Effect of Folate and/or Vitamin B12 Supplementation between 6 to 30 Months of Age on Markers of Cardiovascular Illness at School Age: A Secondary Analysis

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**Objectives:** Deficiencies of vitamin B12 and folate in childhood are associated with cardiovascular risk in later life. The main objective of this analysis is to measure the effect of vitamin B12 and/or folic acid supplementation in children between 6 to 30 months of age on biochemical markers of cardiovascular risk at school age.

**Methods:** This is a follow-up study of a randomized,  $2 \times 2$  factorial, double-blind, placebo-controlled trial which assessed the effect of 2 recommended daily allowances of vitamin B12 and/or folic acid supplementation for 6 months on the risk of common infections in children aged between 6 to 30 months. The follow-up study was done 6 years later. The outcomes of the current

analyses were plasma concentrations of total homocysteine, leptin, high molecular weight (HMW) adiponectin, and total adiponectin. We used multivariable linear regression to measure the effect of vitamin B12, folic acid, or both during early childhood on these outcomes. We included interaction terms in the statistical models to measure whether the two vitamins modified the effect of each other.

**Results:** Compared to the placebo, giving both B12 and folate supplementation resulted in 1.19  $\mu$ mol/L (95% confidence interval: 0.09, 2.30) lower total homocysteine concentration at 7 years of age. There was no effect of B12 and folate supplementation on any of the other biomarkers. The effect of folic acid or vitamin B12 alone did not reach statistical significance for any of the outcomes.

**Conclusions:** Vitamin B12 and folic acid supplementation in early life resulted in lower plasma homocysteine at school age. Elevated homocysteine is a risk factor for many illnesses and our findings support improving the status of these vitamins in early life.

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