteoporosis and reduction in risk of invasive breast cancer in postmenopausal women at high risk for invasive breast cancer.²¹

From a managed care perspective, decisions must be made as to which postmenopausal women with osteoporosis should be on raloxifene to reduce risk of breast cancer. Identifying those patients who would benefit the most while still minimizing the costs to society and the individual health plan must be done. This may include stratifying patients into various risk groups and deciding that only high-risk patients should be offered preventative therapy.

Exhibit 6 lists the known risk factors for developing breast cancer.^{22,23} The strongest risk factors are advancing age, family history of invasive breast cancer (first-degree relative), and history of atypical hyperplasia or lobular carcinoma in situ. There are no data available regarding the effect of raloxifene on invasive breast cancer incidence in women with inherited mutations (BRCA1, BRCA2).²¹

A woman's risk of developing breast cancer over the next five years can be estimated using a risk assessment tool commonly known as the Gail model available at www.cancer.gov/bcrisktool. Estimates from this tool only apply to woman greater than 35 years of age in the general U.S. population. For example, the five-year estimated risk for a 65-year-old white female (began menstrual periods at 12, first live birth at 20, no abnormal breast biopsies, no first degree relatives with breast cancer) is 1.5 percent compared to 2 percent for the average 65 year old woman. If she had given birth after the age of 30 and had one first degree relative with cancer, her estimated risk would be 3.3 percent. Clinicians can use this estimate to help individual patients considering raloxifene therapy estimate the potential benefit. However, the validity, feasibility, and impact of using the Gail model to identify appropriate candidates for chemoprevention have not been tested in a primary care setting. Although the tool has been used with success in clinics for women with strong family histories of breast cancer, more specific methods of estimating risk are appropriate for women known to have breast cancer-producing mutations in the BRCA1 or BRCA2 genes. Other factors also may affect risk and are not accounted for by the tool.

The U.S. Preventive Services Task Force recommends against routine use of raloxifene (or tamoxifen) for the primary prevention of breast cancer in women at low or average risk for breast cancer (Grade D recommendation).²⁴ The group recommends clinicians discuss chemoprevention with women at high risk for breast cancer and at low risk

for adverse effects of chemoprevention (Grade B). Although these are 2008 recommendations, they do not include the fact that raloxifene is now approved for preventing breast cancer in women being treated for osteoporosis. The recommendations also do not define low, average, or high risk.

In determining who are the best candidates for chemoprevention in general, it should be noted that primary prevention with SERMs like tamoxifen or raloxifene has not been proven to improve overall survival. Also, the optimal duration of chemoprevention is unknown. At least with tamoxifen, studies indicate that treatment beyond five years does not provide any additional benefit.²³ Typically for treatment of osteoporosis, therapy is continued for a lifetime and thus raloxifene for both osteoporosis and breast cancer prevention would be continued indefinitely. Presented with the potential benefits and harms and questions that remain, many women may decline treatment.

Conclusion

Osteoporosis and breast cancer affect a significant number of women. There are now numerous choices for osteoporosis treatment and a treatment to prevent the development of breast cancer while also managing osteoporosis. Bisphosphonates are generally considered first line therapy of osteoporosis because they decrease vertebral, non-vertebral fractures, and hip fractures. Raloxifene should be considered for osteoporosis treatment in patients at significant risk for invasive breast cancer. JMCM

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