

# Clinical trials of antioxydants for cardiovascular prevention in primary prevention

TrialResults-center [www.trialresultscenter.org](http://www.trialresultscenter.org)

## 1 antioxydant

Trial	Treatments	Patients	Trials design and methods
<b>vitamin E vs control</b>			
<b>PPP , 2001</b> n=2231/2264 follow-up: 3.6y	vitamin E (300 mg/day) versus no vitamin E	men and women aged 50 years or greater, with at least one of the major recognised cardiovascular risk factors	Factorial plan open Italy
<b>beta carotene vs placebo</b>			
<b>ATBC beta carotene , 1994</b> n=14560/14573 follow-up: 6.1 median (range 5-8y)	beta carotene 20mg four times daily versus placebo	male smokers 50 to 69 years of age from southwestern Finland	Factorial plan double-blind Southwestern Finland
<b>CARET beta carotene , 1996</b> n=9420/8894 follow-up: 4 y	combination of 30 mg of beta carotene per day and 25,000 IU of retinol (vitamin A) in the form of retinyl palmitate per day versus placebo	smokers, former smokers, and workers exposed to asbestos	Parallel groups double-blind USA
<b>PHS beta carotene , 1996</b> n=11036/1035 follow-up: 12 y	beta carotene 50 mg on alternate days versus placebo	male physicians, 40 to 84 years of age with no history of cancer (except nonmelanoma skin cancer), myocardial infarction, stroke, or transient cerebral ischemia	Factorial plan double-blind USA
<b>WHS beta carotene , 1999</b> [NCT00000479] n=19939/19937 follow-up: 2.1y (range 0 - 2.72y)	beta carotene 50mg four times daily versus placebo	female health professionals, aged 45 years or older and without a history of cancer (except nonmelanoma skin cancer), coronary heart disease, or cerebrovascular disease	Factorial plan double-blind USA
<b>combination vs placebo</b>			
<b>PHS II beta carotene , 2003</b> [NCT00270647] n=2967/2989 follow-up: 8 years	400 IU of vitamin E every other day and 500 mg of vitamin C daily versus placebo	US male physicians enrolled, aged 50 years or older	Factorial plan double-blind
<b>SUVIMAX , 2005</b> n=6481/6536 follow-up: 7.5 years	single daily capsule of combination of antioxydants: 120 mg of ascorbic acid, 30 mg of vitamin E, 6 mg of beta carotene, 100 g of selenium, and 20 mg of zinc versus matched placebo	women aged 35-60 years and men aged 45-60 years	Parallel groups double-blind France
<b>vitamin C vs placebo</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>PHS II vitamin C , 2008</b> [NCT00270647] n=7329/7312 follow-up: 8 years (mean)	vitamin C 500mg daily versus placebo	US male physicians aged 50 years or older	Factorial plan double blind US
<b>vitamin E vs placebo</b>			
<b>ATBC vitamin E , 1994</b> n=14564/14569 follow-up: 6.1 median (range 5-8y)	vitamin E (alpha-tocopherol) 50mg/d versus placebo	male smokers 50 to 69 years of age from southwestern Finland	Factorial plan double-blind Southwestern Finland
<b>WHS vitamin E , 2005</b> [NCT00000479] n=19937/19939 follow-up: 10.1 y	vitamin E 600 IU every other day (-tocopherol) versus placebo	apparently healthy US women aged at least 45 years	Factorial plan double-blind US
<b>PHS II vitamin E , 2008</b> [NCT00270647] n=7315/7326 follow-up: 8 years (mean)	vitamin E 400IU every two days versus placebo	US male physicians aged 50 years or older	double blind US
<b>AREDS , 2001</b> n=2370/2387 follow-up: 6.3 y	daily supplementation of antioxidants (500 mg of vitamin C, 400 IU of vitamin E, and 15 mg of beta carotene) versus placebo	patients with age-related lens opacities and visual acuity loss	Factorial plan double-blind USA
<b>Linxian , 1993</b> n=14792/14792 follow-up: 5y	-	Apparently healthy Individuals of ages 40-69	

2

## References

### PPP, 2001:

de Gaetano G Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. Collaborative Group of the Primary Prevention Project. Lancet 2001 Jan 13;357:89-95 [[11197445](#)]

### ATBC beta carotene, 1994:

The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. N Engl J Med 1994 Apr 14;330:1029-35 [[8127329](#)]

Kataja-Tuomola MK, Kontto JP, Mnnist S, Albanes D, Virtamo JR Effect of alpha-tocopherol and beta-carotene supplementation on macrovascular complications and total mortality from diabetes: results of the ATBC Study. Ann Med 2010 Apr;42:178-86 [[20350251](#)]

### CARET beta carotene, 1996:

Omenn GS, Goodman GE, Thornquist MD, Balmes J, Cullen MR, Glass A, Keogh JP, Meyskens FL, Valanis B, Williams JH, Barnhart S, Hammar S Effects of a combination of beta carotene and vitamin A on lung cancer and cardiovascular disease. N Engl J Med 1996 May 2;334:1150-5 [[8602180](#)]

Goodman GE, Thornquist MD, Balmes J, Cullen MR, Meyskens FL Jr, Omenn GS, Valanis B, Williams JH Jr The Beta-Carotene and Retinol Efficacy Trial: incidence of lung cancer and cardiovascular disease mortality during 6-year follow-up after stopping beta-carotene and retinol supplements. J Natl Cancer Inst 2004;96:1743-50 [[15572756](#)] [10.1093/jnci/djh320](#)

### PHS beta carotene, 1996:

Hennekens CH, Buring JE, Manson JE, Stampfer M, Rosner B, Cook NR, Belanger C, LaMotte F, Gaziano JM, Ridker PM, Willett W, Peto R Lack of effect of long-term supplementation with beta carotene on the incidence of malignant neoplasms and cardiovascular disease. N Engl J Med 1996 May 2;334:1145-9 [[8602179](#)]

### **WHS beta carotene, 1999:**

Lee IM, Cook NR, Manson JE, Buring JE, Hennekens CH Beta-carotene supplementation and incidence of cancer and cardiovascular disease: the Women's Health Study. *J Natl Cancer Inst* 1999 Dec 15;91:2102-6 [[10601381](#)]

Lee IM, Cook NR, Gaziano JM, Gordon D, Ridker PM, Manson JE, Hennekens CH, Buring JE Vitamin E in the primary prevention of cardiovascular disease and cancer: the Women's Health Study: a randomized controlled trial. *JAMA* 2005;294:56-65 [[15998891](#)] [10.1001/jama.294.1.56](#)

Buring JE, Hennekens CH. The WomensHealth Study: rationale and background. *J Myocardial Ischemia* 1992;4:3040

### **PHS II beta carotene, 2003:**

Christen WG, Gaziano JM, Hennekens CH 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. *Ann Epidemiol* 2000;10:125-34 [[10691066](#)]

Grodstein F, Kang JH, Glynn RJ, Cook NR, Gaziano JM A randomized trial of beta carotene supplementation and cognitive function in men: the Physicians' Health Study II. *Arch Intern Med* 2007;167:2184-90 [[17998490](#)]

Sesso HD, Buring JE, Christen WG, Kurth T, Belanger C, MacFadyen J, Bubes V, Manson JE, Glynn RJ, Gaziano JM Vitamins E and C in the prevention of cardiovascular disease in men: the Physicians' Health Study II randomized controlled trial. *JAMA* 2008;300:2123-33 [[18997197](#)]

### **SUVIMAX, 2005:**

Hercberg S, Galan P, Preziosi P, Bertrais S, Mennen L, Malvy D, Roussel AM, Favier A, Brianon S The SU.VI.MAX Study: a randomized, placebo-controlled trial of the health effects of antioxidant vitamins and minerals. *Arch Intern Med* 2004 Nov 22;164:2335-42 [[15557412](#)]

Hercberg S, Preziosi P, Brianon S, Galan P, Triol I, Malvy D, Roussel AM, Favier A A primary prevention trial using nutritional doses of antioxidant vitamins and minerals in cardiovascular diseases and cancers in a general population: the SU.VI.MAX study—design, methods, and participant characteristics. *Supplementation en Vitamines et Minéraux Antioxydants. Control Clin Trials* 1998;19:336-51 [[9683310](#)]

Hercberg S, Galan P, Preziosi P, Roussel AM, Arnaud J, Richard MJ, Malvy D, Paul-Dauphin A, Brianon S, Favier A Background and rationale behind the SU.VI.MAX Study, a prevention trial using nutritional doses of a combination of antioxidant vitamins and minerals to reduce cardiovascular diseases and cancers. *Supplementation en Vitamines et Minéraux Antioxydants Study. Int J Vitam Nutr Res* 1998;68:3-20 [[9503043](#)]

### **PHS II vitamin C, 2008:**

Sesso HD, Buring JE, Christen WG, Kurth T, Belanger C, Macfadyen J, Bubes V, Manson JE, Glynn RJ, Gaziano JM Vitamins E and C in the Prevention of Cardiovascular Disease in Men: The Physicians' Health Study II Randomized Controlled Trial. *JAMA* 2008;: [[18997197](#)]

### **ATBC vitamin E, 1994:**

The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. *N Engl J Med* 1994 Apr 14;330:1029-35 [[8127329](#)]

Kataja-Tuomola MK, Kontto JP, Mnnist S, Albanes D, Virtamo JR Effect of alpha-tocopherol and beta-carotene supplementation on macrovascular complications and total mortality from diabetes: results of the ATBC Study. *Ann Med* 2010 Apr;42:178-86 [[20350251](#)]

Leppl JM, Virtamo J, Fogelholm R, Huttunen JK, Albanes D, Taylor PR, Heinonen OP Controlled trial of alpha-tocopherol and beta-carotene supplements on stroke incidence and mortality in male smokers. *Arterioscler Thromb Vasc Biol* 2000;20:230-5 [[10634823](#)]

### **WHS vitamin E, 2005:**

Lee IM, Cook NR, Gaziano JM, Gordon D, Ridker PM, Manson JE, Hennekens CH, Buring JE Vitamin E in the primary prevention of cardiovascular disease and cancer: the Women's Health Study: a randomized controlled trial. *JAMA* 2005;294:56-65 [[15998891](#)] [10.1001/jama.294.1.56](#)

### **PHS II vitamin E, 2008:**

Sesso HD, Buring JE, Christen WG, Kurth T, Belanger C, MacFadyen J, Bubes V, Manson JE, Glynn RJ, Gaziano JM Vitamins E and C in the prevention of cardiovascular disease in men: the Physicians' Health Study II randomized controlled trial. *JAMA* 2008 Nov 12;300:2123-33 [[18997197](#)]

### **AREDS, 2001:**

A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E and beta carotene for age-related cataract and vision loss: AREDS report no. 9. *Arch Ophthalmol* 2001 Oct;119:1439-52 [[11594943](#)]

### **Linxian, 1993:**

Blot WJ, Li JY, Taylor PR, Guo W, Dawsey S, Wang GQ, Yang CS, Zheng SF, Gail M, Li GY Nutrition intervention trials in Linxian, China: supplementation with specific vitamin/mineral combinations, cancer incidence, and disease-specific mortality in the general population. *J Natl Cancer Inst* 1993;85:1483-92 [[8360931](#)]

Mark SD, Wang W, Fraumeni JF Jr, Li JY, Taylor PR, Wang GQ, Guo W, Dawsey SM, Li B, Blot WJ Lowered risks of hypertension and cerebrovascular disease after vitamin/mineral supplementation: the Linxian Nutrition Intervention Trial. *Am J Epidemiol* 1996 Apr 1;143:658-64 [[8651227](#)]

## **2 About TrialResults-center.org**

TrialResults-center is an innovative knowledge database that collects the results of RCTs and provides dynamic interactive systematic reviews and meta-analysis in the field of all major heart and vessels diseases.

The TrialResults-center database provides a unique view of the treatment efficacy based on all data provided directly from clinical trial results, offering a valuable alternative to personal bibliographic search, published meta-analysis, etc. Furthermore, it would allow comparing easily the various concurrent therapeutic for the same clinical condition.

Rigorous meta-analysis method is used to populate TrialResults-center: widespread search of published and non published trials, study selection using pre-specified criteria, data extraction using standard form.

TrialResults-center is continually updated on a weekly basis. We continually search all new results (whatever their publication channel) and these news results are immediately added to the database with a maximum of 1 week.

TrialResults-center is non-profit and self-funded.