

Timing of Hormone replacement therapy (HRT) initiation and digital cognitive outcomes in postmenopausal women

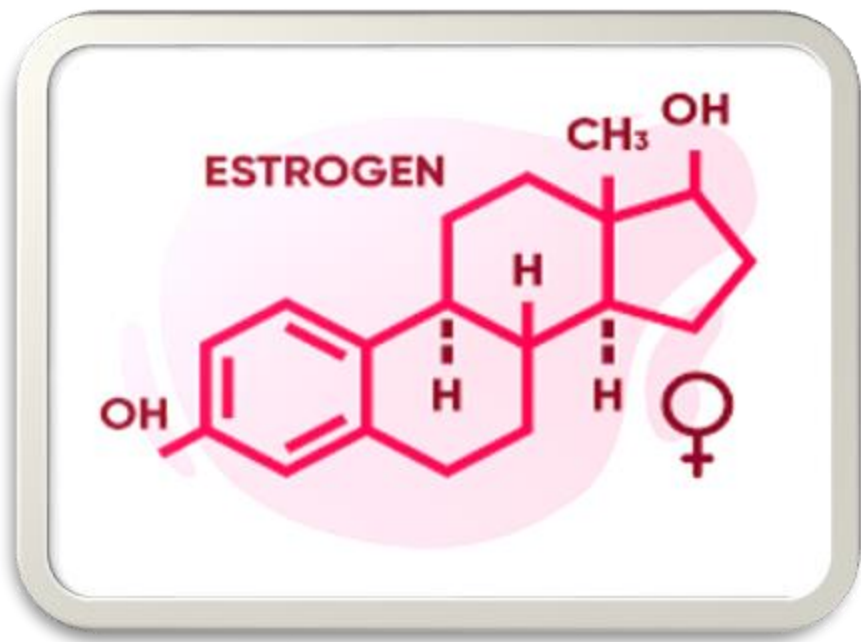
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Postmenopausal women account for over 60% of individuals with Alzheimer’s disease and related dementias (ADRD) and estrogen is thought to be neuroprotective. However, research on hormone replacement therapy (HRT) and its association with cognition has been inconclusive. In our study of 58 postmenopausal women, timing of HRT initiation was not associated with digital cognitive screening performance. More studies are needed to further assess estrogen's effect on the aging brain.

- Women are disproportionately affected by ADRD. This cannot only be explained by their longer lifespan
- Estrogen is thought to be neuroprotective. Its decline after menopause may increase risk for cognitive decline.

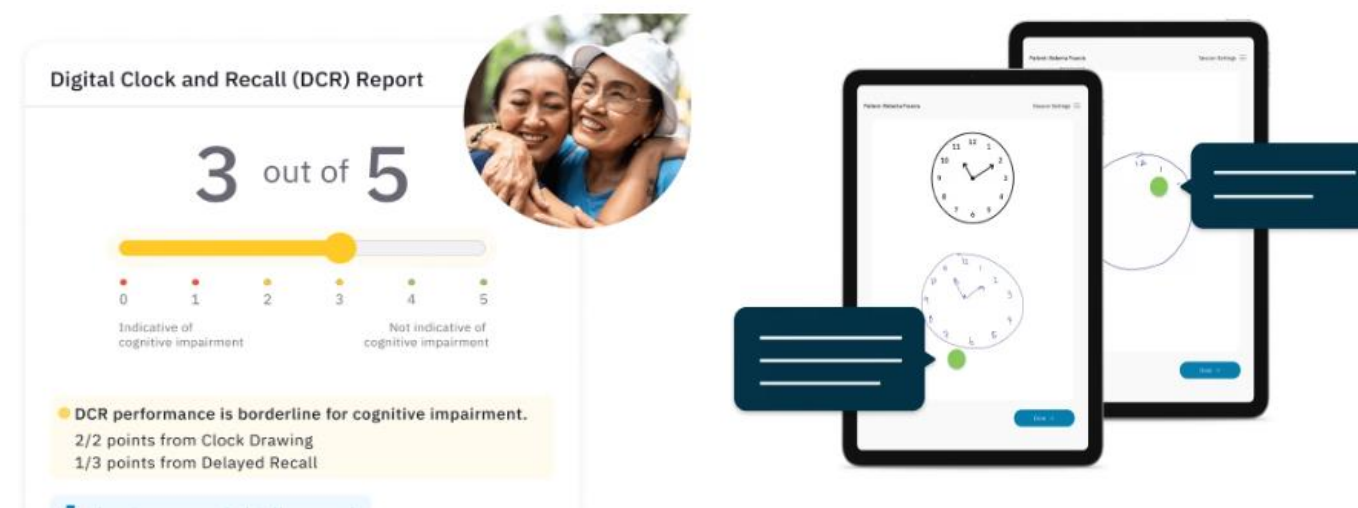


- Existing studies describe a critical window hypothesis: HRT may benefit cognition if started during perimenopause or early postmenopause.

AIM

This study examined the association between timing of HRT initiation in relation to menopause and digital cognitive performance in postmenopausal women.

- Study Sample: postmenopausal women from the Integrated Women’s Health Center and Nurse Practitioner’s Group at Columbia
- Participants completed:
 1. Core Cognitive Evaluation (CCE): total score range 0-5
 - 3-word recall + clock drawing
 2. Continuous 100-point clock score that assessed multidomain cognition
- HRT timing = HRT age - menopause age
 - This data was collected in a Women's Heath Survey
- Linear regression models examined associations between timing of HRT initiation and cognitive outcomes, adjusting for age, education, menopause age, and HRT duration.



- The sample included 58 postmenopausal women (mean age=62.5±9.4 years; mean education=17.1±9.4 years; 72% White).
 - CCE score: 4 ± 1
 - 100-point clock score: 78.3 ± 20.1

Cognitive Status	Total CCE Score Range	% of total Sample
Impaired	0-1	1.7%
Borderline	2-3	22.4%
Normal	4-5	75.8%

- The overall regression model predicting the 100-point clock score was significant (F=2.3, p=.048).
- HRT initiation timing was not independently associated with either the 100-point clock score (p=.207) or total CCE score (p=.150).
- Younger age at HRT initiation was also not associated with better cognitive scores.

Separate Stratified Analyses	Association with 100-point Clock Score	Association with Total CCE score
Only Current HRT Users (n=42)	P= 0.179	P= 0.296
Excluded participants with history of stroke or MS (n= 5)	P= 0.126	P= 0.200



In this cohort, timing of HRT initiation was not associated with cognitive screening performance.

These null findings may reflect the cross-sectional design of the study, variability in age at time of testing and years since menopause, and limited sample size.

Larger longitudinal studies and attention to specific type of HRT are needed to clarify the impact of HRT timing on cognitive outcomes in postmenopausal women.

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