

## Estrogen Therapy Does Not Reduce Dementia Risk When Started in Older Women

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**T**he most common form of postmenopausal estrogen therapy does not prevent dementia or a decline in memory function when started in women aged 65 and older according to research reported by scientists from the Women's Health Initiative Memory Study in two articles in this week's issue of the *Journal of the American Medical Association (JAMA)*.

"Starting estrogen in women 65 years and older to prevent dementia or cognitive decline is not recommended," said Robert D. Langer, M.D., M.P.H., the principal investigator for the Women's Health Initiative Memory Study (WHIMS), and a professor of family and preventive medicine at the University of California, San Diego (UCSD) School of Medicine.

The study was designed to test whether the most common forms of estrogen alone, or estrogen plus progestin, lowered the risk of dementia or memory impairment in older women.

Last spring, the researchers reported the first results from the study – that conjugated equine estrogen plus medroxyprogesterone acetate (Prempro™) doubled the risk of dementia in older women and did not benefit global cognition (memory and other basic mental abilities like concentration, language and abstract reasoning). When that study was published researchers weren't sure if the results would also apply to estrogen alone (Premarin™ in this study), which is given to women whose uterus has been removed.

Now, in *JAMA*, the researchers report on the group of women who took conjugated equine estrogen alone.

"We found a similar, but weaker, trend toward increased risk of dementia among the women taking estrogen alone," said Langer. "For every 10,000 women aged 65 or older started on estrogen alone there would be 12 extra cases of dementia per year. In 10,000 women aged 65 or older started on the combined hormone therapy tested there would be an additional 23 cases of dementia per year. Hormone therapy initiated at older ages does not prevent dementia – as was thought when we began this research."

The researchers also found that global cognition did not improve in women taking hormone therapy. In fact it was adversely affected.

“This adverse effect was relatively small overall, but was more pronounced for women who started with relatively lower cognitive function,” said Mark Espeland, Ph.D., Professor of Public Health Sciences at Wake Forest University Baptist Medical Center and a WHIMS Co-investigator.

WHIMS involved about 7,500 women between the ages of 65 and 79 who were free of dementia when the study started in 1995. Dementia occurs when memory, judgment and other thinking abilities decline substantially, to the point that it interferes with basic day-to-day activities.

Alzheimer’s disease was the most common form of dementia found among WHIMS participants.

The study also measured noticeable, but less severe declines in cognitive function, which affect 20 percent to 30 percent of older adults and, for some, strongly predict dementia and future institutionalization. Neither form of hormone therapy prevented the declines.

WHIMS was conducted at 39 centers across the United States. For the estrogen-alone study, about 3,000 women were assigned to take either a daily tablet of conjugated equine estrogen, sold as Premarinä, or an inactive placebo or “dummy” pill. Another 4,500 women took either a daily combination tablet with conjugated equine estrogen plus medroxyprogesterone acetate, sold as Prempro™, or a placebo.

WHIMS is part of the larger Women’s Health Initiative (WHI), designed to study the effects of hormone therapy as well as the long-term effects of a high-fiber, low-fat diet on heart disease and how vitamin D and calcium affect bone density and fracture rates. These two trials of WHI will continue through 2005.

In July 2002, women in WHI and WHIMS were told to stop taking the estrogen plus progestin therapy because the risks for developing breast cancer, strokes and cardiovascular disease outweighed the benefits. In March 2004, women in the estrogen-alone study were told to stop taking their drugs due to an increased risk of stroke, along with no difference for heart disease or breast cancer. Both groups of women are still being followed to determine the long-term effects of hormone therapy.

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