

# Clinical trials of vitamin E

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## 1 cardiovascular prevention

| Trial  | Treatments   | Patients   | Trials design and methods  |
|--|--|--|--|
| <b>vitamin E vs control</b>  |  |  |  |
| <b>GISSI , 1999</b><br>n=5660/5664<br>follow-up: 3.5y                                  | vitamin E 300mg/d<br>versus<br>no vitamine E                               | patients with recent (3 months)<br>myocardial infarction   | Factorial plan<br>open<br>Italy  |
| <b>PPP , 2001</b><br>n=2231/2264<br>follow-up: 3.6y                                    | vitamin E (300 mg/day)<br>versus<br>no vitamin E                           | men and women aged 50 years or greater,<br>with at least one of the major recognised<br>cardiovascular risk factors  | Factorial plan<br>open<br>Italy  |
| <b>vitamin E vs placebo</b>  |  |  |  |
| <b>CHAOS , 1996</b><br>n=1035/967<br>follow-up: 1.5y                                   | vitamin E 400-800UI/d (alpha<br>tocopherol)<br>versus<br>identical placebo | patients with angiographically proven<br>coronary atherosclerosis  | Parallel groups<br>double-blind<br>UK  |
| <b>SPACE , 2000</b><br>n=97/99<br>follow-up: 1.42 years                                | vitamin E 800 IU daily<br>versus<br>matching placebo                       | Haemodialysis patients aged 40-75 years<br>with pre-existing cardiovascular disease  | Parallel groups<br>double -blind<br>Israel   |
| <b>HOPE , 2000</b><br>n=4761/4780<br>follow-up: 4.5y                                   | vitamin E 400IU/d from natural sources<br>versus<br>matching placebo       | women and men 55 years of age or older<br>who were at high risk for cardiovascular<br>events because they had cardiovascular<br>disease or diabetes in addition to one<br>other risk factor. | Factorial plan<br>double-blind<br>Multinational: Canada, USA, Europe,<br>South America |
| <b>ATBC vitamin E , 1994</b><br>n=14564/14569<br>follow-up: 6.1 median<br>(range 5-8y) | vitamin E (alpha-tocopherol) 50mg/d<br>versus<br>placebo                   | male smokers 50 to 69 years of age from<br>southwestern Finland  | Factorial plan<br>double-blind<br>Southwestern Finland                                 |
| <b>WACS vitamin E , 2007</b><br>[NCT00000541]<br>n=4083/4088<br>follow-up: 9.4 years   | vitamin E (600IU every two days)<br>versus<br>placebo                      | female health professionals at increased<br>risk (40 years or older with a history of<br>CVD or 3 or more CVD risk factors)  | Factorial plan<br>double blind<br>US   |

continued...

| <b>Trial</b>  | <b>Treatments</b>   | <b>Patients</b>  | <b>Trials design and methods</b>                                  |
|---|---|--|---|
| <b>WHS vitamin E , 2005</b><br>[NCT00000479]<br>n=19937/19939<br>follow-up: 10.1 y          | vitamin E 600 IU every other day (-tocopherol)<br>versus<br>placebo   | apparently healthy US women aged at least 45 years   | Factorial plan<br>double-blind<br>US                              |
| <b>PHS II vitamin E , 2008</b><br>[NCT00270647]<br>n=7315/7326<br>follow-up: 8 years (mean) | vitamin E 400IU every two days<br>versus<br>placebo   | US male physicians aged 50 years or older  | double blind<br>US  |
| <b>HOPE renal insufficiency subgroup , 2004</b><br>n=499/494<br>follow-up: 4.5y             | vitamin E 400 IU/day, natural<br>versus<br>placebo  | patients with either known cardiovascular disease or diabetes and at least one additional coronary risk factor and renal insufficiency (sub group) | Factorial plan<br>double-blind<br>North and South America, Europe |
| <b>ASAP , 2000</b><br>n=260/260<br>follow-up: 3 years                                       | d-alpha-tocopherol 91 mg (136 IU) twice daily<br>versus<br>placebo  | smoking and nonsmoking men and postmenopausal women aged 45-69 years with serum cholesterol $\geq$ 5.0 mmol/l                                      | Factorial plan<br>double-blind<br>Finland                         |
| <b>ATBC 2nd prev subgroup (vitamin E) , 1998</b><br>n=916/879<br>follow-up: 3.79 y          | alpha tocopherol (vitamin E) 50 mg/day<br>versus<br>placebo   | patients enrolled in the ATBC trial and who had angina pectoris in the Rose chest pain questionnaire at baseline                                   | Factorial plan<br>double-blind<br>Finland                         |
| <b>AREDS , 2001</b><br>n=2370/2387<br>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)<br>versus<br>placebo | patients with age-related lens opacities and visual acuity loss  | Factorial plan<br>double-blind<br>USA                             |
| <b>Linxian , 1993</b><br>n=14792/14792<br>follow-up: 5y                                     | -   | Apparently healthy Individuals of ages 40-69   |   |

More details and results :

- antioxidants for cardiovascular prevention in all type of patients at <http://www.trialresultscenter.org/go-Q131>
- antioxidants for cardiovascular prevention in patients with renal disease at <http://www.trialresultscenter.org/go-Q432>
- antioxidants for cardiovascular prevention in primary prevention at <http://www.trialresultscenter.org/go-Q433>
- antioxidants for cardiovascular prevention in secondary prevention at <http://www.trialresultscenter.org/go-Q434>

## References

**GISSI, 1999:**

Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico. *Lancet* 1999 Aug 7;354:447-55 [[10465168](#)]

**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](#)]

**CHAOS, 1996:**

Stephens NG, Parsons A, Schofield PM, Kelly F, Cheeseman K, Mitchinson MJ Randomised controlled trial of vitamin E in patients with coronary disease: Cambridge Heart Antioxidant Study (CHAOS) *Lancet* 1996 Mar 23;347:781-6 [[8622332](#)]

**SPACE, 2000:**

Boaz M, Smetana S, Weinstein T, Matas Z, Gafter U, Iaina A, Knecht A, Weissgarten Y, Brunner D, Fainaru M, Green MS Secondary prevention with antioxidants of cardiovascular disease in endstage renal disease (SPACE): randomised placebo-controlled trial. *Lancet* 2000 Oct 7;356:1213-8 [[11072938](#)]

**HOPE, 2000:**

Yusuf S, Dagenais G, Pogue J, Bosch J, Sleight P Vitamin E supplementation and cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med* 2000 Jan 20;342:154-60 [[10639540](#)]

Lonn E, Bosch J, Yusuf S, Sheridan P, Pogue J, Arnold JM, Ross C, Arnold A, Sleight P, Probstfield J, Dagenais GR Effects of long-term vitamin E supplementation on cardiovascular events and cancer: a randomized controlled trial. *JAMA* 2005 Mar 16;293:1338-47 [[15769967](#)]

**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](#)]

Lepl J, 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](#)]

**WACS vitamin E, 2007:**

Cook NR, Albert CM, Gaziano JM, Zaharris E, MacFadyen J, Danielson E, Buring JE, Manson JE A randomized factorial trial of vitamins C and E and beta carotene in the secondary prevention of cardiovascular events in women: results from the Women's Antioxidant Cardiovascular Study. *Arch Intern Med* 2007;167:1610-8 [[17698683](#)]

Manson JE, Gaziano JM, Spelsberg A, Ridker PM, Cook NR, Buring JE, Willett WC, Hennekens CH A secondary prevention trial of antioxidant vitamins and cardiovascular disease in women. Rationale, design, and methods. The WACS Research Group. *Ann Epidemiol* 1995;5:261-9 [[8520707](#)]

**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](#)]

**HOPE renal insufficiency subgroup, 2004:**

Mann JF, Lonn EM, Yi Q, Gerstein HC, Hoogwerf BJ, Pogue J, Bosch J, Dagenais GR, Yusuf S Effects of vitamin E on cardiovascular outcomes in people with mild-to-moderate renal insufficiency: results of the HOPE study. *Kidney Int* 2004;65:1375-80 [[15086477](#)] [10.1111/j.1523-1755.2004.00513.x](#)

**ASAP, 2000:**

Leppel 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](#)]

Salonen JT, Nyyssnen K, Salonen R, Lakka HM, Kaikkonen J, Porkkala-Sarataho E, Voutilainen S, Lakka TA, Rissanen T, Leskinen L, Tuomainen TP, Valkonen VP, Ristonmaa U, Poulsen HE Antioxidant Supplementation in Atherosclerosis Prevention (ASAP) study: a randomized trial of the effect of vitamins E and C on 3-year progression of carotid atherosclerosis. *J Intern Med* 2000;248:377-86 [[11123502](#)]

Salonen RM, Nyyssnen K, Kaikkonen J, Porkkala-Sarataho E, Voutilainen S, Rissanen TH, Tuomainen TP, Valkonen VP, Ristonmaa U, Lakka HM, Vanharanta M, Salonen JT, Poulsen HE Six-year effect of combined vitamin C and E supplementation on atherosclerotic progression: the Antioxidant Supplementation in Atherosclerosis Prevention (ASAP) Study. *Circulation* 2003;107:947-53 [[12600905](#)]

**ATBC 2nd prev subgroup (vitamin E), 1998:**

Rapola JM, Virtamo J, Ripatti S, Haukka JK, Huttunen JK, Albanes D, Taylor PR, Heinonen OP Effects of alpha tocopherol and beta carotene supplements on symptoms, progression, and prognosis of angina pectoris. *Heart* 1998;79:454-8 [[9659191](#)]

Rapola JM, Virtamo J, Ripatti S, Huttunen JK, Albanes D, Taylor PR, Heinonen OP Randomised trial of alpha-tocopherol and beta-carotene supplements on incidence of major coronary events in men with previous myocardial infarction. *Lancet* 1997;349:1715-20 [[9193380](#)] [10.1016/S0140-6736\(97\)01234-8](#)

**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](#)]

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