COMPANION, 2003

MENOPAUSE

One Woman's Story, Every Woman's Story

National Institute on Aging

Why a Companion Booklet?

In the 2 1/2 years since printing *Menopause: One Woman's Story, Every Woman's Story—A Resource for Making Healthy Choices*, there have been several significant research findings involving the treatment used for the symptoms of menopause. This companion explains the most important new studies. It is designed to be read in conjunction with the full *Menopause* booklet. We've tagged some of the updated material with page numbers from the full *Menopause* booklet where more detailed information is available. So, by combining this information with the earlier booklet, you will have the most up-to-date information to help make a decision about whether menopausal hormone therapy is right for you. Information about ordering the full booklet or more copies of this companion is at the end.

Terminology

The terms that describe the use of estrogen with or without a progestin to treat the symptoms of menopause are changing.

THERAPY	WAS	NOW
Using estrogen with or without progestin	hormone replacement therapy (HRT)	menopausal hormone therapy (MHT)
Using estrogen alone	estrogen replacement therapy (ERT)	estrogen therapy (ET)
Using estrogen with a progestin	hormone replacement therapy (HRT)	estrogen-progestin therapy (EPT)

Risks and Benefits of Hormones

This is a confusing time for any woman dealing with the symptoms of menopause. In the past, women were told that using menopausal hormone therapy would control their hot flashes and vaginal dryness while protecting them from heart disease and osteoporosis. Results from the Women's Health Initiative (WHI) in 2002 did confirm some of these uses, but questioned others. While all the answers are still not in, the latest results do give women more information to use when considering their choices.

Prempro™ is a pill containing:
- 0.625 mg of conjugated equine estrogens (CEEs) and
- 2.5 mg of a progestin called medroxyprogesterone acetate (MPA).

Premarin™ is a pill containing only 0.625 mg of CEEs, without the MPA.

A placebo looks like the hormone pills, but has no hormones in it.

Page 23 discusses the WHI trial which included women between the ages of 50 and 79 when they entered the study. The WHI was designed to help women and their doctors know the benefits and risks of using menopausal hormone therapy (MHT) to prevent chronic illnesses such as heart disease. It was planned to run for 8 1/2 years. In July 2002, part of the study was stopped—more than 3 years early.

Why did this happen? In the part of the study that was stopped, each day women received Prempro™ (see sidebar) or a placebo (see sidebar). Scientists stopped this arm of the WHI research when they found that the possible risks of this estrogen-progestin therapy (EPT) exceeded the safety limits established at the outset of the study. A second part of the research where women were given Premarin™ (see sidebar) or a placebo is continuing, and the risks and benefits are being monitored carefully.

What were the risks?

WHI scientists found that women using this combined estrogen plus progestin (EPT) had more heart attacks, breast cancers, blood clots, and strokes than women not receiving any hormones. Some of these results were not a surprise. Experts had already suspected that using estrogen plus progestin could add to a woman's chance of developing breast cancer or a blood clot. The increase in heart disease was unexpected because scientists had hoped to *lower* the risk of heart disease by giving women in the study this combination.

Another surprise finding was reported in May 2003. Investigators in a WHI substudy, called the Women's Health

Initiative Memory Study (WHIMS), reported that women over age 65 using Prempro™ were at twice the risk for developing dementia as women not using any hormones and were also not protected from cognitive decline. This was unexpected because earlier studies had suggested that estrogen plus progestin might prevent or delay some of the serious cognitive problems that occur in some older women.

Were there benefits?

The WHI had some positive findings, too. Women taking combined estrogen plus progestin had fewer cases of colon cancer and a decrease in the number of bone fractures. These results were expected. Earlier studies had suggested that estrogen plus progestin might prevent colon cancer and protect against bone fractures. At the time the WHI study began, there were few treatments for osteoporosis. Now several drugs are available.

Often women believe that relief from menopausal symptoms improves their daily functioning and quality-of-life. But, the WHI study of women ages 50 to 79 reported in May 2003 that Prempro™ did not change how women described their mood, energy level, sexual satisfaction, or general health. Women did, however, after 1 year have a small, but meaningful improvement in sleep, physical functioning, and bodily pain. After 3 years, there were no benefits. Younger women in the WHI (those ages 50 to 54) with moderate to severe hot flashes and/or night sweats, found Prempro™ improved their hot flashes/night sweats and sleep, but nothing else.

How big are the risks or benefits?

There are two ways to describe the WHI results. One is *relative risk*. In the WHI relative risk compares the chance of one woman who takes combined estrogen plus progestin getting a health problem with that risk in another woman who does not take any menopausal hormone therapy. Relative risk is usually expressed as a number in decimal form, but may be easier to understand as a percentage. In the WHI and the WHIMS substudy the relative risks of using this combined estrogen plus progestin are shown in the top part of the chart below.

The second way to describe these results is *absolute risk*. This tells us the number of health problems that result from, or are prevented by, using estrogen plus progestin. It is usually expressed as the number of cases per people treated. For the WHI and the WHIMS substudy, changes in the absolute risk in 10,000 women receiving this combined estrogen plus progestin yearly are shown in the bottom part of the chart below.

	RISK/BENEFIT	CHANGE	
RELATIVE RISK	Heart attack	1.29	29% increase
	Breast cancer	1.26	26% increase
	Stroke	1.41	41% increase
	Blood clot	2.11	111% increase
	Dementia	2.05	105% increase in women over age 65
	Hip fracture	0.66	33% decrease
	Colon cancer	0.63	37% decrease

	RISK/BENEFIT	CHANGE PER YEAR
ABSOLUTE RISK	Heart attack	7 more cases in 10,000 women
	Breast cancer	8 more cases in 10,000 women
	Stroke	8 more cases in 10,000 women
	Blood clot	18 more cases in 10,000 women
	Dementia	23 more cases in 10,000 women over age 65
	Hip fracture	5 fewer cases in 10,000 women
	Colon cancer	6 fewer cases in 10,000 women

Questions remain

Experts still have questions. These include:

- **How long is it safe to use menopausal hormone therapy to manage symptoms?** In the WHI study of women age 50 to 79, the increase in breast cancer did not develop until after 4 years of use, but the extra cases of heart disease, stroke, blood clots, and, in WHIMS, cognitive decline in women age 65 and older began within 2 years after starting this combined estrogen plus progestin.
- **Will these results prove true for other types of estrogen and progestin?** Scientists don't know. The WHI looked only at Premarin™ and Prempro™, which were the two most commonly prescribed types of menopausal hormone therapy when the study began.
- **What about forms other than pills, like patches or creams?** These have not been studied as thoroughly as the hormones used in the WHI project, and no information is available to compare them.
- **Will smaller doses of these hormones have lower risks? Lower benefits?** Experts don't know. New information may become available as other studies are concluded.
- **If a woman decides to stop using estrogen alone or estrogen plus progestin, what is the best way?** Some doctors suggest tapering off—reducing the dose gradually. Others say it's fine to just stop.
- **Does progestin cause the increased risk of health problems from using this combined estrogen plus progestin?** Experts don't know. More study is needed. But we do know that taking estrogen without a progestin does cause a thickening of the lining of the uterus and slightly increases a woman's risk of cancer of the lining of the uterus (endometrial cancer). That is why estrogen alone is only recommended for use in women who have had a hysterectomy.

- **Does estrogen protect your mind from the effects of growing older or even Alzheimer's disease?** The part of WHIMS using estrogen only is continuing and may provide a better understanding.
- **Does estrogen alone cause ovarian cancer?** In 2002 an observational study of women using estrogen alone found that the cases of ovarian cancer almost doubled after 10 to 19 years of estrogen use, and more than doubled after 20 years. The absolute risks in 10,000 women each year are shown in the chart below. This is being studied in the estrogen alone part of the WHI.

ABSOLUTE RISK	
Using no hormones, after 10–19 years	4.4 cases in 10,000 women
Using estrogen alone for 10–19 years	7 cases in 10,000 women
Using estrogen alone for 20 years or more	14 cases in 10,000 women

In Summary

Since 2002, studies from the WHI have reported that women using a particular combination estrogen-progestin therapy were at increased risk for heart disease, stroke, blood clots, breast cancer, and dementia, but were at decreased risk for colorectal cancer and bone fracture. The therapy also only slightly improved hot flashes, sleep, and physical functioning in the women studied.

The surprising findings from this study were that the estrogen-progestin therapy used did not prevent heart disease or cognitive decline. Lifestyle changes and other medications are more effective for protecting the heart than using this combined estrogen plus progestin (page 24).

Menopausal hormone therapy—whether estrogen alone or estrogen plus progestin—is a single treatment with several uses. It is still approved by the Food and Drug Administration for controlling the symptoms of

menopause, especially hot flashes, night sweats, and vaginal dryness, but also for protecting women from osteoporosis. At present, experts suggest that women use menopausal hormone therapy, if they need to, for the shortest time necessary at the lowest dose that works. The booklet *Menopause* discusses the other uses for menopausal hormone therapy on pages 6–7, 13, 14, and 24.

What Do I Do Now?

Talk to your doctor. It doesn't matter if you are currently using menopausal hormone therapy or if you are just starting to think about taking it to help with hot flashes or vaginal dryness. In any case, you can use the WHI study results to help make health care decisions that will match your own health risks and medical needs.

Remember, the final story on estrogen and progestin has not been written yet. Even the WHI study is not complete because scientists are still studying all the information collected. The women who took estrogen plus progestin as part of the WHI and the WHIMS substudy will continue to be checked on for several years. So, whatever you decide, at no point is your decision about using menopausal hormone therapy final. You can start or stop this treatment at any time. You and your doctor should review it carefully at your regular checkup. Take into consideration things like: Have there been any changes in your medical history or that of close family members? Have there been new research findings? Regardless of your decision, follow the general

recommendations about staying healthy found on pages 26–28 of the larger *Menopause* book as the first step in a healthy life for years to come.

If you have received this companion without the *Menopause* book or would like more copies of either one, contact 1-800-222-2225 for your free publications.

RESOURCES

Menopause: One Woman's Story, Every Woman's Story—A Resource for Making Healthy Choices
http://www.nia.nih.gov/health/pubs/menopause/menopause.pdf

Report of the WHI results, July 2002
Writing Group for the Women's Health Initiative Investigators. "Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women: Principal Results From the Women's Health Initiative Randomized Controlled Trial." *JAMA*. 2002; 288:321–333.

Report of the WHI quality-of-life results, May 2003
Hays J, Ockene JK, Brunner RL, Kotchen JM, Manson JE, Patterson RE, Aragaki AK, Shumaker SA, Brzyski RG, LaCroix AZ, Granek IA, and Valanis BG. "Effects of Estrogen/Progestin on Health-Related Quality of Life." *New England Journal of Medicine*. 2003; 348:19:1839–1854.

Two Reports of the WHIMS results, May 2003
Shumaker SA, Legault C, Rapp SR, Thal L, Wallace RB, Ockene JK, Hendrix SL, Jones III BN, Assaf AR, Jackson RD, Kotchen JM, Wassertheil-Smoller S, and Wactawski-Wende J, for the WHIMS Investigators. "Estrogen Plus Progestin and the Incidence of Dementia and Mild Cognitive Impairment in Postmenopausal

Women: The Women's Health Initiative Memory Study: A Randomized Controlled Trial." *JAMA*. 2003; 289:2651–2662.

Rapp SR, Espeland MA, Shumaker SA, Henderson VW, Brunner RL, Manson JE, Gass MLS, Stefanick ML, Lane DS, Hays J, Johnson KC, Coker LH, Dailey M, Bowen D, for the WHIMS Investigators. "Effect of Estrogen Plus Progestin on Global Cognitive Function in Postmenopausal Women: The Women's Health Initiative Memory Study: A Randomized Controlled Trial." *JAMA*. 2003; 2898:2663–2672.

Understanding Risk: What Do Those Headlines Really Mean?
http://www.niapublications.org/engagepages/risk.asp

National Institutes of Health (NIH) Menopausal Hormone Therapy Web Site
http://www.nih.gov/PHTindex.htm

Women's Health Initiative (WHI) Web Site
http://www.nhlbi.nih.gov/whi/

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