

# Clinical trials of antioxidants for cardiovascular prevention in all type of patients

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

## 1 antioxidant

Trial	Treatments	Patients	Trials design and methods
<b>vitamin E vs control</b>			
<b>GISSI , 1999</b> n=5660/5664 follow-up: 3.5y	vitamin E 300mg/d versus no vitamin E	patients with recent (3 months) myocardial infarction	Factorial plan open Italy
<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>acetylcysteine vs placebo</b>			
<b>Tepel , 2003</b> n=64/70 follow-up: 14.5 y	acetylcysteine 600 mg twice daily versus placebo	patients undergoing maintenance hemodialysis for a minimum of 3 months 3 times weekly in an ambulatory center	Parallel groups double-blind Germany
<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>NSCP (Green) beta carotene , 1999</b> n=820/801 follow-up: 4.5 y	beta carotene 30mg four times daily versus placebo	residents of Nambour	Factorial plan double-blind Queensland, Australia
<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>SCP beta carotene , 1990</b> n=913/892 follow-up: 4.02 years	beta carotene 50mg four times daily versus placebo	Age <85 years (most <65 years); previous non-melanoma skin cancer; 69% male	Parallel groups double-blind USA

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>WACS beta-caroten , 2007</b> [NCT00000541] n=4084/4087 follow-up: 9.4 years	beta carotene (Lurotin) 50 mg every two days versus placebo	female health professionals at increased risk (40 years or older with a history of CVD or 3 or more CVD risk factors)	Factorial plan double blind
<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 (multivitamin) , 2012</b> [NCT00270647] n=7317/7324 follow-up: 11.2y (median)	Daily multivitamin versus placebo	male US physicians initially aged 50 years or older	Parallel groups double-blind USA
<b>POPADAD (antioxydant) , 2008</b> [ISRCTN53295293] n=640/636 follow-up:	antioxidant capsule containing (alpha-tocopherol 200 mg, ascorbic acid 100 mg, pyridoxine hydrochloride 25 mg, zinc sulphate 10 mg, nicotinamide 10 mg, lecithin 9.4 mg, and sodium selenite 0.8 mg) versus placebo	patients with diabetes mellitus and asymptomatic peripheral arterial disease	Factorial plan double blind Scotland
<b>HATS , 2001</b> n=84/76 follow-up:	antioxidant-therapy (vitamins) versus placebo	patients with coronary disease, low HDL cholesterol levels and normal LDL cholesterol	Factorial plan double-blind USA, Canada
<b>MVP , 1997</b> n=158/159 follow-up: 6 montsh	multivitamins (30,000 IU of beta carotene, 500 mg of vitamin C, and 700 IU of vitamin E) for four weeks before and six months after angioplasty versus placebo	patient undergoing angioplasty	Factorial plan double-blind Canada
<b>HPS antioxidant , 2002</b> n=10269/10267 follow-up: jul 1994 - may 1997	antioxidant vitamin supplementation (600 mg vitamin E, 250 mg vitamin C, and 20 mg -carotene daily) versus matching placebo	UK adults (aged 4080) with coronary disease, other occlusive arterial disease, or diabetes	Factorial plan double-blind UK
<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

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>WAVE (Waters) , 2002</b> n=212/211 follow-up: 2.8 years	400 IU of vitamin E twice daily plus 500 mg of vitamin C twice daily versus placebo	postmenopausal women with at least one 15% to 75% coronary stenosis	Factorial plan double-blind US, Canada
<b>succinobucol vs placebo</b>			
<b>ARISE , 2008</b> [NCT00066898] n=3078/3066 follow-up: 24 mo (range 12-36 mo)	succinobucol 300 mg once daily versus placebo	patients with recent (14-365 days) acute coronary syndromes already managed with conventional treatments	Parallel groups double blind Canada, US, UK, South Africa
<b>vitamin C vs placebo</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>WACS vitamin C , 2007</b> [NCT00000541] n=4087/4084 follow-up: 9.4 years	vitamin C (ascorbic acid) 500 mg/d versus placebo	female health professionals at increased risk (40 years or older with a history of CVD or 3 or more CVD risk factors)	double blind US
<b>vitamin E vs placebo</b>			
<b>CHAOS , 1996</b> n=1035/967 follow-up: 1.5y	vitamin E 400-800IU/d (alpha tocopherol) versus identical placebo	patients with angiographically proven coronary atherosclerosis	Parallel groups double-blind UK
<b>HOPE , 2000</b> n=4761/4780 follow-up: 4.5y	vitamin E 400IU/d from natural sources versus matching placebo	women and men 55 years of age or older who were at high risk for cardiovascular events because they had cardiovascular disease or diabetes in addition to one other risk factor.	Factorial plan double-blind Multinational: Canada, USA, Europe, South America
<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>WACS vitamin E , 2007</b> [NCT00000541] n=4083/4088 follow-up: 9.4 years	vitamin E (600IU every two days) versus placebo	female health professionals at increased risk (40 years or older with a history of CVD or 3 or more CVD risk factors)	Factorial plan double blind US
<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

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>ASAP , 2000</b> n=260/260 follow-up: 3 years	d-alpha-tocopherol 91 mg (136 IU) twice daily versus placebo	smoking and nonsmoking men and postmenopausal women aged 45-69 years with serum cholesterol $\geq$ 5.0 mmol/l	Factorial plan double-blind Finland
<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	

## 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](#)]

### Tepel, 2003:

Tepel M, van der Giet M, Statz M, Jankowski J, Zidek W The antioxidant acetylcysteine reduces cardiovascular events in patients with end-stage renal failure: a randomized, controlled trial. *Circulation* 2003;107:992-5 [[12600912](#)]

### 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](#)

### NSCP (Green) beta carotene, 1999:

Green A, Williams G, Neale R, Hart V, Leslie D, Parsons P, Marks GC, Gaffney P, Battistutta D, Frost C, Lang C, Russell A Daily sunscreen application and betacarotene supplementation in prevention of basal-cell and squamous-cell carcinomas of the skin: a randomised controlled trial. *Lancet* 1999 Aug 28;354:723-9 [[10475183](#)]

### 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](#)]

### SCP beta carotene, 1990:

Greenberg ER, Baron JA, Stukel TA, Stevens MM, Mandel JS, Spencer SK, Elias PM, Lowe N, Nierenberg DW, Bayrd G A clinical trial of beta carotene to prevent basal-cell and squamous-cell cancers of the skin. The Skin Cancer Prevention Study Group. *N Engl J Med* 1990 Sep 20;323:789-95 [[2202901](#)]

### **WACS beta-caroten, 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 Aug 13-27;167:1610-8 [[17698683](#)]

Bassuk SS, Albert CM, Cook NR, Zaharris E, MacFadyen JG, Danielson E, Van Denburgh M, Buring JE, Manson JE The Women's Antioxidant Cardiovascular Study: design and baseline characteristics of participants. *J Womens Health (Larchmt)* 2004;13:99-117 [[15006283](#)] [10.1089/154099904322836519](#)

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 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 (multivitamin), 2012:**

Sesso HD, Christen WG, Bubes V, Smith JP, MacFadyen J, Schvartz M, Manson JE, Glynn RJ, Buring JE, Gaziano JM Multivitamins in the prevention of cardiovascular disease in men: the Physicians' Health Study II randomized controlled trial. *JAMA* 2012 Nov 7;308:1751-60 [[23117775](#)] [10.1001/jama.2012.14805](#)

Sesso HD, Christen WG, Bubes V, Smith JP, Macfadyen J, Schvartz M, Manson JE, Glynn RJ, Buring JE, Gaziano JM Multivitamins in the Prevention of Cardiovascular Disease in Men: The Physicians' Health Study II Randomized Controlled Trial. *JAMA* 2012;308:1751-60 [[23117775](#)]

### **POPADAD (antioxydant), 2008:**

Belch J, MacCuish A, Campbell I, Cobbe S, Taylor R, Prescott R, Lee R, Bancroft J, MacEwan S, Shepherd J, Macfarlane P, Morris A, Jung R, Kelly C, Connacher A, Peden N, Jamieson A, Matthews D, Leese G, McKnight J, O'Brien I, Semple C, Petrie J, Gordon D, The prevention of progression of arterial disease and diabetes (POPADAD) trial: factorial randomised placebo controlled trial of aspirin and antioxidants in patients with diabetes and asymptomatic peripheral arterial disease. *BMJ* 2008 Oct 16;337:a1840 [[18927173](#)]

### **HATS, 2001:**

Brown BG, Zhao XQ, Chait A, Fisher LD, Cheung MC, Morse JS, Dowdy AA, Marino EK, Bolson EL, Alaupovic P, Frohlich J, Albers JJ Simvastatin and niacin, antioxidant vitamins, or the combination for the prevention of coronary disease. *N Engl J Med* 2001;345:1583-92 [[11757504](#)]

### **MVP, 1997:**

Tardif JC, Ct G, Lesprance J, Bourassa M, Lambert J, Doucet S, Bilodeau L, Nattel S, de Guise P Probuco and multivitamins in the prevention of restenosis after coronary angioplasty. Multivitamins and Probuco Study Group. *N Engl J Med* 1997;337:365-72 [[9241125](#)]

### **HPS antioxidant, 2002:**

MRC/BHF Heart Protection Study of antioxidant vitamin supplementation in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002 Jul 6;360:23-33 [[12114037](#)]

### **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](#)]

#### **WAVE (Waters), 2002:**

Waters DD, Alderman EL, Hsia J, Howard BV, Cobb FR, Rogers WJ, Ouyang P, Thompson P, Tardif JC, Higginson L, Bittner V, Steffes M, Gordon DJ, Proschan M, Younes N, Verter JI Effects of hormone replacement therapy and antioxidant vitamin supplements on coronary atherosclerosis in postmenopausal women: a randomized controlled trial. *JAMA* 2002 Nov 20;288:2432-40 [[12435256](#)]

#### **ARISE, 2008:**

Tardif JC, McMurray JJ, Klug E, Small R, Schumi J, Choi J, Cooper J, Scott R, Lewis EF, L'Allier PL, Pfeffer MA Effects of succinobucol (AGI-1067) after an acute coronary syndrome: a randomised, double-blind, placebo-controlled trial. *Lancet* 2008;371:1761-8 [[18502300](#)]

#### **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](#)]

#### **WACS vitamin C, 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](#)]

Bassuk SS, Albert CM, Cook NR, Zaharris E, MacFadyen JG, Danielson E, Van Denburgh M, Buring JE, Manson JE The Women's Antioxidant Cardiovascular Study: design and baseline characteristics of participants. *J Womens Health (Larchmt)* 2004;13:99-117 [[15006283](#)] [10.1089/154099904322836519](#)

#### **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](#)]

#### **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](#)]

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](#)]

#### **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](#)]

**ASAP, 2000:**

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](#)]

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](#)]

**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.