

Do hormone risks outweigh the benefits for some women?

# HRT Update

**B**ased on findings from the Women's Health Initiative (WHI), a UVa community forum was held on July 17 in an attempt to share current information and informed medical opinions from physicians of the UVa Health System. Six hundred people attended a Community Forum, chaired by national expert on women's midlife health, JoAnn V. Pinkerton, M.D. The speakers and the follow-up question and answer session yielded many facts worth sharing. This fact sheet covers findings from the WHI study, the risks and benefits of hormone replacement therapy, a discussion of the value of hormones in preventing disease and treating symptoms of menopause, options available to women, and lifestyle changes you can make. Other speakers included Dearing Johns, M.D., David Brenin, M.D., Karen Johnston, M.D., Jennifer Harvey, M.D., Elizabeth Mandell, M.D. John Schmitt M.D., and Christine Peterson, M.D.

## Q. What is the Women's Health Initiative?

A. This is a large randomized clinical trial funded by the federal government to determine if hormones prevent heart disease. The trial used conjugated equine estrogens 0.625 mg each day and medroxyprogesterone acetate 2.5 mg each day. This is the most commonly prescribed postmenopausal hormone therapy in the United States for women who have a uterus (used each day by more than six million women). There was also an estrogen-only group, a placebo (sugar pill) group and a lifestyles and diet group. Only the estrogen and progesterone group has been stopped. The estrogen-only group is continuing.

## WHI findings

### Q. What were the main findings in the study on estrogen plus progestin?

- A. The main findings show that compared to women taking placebo (sugar) pills:
- The number of women who developed breast cancer was higher in women taking estrogen plus progestin.
  - The numbers of women who developed heart attacks, strokes or blood clots in the lungs and legs were higher in women taking estrogen plus progestin.
  - The numbers of women who had hip and other fractures or colorectal cancer were lower in women taking estrogen plus progestin.
  - There were no differences in the number of women who had endometrial cancer (cancer of the lining of the uterus) or in the number of deaths
  - No increased risk of breast cancer has been observed at this time in women taking estrogen alone versus placebo pills.
  - These new findings highlight the importance of having your annual mammograms and keeping your scheduled appointments.

### Q. What are the conclusions from these findings?

- A. The main conclusions are:
- The estrogen plus progestin combination studied in WHI does not prevent heart disease (0.625 conjugated estrogens and 2.5 mg medroxyprogesterone).
  - For women taking this estrogen plus progestin combination, the risks (increased breast cancer, heart attacks, strokes, and blood clots in the lungs and legs) outweigh the benefits (fewer hip fractures and colon cancers).

## Increased health risks

### Q. What are the increased risks for women taking estrogen plus progestin?

- A. For every 10,000 women taking estrogen plus progestin pills:
- 38 developed breast cancer each year compared to 30 breast cancers for every 10,000 women taking placebo pills each year.
  - 37 developed a heart attack compared to 30 out of every 10,000 women taking placebo pills.
  - 29 had a stroke each year, compared to 21 out of every 10,000 women taking placebo pills.
  - 34 had blood clots in the lungs or legs, compared to 16 women out of every 10,000 women taking placebo pills.

# HRT Update 2

## Health benefits

**Q. What risks are lower for women taking estrogen plus progestin?**

- A. For every 10,000 women taking estrogen plus progestin pills:
- 10 had a hip fracture each year, compared to 15 out of every 10,000 women taking placebo pills each year.
  - 10 developed colon cancer each year, compared to 16 out of every 10,000 women taking placebo pills.

## WHI Conclusions

**Q. How many women were affected?**

- A. Only 2.5% of the women in this study had these events. These results tell us that during one year, for every 10,000 women taking estrogen plus progestin, we would expect:
- 7 more women with heart attacks. In other words, 37 women taking estrogen plus progestin would have heart attacks compared to 30 women taking placebo.
  - 8 more women with strokes.
  - 8 more women with breast cancer.
  - 18 more women with blood clots.

These results also suggest that for every 10,000 women taking estrogen plus progestin, we would expect:

- 6 fewer colorectal cancers.
- 5 fewer hip fractures.
- Fewer fractures in other bones.

In summary, then, more women taking estrogen plus progestin had a serious health event than did women taking placebo. We conclude that estrogen plus progestin does not prevent heart disease and is not beneficial overall.

## Cancer risks

**Q. When did the increased risk of breast cancer become apparent for women taking estrogen plus progestin compared to women taking placebo pills?**

- A. There was no difference in the development of breast cancer during the first 4 years between women taking estrogen plus progestin and those taking placebo pills. After that time, the numbers began to increase. After an average of 5.2 years, there was an increased risk of breast cancer in women taking estrogen plus progestin compared to those taking placebo pills.

**Q. Is there an increased risk of breast cancer in women taking estrogen alone?**

- A. There is no evidence of an increased risk for breast cancer in women taking active estrogen alone, compared to those taking placebo pills, even after an average of 5.2 years. We do not know whether the long-term effects will differ. The Data Safety and Monitoring Board will continue to review participants' health data every 6 months.

**Q. What about the risk of ovarian cancer and hormone use?**

- A. The WHI did not examine ovarian cancer risk. However they did not find or report any increased risk in ovarian cancer at 5 years. In a separate study, however, researchers from the National Cancer Institute have just announced that postmenopausal women who use estrogen-only therapy for 10 years or more have an increased risk for ovarian cancer. Risk increased with length of estrogen use. So far, the studies suggesting possible increase in ovarian cancer risk are observational. We need more data.

**Q. What are breast specialists saying about the WHI results?**

- A. With the new data we have from this study, it means the medical risk/benefit ratio for taking the hormones has become too high for most women. If you are healthy and taking hormones only to prevent hot flashes and other symptoms, HRT may make sense for you. Discuss your goals for therapy carefully with your own doctor. Taking HRT is a very individual decision that each woman needs to make. Breast experts also note that taking estrogen with progestin increases breast tissue density, which makes it harder to read mammograms accurately. When

# HRT Update 3

women stop taking the hormones, the dense white tissue on the mammogram goes away within a few weeks. Remember to have mammograms yearly after age 40, perform monthly breast self-exams and have a doctor examine your breasts at least once a year.

## Heart health

**Q. What do heart experts say about the WHI? Will taking the combined hormones damage my heart?**

A. The new studies show the combination of estrogen plus progestin fails to protect the heart and blood vessels. They do not show definite damage in the heart from taking this combination. There are probably some women who could take hormones safely and benefit, but there is no way to know for sure which women will benefit. Estrogen therapy alone, however, is still being tested in healthy women without a uterus, which suggests that estrogen alone may protect your heart. That said, you should definitely stop hormone therapy if you have had a heart attack, stroke or stroke-like symptoms, or if you have developed a vein clot. You probably should stop hormone therapy if you need to be immobilized because of a broken bone or a need for major surgery, because of blood clotting concerns.

**Q. What is the biggest danger of taking these hormones together, with regard to my heart and blood vessels?**

A. There is an increase in vein clotting early in the course of therapy. In the first one to two years of this combination therapy, clotting in veins is likely to increase. Clotting in veins is different from clotting in arteries that go to the heart. There is still a question about whether there is a significant increase in the risk of heart attack if you are taking estrogen and progestin.

## Hormone use

**Q. Do you have recommendations about other hormone alternatives (lower-dose estrogens, micronized progesterone, natural hormones)?**

A. It is not possible to make specific recommendations about other hormone medications, such as different estrogens or progestins, lower dosages or taking the medication in different ways, such as patches instead of pills. This includes compounded “natural” products. Without scientific clinical trial data, one cannot assume that alternative estrogen plus progestin treatments have the same risks or are any safer than those studied in WHI.

**Q. I am taking prescription hormones, what should I do?**

A. Do not panic or abruptly discontinue your hormones. We recommend that you talk with your health care provider about your individual health risk profile and the hormones you are currently taking. Stopping abruptly may cause a recurrence of menopausal symptoms (even if you did not have them before going on hormones). If you would like to stop taking the hormones, it is better to taper off gradually. It is also possible that benefits could exceed risks for you or that there are alternative lifestyle changes or medications that you can take to lower your health risks. Therefore discussion with your health care provider is important.

## Lifestyle changes

**Q. How much of a difference can lifestyle changes make?**

A. You should try to change your lifestyle to become more healthy, if at all possible. Exercise is the secret to good health. A healthy diet also can go far toward preserving your good health. Don't smoke and quit if you do smoke. There are several good clinical studies that show that controlling high blood pressure and normalizing your cholesterol levels lead to robust benefits to your heart and blood vessels. Those are the most important things you can do for your health before you need medications. Exercise can actually reduce the risk of breast cancer. Some studies show that if you're a postmenopausal woman who exercises aerobically (heart-beat more rapid, building a sweat) four hours a week, you can decrease your breast cancer risk by 15-20 percent. If you only exercise one hour a week, you can decrease your risk by 7 percent. The benefits were even greater for premenopausal women who exercise. The bottom line is that exercise is important for preventing breast cancer as well as for preventing strokes,

# HRT Update 4

heart attacks and clots. Eat a healthy diet, including calcium every day, and eat less saturated fat (solid at room temperature) and more olive and fish oils. Avoiding alcohol can help you reduce your risk of breast cancer and prevent hot flashes. Avoiding drinks with caffeine also can help you prevent hot flashes.

## Heart/blood vessel drugs

**Q. Are there other drugs that can protect my heart and blood vessels from disease?**

A. Raloxifene is being studied to learn how well it might prevent heart disease. We know that in a large trial of women with osteoporosis, there were fewer breast cancer cases and women at highest risk of heart disease had less heart disease than expected. The study has been going for two years and has not been stopped yet for any findings like those of the WHI study. Another trial evaluated men and women who had heart or blood vessel disease or diabetes plus a risk factor to learn the effects of a drug called angiotensin enzyme converting inhibitor. The cardiac protective effect of this drug was greater than the effects seen in the WHI. Ask your doctor about all of the options for your heart, including lifestyle options. Statins have been shown to lower cholesterol and to decrease heart events in both women and men with and without heart disease.

## Bone protection

**Q. What can I do if I want to keep taking the hormones for bone protection?**

A. You have to look closely at your personal history and risk factors. If you have a high risk of osteoporosis or colon cancer for example, you might choose to continue taking estrogen and progestin pills to prevent a broken hip and colon cancer. We still don't know the safest preparation that will give us these protective effects, however. You should also explore with your doctor alternative medicines that could also protect your bones, such as the bisphosphonate family of drugs, known as Fosamax or Actonel. Miacalcin, which helps protect the backbone, usually is used by women who can't take bisphosphonates. Raloxifene is a different type of drug that appears to decrease stimulation to breast (compared with estrogen) while it helps protect bone. Don't forget, also, that your body needs calcium before, during and after menopause. You'll probably need to supplement your diet with calcium, and as you age, you'll need Vitamin D to aid with absorption. If you have had severe bone loss, magnesium supplements may help you absorb calcium better.

## Neurological effects

**Q. Did the WHI look at nervous system effects?**

A. No, but several small studies suggest that estrogen can benefit the brain, by increasing nerve activity in the brain and preventing Alzheimer's disease. We still need a sound, randomized large trial that looks primarily at neurological effects.

## WHI findings

***These results do not apply to women who had a hysterectomy and are on estrogen alone.***

The Data Safety Monitoring Board recommended that the study of estrogen alone continue as planned. The balance of risks and benefits for women in the estrogen alone study is still uncertain. ***It is important to note that, to date, women in the estrogen alone study have not shown an increased risk of breast cancer.*** (See chart on page 5.)

# HRT Update 5

Condition	For each year,		
	If you are post-menopausal and are taking <u>no hormones</u> , your risks are:	If you are taking <b>Premarin 0.625 mg and Provera 2.5 mg</b> daily, your risks are:	The increase (or decrease) in risk due to this particular form of HRT is:
Coronary heart disease	30 per 10,000	37 per 10,000	7 extra per 10,000
Stroke	21 per 10,000	29 per 10,000	8 extra per 10,000
Pulmonary embolism	8 per 10,000	16 per 10,000	8 extra per 10,000
Invasive breast cancer	30 per 10,000	38 per 10,000	8 extra per 10,000
Colorectal cancer	16 per 10,000	10 per 10,000	6 fewer per 10,000
Overall (all 5 conditions)	151 per 10,000	170 per 10,000	19 per 10,000
[For five years of hormone treatment]			100 per 10,000 (= 1%) In other words, if 100 women take this form of HRT for 5 years, one of those women will develop one of these conditions because of the medication.

From Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women. *JAMA*, July 17, 2002; 288(3):321-33.

## Resources:

[www.Menopause.org](http://www.Menopause.org)

[www.WHI.org/faq](http://www.WHI.org/faq)

adapted from the WHI FAQ website, July 15, 2002 and incorporating comments from the 7/17 UVa Community Forum

