



## Proposed Care Management for Women with Estrogen Deficiency: Identification, Risk Stratification, and Treatment

... we have the potential to identify and manage the care of all women who have estrogen deficiency ...

### Introduction

For years, we have understood the importance of managing the care of women with estrogen deficiency: Women's risk for death from hip fracture and ischemic heart disease increase significantly after menopause.<sup>1</sup> Population care management programs have been developed to improve quality of life and to reduce utilization of expensive resources for patients who have preventable diseases.<sup>2</sup> Newly developed information technology systems within Kaiser Permanente (KP) make it possible to identify and stratify risks for chronic illnesses such as congestive heart failure, diabetes mellitus, and asthma. Using this technology, we have the potential to identify and manage the care of all women who have estrogen deficiency: Selection algorithms can be integrated into current data systems to educate and improve the overall care of menopausal women who are at risk for complications of estrogen deficiency (eg, coronary artery disease, and osteoporosis).

This article describes a proposed model of care that has been developed to help manage the care of estrogen-deficient menopausal women.

### Management of Estrogen Deficiency: The Problem

In general, estrogen deficiency among women is poorly managed: Fewer than 20% of US women over age 50 years are adequately treated for estrogen deficiency. This statistic suggests that we have substantial room for improvement. Moreover, as our adult population ages, the number of women who become estrogen-deficient will increase. There is a growing concern that many of these women will not be treated for estrogen deficiency.

Management of estrogen deficiency is a subject of interest to many clinicians who care for women who have had hysterectomy or who become menopausal. Clinicians are aware that hormone replacement therapy (HRT) in women decreases symptoms of menopause and decreases their risk for death associated with hip fracture and heart disease; indeed, mortality among women who use postmenopausal hormones is lower than among nonusers. However, the survival benefit of HRT use diminishes with longer duration because prolonged HRT use is associated with a slightly increased risk of breast cancer.<sup>3,4</sup> In the United States, hip fracture kills approximately

65,000 women per year, heart disease kills about 233,000 women per year, and breast cancer kills about 43,000 women per year.<sup>5</sup> Some authors<sup>1,6</sup> have suggested that the decrease in risk of heart disease outweighs the risk of breast cancer.

Despite the known benefits of HRT, however, many women choose to not take estrogen replacement. In one study,<sup>7</sup> current use of HRT was reported by 58.7% of women who had hysterectomy and by 19.6% of women who did not have hysterectomy. Most women either do not fill prescriptions for HRT or discontinue treatment within one year after starting HRT.<sup>8</sup>

### Recent and Proposed Ways to Improve Identification and Management of Estrogen Deficiency

In general, women are not well informed about the risks and benefits of HRT. The Health Plan Employer Data and Information Set (HEDIS), which is maintained by the National Committee for Quality Assurance (NCQA), now uses a set of standardized performance measures to assure purchasers and consumers of health care that their managed care organizations are informing women who may have estrogen deficiency about the risks and benefits of HRT as well as alternatives to this therapy. Specifically, HEDIS will be sending to members of managed care organizations a questionnaire which focuses on exposure to counseling, breadth of counseling, and personalization of counseling. In addition, the American Association of Clinical Endocrinologists (AACE) has outlined educational guidelines<sup>10</sup> to help clinicians manage their patients' menopausal symptoms (Table 1).

As a managed care organization, we must be held accountable for our management of the care of women with estrogen deficiency. By using tracking systems to screen women for estrogen deficiency, by educating women about estrogen deficiency, and by improving compliance with prescribed treatment regimens, treatment programs could decrease the incidence of osteoporotic fracture and coronary artery disease in women with estrogen deficiency. Successful preventive therapy for these women could then have a dramatic impact on health care expenditures over the next two decades. A care management program is therefore needed and should include population identification, risk stratification, and models of care for estrogen-deficient menopausal women.



PHILIP J. TUSO, MD, FACP, is the Assistant Chief, Internal Medicine, for the Lancaster Medical Offices. He has been a Permanente Medical Group physician for six years. He has authored over 20 research articles, and has won numerous awards. E-mail: philip.j.tuso@kp.org

### Proposed Population-Based Care Management Model

Women should start receiving counseling in their mid- to late forties, when most women are perimenopausal or menopausal. These Health Plan members could receive counseling by a case manager with or without attending classes that review the risks and benefits of managing estrogen deficiency as well as alternative methods of managing this condition. Members seen in primary care clinics for routine examination or for cancer screening (mam-

mography, Pap smear) or who attend the counseling sessions or classes can be asked to complete a simple self-examination tool (Table 2). Responses to the questionnaire can be used to identify members as being at low, medium, or high risk for complications associated with untreated estrogen deficiency. Feedback to primary care providers on percentage of impaneled women aged >45 years who are receiving HRT may increase the percentage of women who are appropriately counseled on the risks and benefits of HRT as well as on alternatives to this method

**Table 1. AACE Educational guidelines for hormone replacement therapy<sup>10</sup>: risks, benefits, and alternatives**

<p>Benefits of hormone replacement therapy</p> <ul style="list-style-type: none"> <li>• Prevention of cardiovascular disease</li> <li>• Prevention of osteoporosis</li> <li>• prevention of menopause symptoms (“hot flushes,” mood alteration, depression, sleep disturbance, vaginal dryness)</li> </ul>
<p>Risks of hormone replacement therapy</p> <ul style="list-style-type: none"> <li>• Thromboembolism (blood clots)</li> <li>• Cholelithiasis (gallstones)</li> <li>• Endometrial cancer (women with a uterus who receive estrogen but not progestin replacement)</li> <li>• Abnormal vaginal bleeding</li> <li>• Possible increase risk of breast cancer</li> </ul>
<p>Alternative therapies to hormone replacement therapy</p> <ul style="list-style-type: none"> <li>• Prevention of menopausal symptoms:                             <ul style="list-style-type: none"> <li>Flaxseed and phytoestrogens (soy products and herbal preparations<sup>a</sup>)</li> <li>Vaginal lubricants</li> </ul> </li> <li>• Prevention of coronary artery disease:                             <ul style="list-style-type: none"> <li>Smoking cessation</li> <li>Lipid management</li> <li>Blood pressure management</li> <li>Glucose control</li> </ul> </li> <li>• Prevention of osteoporosis:                             <ul style="list-style-type: none"> <li>Smoking cessation</li> <li>Exercise</li> <li>Vitamin D and calcium supplementation</li> <li>Selective estrogen receptor modulators (raloxifene)</li> <li>Biphosphonates (alendronate)</li> <li>Calcitonin</li> </ul> </li> </ul>
<p><sup>a</sup> Reasons why Health Plan members should consult a physician before taking herbal supplements and phytoestrogens for management of estrogen deficiency:</p> <ul style="list-style-type: none"> <li>• not all herbs are safe</li> <li>• not all herbs are standardized</li> <li>• herbal preparations may be contaminated</li> <li>• herbal preparations may interact with prescription medication</li> <li>• effectiveness of herbal preparations may not be evidence-based</li> </ul>

Responses to the questionnaire can be used to identify members as being at low, medium, or high risk for complications associated with untreated estrogen deficiency.

of managing estrogen deficiency. Models of care (Table 3) could help guide members, staff, care managers, and clinicians in developing the best management plan for each Health Plan member.

**Table 2. Proposed self-examination tool for women**

**Question A: Menopausal symptoms**

Do you have a history of:

- depression?
- urinary incontinence?
- vaginal dryness?
- hot flushes?
- difficulty sleeping?
- painful intercourse?

**Question B: Risk factors for osteoporosis**

Do you have a history of:

- fracture after age 50 years?
- parents or siblings who had fracture after age 50 years?
- taking medications such as prednisone or corticosteroid drugs?
- total hysterectomy?
- tobacco use?

**Question C: Risk factors for coronary artery disease**

Do you have a history of:

- diabetes mellitus?
- high blood pressure?
- high cholesterol level (LCL-C > 160 mg/dL [4.14 mmol/L])?
- heart attack?
- angiogram with abnormal findings?
- parents or siblings with history of heart attack or stroke?
- tobacco use?

**Question D: Risk factors for breast cancer**

Do you have

- personal history of breast cancer?
- personal history of breast biopsy done to rule out diagnosis of breast cancer?
- mother or sisters with history of treatment for breast cancer?
- family history of bilateral breast cancer?

**Risk groups:**

- More than two symptoms of menopause (Question A)
- More than two risk factors for coronary artery disease (Question B)
- More than two risk factors for osteoporosis (Question C)
- History of breast cancer or high risk for breast cancer (Question D)
- Postmenopausal woman who does not receive hormone replacement therapy

**Women with no regular primary care physician**

Risk for complications by number of risk factors:

- High risk for complications: 4-6 risk factors
- Medium risk for complications: 1-3 risk factors
- Low risk for complications: 0 risk factors

Women who decide to take HRT should have easy access to clinics or practitioners who can provide education on the most appropriate treatment plan and who can arrange for follow-up consultation to answer any questions and, if necessary, to adjust therapy. For women who have not had hysterectomy, HRT should include estrogen and progestin agents because unopposed estrogen therapy in women with a uterus has been associated with endometrial cancer. Women who have had hysterectomy need only estrogen replacement. Multiple HRT regimens have been developed.<sup>10</sup> For women with a uterus, these regimens commonly prescribe 0.625 mg equine estrogen taken orally every day with daily or cycled medroxyprogesterone at a dosage of 5 mg to 10 mg per day.

Hormone replacement therapy is contraindicated in women who have a history of breast or uterine cancer, thromboembolism, undiagnosed genital bleeding, gallbladder disease, or undiagnosed headache with or without hypertension.<sup>10,11</sup> For women in whom HRT is not well tolerated or for whom HRT is contraindicated or not selected, alternative therapy for preventing osteoporosis includes vitamin D and calcium supplementation, selective estrogen receptor modulators (raloxifene), biphosphonates (alendronate), phytoestrogens, and calcitonin.<sup>10</sup> In addition to having protective effects on bone, raloxifene may also lower LDL cholesterol levels. Alendronate has been shown to have no effect on reduction of symptoms associated with menopause but has been approved for both prevention and treatment of osteoporosis. Alendronate has not been shown to reduce cardiac mortality associated with estrogen deficiency.<sup>12</sup>

The effects of HRT, alendronate, and raloxifene on bone disease, coronary artery disease, menopausal symptoms, breast cancer, and thromboembolism are summarized in Table 4. As stated above, HRT, alendronate, and raloxifene all help to prevent osteoporosis. The cardioprotective effects of HRT have been well documented.<sup>13</sup> Of all 3 treatments—HRT, alendronate, and raloxifene—HRT is best for managing menopausal symptoms. Raloxifene and HRT may cause thromboembolic disease.

Menopausal symptoms are easily managed with HRT but are difficult to treat without estrogen replacement. Flaxseed, soy products, and certain herb products contain phytoestrogen, which may inhibit release of luteinizing hormone and subsequently help women with hot flushes and mood irregularity.<sup>14</sup> Vaginal dry-

**Table 3. Proposed models of care for women with estrogen deficiency**

Low risk for complications:

- Yearly flu vaccine and routine immunizations per KP Regional guidelines
- Smoking cessation
- Mammogram, Pap smear, LDL cholesterol level tested per guidelines
- Vitamin D (400 IU/day) and calcium (1000-1500 mg/day) supplementation
- Routine contact with primary care provider at least once per year
- Osteoporosis preventive therapy per KP Regional guidelines
- Basic menopause education

Medium risk for complications (all low-risk-group actions)

- Assure all members assigned to a primary care practitioner
- Consider referral to endocrinology clinic for women with risk factors for osteoporosis
- Consider referral to cardiology clinic and/or cholesterol clinic for women with risk factors for coronary artery disease
- Review medication/vitamin compliance (eg. calcium supplementation, Vitamin D, hormone replacement therapy, alendronate)
- Written treatment plan and refer for group menopause class
- Telephone follow-up to assure self-care skills assimilated

High risk for complications (all low- and medium-risk-group actions):

- Referral to specialist if indicated (endocrinology, cardiology, psychiatry, or cholesterol clinic, or any combination)
- Review treatment plan for management of coronary artery disease and osteoporosis

ness can be managed with phytoestrogen creams or with nonprescription, water-based lubricants.<sup>15</sup> Use of herbal remedies is not without risk (Table 1), and members should review their use of herbal supplements with their health care practitioners.<sup>16</sup>

All Health Plan members should be screened for diabetes mellitus, hypertension, and hyperlipidemia, and appropriate treatment should be initiated according to KP Regional guidelines. Women at risk for coronary artery disease should be screened carefully to ensure that optimum LDL levels have been achieved. After receiving dietary counseling, Health Plan members at very high risk for coronary artery disease may be considered candidates for "statin" therapy.<sup>17</sup> All members who smoke should be advised to stop. Education classes and individual counseling should emphasize the importance of exercise as well as vitamin D and calcium supplementation.<sup>18</sup> Care of women in the high-risk group should be managed aggressively by these members' primary care practitioner or referred to a specialist, as appropriate. Some medical centers may consider developing clinics to manage the care of female members who are at risk for complications associated with estrogen deficiency. Teams may consist of representatives from the adult medicine and

obstetrics-gynecology departments and use a care management strategy that includes long-term continuity of care as well as special expertise in managing multiple risk factors.

#### The Problem of Noncompliance

Two important reasons exist for noncompliance with HRT: 1) side effects resulting from initiation of HRT and 2) belief that an increased risk of breast

**Table 4. Effects of using hormone replacement therapy (HRT), alendronate, and raloxifene for medical management of estrogen deficiency**

	HRT	Alendronate	Raloxifene
Bone density	+	+	+
Coronary artery disease	+	no effect	+
Menopausal symptoms	+	no effect	-
Breast cancer	+	no effect	+
Thromboembolism	+	no effect	+

+ = positive effect; - = negative effect



*Well-organized education programs and access to counselors should be made available to women who have questions about HRT before they consider stopping treatment.*

cancer is associated with estrogen replacement. An estimated 20%-30% of women who initiate HRT discontinue it within one year after starting treatment.<sup>8</sup> Many women are concerned about associated problems, ie, abnormal uterine bleeding and the inconvenience of taking hormones for the rest of their lives. Well-organized education programs and access to counselors should be made available to women who have questions about HRT before they consider stopping treatment.

Many women avoid HRT because of the fear that by taking estrogen replacement they will increase their risk of developing breast cancer. In 1997, the results of a collaborative reanalysis of the effects of HRT on women were reported from 51 epidemiologic studies of 52,705 women with breast cancer and 108,411 women without breast cancer.<sup>19</sup> The results demonstrated that an increased risk of breast cancer in estrogen users might not be conclusive.

Women should know that multiple studies published over the past 20 years fail to show that estrogen use increases women's risk for breast cancer.<sup>10</sup> To ensure that all members receive counseling and comply with prescribed treatment regimens—and to assess the program's overall success—measurable outcomes such as those proposed (Table 5) should be monitored continuously.

### Conclusion

Information technology is revolutionizing the way we care for patients. Specifically, we now have the tools to identify and stratify risks for many chronic illnesses and to manage the care of large numbers of Health Plan members with these chronic illnesses. Over the next few years, we will therefore shift many of our resources from disease treatment to disease prevention. In this context, population-based care management for women represents the next phase

<b>Table 5. Overview of proposed population-based care management for women with estrogen deficiency</b>
1. Screen and educate all women at risk for estrogen deficiency on the risk and benefits of hormone replacement therapy as well as alternatives to this therapy.
2. Design questionnaire (eg, Tables 1 and 2) as an outreach tool to educate women and staff members about risk of complications associated with estrogen deficiency. Women can use tool for self-examination to determine risk for complications. Develop models of care (eg, Table 3) to help members and staff determine the care modality appropriate for each member. Develop care management programs to allow women aged >45 years to self-refer to educational programs (ie, lectures, tapes), to case managers, or to specialists.
3. After completing self-evaluation questionnaires during outreach programs, at routine clinic visits, or at hospital admission, identify members at risk for complications of estrogen deficiency. Multiple points of contact at which this population can be identified: <ul style="list-style-type: none"> <li>• at entry programs for new members and at educational programs</li> <li>• at visit for mammogram or Pap smear</li> <li>• at orthopedic clinic evaluation for fracture</li> <li>• at cholesterol clinic evaluation for hyperlipidemia</li> <li>• at gynecology clinic follow-up after hysterectomy</li> <li>• at surgical clinic visit for treatment of breast lump or malignancy</li> <li>• at Kaiser Permanente Web site</li> <li>• in educational letters mailed to female members on their 45<sup>th</sup> birthday</li> </ul>
4. Develop database to record questionnaire response (ie, to determine percentage of women at high, medium, or low risk for complications of estrogen deficiency)
5. Develop database of measurable outcomes to monitor percentage of women aged >45 years who <ul style="list-style-type: none"> <li>• meet LDL cholesterol goals for age per KP Regional guidelines (see laboratory database)</li> <li>• comply with prescribed hormone replacement regimen (see pharmacy database)</li> <li>• had fracture during the past year (see hospital/clinic diagnostic code)</li> <li>• had myocardial infarction during the past year (hospital/diagnostic code)</li> </ul>

of care management: after individual Health Plan members are stratified according to their health risks, long-term medical complications in these members can be prevented through routine medical evaluations given by health care practitioners, yearly reminder letters, and recommended participation in health education programs or seminars. Population-based care management of women with estrogen deficiency can be modeled after highly successful care management programs currently used by KP for management of asthma, congestive heart failure, and diabetes mellitus.

Considering these emerging needs and capabilities, a goal of our health maintenance organization should be to inform all women of the risks and benefits of hormone replacement therapy as well as its alternatives. ❖

#### References

1. Wood H, Wang-Dheng R, Nattinger AB. Postmenopausal hormone replacement: are two hormones better than one? *J Gen Int Med* 1993 Aug;8(8):451-8; 1993.
2. Bodenheimer T. Disease management—promises and pitfalls. *N Engl J Med* 1999 Apr 15;340:1202-5.
3. Grady D, Rubin SM, Petitti DB, Fox CS, Black D, Ettinger B, et al. Hormone therapy to prevent disease and prolong life in postmenopausal women. *Ann Intern Med* 1992 Dec 15;117(12):1016-37.
4. Grodstein F, Stampfer MJ, Colditz GA, Willett WC, Manson JE, Joffe M, et al. Postmenopausal hormone therapy and mortality. *N Engl J Med* 1997 Jun 19;336(25):1769-75.
5. Jacobsen SJ, Goldberg J, Miles TP, Brody JA, Stiers W, Rimm AA. Race and sex differences in mortality following fracture of the hip. *Am J Public Health* 1992 Aug;82(8):1147-50.
6. Col NF, Eckman MH, Karas RH, Pauker SG, Goldberg RJ, Ross EM, et al. Patient-specific decisions about hormone replacement therapy in postmenopausal women. *JAMA* 1997 Apr 9;277(14):1140-7.
7. Keating NL, Cleary PD, Rossi AS, Zaslavsky AM, Ayanian JZ. Use of hormone replacement therapy by postmenopausal women in the United States. *Ann Intern Med* 1999 Apr 6;130(7):545-53.
8. Ravnikaar VA. Compliance with hormone replacement therapy: are women receiving the full impact of hormone replacement therapy preventive health benefits? *Women's Health Issues* 1992 Summer;2(2):75-80; discussion 80-2.
9. HEDIS 2000, Vol. 3: Specifications for Survey Measures. HEDIS Protocol for Administering CAHPS® 2.0H Survey. Management of Menopause Survey. Washington, DC: NCQA Publications; 1999. p. 41-54. Item No. 10236-100-00.
10. American Association of Clinical Endocrinologists. AACE medical guidelines for clinical practice for management of menopause. *Endocrine Pract* 1999 Nov-Dec;5(6):355-66.
11. Pérez Gutthann S, Garcia Rodríguez LA, Castellsague J, Duque Oliart A. Hormone replacement therapy and risk of venous thromboembolism: population-based case-control study. *Br Med J* 1997 Mar 15;314(7083):796-800.
12. Liberman UA, Weiss SR, Broll J, Minne HW, Quann H, Bell NH, et al. Effects of oral alendronate on bone mineral density and the incidence of fractures in postmenopausal osteoporosis. The Alendronate Phase III Osteoporosis Treatment Study Group. *N Engl J Med* 1995 Nov 30;333(22):1437-43.
13. Stampfer MJ, Colditz GA, Willett WC, Manson JE, Rosner B, Speizer FE et al. Postmenopausal estrogen therapy and cardiovascular disease. Ten-year follow-up from the nurses' health study. *N Engl J Med* 1991 Sep 12;325(11):756-62.
14. Lieberman S. A review of the effectiveness of Cimicifuga racemosa (black cohosh) for the symptoms of menopause. *J Women's Health* 1998 Jun;7(5):525-9.
15. Nyirjesy P, Weitz MV, Grody MH, Lorber B. Over-the-counter and alternative medicines in the treatment of chronic vaginal symptoms. *Obstet Gynecol* 1997 Jul;90(1):50-3.
16. Tuso PJ. The herbal medicine pharmacy: what Kaiser Permanente providers need to know. *Permanente J* 1999 Winter;3(1):33-7.
17. Darling GM, Johns JA, McCloud PI, Davis SR. Estrogen and progestin compared with simvastatin for hypercholesterolemia in postmenopausal women. *N Engl J Med* 1997 Aug 28;337(9):595-601.
18. Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. *N Engl J Med* 1997 Sep 4;337(10):670-6.
19. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52,705 women with breast cancer and 108,411 women without breast cancer. Collaborative Group on the Hormonal Factors in Breast Cancer [published erratum appears in *Lancet* 1997 Nov 15;350(9089):1484]. *Lancet* 1997 Oct 11;350(9084):1047-59.

## Journey

It is good to have an end to journey toward;  
but it is the journey that matters, in the end.

*Ursula K. LeGuin, award-winning science fiction  
and fantasy author*