

HRT Update

Do the Benefits Outweigh the Risk for Some Women?

JoAnn V. Pinkerton, MD

adapted from the WHI FAQ website. 7/15/02

What is the Women's Health Initiative? 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 a 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.

The Women's Place

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).

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.

Q. What are the reduced risks 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.

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. 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 prior to going on hormones). If the decision is made to stop hormones, it is preferable to taper off more gradually. It is also possible that benefits exceed risks for you or that there are alternative lifestyle changes or medications which you can take to lower your health risks. Therefore discussion with your health care provider is important.

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.

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.

Condition	For each year,		
	If you are postmenopausal and are taking no hormones , your risks are:	If you are taking Premarin 0.625 mg and Provera 2.5 mg 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
<i>Colorectal cancer</i>	16 per 10,000	10 per 10,000	<i>6 fewer per 10,000</i>
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.

