Clinical trials of cholesterol lowering intervention for cardiovascular prevention in patients with prior MI or with CHD

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1 diet

Trial	Treatments	Patients	Trials design and methods
diet vs usual diet			
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 domicilary care, age>55, with or without CHD	Parallel groups double blind USA
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
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
low fat diet vs mediterranean-style diet			
Tuttle , 2008 n=NA follow-up: 24 months	low-fat versus Mediterranean-style diets	First MI survivors	Parallel groups open

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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]

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]

2 ezetimibe

Trial	Treatments	Patients	Trials design and methods
ezetimibe vs control			
IMPROVE-IT , 2014 [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

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, Tershakovec 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]

3 fibrates

Trial	Treatments	Patients	Trials design and methods
bezafibrate vs placebo			
SENDCAP , 1998 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

continued...

Trial	Treatments	Patients	Trials design and methods
gemfibrozil vs placebo			
HHS (Frick)(secondary prev subgroup) , 1993 n=311/317 follow-up: 5.0 years	gemfibrozil 600 mg twice daily versus placebo	individuals who exhibited symptoms and signs of possible coronary heart disease	Parallel groups double blind Sweden
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

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Frick MH, Heinonen OP, Huttunen JK, Koskinen P, Mnttri M, Manninen V Efficacy of gemfibrozil in dyslipidaemic subjects with suspected heart disease. An ancillary study in the Helsinki Heart Study frame population. Ann Med 1993;25:41-5 [8435186]

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Frick MH, Syvnne 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. Lopid Coronary Angiography Trial (LOCAT) Study Group. Circulation 1997;96:2137-43 [9337181]

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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]

4 hormones

Trial	Treatments	Patients	Trials design and methods
estrogen vs placebo			
CDP estrogen 2.5 , 1975 n=1101/2789 follow-up: 4.7 years	estrogen 2.5 mg daily versus placebo	-	Parallel groups

continued...

Trial	Treatments	Patients	Trials design and methods
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
estrogen or thyroxine vs placebo			
VA drugs (Estrogen or thyroxine) , 1968 n=427/143 follow-up: 65279;3.2 years	estrogen or thyroxine versus placebo	-	Parallel groups
thyroxine vs placebo			
CDP tyroxine , 1975 n=1083/2715 follow-up: 3.0 years	thyroxine versus placebo	-	Parallel groups

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5 inhibitor of lipoprotein-associated phospholipase

Trial	Treatments	Patients	Trials design and methods
darapladib vs placebo			
SOLID-TIMI 52 [NCT01000727] n=NA follow-up:	-	-	

References

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O'Donoghue ML, Braunwald E, White HD, Steen DP, Lukas MA, Tarka E, Steg PG, Hochman JS, Bode C, Maggioni AP, Im K, Shannon JB, Davies RY, Murphy SA, Crugnale SE, Wiviott SD, Bonaca MP, Watson DF, Weaver WD, Serruys PW, Cannon CP Effect of Darapladib on Major Coronary Events After an Acute Coronary Syndrome: The SOLID-TIMI 52 Randomized Clinical Trial. JAMA 2014 Aug 31;: [25173516] 10.1001/jama.2014.11061

6 niacin

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

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CDP niacin, 1975:

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7 other cholesterol lowering drugs

Trial	Treatments	Patients	Trials design and methods
colestipol-niacin vs placebo			
CLAS , 1987 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
various drugs vs placebo			
HARP , 1994 [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
various drugs vs usual care			
SCRIP , 1994 [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

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8 Probucol

Trial	Treatments	Patients	Trials design and methods
Probucol vs placebo			
McCaughan , 1981 n=88/30 follow-up: 1 year	probucol versus placebo	hypercholesterolemic men	Parallel groups double-blind

continued...

Trial	Treatments	Patients	Trials design and methods
Tardif , 1997 n=160/157 follow-up: 0.5 years	probucol 500 mg versus placebo	patients undergoing PTCA	Parallel groups open

References

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9 resins

Trial	Treatments	Patients	Trials design and methods
cholestyramine vs control			
STARS (cholestyramine) , 1992 n=30/30 follow-up: 3 years	cholestyramine versus diet	patients with angina or past myocardial infarction	
colestipol vs placebo			
Gross , 1973 n=23/29 follow-up: 65279;1.0 years	colestipol versus placebo		Parallel groups

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]

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10 statins

Trial	Treatments	Patients	Trials design and methods
any statin vs no statin			

continued...

Trial	Treatments	Patients	Trials design and methods
Sakamoto , 2006 n=241/245 follow-up: up to 24 months	any available statin versus no statin	Japanese patients with AMI within 96 hours of AMI onset	Parallel groups open Japan
atorvastatin vs placebo			
MIRACL , 2001 n=1538/1548 follow-up: 1 and 4 months	Atorvastatin, 80 mg (early initiation) versus Placebo	unstable angina or nonQ-wave acute MI	Parallel groups Double blind Europe, North America, South Africa, and Australasia
macin , 2005 n=NA follow-up: 30 days	atorvastatin 40 mg daily for 30 days versus placebo	patients admitted within 48 hours of onset of ACS with CRP levels >or =1.4 mg/dL	Parallel groups double-blind
fluvastatin vs placebo			
LIPS (sub groups) , 2002 n=417/407 follow-up: 1, 4, and 6 months	Fluvastatin, 80 mg versus Placebo	patients with unstable angina and successful first percutaneous coronary intervention	Parallel groups double blind Europe, Canada, and Brazil
FLORIDA , 2002 n=265/275 follow-up: 1, 4, and 6 months	Fluvastatin, 80 mg (early initiation) versus Placebo	patients with an AMI and total cholesterol of <6.5 mmol.l	Parallel groups double blind The Netherlands
FLARE , 1999 n=409/425 follow-up: 40 weeks	fluvastatin 40 mg twice daily versus placebo	successful coronary balloon angioplasty	Parallel groups double blind
LCAS , 1997 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
Riegger et al. , 1999 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
Czech trial *ongoing* [NCT00171275] n=NA follow-up: 52 weeks	fluvastatin versus placebo	-	Parallel groups double blind
pravastatin vs placebo			
LAMIL , 1997 n=36/33 follow-up: 1 and 3 months	Pravastatin, 10-20 mg (starting at D3) versus Placebo	patients suffering an acute myocardial infarction	Parallel groups double blind Belgium
RECIFE , 1999 n=30/30 follow-up: 1.5 months	Pravastatin, 40 mg versus Placebo	Patients with acute myocardial infarction or unstable angina and total cholesterol levels at admission >=5.2 mmol/L or LDL >=3.4 mmol/L	Parallel groups double blind Canada

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Trial	Treatments	Patients	Trials design and methods
PAIS , 2001 n=50/49 follow-up: 1 and 3 months	Pravastatin, 40 mg (initiated within 48 hours of hospital admission) versus Placebo	patients with acute coronary syndromes	Parallel groups double blind The Netherlands
PACT , 2004 n=1710/1698 follow-up: 1 months	Pravastatin, 20-40 mg within 24 hours of the onset of symptoms in versus Placebo	patients with unstable angina, non-ST-segment elevation myocardial infarction, or ST-segment elevation myocardial infarction within 24 hours of the onset of symptoms	Parallel groups double blind Australia
CARE , 1996 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
LIPID , 1998 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
simvastatin vs placebo			
4S , 1994 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
A to Z , 2004 n=2265/2232 follow-up: 1 and 4 months	Simvastatin, 40-80 mg early initiation versus Placebo	patient with an acute coronary syndrome (ACS)	Parallel groups Double aveugle 41 countries
Ren , 2009 n=NA follow-up:	simvastatin (40 mg/d for 4 weeks) versus placebo	patients with unstable angina pectoris	Parallel groups double-blind
CIS , 1997 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
HPS , 2002 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
atorvastatin vs usual care			
Colivicchi , 2002 n=40/41 follow-up: 1, 3, and 6 months	Atorvastatin, 80 mg daily early initiation versus Usual care	unstable angina pectoris or non-Q-wave myocardial infarction	Parallel groups open Italy
ESTABLISH , 2004 n=35/35 follow-up: 1, 4, and 6 months	Atorvastatin, 20 mg early initiation versus Usual care	patients with ACS undergoing emergency coronary angiography and percutaneous coronary intervention	Parallel groups open Japan

continued...

Trial	Treatments	Patients	Trials design and methods
GREACE , 2002 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
lovastatin vs usual care			
CLAPT , 1999 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 underwenting PTCA	Parallel groups open (blind assessement)
Sahni , 1991 n=79/78 follow-up: 2 years	lovastatin 20-40mg/d versus conventional therapy alone	patients undergoing successful PTCA	Parallel groups open
pravastatin vs usual care			
L-CAD , 2000 n=70/56 follow-up: 1, 4, and 6 months	Pravastatin, 20-40 mg (strating on average at D6) versus Usual care	patients with acute coronary syndrome	Parallel groups open Germany
PTT , 2002 n=79/85 follow-up: 1 and 6 months	Pravastatin, 40 mg versus Usual care	patients who underwent coronary balloon angioplasty of the infarct-related artery during the first month of acute myocardial infarction	Parallel groups open Turkey
OACIS-LIPID , 2008 n=176/177 follow-up: 9 months	pravastatin 10 mg/daily versus no pravastatin	patients with AMI who had plasma total cholesterol levels of 200-250 mg/dl and triglyceride levels <300 mg/dl	Parallel groups open
GISSI Prevenzione , 2000 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
pitavastatin vs atorvastatin			
JAPAN ACS , 2009 [NCT00242944] n=307 follow-up: 8-12 months	pitavastatin 4 mg daily versus atorvastatin 20mg daily	patients with acute coronary syndrome undergoing IVUS-guided percutaneous coronary intervention	Parallel groups open Japan
atorvastatin vs pravastatin			
PROVE IT - TIMI 22 , 2004 n=2099/2063 follow-up: 24 mo (18-36 mo)	80 mg of atorvastatin daily (intensive therapy). versus 40 mg of pravastatin daily (standard therapy)	patients who had been hospitalized for an acute coronary syndrome within the preceding 10 days	Parallel groups double blind UK, US, AUstralia, Italy, France, Germany, Spain, Canada

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11 statins high dose

Trial	Treatments	Patients	Trials design and methods
atorvastatin high dose vs atorvastatin			
TNT , 2005 [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
atorvastatin high dose vs lovastatin			
Vascular basis , 2005 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
atorvastatin high dose vs pravastatin			
PROVE-IT , 2004 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
REVERSAL , 2004 n=327/327 follow-up: 1.5 years	atorvastatin 80 mg daily versus Pravastatin(40 mg)	Chronic coronary artery disease	Parallel groups double blind
SAGE , 2007 n=446/445 follow-up: 1 years	atorvastatin 80 mg daily versus pravastatin(40 mg)	Chronic coronary artery disease	Parallel groups double blind
atorvastatin high dose vs simvastatin			

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Trial	Treatments	Patients	Trials design and methods
IDEAL , 2005 [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
simvastatin high dose vs simvastatin			
SEARCH , 2010 [NCT00124072] n=6031/6033 follow-up: 6.7 years (mean)	simvastatin 80 mg daily versus simvastatin 20mg daily	MI survivors	Parallel groups

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Vascular basis, 2005:
PROVE-IT, 2004:
REVERSAL, 2004:
SAGE, 2007:
IDEAL, 2005:
SEARCH, 2010:

12 surgery

Trial	Treatments	Patients	Trials design and methods
partial ileum bypass surgery vs no surgery			
POSCH , 1990 [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

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13 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.

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