

Clinical trials of folic acid

TrialResults-center www.trialresultscenter.org

1 post stroke

Trial	Treatments	Patients	Trials design and methods
folic acid, vit B12 and vit B6 vs placebo			
VITATOPS , 2010 [NCT00097669X]]n=4089/4075 follow-up: 3.4 y	folic acid and vitamins B12 and B6 in a single tablet versus placebo	patients with recent stroke or TIA (within the past seven months)
Parallel groups double-blind 20 countries			
high dose - folic acid, vit B12 and vit B6 vs low dose - folic acid, vit B12 and vit B6			
VISP (Toole) , 2004 n=1827/1853 follow-up: 2 y	high-dose of folic acid, pyridoxine (vitamin B6), and cobalamin (vitamin B12) versus low-dose of folic acid, pyridoxine (vitamin B6), and cobalamin (vitamin B12)	adults with nondisabling cerebral infarction	Parallel groups double blind United States, Canada, Scotland

More details and results :

- prevention for post stroke in patients with prior stroke or TIA at <http://www.trialresultscenter.org/go-Q421>

References

VITATOPS, 2010:

Hankey GJ. The Vitamins to Prevent Stroke (VITATOPS) trial: Results of a double-blind, placebo-controlled, randomised trial of B-vitamin therapy in 8164 patients with recent transient ischaemic attack or stroke. 2010 European Stroke Conference: May 26, 2010; Barcelona, Spain

B vitamins in patients with recent transient ischaemic attack or stroke in the VITAMINS TO Prevent Stroke (VITATOPS) trial: a randomised, double-blind, parallel, placebo-controlled trial. Lancet Neurol 2010 Aug 3;: [20688574] [10.1016/S1474-4422\(10\)70187-3](https://doi.org/10.1016/S1474-4422(10)70187-3)

VISP (Toole), 2004:

Spence JD, Bang H, Chambless LE, Stampfer MJ Vitamin Intervention For Stroke Prevention trial: an efficacy analysis. Stroke 2005 Nov;36:2404-9 [16239629]

Toole JF, Malinow MR, Chambless LE, Spence JD, Pettigrew LC, Howard VJ, Sides EG, Wang CH, Stampfer M Lowering homocysteine in patients with ischemic stroke to prevent recurrent stroke, myocardial infarction, and death: the Vitamin Intervention for Stroke Prevention (VISP) randomized controlled trial. JAMA 2004 Feb 4;291:565-75 [14762035]

2 cardiovascular prevention

Trial	Treatments	Patients	Trials design and methods
folic acid vs control			
FOLARDA (Liem) , 2004 n=140/143 follow-up: 1 year	folic acid 5 mg per day for 1 year versus usual care	patients with acute MI and total cholesterol >6.5 mmol/l	Parallel groups open The Netherlands
GOES (Liem) , 2003 n=300/293 follow-up: 24 months	folic acid 0.5 mg per day versus usual care	patients with stable coronary artery disease	Parallel groups open The Netherlands
folic acid, B12 vs control			
NORVIT (folic acid + B12) (Bonaa) , 2006 [NCT00266487] n=1872/1877 follow-up: 36 months	folic acid 0.8mg and B12 0.4 mg daily versus no folic acid and B12	men and women who had had an acute myocardial infarction within seven days before	Factorial plan double-blind Norway
folic acid, vit B12 and vit B6 vs control			
NORVIT (folic acid, B12 and vit B6) (Bonaa) , 2006 [NCT00266487] n=937/943 follow-up: 36 months	0.8 mg of folic acid, 0.4 mg of vitamin B12, and 40 mg of vitamin B6 versus placebo	men and women who had had an acute myocardial infarction within seven days	Factorial plan double-blind Norway
folic acid vs placebo			
CSPPT , 2015 [NCT00794885] n=10348/10354 follow-up:	enalapril 10 mg / folic acid 0.8 mg daily versus Enalapril maleate 10 mg daily	patients with primary hypertension	Parallel groups double-blind China
CHAOS-2 , 2002 n=942/940 follow-up: 1.7 y	folic acid 5 mg per day (for 2 years) versus placebo	patient with CHD	Parallel groups double blind
folic acid, B12 vs placebo			

continued...

Trial	Treatments	Patients	Trials design and methods
WENBIT (folic ac,B12) , 2008 [NCT00354081] n=772/780 follow-up: 38.4 mo	folic acid 0.8mg, vit B12 0.4mg daily versus placebo	adult participants undergoing coronary angiography	Factorial plan double blind Norway
SEARCH , 2007 [NCT00124072] n=6033/6031 follow-up: 7 years	folic acid 2mg/d + vitamin B12 1mg/d versus placebo	patients survivors of myocardial infarction	Factorial plan double blind UK
folic acid, vit B12 and vit B6 vs placebo			
VITATOPS , 2010 [NCT00097669X]] n=4089/4075 follow-up: 3.4 y	folic acid and vitamins B12 and B6 in a single tablet versus placebo	patients with recent stroke or TIA (within the past seven months)
Parallel groups double-blind 20 countries			
SU.FOL.OM3 [ISRCTN41926726] n=1242/1259 follow-up:	supplementation with natural foLate, vitamin B6 and B12 versus placebo	patients with coronary or cerebral event within the previous 12 months	Parallel groups double-blind France
HOPE-2 (Lonn) , 2006 [NCT00106886] n=2758/2764 follow-up: Jan 2000 - dec 2000	folic acid, 2.5 mg, vitamin B6,50 mg and vitamin B12, 1mg versus placebo	patients 55 years of age or older who had vascular disease or diabetes and additional risk factors for atherosclerosis	Parallel groups double blind 13 countries
WAFACS , 2008 [NCT00000541] n=2721/2721 follow-up: 7.3 y	folic acid 2.5mg, vitamin B6 50mg, and vitamin B12 1mg daily versus placebo	women aged 42 years or older, with either a history of CVD or 3 or more coronary risk factors	Parallel groups double blind US
high dose - folic acid, vit B12 and vit B6 vs low dose - folic acid, vit B12 and vit B6			
VISP (Toole) , 2004 n=1827/1853 follow-up: 2 y	high-dose of folic acid, pyridoxine (vitamin B6), and cobalamin (vitamin B12) versus low-dose of folic acid, pyridoxine (vitamin B6), and cobalamin (vitamin B12)	adults with nondisabling cerebral infarction	Parallel groups double blind United States, Canada, Scotland

More details and results :

- plasma homocysteine lowering intervention for cardiovascular prevention in all type of patients at <http://www.trialresultscenter.org/go-Q127>

References

FOLARDA (Liem), 2004:

Liem AH, van Boven AJ, Veeger NJ, Withagen AJ, Robles de Medina RM, Tijssen JG, van Veldhuisen DJ Efficacy of folic acid when added to statin therapy in patients with hypercholesterolemia following acute myocardial infarction: a randomised pilot trial. *Int J Cardiol* 2004;93:175-9 [[14975544](#)] [10.1016/j.ijcard.2003.02.001](#)

GOES (Liem), 2003:

Liem A, Reynierse-Buitenwerf GH, Zwinderman AH, Jukema JW, van Veldhuisen DJ Secondary prevention with folic acid: effects on clinical outcomes. *J Am Coll Cardiol* 2003;41:2105-13 [[12821232](#)]

Liem A, Reynierse-Buitenwerf GH, Zwinderman AH, Jukema JW, van Veldhuisen DJ Secondary prevention with folic acid: results of the Goes extension study. *Heart* 2005;91:1213-4 [[16103563](#)] [10.1136/hrt.2004.035030](#)

NORVIT (folic acid + B12) (Bonna), 2006:

Bnaa KH, Njlstad I, Ueland PM, Schirmer H, Tverdal A, Steigen T, Wang H, Nordrehaug JE, Arnesen E, Rasmussen K Homocysteine lowering and cardiovascular events after acute myocardial infarction. *N Engl J Med* 2006;354:1578-88 [[16531614](#)] [10.1056/NEJMoa055227](#)

NORVIT (folic acid, B12 and vit B6) (Bonna), 2006:

Bnaa KH, Njlstad I, Ueland PM, Schirmer H, Tverdal A, Steigen T, Wang H, Nordrehaug JE, Arnesen E, Rasmussen K Homocysteine lowering and cardiovascular events after acute myocardial infarction. *N Engl J Med* 2006;354:1578-88 [[16531614](#)] [10.1056/NEJMoa055227](#)

CSPPT, 2015:

Huo Y, Li J, Qin X, Huang Y, Wang X, Gottesman RF, Tang G, Wang B, Chen D, He M, Fu J, Cai Y, Shi X, Zhang Y, Cui Y, Sun N, Li X, Cheng X, Wang J, Yang X, Yang T, Xiao C, Zhao G, Dong Q, Zhu D, Wang X, Ge J, Zhao L, Hu D, Liu L, Hou FF Efficacy of Folic Acid Therapy in Primary Prevention of Stroke Among Adults With Hypertension in China: The CSPPT Randomized Clinical Trial. *JAMA* 2015 Mar 15;: [[25771069](#)] [10.1001/jama.2015.2274](#)

CHAOS-2, 2002:

Baker F, Picton D, Blackwood S, Hunt J, Erskine M, Dyas M, et al. Baker F, Picton D, Blackwood S, Hunt J, Blinded comparison of folic acid and placebo in patients with ischaemic heart disease: an outcome trial [abstract] *Circulation* 2002;106(Suppl II):741.

WENBIT (folic ac,B12), 2008:

Ebbing M, Bleie , Ueland PM, Nordrehaug JE, Nilsen DW, Vollset SE, Refsum H, Pedersen EK, Nygrd O *JAMA* 2008;300:795-804 [[18714059](#)] [10.1001/jama.300.7.795](#)

SEARCH, 2007:

Bowman L, Armitage J, Bulbulia R, Parish S, Collins R Study of the effectiveness of additional reductions in cholesterol and homocysteine (SEARCH): characteristics of a randomized trial among 12064 myocardial infarction survivors. *Am Heart J* 2007 Nov;154:815-23, 823.e1-6 [[17967584](#)]

MacMahon M, Kirkpatrick C, Cummings CE, Clayton A, Robinson PJ, Tomiak RH, Liu M, Kush D, Tobert J A pilot study with simvastatin and folic acid/vitamin B12 in preparation for the Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH). *Nutr Metab Cardiovasc Dis* 2000 Aug;10:195-203 [[11079257](#)]

Armitage JM, Bowman L, Clarke RJ, Wallendszus K, Bulbulia R, Rahimi K, Haynes R, Parish S, Sleight P, Peto R, Collins R Effects of Homocysteine-Lowering With Folic Acid Plus Vitamin B12 vs Placebo on Mortality and Major Morbidity in Myocardial Infarction Survivors: A Randomized Trial. *JAMA* 2010 Jun 23;303:2486-94 [[20571015](#)] [10.1001/jama.2010.840](#)

Armitage JM, Bowman L, Clarke RJ, Wallendszus K, Bulbulia R, Rahimi K, Haynes R, Parish S, Sleight P, Peto R, Collins R Effects of homocysteine-lowering with folic acid plus vitamin B12 vs placebo on mortality and major morbidity in myocardial infarction survivors: a randomized trial. *JAMA* 2010;303:2486-94 [[20571015](#)] [10.1001/jama.2010.840](#)

VITATOPS, 2010:

Hankey GJ. The Vitamins to Prevent Stroke (VITATOPS) trial: Results of a double-blind, placebo-controlled, randomised trial of B-vitamin therapy in 8164 patients with recent transient ischaemic attack or stroke. 2010 European Stroke Conference: May 26, 2010; Barcelona, Spain

B vitamins in patients with recent transient ischaemic attack or stroke in the VITamins TO Prevent Stroke (VITATOPS) trial: a randomised, double-blind, parallel, placebo-controlled trial. *Lancet Neurol* 2010 Aug 3;: [[20688574](#)] [10.1016/S1474-4422\(10\)70187-3](#)

SU.FOL.OM3, :

Galan P, Kesse-Guyot E, Czernichow S, Briancon S, Blacher J, Hercberg S Effects of B vitamins and omega 3 fatty acids on cardiovascular diseases: a randomised placebo controlled trial. *BMJ* 2010;341:c6273 [[21115589](#)]

HOPE-2 (Lonn), 2006:

Lonn E, Yusuf S, Arnold MJ, Sheridan P, Pogue J, Micks M, McQueen MJ, Probstfield J, Fodor G, Held C, Genest J Jr Homocysteine lowering with folic acid and B vitamins in vascular disease. *N Engl J Med* 2006 Apr 13;354:1567-77 [[16531613](#)]

Ray JG, Kearon C, Yi Q, Sheridan P, Lonn E Homocysteine-lowering therapy and risk for venous thromboembolism: a randomized trial. *Ann Intern Med* 2007 Jun 5;146:761-7 [[17470822](#)]

Sawka AM, Ray JG, Yi Q, Josse RG, Lonn E Randomized clinical trial of homocysteine level lowering therapy and fractures. *Arch Intern Med* 2007 Oct 22;167:2136-9 [[17954810](#)]

Mann JF, Sheridan P, McQueen MJ, Held C, Arnold JM, Fodor G, Yusuf S, Lonn EM Homocysteine lowering with folic acid and B vitamins in people with chronic kidney disease—results of the renal Hope-2 study. *Nephrol Dial Transplant* 2008 Feb;23:645-53 [[18003666](#)]

Saposnik G, Ray JG, Sheridan P, McQueen M, Lonn E Homocysteine-lowering therapy and stroke risk, severity, and disability: additional findings from the HOPE 2 trial. *Stroke* 2009;40:1365-72 [[19228852](#)]

Lonn E, Held C, Arnold JM, Probstfield J, McQueen M, Micks M, Pogue J, Sheridan P, Bosch J, Genest J, Yusuf S Rationale, design and baseline characteristics of a large, simple, randomized trial of combined folic acid and vitamins B6 and B12 in high-risk patients: the Heart Outcomes Prevention Evaluation (HOPE)-2 trial. *Can J Cardiol* 2006;22:47-53 [[16450017](#)]

WAFACS, 2008:

Albert CM, Cook NR, Gaziano JM, Zaharris E, MacFadyen J, Danielson E, Buring JE, Manson JE Effect of folic acid and B vitamins on risk of cardiovascular events and total mortality among women at high risk for cardiovascular disease: a randomized trial. *JAMA* 2008 May 7;299:2027-36 [[18460663](#)]

Song Y, Cook NR, Albert CM, Van Denburgh M, Manson JE Effect of homocysteine-lowering treatment with folic Acid and B vitamins on risk of type 2 diabetes in women: a randomized, controlled trial. *Diabetes* 2009;58:1921-8 [[19491213](#)]

VISP (Toole), 2004:

Spence JD, Bang H, Chambless LE, Stampfer MJ Vitamin Intervention For Stroke Prevention trial: an efficacy analysis. *Stroke* 2005 Nov;36:2404-9 [[16239629](#)]

Toole JF, Malinow MR, Chambless LE, Spence JD, Pettigrew LC, Howard VJ, Sides EG, Wang CH, Stampfer M Lowering homocysteine in patients with ischemic stroke to prevent recurrent stroke, myocardial infarction, and death: the Vitamin Intervention for Stroke Prevention (VISP) randomized controlled trial. *JAMA* 2004 Feb 4;291:565-75 [[14762035](#)]

Entry terms: Folic Acid, Vitamin M, Pteroylglutamic Acid, Folate, Folvite, Folacin,