

# Abstract

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## Low vitamin B-12 status and risk of cognitive decline in older adults.

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**BACKGROUND:** Elevated total homocysteine (tHcy) concentrations have been associated with cognitive impairment, but it is unclear whether low vitamin B-12 or folate status is responsible for cognitive decline.

**OBJECTIVE:** We examined the associations of cognitive decline with vitamin B-12 and folate status in a longitudinal cohort study performed from 1993 to 2003 in Oxford, United Kingdom.

**DESIGN:** Cognitive function was assessed with the Mini-Mental State Examination on  $\geq 3$  occasions during 10 y and related to serum concentrations of vitamin B-12, holotranscobalamin (holoTC), tHcy, methylmalonic acid (MMA), and folate with the use of linear mixed models in 1648 participants who provided blood in 1995.

**RESULTS:** Cognitive function declined abruptly at younger ages in some participants but remained intact in others until very old age. In multivariate regression analyses after adjustment for established risk factors, concentrations of holoTC (a marker of reduced vitamin B-12 status), tHcy, and MMA predicted cognitive decline, but folate did not. A doubling in holoTC concentrations (from 50 to 100 pmol/L) was associated with a 30% slower rate of cognitive decline (-0.137 to -0.083), whereas a doubling in tHcy (from 10 to 20  $\mu\text{mol/L}$ ) or MMA (from 0.25 to 0.50  $\mu\text{mol/L}$ ) was associated with >50% more rapid cognitive decline (-0.090 to -0.169) and (-0.104 to -0.169), respectively. After adjustment for all vitamin markers simultaneously, the associations of cognitive decline with holoTC and MMA remained significant.

**CONCLUSIONS:** Low vitamin B-12 status was associated with more rapid cognitive decline. Randomized trials are required to determine the relevance of vitamin B-12 supplementation for prevention of dementia.

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