

**Results from the WHIMSY Study:  
No Long-Term Effects on Cognitive Function of Postmenopausal Hormone Therapy  
Prescribed to Women Aged 50-55 Years**

The Women's Health Initiative Study of Memory in Younger Women (WHIMSY) studied participants who were enrolled in the WHI Hormone Trials to assess the impact of hormone therapy (specifically, conjugated equine estrogens) on cognitive functioning when taken by postmenopausal women aged 50-55. The principle findings of this study was that hormone therapy did not affect overall cognitive function or any of the specific elements measured that formed the assessment of cognitive function.

**1. Why was this study conducted?**

During the Women's Health Initiative Hormone Trials, participants took study pills containing either an inactive placebo or conjugated equine estrogens (CEE), which was the most popular type of hormone therapy used in the US at the time. Women without a uterus took CEE alone, while women with a uterus took a pill that combined CEE with medroxyprogesterone (CCC+MPA). Research by the Women's Health Initiative Memory Study (WHIMS), a subset of women aged 65 years and older at enrollment, found that hormone therapy produced small losses in cognitive functioning (e.g., memory and attention). However, it was not known whether hormone therapy affects memory and other cognitive function in women younger than 65 years, which is when postmenopausal hormone therapy is commonly prescribed. Some studies have suggested that hormone therapy may actually benefit cognition if it is prescribed when women are just starting or going through menopause. The goal of WHIMSY was to assess the impact on cognitive function of CEE hormone therapy when it is taken by women aged 50-55.

**2. Who enrolled in the WHIMSY study?**

The participants in WHIMSY were women who joined the WHI Hormone Trials when they were aged 50-55. The WHI trials ended in 2002 (for CEE+MPA) and 2004 (for CEE). Overall, women had been in the study for an average of 7 years. Once the WHI trials ended, only 4% of the women reported using hormone therapy at any time after the study ended.

About 7 years after the WHI trials ended, we asked these women to participate in annual telephone interviews to assess their cognitive function, when their average age was 67 years. A total of 1,326 women agreed to participate.

About 40% of these women had a hysterectomy prior to joining the WHI Hormone Trials. For these women at the time of WHI enrollment, an average of 8 years had passed since their last menstrual period. For women with no prior hysterectomy, it had been an average of 4 years since their last menstrual period. Overall, 47% of the women had their last menstrual period within 5 years of WHI enrollment. About half of the women had used some form of postmenopausal hormone therapy before joining WHI.

**3. What was measured in WHIMSY?**

We are reporting results of the first two annual telephone interviews. These interviews measured global (i.e., overall) cognitive function and some of its parts: verbal memory, attention, executive function, verbal fluency, and working memory.

#### **4. What are the primary findings of the study?**

There was no overall difference in cognitive function between women who had taken study pills containing active hormones compared to women who had taken placebo study pills during the 7 years of the WHI study. This was true for global cognitive function, as well as the individual components.

The primary finding of the study is that conjugated equine estrogen therapies, when taken by women aged 50-55 years, produce no long-term benefit or harm for memory or other cognitive functions. There were no noticeable differences between CEE and CEE+MPA in their effects on cognitive function.

#### **5. What else was learned?**

WHIMSY was designed to see whether hormone therapies affected cognitive function depending on a woman's hysterectomy status, prior use of hormone therapy, or time since her last menstrual period.

Overall, for global cognitive function, no differences were found. Also, no differences were found for any part of cognitive function depending on time since women's last menstrual periods. Among women who had a prior hysterectomy or had used (but had stopped) hormone therapy in the past, there was some evidence that verbal fluency may have been lower in women taking hormones. However, this difference was small and would not be noticeable by an individual woman. Also, we cannot rule out that this may have been a chance finding.

#### **6. What is still to be learned?**

WHIMSY will continue to follow women with annual telephone interviews to learn whether previous use of hormones has effects on how cognitive function changes over time. It may also identify other factors during women's mid-life that are linked to better cognitive function later in life.

#### **7. What was not learned from WHIMSY?**

Because women enrolled in WHI were all postmenopausal, many by several years, WHIMSY is unable to assess the impact of this (CEE) therapy if it is started during the menopause transition. WHIMSY assessed effects on cognitive function only several years after treatment was stopped; we cannot describe the effects of hormone therapy on cognitive function in younger women while they were on active therapy.

In addition, WHIMSY assessed only conjugated equine estrogen (CEE) therapies. Its findings may not extend to other hormone therapy preparations.

**8. Who sponsored the study?**

WHIMSY was sponsored by the National Institute on Aging and the National Heart, Lung and Blood Institute. The study also made use of data and infrastructure provide by the National Heart, Lung, and Blood Institute. The hormone therapy used in the WHI hormone trials was provided by Wyeth-Ayerst Laboratories (now Pfizer).