

Fischer LM, da Costa K-A, Kwock L, Galanko J, Zeisel SH. Dietary choline requirements of women: effects of estrogen and genetic variation, *Am J Clin Nutr* 2010;92:1112-1119.

Background: Choline is obtained from the diet and from the biosynthesis of phosphatidylcholine. Phosphatidylcholine is catalyzed by the enzyme phosphatidylethanolamine-*N*-methyltransferase (PEMT), which is induced by estrogen. Because they have lower estrogen concentrations, postmenopausal women are more susceptible to the risk of organ dysfunction in response to a low-choline diet. A common genetic polymorphism (rs12325817) in the *PEMT* gene can also increase this risk.

Objective: The objective was to determine whether the risk of low choline–related organ dysfunction increases with the number of alleles of rs12325817 in premenopausal women and whether postmenopausal women (with or without rs12325817) treated with estrogen are more resistant to developing such symptoms.

Design: Premenopausal women ($n = 27$) consumed a choline-sufficient diet followed by a very-low-choline diet until they developed organ dysfunction (or for 42 d), which was followed by a high-choline diet. Postmenopausal women ($n = 22$) were placed on the same diets but were first randomly assigned to receive estrogen or a placebo. The women were monitored for organ dysfunction and plasma choline metabolites and were genotyped for rs12325817.

Results: A dose-response effect of rs12325817 on the risk of choline-related organ dysfunction was observed in premenopausal women: 80%, 43%, and 13% of women with 2, 1, or 0 alleles, respectively, developed organ dysfunction. Among postmenopausal women, 73% who received placebo but only 18% who received estrogen developed organ dysfunction during the low-choline diet.

Conclusions: Because of their lower estrogen concentrations, postmenopausal women have a higher dietary requirement for choline than do premenopausal women. Choline requirements for both groups of women are further increased by rs12325817. This trial was registered at clinicaltrials.gov as [NCT00065546](https://clinicaltrials.gov/ct2/show/study/NCT00065546).