

Clinical trials of antioxidants for cardiovascular prevention in secondary prevention

TrialResults-center www.trialresultscenter.org

1 antioxidant

Trial	Treatments	Patients	Trials design and methods
vitamin E vs control			
GISSI , 1999 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
beta carotene vs placebo			
ATBC 2nd prev subgroup (beta carotene) , 1998 n=876/919 follow-up: 3.79 y	synthetic beta carotene 20 mg daily versus placebo	patients enrolled in the ATBC trial and who had angina pectoris in the Rose chest pain questionnaire at baseline	Factorial plan double-blind Finland
WACS beta-carotene , 2007 [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
combination vs placebo			
HATS , 2001 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
MVP , 1997 n=158/159 follow-up: 6 monthsh	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
HPS antioxidant , 2002 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
WAVE (Waters) , 2002 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
vitamin C vs placebo			

continued...

Trial	Treatments	Patients	Trials design and methods
WACS vitamin C , 2007 [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
vitamin E vs placebo			
CHAOS , 1996 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
SPACE , 2000 n=97/99 follow-up: 1.42 years	vitamin E 800 IU daily versus matching placebo	Haemodialysis patients aged 40-75 years with pre-existing cardiovascular disease	Parallel groups double -blind Israel
HOPE , 2000 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
WACS vitamin E , 2007 [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
HOPE renal insufficiency subgroup , 2004 n=499/494 follow-up: 4.5y	vitamin E 400 IU/day, natural versus placebo	patients with either known cardiovascular disease or diabetes and at least one additional coronary risk factor and renal insufficiency (sub group)	Factorial plan double-blind North and South America, Europe
ATBC 2nd prev subgroup (vitamin E) , 1998 n=916/879 follow-up: 3.79 y	alpha tocopherol (vitamin E) 50 mg/day versus placebo	patients enrolled in the ATBC trial and who had angina pectoris in the Rose chest pain questionnaire at baseline	Factorial plan double-blind Finland

2

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](#)]

ATBC 2nd prev subgroup (b carotene), 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](#)]

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](#)]

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](#)]

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](#)]

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](#)]

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](#)]

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](#)]

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](#)

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](#)

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.