

WHI Study in a nutshell

## Estrogen-progestin versus placebo

This phase studied [estrogen](#), specifically conjugated equine estrogen, plus [progestin](#) ([Prempro](#), [Wyeth](#)) compared to [placebo](#) (the "WHI-E+P" trial), among healthy postmenopausal women.

This trial found that, compared with placebo, women receiving estrogen plus progestin experienced:<sup>[1]</sup>

- increased risk of [myocardial infarction](#) ("heart attack")
- increased risk of [stroke](#)
- increased risk of blood clots, including [deep venous thrombosis](#) (DVT) and [pulmonary embolism](#) (PE)
- increased risk of [breast cancer](#)
- decreased risk of [colorectal cancer](#)
- fewer fractures

The trial was ended early in 2002 when the researchers found that the subjects with estrogen plus progestin had a greater incidence of coronary heart disease, breast cancer, stroke, and pulmonary embolism than the subjects receiving placebo.<sup>[2]</sup> Hormone replacement therapy use declined in the U.S. and around the world, followed by a decline in breast cancer.<sup>[3]</sup>

## Conjugated estrogen versus placebo

This trial studied [estrogen](#), specifically conjugated equine estrogen ([Premarin](#), [Wyeth](#)), alone versus placebo (the "WHI-CEE" trial) in women with prior hysterectomy.

The trial was conducted among women with hysterectomy so that estrogen could be administered without a progestin. In women with a uterus, a progestin is needed to counteract the risk of [endometrial cancer](#) posed by unopposed estrogen.

Major results of this study were that, compared with placebo, women receiving estrogen alone experienced:<sup>[1]</sup>

- no difference in risk for [myocardial infarction](#)
- an increased risk of stroke
- an increased risk of blood clots
- an uncertain effect on breast cancer risk
- no difference in risk for [colorectal cancer](#)
- a reduced risk of fracture

What should you know:

- 1) WHI average patient age was 61 years old. That patient population has a higher risk of heart disease. Heart disease risk increased in the first year of taking HRT and then decreased after that time.
- 2) The estrogen alone arm of the study did not show an increased risk of breast cancer.
- 3) It is thought that perhaps the type of progesterone that was used in the study, medroxyprogesterone acetate, contributed to the increased risk of breast cancer. We now use other types of progesterone that may be safer, but that is unknown at this time.
- 4) Transdermal methods of delivery of estrogen should reduce the risk of blood clots and stroke due to the fact that only oral estrogen affects the P450 clotting system in the liver, so patches, creams and pellet therapy should minimize the increased risk of blood clot and stroke.
- 5) Is pellet therapy safer than prescription HRT? Small studies show that testosterone has a protective effect on the breast, however, large studies, such as WHI have not been done, so theoretically, pellet therapy is as safe as HRT.

Please initial the following key points:

\_\_\_ I understand that there may be an increased risk of breast cancer using any form of HRT over time.

\_\_\_ I understand there is an increased risk of blood clot and stroke that is optimized by patches, creams and pellet therapy.

\_\_\_ I understand there may be an increased risk of heart disease in the first year of use if using progesterone therapy.

\_\_\_ I understand that pellet therapy is not covered by most insurances and is an out of pocket cost, but I may submit charges to see if they will be covered by my insurance company.

\_\_\_ Risk of pellet therapy is pain at insertion site, infection, bleeding, side effects such as facial hair growth, acne, hair loss on scalp, breast tenderness and that I should notify my doctor if I have any of these side effects.

\_\_\_ I will need to take progesterone therapy if I have a uterus to avoid an increased risk of uterine cancer from unopposed estrogen therapy.

\_\_\_ I have had all my questions answered and would like to use the following method of hormone replacement therapy: \_\_\_ oral prescription, \_\_\_ transdermal patch, \_\_\_ bioidentical pellet therapy.

\_\_\_\_\_  
Signature

\_\_\_\_\_  
date

