

# Clinical trials of cholesterol lowering intervention for cardiovascular prevention in all chronic situations

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

## 1 colestipol-niacin

Trial	Treatments	Patients	Trials design and methods
<b>colestipol-niacin vs placebo</b>			
<b>CLAS , 1987</b> n=94/94 follow-up: 2 ans	Colestipol + Niacin 30 g / j 3-12 g / j (titr sur chaque patient sur la base de la baisse de cholestrol sanguin) versus placebo: methyl cellulose	Patients coronariens avec antcdent de revascularisation chirurgicale coronarienne.	Parallel groups Non dterminable
<b>CLAS , 1987</b> n=NA follow-up: 65279;2 years	colestipol + niacin versus placebo	nonsmoking men aged 40 to 59 years with previous coronary bypass surgery	Parallel groups double blind

## References

### CLAS, 1987:

Blankenhorn DH, Brooks SH. Angiographic trials of lipid-lowering therapy. *Arteriosclerosis* 1981; 1: 242-249.

The Cholesterol Lowering Atherosclerosis Study (CLAS): design, methods, and baseline results. Blankenhorn DH, Johnson RL, Nessim SA, Azen SP, Sanmarco ME, Selzer RH *Control Clin Trials* 1987 Dec;8:356-87 [3327654]

Beneficial effects of combined colestipol-niacin therapy on coronary atherosclerosis and coronary venous bypass grafts. Blankenhorn DH, Nessim SA, Johnson RL, Sanmarco ME, Azen SP, Cashin-Hemphill L *JAMA* 1987 Jun 19;257:3233-40 [3295315]

Comparison of computer- and human-derived coronary angiographic end-point measures for controlled therapy trials. Mack WJ, Selzer RH, Pogoda JM, Lee PL, Shircore AM, Azen SP, Blankenhorn DH *Arterioscler Thromb* 1992 Mar;12:348-56 [1547194]

### CLAS, 1987:

Blankenhorn DH, Johnson RL, Nessim SA, Azen SP, Sanmarco ME, Selzer RH The Cholesterol Lowering Atherosclerosis Study (CLAS): design, methods, and baseline results. *Control Clin Trials* 1987;8:356-87 [3327654]

Cashin-Hemphill L, Mack WJ, Pogoda JM, Sanmarco ME, Azen SP, Blankenhorn DH Beneficial effects of colestipol-niacin on coronary atherosclerosis. A 4-year follow-up. *JAMA* 1990;264:3013-7 [2243429]

Blankenhorn DH, Nessim SA, Johnson RL, Sanmarco ME, Azen SP, Cashin-Hemphill L Beneficial effects of combined colestipol-niacin therapy on coronary atherosclerosis and coronary venous bypass grafts. *JAMA* 1987;257:3233-40 [3295315]

Blankenhorn DH, Azen SP, Crawford DW, Nessim SA, Sanmarco ME, Selzer RH, Shircore AM, Wickham EC Effects of colestipol-niacin therapy on human femoral atherosclerosis. *Circulation* 1991;83:438-47 [1991366]

## 2 combination therapies

Trial	Treatments	Patients	Trials design and methods
<b>intensive lipid-lowering therapy vs diet</b>			
<b>FATS , 1990</b> [NCT00000512] n=94/52 follow-up: 2.5 years	intensive lipid-lowering therapy with various drugs versus placebo	men no more than 62 years of age who had apolipoprotein B levels greater than or equal to 125 mg per deciliter, documented coronary artery disease, and a family history of vascular disease	Parallel groups open Japan
<b>colestipol+clofibrate vs placebo</b>			
<b>SCOR , 1990</b> n=48/49 follow-up: 2.0 years	colestipol (15 to 30mg/d) + clofibrate (2g/d) versus diet	patients with primary hypercholesterolemia	Parallel groups

## References

### FATS, 1990:

Brown G, Albers JJ, Fisher LD, Schaefer SM, Lin JT, Kaplan C, Zhao XQ, Bisson BD, Fitzpatrick VF, Dodge HT Regression of coronary artery disease as a result of intensive lipid-lowering therapy in men with high levels of apolipoprotein B. N Engl J Med 1990 Nov 8;323:1289-98 [2215615]

### SCOR, 1990:

Sepowitz AH, Smith FR, Berns L, Eder HA, Goodman DS Comparison of the effects of colestipol hydrochloride and clofibrate on plasma lipids and lipoproteins in the treatment of hypercholesterolemia. Atherosclerosis 1981;39:35-43 [7018502]

2

## 3 diet

Trial	Treatments	Patients	Trials design and methods
<b>diet vs usual diet</b>			
<b>Black , 1994</b> n=56/55 follow-up: 2.0 years	diet with 20 percent of total caloric intake as fat versus usual diet	patients with nonmelanoma skin cancer	Parallel groups open
<b>Finnish Mental Hospital (Miettinen) , 1985</b> n=612/610 follow-up: 6.0 years	cholesterol-lowering diet (low in saturated fats and cholesterol and relatively high in polyunsaturated fats) versus usual diet	middle-aged institutionalized women without CHD	Cluster-randomized cross-ove open, blind assessment Finland
<b>Goteborg , 1986</b> n=10004/20028 follow-up: 10 years	multifactorial intervention programme versus no intervention	men, 47-55 years old at entry	Parallel groups open Sweden
<b>Gteborg (Wilhelmsen) , 1986</b> n=10004/20028 follow-up: 10.0 years	multifactorial intervention programme versus usual care	men, 47-55 years old at entry	Parallel groups open

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Hjermann , 1981 n=604/628 follow-up: 6.5 years	diet versus usual diet	healthy, normotensive men at high risk of coronary heart disease	Parallel groups open Sweden
Kallio , 1979 n=188/187 follow-up: 3.0 years	diet (multifactorial intervention programme) versus usual diet	patients below 65 years who had an acute myocardial infarction	Parallel groups open
Los Angeles VA (Dayton) , 1969 n=424/422 follow-up: 65279;8.0 y	diet versus usual diet	men in domiciliary care, age>55, with or without CHD	Parallel groups double blind USA
Minnesota coronary survey (Frantz) , 1975 n=2197/2196 follow-up: 1.1 y (max 4.5y)	cholesterol lowering diet versus control diet	65279;Adult residents of mental hospitals; no illness restrictions, no cholesterol concentration requirements	Parallel groups double-blind USA
MRC low fat , 1965 n=123/129 follow-up: 3 y	-	-	Parallel groups open
MRC Soya , 1968 n=199/194 follow-up: 3.5 y	Rgime pauvre en graisses satures + 85 g/j d'huile de soja versus usual diet	ambulatory men with recent MI	Parallel groups open, blind assessment
MRFIT , 1982 n=6428/6438 follow-up: 6.5 y	multifactor intervention program versus usual diet	high-risk men aged 35 to 57 years	Parallel groups open
Ornish , 1990 n=28/20 follow-up: 1.0 y	low-fat vegetarian diet, stopping smoking, stress management training, and moderate exercise versus usual-care	Patients with angiographically documented coronary artery disease	Parallel groups open USA
Oslo Diet Heart Study (Leren) , 1966 n=206/206 follow-up: 5 y (11y)	diet versus usual care	middle-aged ambulatory men with prior MI	Parallel groups open, blind assessment
Rose , 1965 n=28/26 follow-up: 1.2 years	Rgime restreint en graisses + 80 g/j huile de mas versus usual diet	men, <70 years	Parallel groups open
Singh , 1992 n=204/202 follow-up: 65279;2.0 years	strict diet versus usual diet	patients with suspected acute myocardial infarction	Parallel groups open
STARS (St Thomas, diet) , 1992 n=30/30 follow-up: 3.0 years	dietary advice versus usual diet	patients with angina or past myocardial infarction	open, blind assessment

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Veterans Ad. (Dayton) , 1969</b> n=424/422 follow-up: 3.6 and 8 y	cholesterol lowering diet versus usual diet	men in domiciliary care, age>55, with or without CHD	Parallel groups double blind USA
<b>WHI low fat , 2005</b> [NCT00000611] n=19541/29294 follow-up: 8.1y mean	dietary modification intervention to promote dietary change with the goals of reducing intake of total fat to 20% of energy and increasing consumption of vegetables and fruit to at least 5 servings daily and grains to at least 6 servings daily versus usual diet	postmenopausal women, aged 50 to 79 years, without prior breast cancer	Parallel groups open US
<b>WHO Collaborative , 1986</b> n=30489/26971 follow-up: 5.5 years	multifactorial prevention versus usual diet	middle-aged men	Parallel groups open Belgium, Italy, Poland, UK
<b>Woodhill , 1966</b> n=221/237 follow-up: <7 years	diet versus usual diet	men, 30-59 years	Parallel groups open
<b>low fat diet vs mediterranean-style diet</b>			
<b>Tuttle , 2008</b> n=NA follow-up: 24 months	low-fat versus Mediterranean-style diets	First MI survivors	Parallel groups open

4

## References

### Black, 1994:

Black HS, Herd JA, Goldberg LH, Wolf JE Jr, Thornby JI, Rosen T, Bruce S, Tschen JA, Foreyt JP, Scott LW Effect of a low-fat diet on the incidence of actinic keratosis. *N Engl J Med* 1994;330:1272-5 [8145782]

### Finnish Mental Hospital (Miettinen), 1985:

European collaborative trial of multifactorial prevention of coronary heart disease: final report on the 6-year results. World Health Organisation European Collaborative Group. *Lancet* 1986;1:869-72 [2870351]

Miettinen TA, Huttunen JK, Naukkarinen V, Strandberg T, Mattila S, Kumlin T, Sarna S Multifactorial primary prevention of cardiovascular diseases in middle-aged men. Risk factor changes, incidence, and mortality. *JAMA* 1985;254:2097-102 [4046137]

Miettinen M, Turpeinen O, Karvonen MJ, Pekkarinen M, Paavilainen E, Elosuo R Dietary prevention of coronary heart disease in women: the Finnish mental hospital study. *Int J Epidemiol* 1983;12:17-25 [6840954]

### Goteborg, 1986:

Wilhelmsen L, Berglund G, Elmfeldt D, Tibblin G, Wedel H, Pennert K, Vedin A, Wilhelmsson C, Werk L The multifactor primary prevention trial in Gteborg, Sweden. *Eur Heart J* 1986;7:279-88 [3720755]

### Gteborg (Wilhelmsen), 1986:

Wilhelmsen L, Berglund G, Elmfeldt D, Tibblin G, Wedel H, Pennert K, Vedin A, Wilhelmsson C, Werk L The multifactor primary prevention trial in Gteborg, Sweden. *Eur Heart J* 1986;7:279-88 [3720755]

### Hjermann, 1981:

Hjermann I, Velve Byre K, Holme I, Leren P Effect of diet and smoking intervention on the incidence of coronary heart disease. Report from the Oslo Study Group of a randomised trial in healthy men. *Lancet* 1981;2:1303-10 [6118715]

**Kallio, 1979:**

Kallio V, Hmlinen H, Hakkila J, Luurila OJ Reduction in sudden deaths by a multifactorial intervention programme after acute myocardial infarction. *Lancet* 1979;2:1091-4 [91836]

**Los Angeles VA (Dayton), 1969:**

Rogers MC Sir John Scott Burdon-Sanderson (1828-1905): a pioneer in electrophysiology. *Circulation* 1969;40:1-2 [4893441]

Dayton S, Pearce ML Diet high in unsaturated fat. A controlled clinical trial. *Minn Med* 1969;52:1237-42 [4896402]

**Minnesota coronary survey (Frantz), 1975:**

Frantz ID Jr, Dawson EA, Ashman PL, Gatewood LC, Bartsch GE, Kuba K, Brewer ER Test of effect of lipid lowering by diet on cardiovascular risk. The Minnesota Coronary Survey. *Arteriosclerosis* 1989;9:129-35 [2643423]

**MRC low fat, 1965:**

, Low-fat diet in myocardial infarction: A controlled trial. *Lancet* 1965; 2:501-4 [4158171]

**MRC Soya, 1968:**

, Controlled trial of soya-bean oil in myocardial infarction. *Lancet* 1968; 2:693-9 [4175085]

**MRFIT, 1982:**

Multiple risk factor intervention trial. Risk factor changes and mortality results. Multiple Risk Factor Intervention Trial Research Group. *JAMA* 1982;248:1465-77 [7050440]

**Ornish, 1990:**

Ornish D, Brown SE, Scherwitz LW, Billings JH, Armstrong WT, Ports TA, McLanahan SM, Kirkeeide RL, Brand RJ, Gould KL Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial. *Lancet* 1990;336:129-33 [1973470]

**Oslo Diet Heart Study (Leren), 1966:**

Leren P, The Oslo diet-heart study. Eleven-year report. *Circulation* 1970; 42:935-42 [5477261]

**Rose, 1965:**

ROSE GA, THOMSON WB, WILLIAMS RT CORN OIL IN TREATMENT OF ISCHAEMIC HEART DISEASE. *Br Med J* 1965 Jun 12;1:1531-3 [14288105]

**Singh, 1992:**

Singh RB, Rastogi SS, Verma R, Laxmi B, Singh R, Ghosh S, Niaz MA Randomised controlled trial of cardioprotective diet in patients with recent acute myocardial infarction: results of one year follow up. *BMJ* 1992;304:1015-9 [1586782]

**STARS (St Thomas, diet), 1992:**

Watts GF, Lewis B, Brunt JN, Lewis ES, Coltart DJ, Smith LD, Mann JI, Swan AV Effects on coronary artery disease of lipid-lowering diet, or diet plus cholestyramine, in the St Thomas' Atherosclerosis Regression Study (STARS) *Lancet* 1992;339:563-9 [1347091]

**Veterans Ad. (Dayton), 1969:**

Dayton S, Pearce ML, Hashimoto S, Dixon WJ, Tomiyasu U. A controlled clinical trial of a diet high in unsaturated fat in preventing complications of atherosclerosis. *Circulation* 1969; 40(supp 2):1-55 [0]

**WHI low fat, 2005:**

Howard BV, Van Horn L, Hsia J, Manson JE, Stefanick ML, Wassertheil-Smoller S, Kuller LH, LaCroix AZ, Langer RD, Lasser NL, Lewis CE, Limacher MC, Margolis KL, Mysiw WJ, Ockene JK, Parker LM, Perri MG, Phillips L, Prentice RL, Robbins J, Rossouw JE, Sarto Low-fat dietary pattern and risk of cardiovascular disease: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. *JAMA* 2006 Feb 8;295:655-66 [16467234]

**WHO Collaborative, 1986:**

European collaborative trial of multifactorial prevention of coronary heart disease: final report on the 6-year results. World Health Organisation European Collaborative Group. *Lancet* 1986;1:869-72 [2870351]

**Woodhill, 1966:**

Woodhill JM, Palmer AJ, Leelarthapin B, McGilchrist C, Blacket RB, Low fat, low cholesterol diet in secondary prevention of coronary heart disease. *Adv Exp Med Biol* 1978; 109:317-30 [727035]

**Tuttle, 2008:**

Tuttle KR, Shuler LA, Packard DP, Milton JE, Daratha KB, Bibus DM, Short RA Comparison of low-fat versus Mediterranean-style dietary intervention after first myocardial infarction (from The Heart Institute of Spokane Diet Intervention and Evaluation Trial). *Am J Cardiol* 2008;101:1523-30 [18489927]

## 4 ezetimibe

Trial	Treatments	Patients	Trials design and methods
<b>ezetimibe vs control</b>			
<b>IMPROVE-IT , 2014</b> [NCT00202878] n=9067/9077 follow-up: 5.68 years	10 mg/day of ezetimibe and 40 mg/day of simvastatin versus simvastatin 40 mg/day	subjects with stabilized high-risk acute coronary syndrome	Parallel groups double blind 39 countries
<b>ezetimibe+simvastatin vs placebo</b>			
<b>SHARP , 2010</b> [NCT00125593] n=4193/4191 follow-up: 4.9 years	Simvastatin 20mg/Ezetimibe 10mg versus placebo	patients with established chronic kidney disease (dialysis or pre-dialysis)	Parallel groups double-blind 20 countries
<b>ezetimibe vs niacin</b>			
<b>ARBITER-HALTS 6 , 2010</b> n=NA follow-up: 14 months	addition of ezetimibe (10 mg/daily) to statin therapy versus extended-release niacin 2000 mg/daily	patients at high risk for vascular disease but with LDL-cholesterol levels <100 mg/dL and moderately low HDL-cholesterol levels (<50 mg/dL)	Parallel groups open

## References

**IMPROVE-IT, 2014:**

Cannon CP, Blazing MA, Giugliano RP, McCagg A, White JA, Theroux P, Darius H, Lewis BS, Ophuis TO, Jukema JW, De Ferrari GM, Ruzyllo W, De Lucca P, Im K, Bohula EA, Reist C, Wiviott SD, Tereshakovec AM, Musliner TA, Braunwald E, Califf RM Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes. *N Engl J Med* 2015;372:2387-97 [26039521]

**SHARP, 2010:**

Sharp Collaborative Group Study of Heart and Renal Protection (SHARP): Randomized trial to assess the effects of lowering low-density lipoprotein cholesterol among 9,438 patients with chronic kidney disease. *Am Heart J* 2010 Nov;160:785-794.e10 [21095263] [10.1016/j.ahj.2010.08.012](https://doi.org/10.1016/j.ahj.2010.08.012)

Baigent C, Landray MJ, Reith C, Emberson J, Wheeler DC, Tomson C, Wanner C, Krane V, Cass A, Craig J, Neal B, Jiang L, Hooi LS, Levin A, Agodoa L, Gaziano M, Kasiske B, Walker R, Massy ZA, Feldt-Rasmussen B, Krairitichai U, Ophascharoensuk V, Fellström B The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial. *Lancet* 2011 Jun 25;377:2181-2192 [21663949] [10.1016/S0140-6736\(11\)60739-3](https://doi.org/10.1016/S0140-6736(11)60739-3)

**ARBITER-HALTS 6, 2010:**

[10.1016/j.jacc.2010.03.017](https://doi.org/10.1016/j.jacc.2010.03.017)

## 5 Fibrates

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>bezafibrate vs placebo</b>			
<b>LEADER trial , 2000</b> n=783/785 follow-up: 5 ans	Bezafibrate: 400 mg/ jour pour les hommes avec cratinimie <135 micromole/litre versus placebo de mme aspect	Stade de la maladie : II.	Parallel groups Double aveugle
<b>BECAIT , 1996</b> n=47/45 follow-up: 5.0 years	bezafibrate 200 mg three times daily versus placebo	dyslipidaemic male survivors of myocardial infarction who were younger than 45 years at the time of the event	Parallel groups double blind Sweden
<b>BIP , 2000</b> n=1548/1542 follow-up: 6.2 y	bezafibrate 400 mg/d versus placebo	patients with a previous myocardial infarction or stable angina, total cholesterol of 180 to 250 mg/dL, HDL-C <or =45 mg/dL, triglycerides <or =300 mg/dL, and low-density lipoprotein cholesterol <or =180 mg/dL	Parallel groups double blind Israel
<b>LEADER , 2002</b> n=783/785 follow-up: 4.6y	bezafibrate 400 mg daily versus placebo	men with lower extremity arterial disease	Parallel groups double-blind UK
<b>SENDCAP , 1998</b> n=81/83 follow-up: 3.0 years	bezafibrate 400 mg daily versus placebo	type 2 diabetic subjects without a history of clinical cardiovascular	Parallel groups double blind UK
<b>clofibrate vs placebo</b>			
<b>Acheson , 1972</b> n=NA follow-up: 6 years	clofibrate versus placebo	cerebral vascular disease	Parallel groups NA UK
<b>Begg , 1971</b> n=76/79 follow-up: 3.5 y	clofibrate versus placebo	peripheral arteriopathy	Parallel groups
<b>CDP Clofibrate , 1975</b> n=1103/2789 follow-up: 6.2 years	clofibrate 1.8 mg/d versus placebo	men, 30-64 y	Parallel groups double blind USA
<b>Cullen , 1974</b> n=20/20 follow-up: 2 years	clofibrate versus placebo		Parallel groups
<b>Hanefeld , 1991</b> n=379/382 follow-up: 5 years	clofibric acid 1.6 g/day versus placebo	newly diagnosed middle-aged (30- to 55-yr-old) patients with non-insulin-dependent diabetes mellitus	Parallel groups double-blind Germany
<b>Harrold , 1969</b> n=30/33 follow-up: 1 years	clofibrate versus placebo	diabetic retinopathy	Parallel groups double-blind

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Newcastle , 1971 n=244/253 follow-up: 3.6 y	clofibrate 1.5-2 g daily versus placebo	Hommes et femmes <65 ans	Parallel groups double blind UK
Scottish , 1971 n=350/367 follow-up: 3.4 years	clofibrate 1.6-2 g daily versus placebo	Hommes et femmes, de 40 69 ans	Parallel groups double blind Scotland
VA Neurology Section , 1974 n=268/264 follow-up: 1.8 years	clofibrate versus placebo	treatment of cerebrovascular disease	Parallel groups USA
WHO clofibrate , 1978 n=5331/5296 follow-up: 5.3 years	clofibrate 1.6 g daily versus olive oil	primary prevention, Hommes, de 30 59 ans	Parallel groups double blind Scotland, Hungary, Czech Republic
<b>etofibrate vs placebo</b>			
Emmerich , 2009 n=NA follow-up: 12 months	etofibrate 1g/j versus placebo	patients with type 2 diabetes mellitus and concomitant diabetic retinopathy	Parallel groups double-blind Germany
<b>fenofibrate vs placebo</b>			
DAIS , 2001 n=207/211 follow-up: 3.3 years	fenofibrate 200 mg/day versus placebo	men and women with type 2 diabetes and coronary atherosclerosis	Parallel groups double-blind Canada, Finland, France, Sweden
FIELD , 2005 [ISRCTN64783481] n=4895/4900 follow-up: 5 years	fenofibrate 200mg/d versus Placebo	participants aged 50-75 years, with type 2 diabetes mellitus, and not taking statin therapy at study entry	Parallel groups double blind Australia, New Zealand, Finland
<b>gemfibrozil vs placebo</b>			
Helsinki (HHS) , 1987 n=2046/2035 follow-up: 5 years	gemfibrozil 1,2 g/d versus placebo	asymptomatic middle-aged men (40 to 55 years of age) with primary dyslipidemia (non-HDL cholesterol greater than or equal to 200 mg per deciliter [5.2 mmol per liter])	Parallel groups double blind Finland
LOCAT , 1997 n=197/198 follow-up: 32 months	gemfibrozil 1200 mg/d versus placebo	post-coronary bypass men, who had an HDL cholesterol concentration <or = 1.1 mmol/L and LDL cholesterol <or = 4.5 mmol/L	Parallel groups double blind Germany
VA-HIT , 1999 [NCT00283335] n=1264/1267 follow-up: 5.1 years	gemfibrozil 1.2g daily versus placebo	men with coronary heart disease, an HDL cholesterol level of 40 mg per deciliter (1.0 mmol per liter) or less, and an LDL cholesterol level of 140 mg per deciliter (3.6 mmol per liter) or less	Parallel groups double blind USA
<b>fenofibrate vs placebo (on top simvastatine)</b>			

continued...



Trial	Treatments	Patients	Trials design and methods
ACCORD lipid , 2010 [NCT00000620] n=2765/2753 follow-up: 4.7y	fenofibrate on top simvastatin versus placebo (on top simvastatine)	high-risk patients with type 2 diabetes	Factorial plan double-blind United States and Canada

## References

### LEADER trial, 2000:

Tom Meade, Riaz Zuhrie, Claire Cook, Jackie Cooper on behalf of MRC Genral Practice Research Framework. Bezafibrate in men with lower extremity arterial disease: randomised controlled trial. *BMJ* 2002; 325: 1139-43

### BECAIT, 1996:

Ruotolo G, Ericsson CG, Tettamanti C, Karpe F, Grip L, Svane B, Nilsson J, de Faire U, Hamsten A Treatment effects on serum lipoprotein lipids, apolipoproteins and low density lipoprotein particle size and relationships of lipoprotein variables to progression of coronary artery disease in the Bezafibrate Coronary Atherosclerosis Intervention Trial (BECAIT). *J Am Coll Cardiol* 1998;32:1648-56 [9822092]

Ericsson CG Results of the Bezafibrate Coronary Atherosclerosis Intervention Trial (BECAIT) and an update on trials now in progress. *Eur Heart J* 1998;19 Suppl H:H37-41 [9717064]

Ericsson CG, Hamsten A, Nilsson J, Grip L, Svane B, de Faire U Angiographic assessment of effects of bezafibrate on progression of coronary artery disease in young male postinfarction patients. *Lancet* 1996;347:849-53 [8622389]

de Faire U, Ericsson CG, Hamsten A, Nilsson J Design features of a five-year Bezafibrate Coronary Atherosclerosis Intervention Trial (BECAIT). *Drugs Exp Clin Res* 1995;21:105-24 [7555614]

### BIP, 2000:

, Secondary prevention by raising HDL cholesterol and reducing triglycerides in patients with coronary artery disease: the Bezafibrate Infarction Prevention (BIP) study. *Circulation* 2000; 102:21-7 [10880410]

Goldenberg I, Boyko V, Tennenbaum A, Tanne D, Behar S, Guetta V Long-term benefit of high-density lipoprotein cholesterol-raising therapy with bezafibrate: 16-year mortality follow-up of the bezafibrate infarction prevention trial. *Arch Intern Med* 2009;169:508-14 [19273782]

### LEADER, 2002:

Meade T, Zuhrie R, Cook C, Cooper J Bezafibrate in men with lower extremity arterial disease: randomised controlled trial. *BMJ* 2002;325:1139 [12433762]

### SENDCAP, 1998:

Elkeles RS, Diamond JR, Poulter C, Dhanjil S, Nicolaidis AN, Mahmood S, Richmond W, Mather H, Sharp P, Feher MD Cardiovascular outcomes in type 2 diabetes. A double-blind placebo-controlled study of bezafibrate: the St. Mary's, Ealing, Northwick Park Diabetes Cardiovascular Disease Prevention (SENDCAP) Study. *Diabetes Care* 1998;21:641-8 [9571357]

### Acheson, 1972:

Acheson J, Hutchinson EC Controlled trial of clofibrate in cerebral vascular disease. *Atherosclerosis* 1972;15:177-83 [4579955]

### Begg, 1971:

Begg TB, Rifkind BM [Evaluation of clofibrate therapy in peripheral arteriopathy] *Minerva Med* 1971;62:3469-75 [5097219]

### CDP Clofibrate, 1975:

, Clofibrate and niacin in coronary heart disease. *JAMA* 1975; 231:360-81 [1088963]

### Cullen, 1974:

### Hanefeld, 1991:

Hanefeld M, Fischer S, Schmechel H, Rothe G, Schulze J, Dude H, Schwanebeck U, Julius U Diabetes Intervention Study. Multi-intervention trial in newly diagnosed NIDDM. *Diabetes Care* 1991;14:308-17 [2060433]

### Harrold, 1969:

Harrold BP, Marmion VJ, Gough KR A double-blind controlled trial of clofibrate in the treatment of diabetic retinopathy. *Diabetes* 1969;18:285-91 [[4894161](#)]

**Newcastle, 1971:**

, Trial of clofibrate in the treatment of ischaemic heart disease. Five-year study by a group of physicians of the Newcastle upon Tyne region. *Br Med J* 1971; 4:767-75 [[4943605](#)]

**Scottish, 1971:**

, Ischaemic heart disease: a secondary prevention trial using clofibrate. Report by a research committee of the Scottish Society of Physicians. *Br Med J* 1971; 4:775-84 [[4943606](#)]

**VA Neurology Section, 1974:**

The treatment of cerebrovascular disease with clofibrate. Final report of the Veterans Administration Cooperative Study of Atherosclerosis, Neurology Section. *Stroke* 1973;4:684-93 [[4723698](#)]

**WHO clofibrate, 1978:**

, WHO cooperative trial on primary prevention of ischaemic heart disease with clofibrate to lower serum cholesterol: final mortality follow-up. Report of the Committee of Principal Investigators. *Lancet* 1984; 2:600-4 [[6147641](#)]

Heady JA, Morris JN, Oliver MF, WHO clofibrate/cholesterol trial: clarifications. *Lancet* 1992; 340:1405-6 [[1360101](#)]

**Emmerich, 2009:**

Emmerich KH, Poritis N, Stelmane I, Klindzane M, Erbler H, Goldsteine J, Grtelmeyer R [Efficacy and safety of etofibrate in patients with non-proliferative diabetic retinopathy] *Klin Monbl Augenheilkd* 2009;226:561-7 [[19644802](#)] [10.1055/s-0028-1109516](#)

**DAIS, 2001:**

Effect of fenofibrate on progression of coronary-artery disease in type 2 diabetes: the Diabetes Atherosclerosis Intervention Study, a randomised study. *Lancet* 2001;357:905-10 [[11289345](#)]

**FIELD, 2005:**

The need for a large-scale trial of fibrate therapy in diabetes: the rationale and design of the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study. [ISRCTN64783481]. *Cardiovasc Diabetol* 2004 Dec 1;3:9 [[15571637](#)]

Scott R, Best J, Forder P, Taskinen MR, Simes J, Barter P, Keech A Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study: baseline characteristics and short-term effects of fenofibrate [ISRCTN64783481]. *Cardiovasc Diabetol* 2005 Aug 22;4:13 [[16111499](#)]

*Lancet* 2005

Keech A, Simes RJ, Barter P, Best J, Scott R, Taskinen MR, Forder P, Pillai A, Davis T, Glasziou P, Drury P, Kesaniemi YA, Sullivan D, Hunt D, Colman P, d'Emden M, Whiting M, Ehnholm C, Laakso M Effects of long-term fenofibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study): randomised controlled trial. *Lancet* 2005 Nov 26;366:1849-61 [[16310551](#)]

Hiukka A, Westerbacka J, Leinonen ES, Watanabe H, Wiklund O, Hulten LM, Salonen JT, Tuomainen TP, Yki-Jrvinen H, Keech AC, Taskinen MR Long-term effects of fenofibrate on carotid intima-media thickness and augmentation index in subjects with type 2 diabetes mellitus. *J Am Coll Cardiol* 2008 Dec 16;52:2190-7 [[19095138](#)] [10.1016/j.jacc.2008.09.049](#)

Hiukka A, Westerbacka J, Leinonen ES, Watanabe H, Wiklund O, Hulten LM, Salonen JT, Tuomainen TP, Yki-Jrvinen H, Keech AC, Taskinen MR Long-term effects of fenofibrate on carotid intima-media thickness and augmentation index in subjects with type 2 diabetes mellitus. *J Am Coll Cardiol* 2008 Dec 16;52:2190-7 [[19095138](#)]

Rajamani K, Colman PG, Li LP, Best JD, Voysey M, D'Emden MC, Laakso M, Baker JR, Keech AC Effect of fenofibrate on amputation events in people with type 2 diabetes mellitus (FIELD study): a prespecified analysis of a randomised controlled trial. *Lancet* 2009 May 23;373:1780-8 [[19465233](#)] [10.1016/S0140-6736\(09\)60698-X](#)

**Helsinki (HHS), 1987:**

Manninen V, Elo MO, Frick MH, Haapa K, Heinonen OP, Heinsalmi P, Helo P, Huttunen JK, Kaitaniemi P, Koskinen P, et al, Lipid alterations and decline in the incidence of coronary heart disease in the Helsinki Heart Study. *JAMA* 1988; 260:641-51 [[3164788](#)]

Frick MH, Elo O, Haapa K, Heinonen OP, Heinsalmi P, Helo P, Huttunen JK, Kaitaniemi P, Koskinen P, Manninen V Helsinki Heart Study: primary-prevention trial with gemfibrozil in middle-aged men with dyslipidemia. Safety of treatment, changes in risk factors, and incidence of coronary heart disease. *N Engl J Med* 1987;317:1237-45 [[3313041](#)]

**LOCAT, 1997:**

Frick MH, Syvonne M, Nieminen MS, Kauma H, Majahalme S, Virtanen V, Kesniemi YA, Pasternack A, Taskinen MR Prevention of the angiographic progression of coronary and vein-graft atherosclerosis by gemfibrozil after coronary bypass surgery in men with low levels of HDL cholesterol. Lipid Coronary Angiography Trial (LOCAT) Study Group. *Circulation*

1997;96:2137-43 [9337181]

### VA-HIT, 1999:

Rubins HB, Robins SJ, Collins D, Fye CL, Anderson JW, Elam MB, Faas FH, Linares E, Schaefer EJ, Schectman G, Wilt TJ, Wittes J, Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group. N Engl J Med 1999; 341:410-8 [10438259]

Adabag AS, Mithani S, Al Aloul B, Collins D, Bertog S, Bloomfield HE Efficacy of gemfibrozil in the primary prevention of atrial fibrillation in a large randomized controlled trial. Am Heart J 2009 May;157:913-8 [19376321]

### ACCORD lipid, 2010:

Effects of Combination Lipid Therapy in Type 2 Diabetes Mellitus. N Engl J Med 2010 Mar 14;: [20228404] 10.1056/NEJMoa1001282

Effects of Medical Therapies on Retinopathy Progression in Type 2 Diabetes. N Engl J Med 2010 Jun 29;: [20587587] 10.1056/NEJMoa1001288

Ismail-Beigi F, Craven T, Banerji MA, Basile J, Calles J, Cohen RM, Cuddihy R, Cushman WC, Genuth S, Grimm RH Jr, Hamilton BP, Hoogwerf B, Karl D, Katz L, Krikorian A, O'Connor P, Pop-Busui R, Schubart U, Simmons D, Taylor H, Thomas A, Weiss D, Hramiak I Effect of intensive treatment of hyperglycaemia on microvascular outcomes in type 2 diabetes: an analysis of the ACCORD randomised trial. Lancet 2010 Jun 29;: [20594588] 10.1016/S0140-6736(10)60576-4

## 6 hormones

11

Trial	Treatments	Patients	Trials design and methods
<b>estrogen vs placebo</b>			
CDP estrogen 2.5 , 1975 n=1101/2789 follow-up: 4.7 years	estrogen 2.5 mg daily versus placebo	-	Parallel groups
CDP estrogen 5 , 1975 n=1119/2788 follow-up: 1.5 years	estrogen 5.0 mg daily versus placebo	-	Parallel groups
Marmorstein , 1962 n=285/147 follow-up: 5.0 y	estrogen versus placebo	-	Parallel groups
Stamler , 1963 n=156/119 follow-up: 5.0 years	estrogen versus placebo	-	Parallel groups
VA Neurology Section (estrogen) , 1966 n=295/287 follow-up: 1.4 years	estrogen versus placebo	-	Parallel groups
<b>estrogen or thyroxine vs placebo</b>			
VA drugs (Estrogen or thyroxine) , 1968 n=427/143 follow-up: 65279;3.2 years	estrogen or thyroxine versus placebo	-	Parallel groups
<b>thyroxine vs placebo</b>			

continued...

Trial	Treatments	Patients	Trials design and methods
<b>CDP tyroxine , 1975</b> n=1083/2715 follow-up: 3.0 years	thyroxine versus placebo	-	Parallel groups

## References

### CDP estrogen 2.5, 1975:

The Coronary Drug Project. Findings leading to discontinuation of the 2.5-mg day estrogen group. The coronary Drug Project Research Group. JAMA 1973;226:652-7 [4356847]

### CDP estrogen 5, 1975:

The Coronary Drug Project. Initial findings leading to modifications of its research protocol. JAMA 1970;214:1303-13 [4320008]

### Marmorstein, 1962:

MARMORSTON J, MOORE FJ, HOPKINS CE, KUZMA OT, WEINER J Clinical studies of long-term estrogen therapy in men with mvocardial infarction. Proc Soc Exp Biol Med 1962;110:400-8 [14470097]

### Stamler, 1963:

SCHWARTZ SO, GREENSPAN I, BROWN ER LEUKEMIA CLUSTER IN NILES, ILL. IMMUNOLOGIC DATA ON FAMILIES OF LEUKEMIC PATIENTS AND OTHERS. JAMA 1963;186:106-8 [14056521]

STAMLER J, PICK R, KATZ LN, PICK A, KAPLAN BM, BERKSON DM, CENTURY D Effectiveness of estrogens for therapy of myocardial infarction in middle-age men. JAMA 1963;183:632-8 [13983325]

### VA Neurology Section (estrogen), 1966:

An evaluation of estrogenic substances in the treatment of cerebral vascular disease. Report of the Veterans Administration Cooperative Study of Atherosclerosis, Neurology Section. Circulation 1966;33:II3-9 [4378175]

### VA drugs (Estrogen or thyroxine), 1968:

### CDP tyroxine, 1975:

The coronary drug project. Findings leading to further modifications of its protocol with respect to dextrothyroxine. The coronary drug project research group. JAMA 1972;220:996-1008 [4337170]

## 7 niacin

Trial	Treatments	Patients	Trials design and methods
<b>niacin vs control</b>			
<b>VA drugs , 1968</b> n=77/143 follow-up: 3.2 years	-	-	Parallel groups double blind
<b>niacin vs placebo</b>			
<b>CDP niacin , 1975</b> n=1119/2789 follow-up: 6.2 years	niacin 3 mg/d versus placebo	Hommes, de 30 64 ans	Parallel groups double blind
<b>niacin vs ezetimibe</b>			

continued...

Trial	Treatments	Patients	Trials design and methods
<a href="#">ARBITER 6-HALTS (niacin vs ezetimibe) , 2009</a> [NCT00397657] n=97/111 follow-up: 14 months	extended-release niacin 1 g/d, titrated to max tolerable dose up to 2 g/d (HDL-focused strategy) versus ezetimibe 10 mg/d (LDL-focused strategy)	patients with known coronary or vascular disease or coronary risk equivalents	Parallel groups open US

## References

### VA drugs, 1968:

Schoch HK. The US Veterans Administration Cardiology drug lipid study: an interim report *Adv Exp Med Biol.* 1968;4:405-420

### CDP niacin, 1975:

, Clofibrate and niacin in coronary heart disease. *JAMA* 1975; 231:360-81 [[1088963](#)]

### ARBITER 6-HALTS (niacin vs ezetimibe), 2009:

Taylor AJ, Villines TC, Stanek EJ, Devine PJ, Griffen L, Miller M, Weissman NJ, Turco M Extended-release niacin or ezetimibe and carotid intima-media thickness. *N Engl J Med* 2009 Nov 26;361:2113-22 [[19915217](#)]

Villines TC, Stanek EJ, Devine PJ, Turco M, Miller M, Weissman NJ, Griffen L, Taylor AJ The ARBITER 6-HALTS Trial (Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol 6-HDL and LDL Treatment Strategies in Atherosclerosis) Final Results and the Impact of Medication Adherence, Dose, and Treatment Duration. *J Am Coll Cardiol* 2010 Apr 8;: [[20399059](#)] [10.1016/j.jacc.2010.03.017](#)

## 8 niacin (on top statin)

Trial	Treatments	Patients	Trials design and methods
<b>niacin vs placebo (on top statin)</b>			
<a href="#">AIM-HIGH , 2011</a> [NCT00120289] n=1718/1691 follow-up: 32 months	high-dose, extended-release niacin in gradually increasing doses up to 2000 mg daily (+ simvastatin) versus placebo	patients with a history of cardiovascular disease, high triglycerides, and low levels of HDL cholesterol	Parallel groups double blind US, Canada
<a href="#">HPS 2-Thrive</a> [NCT00461630] n=12838/12835 follow-up: 3.9y (median)	2 g of extended-release niacin and 40 mg of laropiprant versus placebo	patients with vascular disease	Parallel groups double blind UK, Scandinavia, China
<a href="#">Oxford Niaspan Study , 2009</a> [NCT00232531] n=35/36 follow-up: 1 year	niacin 2g daily (added to statin therapy) versus placebo (statins alone)	patients with low HDL-C (<40 mg/dl) and either a type 2 diabetes with coronary heart disease or a carotid/peripheral atherosclerosis	Parallel groups double blind USA
<a href="#">ARBITER 2 , 2009</a> n=87/80 follow-up: 1 y	long-acting niacin target dose of 1 g/day (added to statin therapy) versus placebo	patients with known coronary artery disease and well controlled on statin therapy	Parallel groups double blind USA

continued...

Trial	Treatments	Patients	Trials design and methods
<b>HATS , 2001</b> n=73/73 follow-up: 3 y	simvastatin plus niacin versus placebo	patients with coronary disease, low HDL cholesterol levels and normal LDL cholesterol levels	Factorial plan double blind USA, Canada

## References

### AIM-HIGH, 2011:

Boden WE, Probstfield JL, Anderson T, Chaitman BR, Desvignes-Nickens P, Koprowicz K, McBride R, Teo K, Weintraub W Niacin in patients with low HDL cholesterol levels receiving intensive statin therapy. N Engl J Med 2011;365:2255-67 [22085343] 10.1056/NEJMoa1107579

### HPS 2-Thrive, :

Landray MJ, Haynes R, Hopewell JC, Parish S, Aung T, Tomson J, Wallendszus K, Craig M, Jiang L, Collins R, Armitage J Effects of extended-release niacin with laropirant in high-risk patients. N Engl J Med 2014 Jul 17;371:203-12 [25014686] 10.1056/NEJMoa1300955

### Oxford Niaspan Study, 2009:

Lee JM, Robson MD, Yu LM, Shirodaria CC, Cunningham C, Kylintireas I, Digby JE, Bannister T, Handa A, Wiesmann F, Durrington PN, Channon KM, Neubauer S, Choudhury RP Effects of high-dose modified-release nicotinic Acid on atherosclerosis and vascular function a randomized, placebo-controlled, magnetic resonance imaging study. J Am Coll Cardiol 2009;54:1787-94 [19874992]

### ARBITER 2, 2009:

Taylor AJ, Sullenberger LE, Lee HJ, Lee JK, Grace KA Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol (ARBITER) 2: a double-blind, placebo-controlled study of extended-release niacin on atherosclerosis progression in secondary prevention patients treated with statins. Circulation 2004;110:3512-7 [15537681]

### 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 Nov 29;345:1583-92 [11757504]

## 9 other cholesterol lowering drugs

Trial	Treatments	Patients	Trials design and methods
<b>clofibrate+niacin vs placebo</b>			
<b>Carlson (Stockholm) , 1977</b> n=279/276 follow-up: 5 years	clofibrate, 1 g twice daily, and nicotinic acid 1 g three times daily versus control	survivors of a myocardial infarction below 70 years of age	Parallel groups open Sweden
<b>colestipol-niacin vs placebo</b>			
<b>CLAS , 1987</b> n=94/94 follow-up: 2 ans	Colestipol + Niacin 30 g / j 3-12 g / j (titr sur chaque patient sur la base de la baisse de cholestrol sanguin) versus placebo: methyl cellulose	Patients coronariens avec antcdent de revascularisation chirurgicale coronarienne.	Parallel groups Non dterminable
<b>CLAS , 1987</b> n=NA follow-up: 65279;2 years	colestipol + niacin versus placebo	nonsmoking men aged 40 to 59 years with previous coronary bypass surgery	Parallel groups double blind

continued...

Trial	Treatments	Patients	Trials design and methods
<b>various drugs vs placebo</b>			
<b>HARP , 1994</b> [NCT00000461] n=40/39 follow-up: 2.5 years	Various drugs (pravastatin, nicotinic acid, cholestyramine, and gemfibrozil stepwise as needed to reach the specified goal (total cholesterol <or = 4.1 mmol/L, ratio of LDL/high-density-lipoprotein [HDL] cholesterol <or = 2.0) versus placebo	normocholesterolaemic patients with coronary heart disease	Parallel groups open
<b>various drugs vs usual care</b>			
<b>SCRIP , 1994</b> [NCT00000508] n=145/155 follow-up: 4.0 years	multifactor risk reduction (Various drugs) versus usual care	patients with angiographically defined coronary atherosclerosis	Parallel groups open

## References

### Carlson (Stockholm), 1977:

Carlson LA, Danielson M, Ekberg I, Klintemar B, Rosenhamer G, Reduction of myocardial reinfarction by the combined treatment with clofibrate and nicotinic acid. *Atherosclerosis* 1977; 28:81-6 [911371]

Carlson LA, Rosenhamer G, Reduction of mortality in the Stockholm Ischaemic Heart Disease Secondary Prevention Study by combined treatment with clofibrate and nicotinic acid. *Acta Med Scand* 1988; 223:405-18 [3287837]

### CLAS, 1987:

Blankenhorn DH, Brooks SH. Angiographic trials of lipid-lowering therapy. *Arteriosclerosis* 1981; 1: 242-249.

The Cholesterol Lowering Atherosclerosis Study (CLAS): design, methods, and baseline results. Blankenhorn DH, Johnson RL, Nessim SA, Azen SP, Sanmarco ME, Selzer RH *Control Clin Trials* 1987 Dec;8:356-87 [3327654]

Beneficial effects of combined colestipol-niacin therapy on coronary atherosclerosis and coronary venous bypass grafts. Blankenhorn DH, Nessim SA, Johnson RL, Sanmarco ME, Azen SP, Cashin-Hemphill L *JAMA* 1987 Jun 19;257:3233-40 [3295315]

Comparison of computer- and human-derived coronary angiographic end-point measures for controlled therapy trials. Mack WJ, Selzer RH, Pogoda JM, Lee PL, Shircore AM, Azen SP, Blankenhorn DH *Arterioscler Thromb* 1992 Mar;12:348-56 [1547194]

### CLAS, 1987:

Blankenhorn DH, Johnson RL, Nessim SA, Azen SP, Sanmarco ME, Selzer RH The Cholesterol Lowering Atherosclerosis Study (CLAS): design, methods, and baseline results. *Control Clin Trials* 1987;8:356-87 [3327654]

Cashin-Hemphill L, Mack WJ, Pogoda JM, Sanmarco ME, Azen SP, Blankenhorn DH Beneficial effects of colestipol-niacin on coronary atherosclerosis. A 4-year follow-up. *JAMA* 1990;264:3013-7 [2243429]

Blankenhorn DH, Nessim SA, Johnson RL, Sanmarco ME, Azen SP, Cashin-Hemphill L Beneficial effects of combined colestipol-niacin therapy on coronary atherosclerosis and coronary venous bypass grafts. *JAMA* 1987;257:3233-40 [3295315]

Blankenhorn DH, Azen SP, Crawford DW, Nessim SA, Sanmarco ME, Selzer RH, Shircore AM, Wickham EC Effects of colestipol-niacin therapy on human femoral atherosclerosis. *Circulation* 1991;83:438-47 [1991366]

### HARP, 1994:

Sacks FM, Pasternak RC, Gibson CM, Rosner B, Stone PH Effect on coronary atherosclerosis of decrease in plasma cholesterol concentrations in normocholesterolaemic patients. Harvard Atherosclerosis Reversibility Project (HARP) Group. *Lancet* 1994;344:1182-6 [7934538]

### SCRIP, 1994:

Haskell WL, Alderman EL, Fair JM, Maron DJ, Mackey SF, Superko HR, Williams PT, Johnstone IM, Champagne MA, Krauss RM Effects of intensive multiple risk factor reduction on coronary atherosclerosis and clinical cardiac events in men and women with coronary artery disease. The Stanford Coronary Risk Intervention Project (SCRIP). Circulation 1994;89:975-90 [8124838]

## 10 Policosanol

Trial	Treatments	Patients	Trials design and methods
<b>policosanol vs control</b>			
Batista , 1996 n=15/14 follow-up: 1.7 years	-	-	Parallel groups
Castano , 2001 n=27/29 follow-up: 2 years	policosanol 10 mg twice daily versus placebo	intermittent claudication	Parallel groups double-blind
Ms , 1999 n=219/218 follow-up: 24 weeks	policosanol 5mg titrted up for 10mg daily versus placebo	patients with type II hypercholesterolemia and additional coronary risk factors	Parallel groups double-blind

## References

### Batista, 1996:

Batista JF, Stsler RJ, Padrn R, Sosa F, Pereztol O, Prez B.P Functional Improvement in Coronary Artery Disease After 20 months of Lipid-Lowering Therapy with Policosanoly Advances in Therapy. 1996;13:137-148imag

### Castano, 2001:

Castao G, Ms Ferreiro R, Fernndez L, Gmez R, Illnait J, Fernndez C A long-term study of policosanol in the treatment of intermittent claudication. Angiology 2001;52:115-25 [11228084]

### Ms, 1999:

Ms R, Castao G, Illnait J, Fernndez L, Fernndez J, Alemn C, Pontigas V, Lescay M Effects of policosanol in patients with type II hypercholesterolemia and additional coronary risk factors. Clin Pharmacol Ther 1999;65:439-47 [10223782]

## 11 probucol

Trial	Treatments	Patients	Trials design and methods
<b>probucol vs control</b>			
FATS Fukosawa (probucol) , 2002 n=82/81 follow-up: 2 years	probucol 500 mg/day versus diet alone	asymptomatic patients with hypercholesterolemia	Parallel groups open Japan
<b>probucol vs placebo</b>			

continued...



<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>PQRST , 1994</b> n=152/151 follow-up: 3 ans	Probucol 1 g / j pendant 3 ans versus placebo, de mme aspect(2 tablettes par jour)pendant 3 ans	Stade II: 70%	Parallel groups Double aveugle
<b>McCaughan , 1981</b> n=88/30 follow-up: 1 year	probucol versus placebo	hypercholesterolemic men	Parallel groups double-blind
<b>PQRST , 1994</b> n=NA follow-up: 3 y	probucol 0.5 g twice daily versus placebo	hypercholesterolemic patients with visible atherosclerosis	Parallel groups double blind
<b>Tardif , 1997</b> n=160/157 follow-up: 0.5 years	probucol 500 mg versus placebo	patients undergoing PTCA	Parallel groups open

## References

### FATS Fukosawa (probucol), 2002:

Sawayama Y, Shimizu C, Maeda N, Tatsukawa M, Kinukawa N, Koyanagi S, Kashiwagi S, Hayashi J Effects of probucol and pravastatin on common carotid atherosclerosis in patients with asymptomatic hypercholesterolemia. Fukuoka Atherosclerosis Trial (FAST). J Am Coll Cardiol 2002 Feb 20;39:610-6 [11849859]

### PQRST, 1994:

Probucol Quantitative Regression Swedish Trial: new angiographic technique to measure atheroma volume of the femoral artery. Erikson U, Nilsson S, Stenport G Am J Cardiol 1988 Jul 25;62:44B-47B [3293416]

Holme I, Malmaeus I, Olsson AG, Nilsson S, Walladius G. Repeated measurements over time: statistical analysis of the angiographic outcomes in the Probucol Quantitative Regression Swedish Trial ( PQRST). Clinical Trials and Meta-Analysis 1993;28:95-108

Development of femoral atherosclerosis in hypercholesterolemic patients during treatment with cholestyramine and probucol/placebo: Probucol Quantitative Regression Swedish Trial (PQRST): a status report. Walldius G, Carlson LA, Erikson U, Olsson AG, Johansson J, Molgaard J, Nilsson S, Stenport G, Kaijser L, Lassvik C, et al Am J Cardiol 1988 Jul 25;62:37B-43B [3293415]

The effect of probucol on femoral atherosclerosis: the Probucol Quantitative Regression Swedish Trial (PQRST). Walldius G, Erikson U, Olsson AG, Bergstrand L, Hadell K, Johansson J, Kaijser L, Lassvik C, Molgaard J, Nilsson S, et al Am J Cardiol 1994 Nov 1;74:875-83 [7977117]

The role of lipids and antioxidative factors for development of atherosclerosis. The Probucol Quantitative Regression Swedish Trial (PQRST). Walldius G, Regnstrom J, Nilsson J, Johansson J, Schafer-Elinder L, Moelgaard J, Hadell K, Olsson AG, Carlson LA Am J Cardiol 1993 Feb 25;71:15B-19B [8434556]

### McCaughan, 1981:

McCaughan D The long-term effects of probucol on serum lipid levels. Arch Intern Med 1981;141:1428-32 [7025778]

### PQRST, 1994:

Walldius G, Erikson U, Olsson AG, Bergstrand L, Hdell K, Johansson J, Kaijser L, Lassvik C, Mlgaard J, Nilsson S The effect of probucol on femoral atherosclerosis: the Probucol Quantitative Regression Swedish Trial (PQRST). Am J Cardiol 1994;74:875-83 [7977117]

Walldius G, Regnstrm J, Nilsson J, Johansson J, Schfer-Elinder L, Moelgaard J, Hdell K, Olsson AG, Carlson LA The role of lipids and antioxidative factors for development of atherosclerosis. The Probucol Quantitative Regression Swedish Trial (PQRST). Am J Cardiol 1993;71:15B-19B [8434556]

Walldius G, Carlson LA, Erikson U, Olsson AG, Johansson J, Mlgaard J, Nilsson S, Stenport G, Kaijser L, Lassvik C Development of femoral atherosclerosis in hypercholesterolemic patients during treatment with cholestyramine and probucol/placebo: Probucol Quantitative Regression Swedish Trial (PQRST): a status report. Am J Cardiol 1988;62:37B-43B [3293415]

Walldius G, Erikson U, Olsson AG, Bergstrand L, Hdell K, Johansson J, Kaijser L, Lassvik C, Mlgaard J, Nilsson S The effect of probucol on femoral atherosclerosis: the Probucol Quantitative Regression Swedish Trial (PQRST). Am J Cardiol 1994;74:875-83 [7977117]

## Tardif, 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]

## 12 resins

Trial	Treatments	Patients	Trials design and methods
<b>cholestyramine vs control</b>			
<b>STARS (cholestyramine) , 1992</b> n=30/30 follow-up: 3 years	cholestyramine versus diet	patients with angina or past myocardial infarction	
<b>cholestyramine vs placebo</b>			
<b>LRC , 1984</b> n=1906/1900 follow-up: 7.4 years	cholestyramine 24 g daily versus placebo	asymptomatic middle-aged men with primary hypercholesterolemia (type II hyperlipoproteinemia)	Parallel groups double blind USA
<b>NHLBI (Brensike) , 1984</b> [NCT00000594] n=71/72 follow-up: 5.0 y	cholestyramine versus placebo	patients with Type II hyperlipoproteinemia and coronary artery disease	Parallel groups double blind
<b>colestipol vs placebo</b>			
<b>Gross , 1973</b> n=23/29 follow-up: 65279;1.0 years	colestipol versus placebo		Parallel groups
<b>Gundersen , 1976</b> n=36/30 follow-up: 0.8 years	colestipol 10g twice daily versus placebo	hypercholesterolemic patients	Parallel groups double-blind
<b>Ruoff , 1978</b> n=21/19 follow-up: 3.2 years	colestipol versus placebo	hypercholesterolemic patients	Parallel groups
<b>Ryan , 1974</b> n=44/48 follow-up: 3.0 years	colestipol15 g/day versus placebo	patients with hypercholesterolemia	Parallel groups
<b>UCS (Dorr) , 1978</b> n=1149/1129 follow-up: 1.9 years	colestipol hydrochloride 32 mg/dl versus placebo	Hommes et femmes, >18 ans	Parallel groups double blind

## References

### STARS (cholestyramine), 1992:

Watts GF, Lewis B, Brunt JN, Lewis ES, Coltart DJ, Smith LD, Mann JI, Swan AV Effects on coronary artery disease of lipid-lowering diet, or diet plus cholestyramine, in the St Thomas' Atherosclerosis Regression Study (STARS) Lancet 1992;339:563-9 [1347091]

### LRC, 1984:

, The Lipid Research Clinics Coronary Primary Prevention Trial results. I. Reduction in incidence of coronary heart disease. JAMA 1984; 251:351-64 [6361299]

**NHLBI (Brensike), 1984:**

Brensike JF, Levy RI, Kelsey SF, Passamani ER, Richardson JM, Loh IK, Stone NJ, Aldrich RF, Battaglini JW, Moriarty DJ Effects of therapy with cholestyramine on progression of coronary arteriosclerosis: results of the NHLBI Type II Coronary Intervention Study. Circulation 1984;69:313-24 [6360414]

Levy RI, Brensike JF, Epstein SE, Kelsey SF, Passamani ER, Richardson JM, Loh IK, Stone NJ, Aldrich RF, Battaglini JW The influence of changes in lipid values induced by cholestyramine and diet on progression of coronary artery disease: results of NHLBI Type II Coronary Intervention Study. Circulation 1984;69:325-37 [6360415]

**Gross, 1973:**

Gross L, Figueredo R Long-term cholesterol-lowering effect of colestipol resin in humans. J Am Geriatr Soc 1973;21:552-6 [4584170]

**Gundersen, 1976:**

Gundersen K, Cooper EE, Ruoff G, Nikolai T, Assenzo JR Cholesterol-lowering effect of colestipol hydrochloride given twice daily in hypercholesterolemic patients. Atherosclerosis 1976;25:303-10 [795441]

**Ruoff, 1978:**

Ruoff G Colestipol hydrochloride for treatment of hypercholesterolemia in a family practice: five-year study. J Am Geriatr Soc 1978;26:121-6 [624819]

**Ryan, 1974:**

Ryan JR, Jain AK, McMahon FG Long-term treatment of hypercholesterolemia with colestipol hydrochloride. Clin Pharmacol Ther 1975;17:83-7 [1091391]

**UCS (Dorr), 1978:**

Dorr AE, Gundersen K, Schneider JC Jr, Spencer TW, Martin WB, Colestipol hydrochloride in hypercholesterolemic patients—effect on serum cholesterol and mortality. J Chronic Dis 1978; 31:5-14 [346598]

## 13 statins

Trial	Treatments	Patients	Trials design and methods
<b>pravastatin vs control</b>			
<b>MEGA , 2006</b> [NCT00211705] n=3866/3966 follow-up: 5.3 y	pravastatin 10 mg daily (20 mg per day if the total cholesterolconcentration did not decrease to 569 mmol/L or less) versus control	patients with hypercholesterolaemia (total cholesterol 569698 mmol/L) and no history of coronary heart disease or stroke	Parallel groups open, blind assessment Japan
<b>Rosuvastatin vs control</b>			
<b>ASTEROID</b> <i>ongoing</i> n=NA follow-up:	-	-	
<b>simvastatin vs control</b>			
<b>Hong , 2005</b> n=106/96 follow-up: 1 year	simvastatin versus no treatment	patients with ischemic heart failure who underwent percutaneous coronary intervention (PCI) for acute myocardial infarction (left ventricular [LV] ejection fraction <40% )	Parallel groups open
<b>atorvastatin vs placebo</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>SPARCL , 2006</b> [NCT00147602] n=2365/2366 follow-up: 4.9y (median)	atorvastatin 80mg daily versus placebo	patients who had had a stroke or TIA within one to six months before study entry, had low-density lipoprotein (LDL) cholesterol levels of 2.6 to 4.9 mmol per liter, and had no known coronary heart disease	Parallel groups double blind
<b>Deutsche Diabetes Dialyse Studie (4D) , 2005</b> n=619/636 follow-up: 4 y (median)	atorvastatin 20mg daily versus matching placebo	patients with type 2 diabetes mellitus on maintenance hemodialysis	Parallel groups double blind
<b>Strey , 2005</b> n=24/24 follow-up: 6 weeks	atorvastatin 40mg versus placebo	patients with stable, symptomatic heart failure (New York Heart Association Class II or III) and a left ventricular ejection fraction <40%	Cross over
<b>ASCOT , 2003</b> n=5168/5137 follow-up: 3.3 years	atorvastatin 10mg/d versus placebo	hypertensive patients aged 40-79 years with at least three other cardiovascular risk factors	Parallel groups double blind UK et Scandinavie
<b>ASPEN , 2006</b> n=1211/1199 follow-up: 4 year	atorvastatin 10mg versus placebo	subjects with type 2 diabetes and LDL cholesterol levels below contemporary guideline targets	Parallel groups double blind 14 countries
<b>Mohler III , 2003</b> n=240/114 follow-up: 1 an	Atorvastatine: 10 mg/ jour ou 80 mg/ jour pendant 12 mois (groupes 1 et 2). versus placebo	Stade de la maladie : II , stable pendant au moins 6 mois.	Parallel groups Double aveugle
<b>CARDS , 2004</b> [NCT00327418] n=1429/1412 follow-up: 3.9 years	atorvastatin 10mg/d versus placebo	patients with type 2 diabetes without high concentrations of LDL-cholesterol and at least one of the following: retinopathy, albuminuria, current smoking, or hypertension.	Parallel groups double blind UK, Irlande
<b>cerivastatin vs placebo</b>			
<b>Laufs , 2004</b> n=8/7 follow-up: mean 20 weeks	cerivastatin 0.4 mg versus placebo	patients with heart failure NYHA II-III caused by non-ischemic dilated cardiomyopathy	Parallel groups double blind
<b>fluvastatin vs placebo</b>			
<b>ALERT , 2003</b> n=1050/1052 follow-up: 5.1 years	fluvastatin versus placebo	renal transplant recipients with total cholesterol 4090 mmol/L.	Parallel groups double blind
<b>ALERT , 2003</b> n=1050/1052 follow-up: 5.1 years	fluvastatin 40 mg daily versus placebo	renal transplant recipients with total cholesterol 4.0-9.0 mmol/L	Parallel groups double-blind Belgium, Denmark, Finland, Germany, Norway,

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>BCAPS , 2001</b> n=395/398 follow-up: 3.0 years	fluvastatin 40 mg once daily versus placebo	subjects who had carotid plaque but no symptoms of carotid artery disease	Factorial plan double-blind Sweden
<b>FLARE , 1999</b> n=409/425 follow-up: 40 weeks	fluvastatin 40 mg twice daily versus placebo	successful coronary balloon angioplasty	Parallel groups double blind
<b>LCAS , 1997</b> n=164/157 follow-up: 2.5 years	fluvastatin 20 mg twice daily versus placebo	men and women aged 35 to 75 years with angiographic CHD and mean low-density lipoprotein (LDL) cholesterol of 115 to 190 mg/dl despite diet	Parallel groups double-blind
<b>LIPS , 2002</b> n=844/833 follow-up: 3.9 years	fluvastatin, 80 mg/d versus placebo	patients (aged 18-80 years) with stable or unstable angina or silent ischemia following successful completion of their first PCI who had baseline total cholesterol levels between 3.5-7.0 mmol/L and with fasting triglyceride levels of less than 4.5 mmol/L	Parallel groups double blind Europe, Canada, and Brazil
<b>Riegger et al. , 1999</b> n=187/178 follow-up: 1.0 years	fluvastatin 40 mg (o.a.d. or b.i.d.) versus placebo	hyperlipidaemic patients with symptomatic, clinically-diagnosed (exercise-ECG) coronary heart disease	Parallel groups double blind
<b>lovastatin vs placebo</b>			
<b>ACAPS , 1994</b> [NCT00000469] n=460/459 follow-up: 2.8 years	lovastatin 20mg daily versus placebo	men and women, 40 to 79 years old, with early carotid atherosclerosis and moderately elevated LDL cholesterol.	Factorial plan double blind USA
<b>AFCAPS/TeXCAPS , 1998</b> n=3304/3301 follow-up: 5.2 years	lovastatin 20-40 mg/d versus placebo	men and women without clinically evident atherosclerotic cardiovascular disease with average total cholesterol (TC) and LDL-C levels and below-average high-density lipoprotein cholesterol (HDL-C) levels	Parallel groups double blind USA
<b>CCAIT , 1994</b> n=165/166 follow-up: 2 years	lovastatin begun at 20 mg/d and titrated to 40 and 80 mg during the first 16 weeks to attain a fasting low-density lipoprotein (LDL) cholesterol $\leq$ 130 mg/dL versus placebo	patients with diffuse but not necessarily severe coronary atherosclerosis documented on a recent arteriogram and with fasting serum cholesterol between 220 and 300 mg/dL	Parallel groups double-blind Canada
<b>CRISP 20mg , 1994</b> [NCT00000477] n=NA follow-up: 1 years	lovastatin 20mg daily versus placebo	elderly (mean 71y) with low-density lipoprotein cholesterol levels greater than 4.1 and less than 5.7 mmol/L	Parallel groups double blind
<b>CRISP 40mg , 1994</b> [NCT00000477] n=NA follow-up: 1 years	lovastatin 40 mg daily versus placebo	elderly (mean 71y) with low-density lipoprotein cholesterol levels greater than 4.1 and less than 5.7 mmol/L	Parallel groups double blind

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Excel , 1991</b> n=6582/1663 follow-up: 0.9 years	lovastatin (20 mg once daily, 40 mg once daily, 20 mg twice daily, or 40 mg twice daily) versus placebo	patients with moderate hypercholesterolemia	Parallel groups double blind
<b>MARS , 1993</b> [NCT00116870] n=123/124 follow-up: 2.0y	lovastatin 80 mg/day versus placebo	patients, 37 to 67 years old, with total cholesterol ranging from 4.92 to 7.64 mmol/L (190 to 295 mg/dL) and angiographically defined coronary artery disease	Parallel groups double blind
<b>Weintraub , 1994</b> n=203/201 follow-up: 0.5 years	lovastatin 40 mg orally twice daily versus placebo	patients undergoing PTCA	Parallel groups double blind
<b>pravastatin vs placebo</b>			
<b>CAIUS , 1996</b> n=151/154 follow-up: 3 years	pravastatin 40mg/d versus placebo	asymptomatic patients with hypercholesterolemia and at least one 1.3 <IMT <3.5 mm in the carotid arteries	Parallel groups double blind Italy
<b>CARE , 1996</b> n=2081/2078 follow-up: 5 years	pravastatin 40 mg/d versus placebo	men and women with myocardial infarction who had plasma totalcholesterol levels below 240 mg per deciliter (mean,209) and low-density lipoprotein (LDL) cholesterollevels of 115 to 174 mg per deciliter	Parallel groups double blind USA, Canada
<b>KAPS , 1995</b> n=224/223 follow-up: 3 years	pravastatin 40mg/d versus placebo	Hypercholesterolemics men with serum LDL-C $\geq$ 4.0 mmol/L and total cholesterol <7.5 mmol/L	Parallel groups double blind Finland
<b>LIPID , 1998</b> n=4512/4502 follow-up: 6.1 years	pravastatin 40 mg/d versus placebo	patients with previous myocardial infarction or unstable angina and a baseline plasma cholesterol concentration of 4.0-7.0 mmol/L	Parallel groups double blind Australie et Nouvelle Zlande
<b>PACT , 2004</b> n=1710/1689 follow-up: 30 days	pravastatin initiated within 24 hours of onset of symptoms and for 4 weeks versus placebo	patients with unstable angina, non-ST-segment elevation myocardial infarction, or ST-segment elevation myocardial infarction <24 hours	Parallel groups double blind
<b>PLAC I , 1995</b> n=206/202 follow-up: 3 y	pravastatin 40mg daily versus placebo	men and women with coronary artery disease and mild to moderate elevations in cholesterol levels	Parallel groups double blind United States
<b>PLAC II , 1995</b> n=75/76 follow-up: 3 y	pravastatin 20-40mg daily versus placebo	coronary patients (men and women )	Parallel groups double blind United States
<b>PMSG , 1993</b> n=530/532 follow-up: 26 weeks	pravastatin 20 mg once daily versus placebo	patients with hypercholesterolemia(serum total cholesterol concentrations of 5.2 to 7.8 mmol/liter) and $\geq$ 2 additional risk factors for atherosclerotic coronary artery disease	Parallel groups double blind

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>PROSPER , 2002</b> n=2891/2913 follow-up: 3.2 years	pravastatin 40mg daily versus placebo	men and women aged 70-82 years with a history of, or risk factors for, vascular disease	Parallel groups double blind Ecosse, Irlande, Pays bas
<b>REGRESS , 1995</b> n=450/435 follow-up: 2 years	pravastatin 40 mg daily versus placebo	symptomatic men with normal to moderately elevated serum cholesterol levels	Parallel groups double blind Netherlands
<b>WOSCOPS , 1995</b> n=3302/3293 follow-up: 4.9 years	pravastatine 40 mg daily versus placebo	men aged 45-64 yr with no history of myocardial infarction and with raised plasma cholesterol levels (LDL cholesterol of at least 155 mg/dL, total cholesterol of at least 252 mg/dL)	Parallel groups double blind Scotland
<b>rosuvastatin vs placebo</b>			
<b>AURORA , 2009</b> n=1391/1385 follow-up: 3.2 y mean (max 5.6y)	rosuvastatin 10 mg daily versus placebo	in patients with end-stage renal disease on hemodialysis	Parallel groups double blind
<b>HOPE 3 , 2016</b> [NCT00468923] n=6361/6344 follow-up:	rosuvastatin 10 mg per day versus placebo	subjects who did not have cardiovascular disease and were at intermediate risk	Factorial plan double-blind 21 countries
<b>CORONA , 2007</b> [NCT00206310] n=2514/2497 follow-up: 32.9 months median	rosuvastatin 10mg/d versus placebo	patients at least 60 years of age with NYHA class II, III, or IV ischemic, systolic heart failure	Parallel groups double blind
<b>Krum , 2007</b> n=40/46 follow-up: 6 months	rosuvastatine 40mg/d versus placebo	patients with systolic (LVEF<40% ) CHF of ischemic or nonischemic etiology	Parallel groups double blind Australia
<b>GISSI-HF rosuvastatine , 2008</b> [NCT00336336] n=2314/2317 follow-up: 3.9y median (IQR 3-4.4)	low-dose rosuvastatin 10 mg daily versus placebo	Patients with NYHA classes II to IV heart failure, whatever the cause and the LVEF and already receiving optimized recommended therapy with no clear indication or contraindication to cholesterol-lowering therapy	Parallel groups double blind Italy
<b>JUPITER , 2008</b> [NCT00239681] n=8901/8901 follow-up: median 1.9 year	rosuvastatin 20 mg daily versus placebo	apparently healthy individuals with low LDL-cholesterol levels of less than 130 mg per deciliter but elevated C-reactive-protein (high-sensitivity C-reactive protein levels of 2.0 mg per liter or higher)	Parallel groups double blind 26 countries
<b>METEOR , 2007</b> [NCT00225589] n=702/282 follow-up:	rosuvastatin 40mg daily versus placebo	individuals, with either age (mean, 57 years) as the only coronary heart disease risk factor or a 10-year Framingham risk score of less than 10% , modest CIMT thickening (1.2-<3.5 mm), and elevated LDL cholesterol	Parallel groups double-blind USA, Europe

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>simvastatin vs placebo</b>			
<b>4S , 1994</b> n=2221/2223 follow-up: 5.4 years	simvastatin 20 or 40 mg/d, target CT between 3 et 5.2 mmol/l versus placebo	patients with angina pectoris or previous myocardial infarction and serum cholesterol 5.5-8.0 mmol/L on a lipid-lowering diet	Parallel groups double blind Scandinavia
<b>Mondillo , 2003</b> n=43/43 follow-up: 6 mois	simvastatine: 40 mg/ jour pendant 6 mois. versus placebo	Stade de la maladie: II.	Parallel groups Double aveugle
<b>Aronow , 2003</b> n=34/35 follow-up: 1 an	simvastatine 40 mg/j versus placebo	Stade II	Parallel groups Non dterminable
<b>Node , 2003</b> n=24/27 follow-up:	simvastatin 10mg/d versus placebo	patients with symptomatic, nonischemic, dilated cardiomyopathy	
<b>CIS , 1997</b> n=129/125 follow-up: 2.3 years	simvastatin 40 mg versus placebo	men with documented coronary artery disease and hypercholesterolaemia	Parallel groups double blind
<b>HPS , 2002</b> n=10269/10267 follow-up: 5 years	simvastatin 40 mg/d versus placebo	adults (aged 40-80 years) with coronary disease, other occlusive arterial disease, or diabete	Factorial plan double blind UK
<b>MAAS , 1994</b> n=193/188 follow-up: 4 y	simvastatin 20 mg daily versus placebo	patients with coronary heart disease	Parallel groups double blind
<b>atorvastatin vs usual care</b>			
<b>GREACE , 2002</b> n=800/800 follow-up: 3 years mean	atorvastatin 10-80 mg/d versus usual care	patients with established coronary heart disease	Parallel groups open
<b>lovastatin vs usual care</b>			
<b>CLAPT , 1999</b> n=112/114 follow-up: 2.0 years	lovastatin begun at 20 mg daily and tritrated up to 80 mg daily versus usual care	patients undergoing PTCA	Parallel groups open (blind assesement)
<b>Sahni , 1991</b> n=79/78 follow-up: 2 years	lovastatin 20-40mg/d versus conventional therapy alone	patients undergoing successful PTCA	Parallel groups open
<b>pravastatin vs usual care</b>			
<b>ALLHAT , 2002</b> [NCT00000542] n=5170/5185 follow-up: 4.8 years	pravastatin 40mg/d versus usual care	older, moderately hypercholesterolemic, hypertensive participants with at least 1 additional CHD risk factor	Factorial plan open USA, Puerto Rico, Canada

continued...



Trial	Treatments	Patients	Trials design and methods
<b>GISSI Prevenzione , 2000</b> n=2138/2133 follow-up: 23 months (mean)	low-dose pravastatin regimen 20 mg daily versus control	recent acute myocardial infarction patients (<= 6 months) with total blood cholesterol >= 200 mg/dl and <250 mg/dl and after a period of 36 months showed plasma cholesterol levels >=200 mg/ dL despite adequate dietary recommendations	Parallel groups open Italy
<b>simvastatin vs ezetimibe</b>			
<b>Landmesser , 2005</b> n=10/10 follow-up:	simvastatin 10mg/d versus ezetimibe 10mg/d	patients with chronic heart failure	

## References

### MEGA, 2006:

Nakamura H, Arakawa K, Itakura H, Kitabatake A, Goto Y, Toyota T, Nakaya N, Nishimoto S, Muranaka M, Yamamoto A, Mizuno K, Ohashi Y Primary prevention of cardiovascular disease with pravastatin in Japan (MEGA Study): a prospective randomised controlled trial. *Lancet* 2006 Sep 30;368:1155-63 [[17011942](#)]

Nakamura H [Primary prevention trial by lowering hyperlipidemia on the cardiovascular disease (MEGA Study)] *Nippon Ronen Igakkai Zasshi* 2009;46:18-21 [[19246826](#)]

### ASTEROID, 0:

#### Hong, 2005:

Hong YJ, Jeong MH, Hyun DW, Hur SH, Kim KB, Kim W, Lim SY, Lee SH, Hong SN, Kang DG, Yun KH, Kim KH, Lee YS, Park HW, Kim JH, Ahn YK, Cho JG, Park JC, Kang JC Prognostic significance of simvastatin therapy in patients with ischemic heart failure who underwent percutaneous coronary intervention for acute myocardial infarction. *Am J Cardiol* 2005;95:619-22 [[15721103](#)]

### SPARCL, 2006:

Amareno P, Bogousslavsky J, Callahan A 3rd, Goldstein LB, Hennerici M, Rudolph AE, Sillesen H, Simunovic L, Szarek M, Welch KM, Zivin JA High-dose atorvastatin after stroke or transient ischemic attack. *N Engl J Med* 2006 Aug 10;355:549-59 [[16899775](#)]

Amareno P, Benavente O, Goldstein LB, Callahan A 3rd, Sillesen H, Hennerici MG, Gilbert S, Rudolph AE, Simunovic L, Zivin JA, Welch KM Results of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial by stroke subtypes. *Stroke* 2009;40:1405-9 [[19228842](#)]

### Deutsche Diabetes Dialyse Studie (4D), 2005:

Wanner C, Krane V, Mrz W, Olschewski M, Mann JF, Ruf G, Ritz E Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis. *N Engl J Med* 2005 Jul 21;353:238-48 [[16034009](#)]

### Strey, 2005:

Strey CH, Young JM, Molyneux SL, George PM, Florkowski CM, Scott RS, Frampton CM Endothelium-ameliorating effects of statin therapy and coenzyme Q10 reductions in chronic heart failure. *Atherosclerosis* 2005;179:201-6 [[15721028](#)]

### ASCOT, 2003:

Sever PS, Dahlof B, Poulter NR, Wedel H, Beevers G, Caulfield M, Collins R, Kjeldsen SE, Kristinsson A, McInnes GT, Mehlsen J, Nieminen M, O'Brien E, Ostergren J, Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. *Lancet* 2003; 361:1149-58 [[12686036](#)]

### ASPEN, 2006:

Knopp RH, d'Emden M, Smilde JG, Pocock SJ Efficacy and safety of atorvastatin in the prevention of cardiovascular end points in subjects with type 2 diabetes: the Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in non-insulin-dependent diabetes mellitus (ASPEN). *Diabetes Care* 2006;29:1478-85 [[16801565](#)]

### Mohler III, 2003:

Cholesterol reduction with atorvastatin improves walking distance in patients with peripheral arterial disease. Mohler ER 3rd, Hiatt WR, Creager MA *Circulation* 2003 Sep 23;108:1481-6 [[12952839](#)]

**CARDS, 2004:**

Colhoun HM, Betteridge DJ, Durrington PN, Hitman GA, Neil HA, Livingstone SJ, Thomason MJ, Mackness MI, Charlton-Menys V, Fuller JH Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. *Lancet* 2004 Aug 21;364:685-96 [[15325833](#)]

**Laufs, 2004:**

Laufs U, Wassmann S, Schackmann S, Heeschen C, Bhm M, Nickenig G Beneficial effects of statins in patients with non-ischemic heart failure. *Z Kardiol* 2004;93:103-8 [[14963675](#)]

**ALERT, 2003:**

Holdaas H, Fellstrom B, Jardine AG, Holme I, Nyberg G, Fauchald P, Gronhagen-Riska C, Madsen S, Neumayer HH, Cole E, Maes B, Ambuhl P, Olsson AG, Hartmann A, Solbu DO, Pedersen TR Effect of fluvastatin on cardiac outcomes in renal transplant recipients: a multicentre, randomised, placebo-controlled trial. *Lancet* 2003 Jun 14;361:2024-31 [[12814712](#)]

**ALERT, 2003:**

Holdaas H, Fellström B, Jardine AG, Holme I, Nyberg G, Fauchald P, Grnhagen-Riska C, Madsen S, Neumayer HH, Cole E, Maes B, Ambuhl P, Olsson AG, Hartmann A, Solbu DO, Pedersen TR Effect of fluvastatin on cardiac outcomes in renal transplant recipients: a multicentre, randomised, placebo-controlled trial. *Lancet* 2003;361:2024-31 [[12814712](#)]

**BCAPS, 2001:**

Hedblad B, Wikstrand J, Janzon L, Wedel H, Berglund G Low-dose metoprolol CR/XL and fluvastatin slow progression of carotid intima-media thickness: Main results from the Beta-Blocker Cholesterol-Lowering Asymptomatic Plaque Study (BCAPS). *Circulation* 2001;103:1721-6 [[11282901](#)]

**FLARE, 1999:**

Serruys PW, Foley DP, Jackson G, Bonnier H, Macaya C, Vrolix M, Branzi A, Shepherd J, Suryapranata H, de Feyter PJ, Melkert R, van Es GA, Pfister PJ A randomized placebo-controlled trial of fluvastatin for prevention of restenosis after successful coronary balloon angioplasty; final results of the fluvastatin angiographic restenosis (FLARE) trial. *Eur Heart J* 1999;20:58-69 [[10075142](#)]

**LCAS, 1997:**

Herd JA, Ballantyne CM, Farmer JA, Ferguson JJ 3rd, Jones PH, West MS, Gould KL, Gotto AM Jr Effects of fluvastatin on coronary atherosclerosis in patients with mild to moderate cholesterol elevations (Lipoprotein and Coronary Atherosclerosis Study [LCAS]). *Am J Cardiol* 1997;80:278-86 [[9264419](#)]

**LIPS, 2002:**

Serruys PW, de Feyter P, Macaya C, Kokott N, Puel J, Vrolix M, Branzi A, Bertolami MC, Jackson G, Strauss B, Meier B, Fluvastatin for prevention of cardiac events following successful first percutaneous coronary intervention: a randomized controlled trial. *JAMA* 2002; 287:3215-22 [[12076217](#)]

**Riegger et al., 1999:**

Riegger G, Abletshauser C, Ludwig M, Schwandt P, Widimsky J, Weidinger G, Welzel D The effect of fluvastatin on cardiac events in patients with symptomatic coronary artery disease during one year of treatment. *Atherosclerosis* 1999;144:263-70 [[10381299](#)]

**ACAPS, 1994:**

Furberg CD, Adams HP Jr, Applegate WB, Byington RP, Espeland MA, Hartwell T, Hunninghake DB, Lefkowitz DS, Probstfield J, Riley WA Effect of lovastatin on early carotid atherosclerosis and cardiovascular events. Asymptomatic Carotid Artery Progression Study (ACAPS) Research Group. *Circulation* 1994;90:1679-87 [[7734010](#)]

Rationale and design for the Asymptomatic Carotid Artery Plaque Study (ACAPS). The ACAPS Group. *Control Clin Trials* 1992;13:293-314 [[1330434](#)]

**AFCAPS/TexCAPS, 1998:**

Downs JR, Clearfield M, Weis S, Whitney E, Shapiro DR, Beere PA, Langendorfer A, Stein EA, Kruyer W, Gotto AM Jr, Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study. *JAMA* 1998; 279:1615-22 [[9613910](#)]

Cui Y, Watson DJ, Girman CJ, Shapiro DR, Gotto AM, Hiserote P, Clearfield MB Effects of increasing high-density lipoprotein cholesterol and decreasing low-density lipoprotein cholesterol on the incidence of first acute coronary events (from the Air Force/Texas Coronary Atherosclerosis Prevention Study). *Am J Cardiol* 2009;104:829-34 [[19733719](#)]

**CCAIT, 1994:**

Probstfield JL, Margitic SE, Byington RP, Espeland MA, Furberg CD Results of the primary outcome measure and clinical events from the Asymptomatic Carotid Artery Progression Study. *Am J Cardiol* 1995;76:47C-53C [[7572686](#)]

Waters D, Higginson L, Gladstone P, Kimball B, LeMay M, Lesprance J Design features of a controlled clinical trial to assess the effect of an HMG CoA reductase inhibitor on the progression of coronary artery disease. Canadian Coronary Atherosclerosis Intervention Trial Investigators Montreal, Ottawa, and Toronto, Canada. *Control Clin Trials* 1993;14:45-74 [[8440094](#)]

Waters D, Higginson L, Gladstone P, Kimball B, Le May M, Boccuzzi SJ, Lesprance J Effects of monotherapy with an HMG-CoA reductase inhibitor on the progression of coronary atherosclerosis as assessed by serial quantitative arteriography. The Canadian Coronary Atherosclerosis Intervention Trial. *Circulation* 1994;89:959-68 [[8124836](#)]

#### **CRISP 20mg, 1994:**

LaRosa JC, Applegate W, Crouse JR 3rd, Hunninghake DB, Grimm R, Knopp R, Eckfeldt JH, Davis CE, Gordon DJ Cholesterol lowering in the elderly. Results of the Cholesterol Reduction in Seniors Program (CRISP) pilot study. *Arch Intern Med* 1994;154:529-39 [[8122946](#)]

Stoy DB, Curtis RC, Dameworth KS, Dowdy AA, Hegland J, Levin JA, Sousoulas BG The successful recruitment of elderly black subjects in a clinical trial: the CRISP experience. Cholesterol Reduction in Seniors Program. *J Natl Med Assoc* 1995;87:280-7 [[7752281](#)]

#### **CRISP 40mg, 1994:**

LaRosa JC, Applegate W, Crouse JR 3rd, Hunninghake DB, Grimm R, Knopp R, Eckfeldt JH, Davis CE, Gordon DJ Cholesterol lowering in the elderly. Results of the Cholesterol Reduction in Seniors Program (CRISP) pilot study. *Arch Intern Med* 1994;154:529-39 [[8122946](#)]

#### **Excel, 1991:**

Bradford RH, Shear CL, Chremos AN, Dujovne C, Downton M, Franklin FA, Gould AL, Hesney M, Higgins J, Hurley DP Expanded Clinical Evaluation of Lovastatin (EXCEL) study results. I. Efficacy in modifying plasma lipoproteins and adverse event profile in 8245 patients with moderate hypercholesterolemia. *Arch Intern Med* 1991;151:43-9 [[1985608](#)]

#### **MARS, 1993:**

Blankenhorn DH, Azen SP, Krams DM, Mack WJ, Cashin-Hemphill L, Hodis HN, DeBoer LW, Mahrer PR, Masteller MJ, Vailas LI, Alaupovic P, Hirsch LJ Coronary angiographic changes with lovastatin therapy. The Monitored Atherosclerosis Regression Study (MARS). *Ann Intern Med* 1993;119:969-76 [[8214993](#)]

#### **Weintraub, 1994:**

Weintraub WS, Boccuzzi SJ, Klein JL, Kosinski AS, King SB 3rd, Ivanhoe R, Cedarholm JC, Stillabower ME, Talley JD, DeMaio SJ Lack of effect of lovastatin on restenosis after coronary angioplasty. Lovastatin Restenosis Trial Study Group. *N Engl J Med* 1994;331:1331-7 [[7935702](#)]

#### **CAIUS, 1996:**

Mercuri M, Bond MG, Sirtori CR, Veglia F, Crepaldi G, Feruglio FS, Descovich G, Ricci G, Rubba P, Mancini M, Gallus G, Bianchi G, D'Al G, Ventura A Pravastatin reduces carotid intima-media thickness progression in an asymptomatic hypercholesterolemic mediterranean population: the Carotid Atherosclerosis Italian Ultrasound Study. *Am J Med* 1996;101:627-34 [[9003110](#)]

#### **CARE, 1996:**

Sacks FM, Pfeffer MA, Moye LA, Rouleau JL, Rutherford JD, Cole TG, Brown L, Warnica JW, Arnold JM, Wun CC, Davis BR, Braunwald E, The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. *N Engl J Med* 1996; 335:1001-9 [[8801446](#)]

Plehn JF, Davis BR, Sacks FM, Rouleau JL, Pfeffer MA, Bernstein V, Cuddy TE, Moy LA, Piller LB, Rutherford J, Simpson LM, Braunwald E Reduction of stroke incidence after myocardial infarction with pravastatin: the Cholesterol and Recurrent Events (CARE) study. The Care Investigators. *Circulation* 1999;99:216-23 [[9892586](#)]

#### **KAPS, 1995:**

Salonen R, Nyssnen K, Porkkala-Sarataho E, Salonen JT The Kuopio Atherosclerosis Prevention Study (KAPS): effect of pravastatin treatment on lipids, oxidation resistance of lipoproteins, and atherosclerotic progression. *Am J Cardiol* 1995;76:34C-39C [[7572684](#)]

Salonen R, Nyssnen K, Porkkala E, Rummukainen J, Belder R, Park JS, Salonen JT Kuopio Atherosclerosis Prevention Study (KAPS). A population-based primary preventive trial of the effect of LDL lowering on atherosclerotic progression in carotid and femoral arteries. *Circulation* 1995;92:1758-64 [[7671358](#)]

#### **LIPID, 1998:**

, Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. *N Engl J Med* 1998; 339:1349-57 [[9841303](#)]

, Long-term effectiveness and safety of pravastatin in 9014 patients with coronary heart disease and average cholesterol concentrations: the LIPID trial follow-up. *Lancet* 2002; 359:1379-87 [[11978335](#)]

Design features and baseline characteristics of the LIPID (Long-Term Intervention with Pravastatin in Ischemic Disease) Study: a randomized trial in patients with previous acute myocardial infarction and/or unstable angina pectoris. *Am J Cardiol* 1995;76:474-9 [[7653447](#)]

#### **PACT, 2004:**

Thompson PL, Meredith I, Amerena J, Campbell TJ, Sloman JG, Harris PJ Effect of pravastatin compared with placebo initiated within 24 hours of onset of acute myocardial infarction or unstable angina: the Pravastatin in Acute Coronary Treatment (PACT) trial. *Am Heart J* 2004;148:e2 [[15215811](#)]

#### **PLAC I, 1995:**

Furberg CD, Pitt B, Byington RP, Park JS, McGovern ME Reduction in coronary events during treatment with pravastatin. PLAC I and PLAC II Investigators. Pravastatin Limitation of Atherosclerosis in the Coronary Arteries. *Am J Cardiol* 1995;76:60C-63C [[7572689](#)]

Pitt B, Ellis SG, Mancini GB, Rosman HS, McGovern ME Design and recruitment in the United States of a multicenter quantitative angiographic trial of pravastatin to limit atherosclerosis in the coronary arteries (PLAC I). *Am J Cardiol* 1993;72:31-5 [[8517425](#)]

Pitt B, Mancini GB, Ellis SG, Rosman HS, Park JS, McGovern ME Pravastatin limitation of atherosclerosis in the coronary arteries (PLAC I): reduction in atherosclerosis progression and clinical events. PLAC I investigation. *J Am Coll Cardiol* 1995;26:1133-9 [[7594023](#)]

#### **PLAC II, 1995:**

Byington RP, Furberg CD, Crouse JR 3rd, Espeland MA, Bond MG Pravastatin, Lipids, and Atherosclerosis in the Carotid Arteries (PLAC-II). *Am J Cardiol* 1995;76:54C-59C [[7572688](#)]

Crouse JR, Byington RP, Bond MG, Espeland MA, Sprinkle JW, McGovern M, Furberg CD Pravastatin, lipids, and atherosclerosis in the carotid arteries: design features of a clinical trial with carotid atherosclerosis outcome. *Control Clin Trials* 1992;13:495-506 [[1334821](#)]

Furberg CD, Byington RP, Crouse JR, Espeland MA Pravastatin, lipids, and major coronary events. *Am J Cardiol* 1994;73:1133-4 [[8198043](#)]

#### **PMSG, 1993:**

Effects of pravastatin in patients with serum total cholesterol levels from 5.2 to 7.8 mmol/liter (200 to 300 mg/dl) plus two additional atherosclerotic risk factors. The Pravastatin Multinational Study Group for Cardiac Risk Patients. *Am J Cardiol* 1993;72:1031-7 [[8213583](#)]

#### **PROSPER, 2002:**

Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, Ford I, Gaw A, Hyland M, Jukema JW, Kamper AM, Macfarlane PW, Meinders AE, Norrie J, Packard CJ, Perry IJ, Stott DJ, Sweeney BJ, Twomey C, Westendorp RG, Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. *Lancet* 2002; 360:1623-30 [[12457784](#)]

#### **REGRESS, 1995:**

Jukema JW, Bruschke AV, van Boven AJ, Reiber JH, Bal ET, Zwinderman AH, Jansen H, Boerma GJ, van Rappard FM, Lie KI Effects of lipid lowering by pravastatin on progression and regression of coronary artery disease in symptomatic men with normal to moderately elevated serum cholesterol levels. The Regression Growth Evaluation Statin Study (REGRESS). *Circulation* 1995;91:2528-40 [[7743614](#)]

van Boven AJ, Jukema JW, Zwinderman AH, Crijs HJ, Lie KI, Bruschke AV Reduction of transient myocardial ischemia with pravastatin in addition to the conventional treatment in patients with angina pectoris. REGRESS Study Group. *Circulation* 1996;94:1503-5 [[8840836](#)]

#### **WOSCOPS, 1995:**

Shepherd J, Cobbe SM, Ford I, Isles CG, Lorimer AR, MacFarlane PW, McKillop JH, Packard CJ, Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. West of Scotland Coronary Prevention Study Group. *N Engl J Med* 1995; 333:1301-7 [[7566020](#)]

A coronary primary prevention study of Scottish men aged 45-64 years: trial design. The West of Scotland Coronary Prevention Study Group. *J Clin Epidemiol* 1992;45:849-60 [[1624967](#)]

#### **AURORA, 2009:**

Fellstrom BC, Jardine AG, Schmieder RE, et al. Rosuvastatin and cardiovascular events in patients undergoing hemodialysis *N Engl J Med* 2009;360:1395-407. [[19332456](#)]

Fellström BC, Jardine AG, Schmieder RE, Holdaas H, Bannister K, Beutler J, Chae DW, Chevaile A, Cobbe SM, Grnhagen-Riska C, De Lima JJ, Lins R, Mayer G, McMahon AW, Parving HH, Remuzzi G, Samuelsson O, Sonkodi S, Sci D, Sleymanlar G, Tsakiris D, Tesar V Rosuvastatin and cardiovascular events in patients undergoing hemodialysis. *N Engl J Med* 2009;360:1395-407 [19332456]

**HOPE 3, 2016:**

Yusuf S, Bosch J, Dagenais G, Zhu J, Xavier D, Liu L, Pais P, Lopez-Jaramillo P, Leiter LA, Dans A, Avezum A, Piegas LS, Parkhomenko A, Keltai K, Keltai M, Sliwa K, Peters RJ, Held C, Chazova I, Yusuf K, Lewis BS, Jansky P, Khunti K, Toff WD, Reid CM, Va Cholesterol Lowering in Intermediate-Risk Persons without Cardiovascular Disease. *N Engl J Med* 2016 Apr 2;: [27040132] 10.1056/NEJMoa1600176

**CORONA, 2007:**

Kjekshus J, Apetrei E, Barrios V, Bhm M, Cleland JG, Cornel JH, Dunselman P, Fonseca C, Goudev A, Grande P, Gullestad L, Hjalmarsen A, Hradec J, Jnosi A, Kamensk G, Komajda M, Korewicki J, Kuusi T, Mach F, Mareev V, McMurray JJ, Ranjith N, Schaufelberg Rosuvastatin in older patients with systolic heart failure. *N Engl J Med* 2007;357:2248-61 [17984166]

**Krum, 2007:**

Krum H, Ashton E, Reid C, Kalff V, Rogers J, Amarena J, Singh B, Tonkin A Double-blind, randomized, placebo-controlled study of high-dose HMG CoA reductase inhibitor therapy on ventricular remodeling, pro-inflammatory cytokines and neurohormonal parameters in patients with chronic systolic heart failure. *J Card Fail* 2007;13:1-7 [17338996]

**GISSI-HF rosuvastatine, 2008:**

Tavazzi L, Tognoni G, Franzosi MG, Latini R, Maggioni AP, Marchioli R, Nicolosi GL, Porcu M Rationale and design of the GISSI heart failure trial: a large trial to assess the effects of n-3 polyunsaturated fatty acids and rosuvastatin in symptomatic congestive heart failure. *Eur J Heart Fail* 2004 Aug;6:635-41 [15302013]

Tavazzi L, Maggioni AP, Marchioli R, Barlera S, Franzosi MG, Latini R, Lucci D, Nicolosi GL, Porcu M, Tognoni G Effect of rosuvastatin in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial. *Lancet* 2008;372:1231-9 [18757089]

**JUPITER, 2008:**

Ridker PM, Danielson E, Fonseca FA, Genest J, Gotto AM Jr, Kastelein JJ, Koenig W, Libby P, Lorenzatti AJ, Macfadyen JG, Nordestgaard BG, Shepherd J, Willerson JT, Glynn RJ Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein. *N Engl J Med* 2008 Nov 9;: [18997196]

**METEOR, 2007:**

Crouse JR 3rd, Raichlen JS, Riley WA, Evans GW, Palmer MK, O'Leary DH, Grobbee DE, Bots ML Effect of rosuvastatin on progression of carotid intima-media thickness in low-risk individuals with subclinical atherosclerosis: the METEOR Trial. *JAMA* 2007 Mar 28;297:1344-53 [17384434]

**4S, 1994:**

, Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S) *Lancet* 1994; 344:1383-9 [7968073]

**Mondillo, 2003:**

Effects of simvastatin on walking performance and symptoms of intermittent claudication in hypercholesterolemic patients with peripheral vascular disease. Mondillo S, Ballo P, Barbati R, Guerrini F, Ammataro T, Agricola E, Pastore M, Borrello F, Belcastro M, Picchi A, Nami R *Am J Med* 2003 Apr 1;114:359-64 [12714124]

**Aronow , 2003:**

Effect of simvastatin versus placebo on treadmill exercise time until the onset of intermittent claudication in older patients with peripheral arterial disease at six months and at one year after treatment. Aronow WS, Nayak D, Woodworth S, Ahn C *Am J Cardiol* 2003 Sep 15;92:711-2 [12972114]

**Node, 2003:**

Node K, Fujita M, Kitakaze M, Hori M, Liao JK Short-term statin therapy improves cardiac function and symptoms in patients with idiopathic dilated cardiomyopathy. *Circulation* 2003;108:839-43 [12885745]

**CIS, 1997:**

Bestehorn HP, Rensing UF, Roskamm H, Betz P, Benesch L, Schemitat K, Blmchen G, Claus J, Mathes P, Kappenberger L, Wieland H, Neiss A The effect of simvastatin on progression of coronary artery disease. The Multicenter coronary Intervention Study (CIS). *Eur Heart J* 1997;18:226-34 [9043838]

**HPS, 2002:**

, MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002; 360:7-22 [12114036]

Armitage J, Collins R Need for large scale randomised evidence about lowering LDL cholesterol in people with diabetes mellitus: MRC/BHF heart protection study and other major trials. *Heart* 2000;84:357-60 [10995396]

MRC/BHF Heart Protection Study of cholesterol-lowering therapy and of antioxidant vitamin supplementation in a wide range of patients at increased risk of coronary heart disease death: early safety and efficacy experience. *Eur Heart J* 1999;20:725-41 [10329064]

**MAAS, 1994:**

Effect of simvastatin on coronary atheroma: the Multicentre Anti-Atheroma Study (MAAS) *Lancet* 1994;344:633-8 [7864934]

**GREACE, 2002:**

Athyros VG, Papageorgiou AA, Mercouris BR, Athyrou VV, Symeonidis AN, Basayannis EO, Demetriadis DS, Kontopoulos AG Treatment with atorvastatin to the National Cholesterol Educational Program goal versus 'usual' care in secondary coronary heart disease prevention. The GREek Atorvastatin and Coronary-heart-disease Evaluation (GREACE) study. *Curr Med Res Opin* 2002;18:220-8 [12201623]

**CLAPT, 1999:**

Kleemann A, Eckert S, von Eckardstein A, Lepper W, Schernikau U, Gleichmann U, Hanrath P, Fleck E, Neiss A, Kerber S, Assmann G, Breithardt and the CLAPT Study Effects of lovastatin on progression of non-dilated and dilated coronary segments and on restenosis in patients after PTCA. The cholesterol lowering atherosclerosis PTCA trial (CLAPT) *Eur Heart J* 1999;20:1393-406 [10487800]

**Sahni, 1991:**

Sahni R, Maniet AR, Voci G, Banka VS Prevention of restenosis by lovastatin after successful coronary angioplasty. *Am Heart J* 1991;121:1600-8 [2035374]

**ALLHAT, 2002:**

, Major outcomes in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin vs usual care: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT). *JAMA* 2002; 288:2998-3007 [12479764]

**GISSI Prevenzione, 2000:**

**Landmesser, 2005:**

30

## 14 statins high dose

Trial	Treatments	Patients	Trials design and methods
<b>atorvastatin high dose vs angioplasty</b>			
<b>AVERT , 1999</b> n=164/177 follow-up: 1.5 years	atorvastatin 80 mg/d versus recommended percutaneous revascularization procedure(angioplasty) followed by usual care, which could include lipid-lowering treatment	patients referred for percutaneous revascularization, with stable coronary artery disease, relatively normal left ventricular function, asymptomatic or mild-to-moderate angina, and a serum level of low-density lipoprotein (LDL) cholesterol of at least 115 mg per deciliter (3.0 mmol per liter)	Parallel groups open US, Europe
<b>atorvastatin high dose vs atorvastatin</b>			
<b>TNT , 2005</b> [NCT00327691] n=4995/5006 follow-up: 4.9 years	80 mg of atorvastatin daily versus 10 mg of atorvastatin daily	Chronic coronary artery disease LDL cholesterol <3.4 mmol/L	Parallel groups double blind 14 countries
<b>atorvastatin high dose vs lovastatin</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Vascular basis , 2005</b> n=197/103 follow-up: 1 year	atorvastatin (80 mg) with or without vitamin C and E versus low dose lovastatin (5 mg)	Chronic coronary artery disease	Parallel groups double blind
<b>atorvastatin high dose vs pravastatin</b>			
<b>PROVE-IT , 2004</b> n=2099/2063 follow-up: 2 years	atorvastatin 80 mg daily versus Pravastatin 40 mg	acute myocardial infarction (with or without electrocardiographic evidence of ST-segment elevation) or highrisk unstable angina) in the preceding 10 days	Parallel groups double blind 8 countries
<b>REVERSAL , 2004</b> n=327/327 follow-up: 1.5 years	atorvastatin 80 mg daily versus Pravastatin(40 mg)	Chronic coronary artery disease	Parallel groups double blind
<b>SAGE , 2007</b> n=446/445 follow-up: 1 years	atorvastatin 80 mg daily versus pravastatin(40 mg)	Chronic coronary artery disease	Parallel groups double blind
<b>atorvastatin high dose vs simvastatin</b>			
<b>IDEAL , 2005</b> [NCT00159835] n=4439/4449 follow-up: 4.8 years	atorvastatin 80mg daily versus simvastatine 20mg/j	Men and women aged 80 years or younger with a history of a definite myocardial infarction and who qualified for statin therapy according to national guidelines	Parallel groups open Denmark, Finland, Iceland, Netherlands, Norway, Sweden
<b>simvastatin high dose vs simvastatin</b>			
<b>SEARCH , 2010</b> [NCT00124072] n=6031/6033 follow-up: 6.7 years (mean)	simvastatin 80 mg daily versus simvastatin 20mg daily	MI survivors	Parallel groups

## References

**AVERT, 1999:**  
**TNT, 2005:**  
**Vascular basis, 2005:**  
**PROVE-IT, 2004:**  
**REVERSAL, 2004:**  
**SAGE, 2007:**  
**IDEAL, 2005:**  
**SEARCH, 2010:**

## 15 strategy

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>aggressive treatment vs standard treatment</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>SANDS , 2008</b> [NCT00047424] n=252/247 follow-up: 3 years	aggressive targets of LDL-C of 70 mg/dL or lower and SBP of 115 mm Hg or lower versus standard targets of LDL-C of 100 mg/dL or lower and SBP of 130 mm Hg or lower	adults with type 2 diabetes	Parallel groups open US

## References

SANDS, 2008:

## 16 surgery

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>partial ileum bypass surgery vs no surgery</b>			
<b>POSCH , 1990</b> [NCT00000490] n=421/417 follow-up: 9.7 years	partial ileum bypass surgery versus no surgery	survivors to a first myocardial infarction	Parallel groups open

## References

POSCH, 1990:

## 17 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.