Postmenopausal hormone therapy with conjugated equine estrogens (CEEs) was not associated with overall sustained benefit or risk to cognitive function when given to women ages 50 to 55 years, according to a report published Online First by *JAMA Internal Medicine*.

The Women's Health Initiative Memory Study (WHIMS) demonstrated that postmenopausal hormone therapy with CEEs, when prescribed to women 65 years and older, caused deficits in global and domain-specific cognitive functioning.

The Women's Health Initiative Memory Study of Younger Women (WHIMSY) tested whether prescribing CEE-based hormone therapy to postmenopausal women ages 50 to 55 years had longer-term effects on cognitive function. The study by Mark A. Espeland, Ph.D., of the Wake Forest School of Medicine, Winston-Salem, N.C., and colleagues presents primary findings from this study.

"Global cognitive function scores from women who had been assigned to CEE-based therapies were similar to those from women assigned to placebo," according to the study results. "Similarly, no overall differences were found for any individual cognitive domain."

The study included 1,326 postmenopausal women, who had started treatment in two randomized placebo-controlled clinical trial of hormone
therapy when they were ages 50 to 55 years. The clinical trials the women participated in compared 0.625mg CEE with or without 2.5mg medroxyprogesterone acetate over an average of seven years.

"Our findings provide reassurance that CEE-based therapies when administered to women earlier in the postmenopausal period do not seem to convey long-term adverse consequences for cognitive function. Although we cannot rule out acute benefits or harm, these do not appear to be present to any degree a mean of seven years after cessation of therapy. One exception may be for minor longer-term disturbances of verbal fluency for women prescribed CEE alone; however this may be a chance finding," the authors conclude.

In an invited commentary, Francine Grodstein, Sc.D., of Brigham and Women's Hospital, Boston, writes: "Approximately 10 years ago, the Women's Health Initiative Memory Study (WHIMS) found that postmenopausal hormone therapy in older women caused nearly two-fold increases in dementia risk, worse rates of cognitive decline over time, and decreased brain volume on magnetic resonance imaging, compared with placebo treatment."

"In the article by Espeland et al, WHIMS investigators report new results from the Women's Health Initiative Memory Study in Younger Women (WHIMSY). The WHIMSY trial cleverly leverages 1,272 participants from the Women's Health Initiative who were aged 50 to 55 years when they were originally assigned to hormone therapy or placebo and reports findings from cognitive assessments administered a mean 7.2 years after treatment was halted," Grodstein continues.

"In these younger women, reassuringly, cognitive function appears similar in those who had been given hormone therapy vs. placebo; that is, there is no evidence in WHIMSY of substantially worse cognitive function associated with hormone use at younger ages," Grodstein
concludes.


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