

WHI (Women's Health Initiative) Update

By Dr Shiau Ee Leng, Editorial Board Member

WHI Update

National Institutes of Health (NIH) established the Women's Health Initiative (WHI) in 1991 to address the most common causes of death, disability and impaired quality of life in postmenopausal women. WHI will address cardiovascular disease, cancer, and osteoporosis. WHI is a 15 year multi-million dollar endeavor, and one of the largest U.S. prevention studies of its kind. The 3 major components of the WHI are:

- a randomized controlled clinical trial of promising but unproven approaches to prevention for Hormone Replacement Therapy Trial (HRT), Dietary Modification Trial (DM) and Calcium/Vitamin D Supplementation Trial (CaD)
- an observational study to identify predictors of disease;
- a study of community approaches to developing healthful behaviors

In July 2002, the investigators stopped the estrogen-plus-progestin study after finding that the associated health risks outweighed the benefits. The researchers are continuing to analyze and report on data from this trial while they complete other WHI studies

Key Findings from the Women's Health Initiative

1 Fracture Risk and Bone Mineral Density (JAMA October 2003)

Summary of results :

After an average of 5.6 years, 733 (8.6%) of women in the Estrogen and Progestin E+P group and 896 (11.1%) women taking placebo (inactive) pills experienced a fracture.

- Overall, there was a 24% reduction in all fractures and a 33% reduction in hip fractures in women assigned to E+P.
- Hip bone density increased 3.7% after 3 years of taking E+P compared to 0.14% in the placebo group.

While it appears HRT will reduce fractures, WHI concludes the risks of E+P outweigh the benefits. In conclusion, treatment with E+P should not be recommended for the prevention and treatment of osteoporosis in women who do not have menopausal symptoms. Other medicines for osteoporosis should be considered. If E+P is prescribed to prevent osteoporosis, women need to be informed of the risks of taking E+P.

2 Gynecologic Cancers and Diagnostic Procedures (JAMA October 2003)

Summary of results:

The WHI investigators report that women randomized to combined estrogen plus progestin (E+P) experienced:

- A 19% decrease in endometrial cancer rates
- A 58% increase in ovarian cancer rates

Thus, women taking E+P have a risk of endometrial cancer that is similar to or slightly less than women taking placebo. Progestin appears to cancel the harmful effect of estrogen in the uterus, as previous studies showed. However, E+P does not completely prevent endometrial cancer, so the bleeding problems that women often have with this therapy must still be monitored via endometrial biopsies. In the WHI study, E+P use was associated with a 5-fold increase in the number of women needing endometrial biopsies.

These results support current recommendations to use the lowest dose of E+P for the shortest duration needed to treat menopausal symptoms.

3 Coronary Heart Disease Risk (NEJM August 2003)

Summary of results :

WHI published the final coronary heart disease (CHD) results for the Estrogen plus Progestin (E+P) study. Findings suggest E+P does not protect the heart and may even increase the risk of coronary heart disease (CHD).

In final analyses, E+P use was associated with:

- A 24% overall increase in the risk of CHD (6 more heart attacks annually per 10,000 women using E+P)
- An 81% increased risk of CHD in the first year after starting E+P

Women who had higher baseline low-density lipoprotein (LDL) cholesterol levels at the beginning of the study were at particularly high risk of CHD with E+P use. No other factors significantly changed the risk of CHD while using E+P.

In conclusion, E+P does not protect the heart and may increase the risk of CHD among generally healthy postmenopausal women, especially during the first year after beginning hormones. E+P should not be started or continued to prevent heart disease.

4 Breast Cancer Risk (JAMA June 2003)

Summary of results :

The 2002 report showed that more women taking E+P developed breast cancer than those taking placebo (inactive) pills. After an average of 5.6 years, 245 of the 8,506 E+P women and 185 of the 8,102 women on placebo developed breast cancer. Of the total cancers, 349 cases were invasive, a type of breast cancer with a greater chance of spreading to other parts of the body. The conclusions below are based on the invasive breast cancer group.

- The increased risk of breast cancer due to E+P was eight additional cases of breast cancer for every 10,000 women over one year
- Overall, there was a 24% increase in the risk for breast cancer due to E+P

Family Practice Skills Courses

During the period November 2003 & February 2004, the College conducted the following courses:

- Men's Health Skills Course
- Pain Management Skills Course

The Men's Health Skills Course was conducted on 12 & 13 November 2003 at Concorde Hotel Ballroom. Workshops on case discussion & implementing disease management strategies and relaxation therapy



The Men's Health skills course involved seminars, workshops and Q & A sessions

were conducted along with the seminar sessions.

The Pain Management Skills Course was conducted on 21 & 28 February 2004 at the auditorium of the Ministry of Health. Workshops conducted were on "Joint injections for orthopaedic disorders" (See *Picture 1*).



Picture 1

These courses were made possible with an educational grant from Pfizer Pte Ltd.

REGISTER NOW!

Atherothrombosis Skills Course

**10 Apr(Sat) &
11 Apr(Sun) 2004**

Venue: MOH Auditorium

**Seminar: 2 - 4 pm
Workshop: 4 - 6 pm**

See page 23. ▶

◀ Page 21 - WHI (Women's Health Initiative) Update

Also, after one year, quite a few more women had abnormal mammograms in the E+P group (9.4%) compared to the placebo group (5.4%); this pattern continued until the study ended. Although we have known from other studies that E+P use increases the density of breast tissue on mammograms, the increase in abnormal mammograms with E+P use seen in this study is a new finding.

Further WHI studies are being done to learn what happens to breast cancer rates and mammograms after E+P use is stopped.

5 Stroke Risk (JAMA May 2003)

This study concluded that women taking active E+P developed more strokes than did those taking placebo (inactive) pills. This updated analysis showed that after an average of 5.6 years, 151 (1.8%) of the 8506 women on estrogen plus progestin and 107 (1.3%) of the 8102 women on placebo developed strokes. There is a 31% increase in the risk for stroke due to E+P.

Most of these strokes were caused by blood clots in the brain. The increased risk of stroke due to E+P was seen in all groups of women studied, including those closest to the menopausal change and those with symptoms like hot flashes disease.

Limitations of WHI

The WHI did not address use of HRT for short-term relief of symptoms. Also, other doses, formulations, routes of administration of E+P, the effects of Progestin separate from Estrogen, the longer term risks & benefits were not taken into account. Also, the non-adherence to E+P was up to 40%. All these may have diluted observed risks & benefits. Therefore whether to start HRT or not, this question will have to be addressed by both the patient concerned and doctor. The doctor & patient should discuss:

- Why was hormone therapy initiated?
- Why should it be continued?
- What are her risks?
- What are her benefits?

All these should incorporate best evidence to arrive at the best decision for the patient herself.

WHI Publications Reference List

1. NHLBI Women's Health Initiative Site <http://www.nhlbi.nih.gov/whi/index.html>
2. Women's Health Initiative Participant Web Site <http://www.whi.org/default.asp>
3. The Clinical Impact of the Women's Health Initiative (WHI): Entering a New Era in Managing Postmenopausal Health Issues <http://www.medscape.com/viewprogram/2152>