

# Abstract

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## **Folate and vitamin B-12 status in relation to anemia, macrocytosis, and cognitive impairment in older Americans in the age of folic acid fortification.**

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**BACKGROUND:** Historic reports on the treatment of pernicious anemia with folic acid suggest that high-level folic acid fortification delays the diagnosis of or exacerbates the effects of vitamin B-12 deficiency, which affects many seniors. This idea is controversial, however, because observational data are few and inconclusive. Furthermore, experimental investigation is unethical.

**OBJECTIVE:** We examined the relations between serum folate and vitamin B-12 status relative to anemia, macrocytosis, and cognitive impairment (ie, Digit Symbol-Coding score < 34) in senior participants in the 1999-2002 US National Health and Nutrition Examination Survey.

**DESIGN:** The subjects had normal serum creatinine concentrations and reported no history of stroke, alcoholism, recent anemia therapy, or diseases of the liver, thyroid, or coronary arteries (n = 1459). We defined low vitamin B-12 status as a serum vitamin B-12 concentration < 148 pmol/L or a serum methylmalonic acid concentration > 210 nmol/L-the maximum of the reference range for serum vitamin B-12-replete participants with normal creatinine.

**RESULTS:** After control for demographic characteristics, cancer, smoking, alcohol intake, serum ferritin, and serum creatinine, low versus normal vitamin B-12 status was associated with anemia [odds ratio (OR): 2.7; 95% CI: 1.7, 4.2], macrocytosis (OR: 1.8; 95% CI: 1.01, 3.3), and cognitive impairment (OR: 2.5; 95% CI: 1.6, 3.8). In the group with a low vitamin B-12 status, serum folate > 59 nmol/L (80th percentile), as opposed to < or = 59 nmol/L, was associated with anemia (OR: 3.1; 95% CI: 1.5, 6.6) and cognitive impairment (OR: 2.6; 95% CI: 1.1, 6.1). In the normal vitamin B-12 group, ORs relating high versus normal serum folate to these outcomes were < 1.0 (P(interaction) < 0.05), but significantly < 1.0 only for cognitive impairment (0.4; 95% CI: 0.2, 0.9).

**CONCLUSION:** In seniors with low vitamin B-12 status, high serum folate was associated with anemia and cognitive impairment. When vitamin B-12 status was normal, however, high serum folate was associated with protection against cognitive impairment.

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