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Thyroid Function and the Risk of Alzheimer Disease

The Framingham Study

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Background Clinical hypothyroidism and hyperthyroidism are recognized causes of reversible dementia, but previous studies relating thyrotropin levels to cognitive performance in clinically euthyroid persons have yielded inconsistent results.

Methods We related serum thyrotropin concentrations measured at baseline (March 1977-November 1979) to the **risk** of Alzheimer disease (AD) in 1864 cognitively intact, clinically euthyroid Framingham original cohort participants (mean age, 71 years; 59% women). Sex-specific Cox proportional hazards models were constructed using tertiles of thyrotropin concentration (tertile 2 as the referent) and adjusting for age, apolipoprotein E ε4 allele status, educational level, plasma homocysteine level, current smoking, body mass index, prevalent stroke, and atrial fibrillation.

Results During a mean follow-up of 12.7 years (range, 1-25 years), 209 participants (142 women) developed AD. Women in the lowest (<1.0 mIU/L) and highest (>2.1 mIU/L) tertiles of serum thyrotropin concentration were at increased **risk** for AD (multivariate-adjusted hazard ratio, 2.39 [95% confidence interval, 1.47-3.87] [*P* < .001] and 2.15 [95% confidence interval, 1.31-3.52] [*P* = .003], respectively) compared with those in the middle tertile. Thyrotropin levels were not related to AD **risk** in men. Analyses excluding individuals receiving thyroid supplementation did not significantly alter these relationships. In analyses limited to participants with serum thyrotropin levels of 0.1 to 10.0 mIU/L, the U-shaped relationship between thyrotropin level and AD **risk** was maintained in women but not when analyses were limited to those with thyrotropin levels of 0.5 to 5.0 mIU/L.

Conclusion Low and high thyrotropin levels were associated with an increased **risk** of incident AD in women but not in men.