

# Abstract

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## Design of Physicians' Health Study II--a randomized trial of beta-carotene, vitamins E and C, and multivitamins, in prevention of cancer, cardiovascular disease, and eye disease, and review of results of completed trials.

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**PURPOSE:** To assess the balance of benefits and risks of supplementation with beta-carotene, vitamin E, vitamin C, and multivitamins on cancer, cardiovascular (CVD), and eye diseases.

**DESIGN:** Physicians' Health Study II (PHS II) is a randomized, double-blind, placebo-controlled trial enrolling 15,000 willing and eligible physicians aged 55 years and older. PHS II will utilize a 2 x 2 x 2 x 2 factorial design to test alternate day beta-carotene, alternate day vitamin E, daily vitamin C, and a daily multivitamin, in the prevention of total and prostate cancer, CVD, and the age-related eye diseases, cataract and macular degeneration.

**PRIOR RESULTS:** The final results of the recently completed Physicians' Health Study I (PHS I), a randomized, double-blind, placebo-controlled trial in 22,071 healthy US male physicians, indicated that beta-carotene supplementation (50 mg on alternate days) had no significant benefit or harm on cancer or CVD during more than 12 years of treatment and follow-up. In regards to cancer, there were possible benefits on total and prostate cancer in those with low baseline levels assigned to beta-carotene, a finding compatible with the Chinese Cancer Prevention Study for combined treatment with beta-carotene, vitamin E, and selenium in a poorly nourished population. Further, with respect to CVD, there were apparent benefits of beta-carotene supplementation on subsequent vascular events among a small subgroup of 333 men with prior angina or revascularization. The currently available data from randomized trials of primary prevention are sparse and inconsistent for vitamin E and non-existent for vitamin C and multivitamins. For eye diseases, namely cataract and age-related macular degeneration, there are no completed large-scale randomized trials of antioxidant vitamins.

**CONCLUSIONS:** PHS II is unique in several respects. PHS II is the only primary prevention trial in apparently healthy men testing the balance of benefits and risks of vitamin E on cancer and CVD. In addition, PHS II is the only primary prevention trial in apparently healthy men to test the balance of benefits and risks of vitamin C, multivitamins, as well as any single antioxidant vitamin, alone and in combination, on cancer, CVD, and eye diseases. Finally, PHS II is the only trial testing a priori the hypotheses that beta-carotene and vitamin E may reduce the risks of prostate cancer. Thus, PHS II will add unique as well as importantly relevant and complementary information to the totality of evidence from other completed and ongoing large-scale randomized trials on the balance of benefits and risks of beta-carotene, vitamin E, vitamin C, and multivitamins alone and in combination on prevention of cancer, CVD and eye diseases.

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