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

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## 1 colestipol-niacin

| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|---|
| **colestipol-niacin vs placebo** | | | |
| CLAS , 1987<br>n=94/94<br>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)<br>versus<br>placebo: methyl cellulose | Patients coronariens avec antcdent de revascularisation chirurgicale coronarienne. | Parallel groups<br>Non dterminable |
| CLAS , 1987<br>n=NA<br>follow-up: 65279;2 years | colestipol + niacin<br>versus<br>placebo | nonsmoking men aged 40 to 59 years with previous coronary bypass surgery | Parallel groups<br>double blind |

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## 2 combination therapies

| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|---|
| **intensive lipid-lowering therapy vs diet** | | | |
| FATS , 1990<br>[NCT00000512]<br>n=94/52<br>follow-up: 2.5 years | intensive lipid-lowering therapy with various drugs<br>versus<br>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<br>open<br>Japan |
| **colestipol+clofibrate vs placebo** | | | |
| SCOR , 1990<br>n=48/49<br>follow-up: 2.0 years | colestipol (15 to 30mg/d) + clofibrate (2g/d)<br>versus<br>diet | patients with primary hypercholesterolemia | Parallel groups |

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# 3 diet

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

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

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| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|---|
| Veterans Ad. (Dayton) , 1969<br>n=424/422<br>follow-up: 3.6 and 8 y | cholesterol lowering diet<br>versus<br>usual diet | men in domicilary care, age>55, with or without CHD | Parallel groups<br>double blind<br>USA |
| WHI low fat , 2005<br>[NCT00000611]<br>n=19541/29294<br>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<br>versus<br>usual diet | postmenopausal women, aged 50 to 79 years, without prior breast cancer | Parallel groups<br>open<br>US |
| WHO Collaborative , 1986<br>n=30489/26971<br>follow-up: 5.5 years | multifactorial prevention<br>versus<br>usual diet | middle-aged men | Parallel groups<br>open<br>Belgium, Italy, Poland, UK |
| Woodhill , 1966<br>n=221/237<br>follow-up: <7 years | diet<br>versus<br>usual diet | men, 30-59 years | Parallel groups<br>open |
| **low fat diet vs mediterranean-style diet** | | | |
| Tuttle , 2008<br>n=NA<br>follow-up: 24 months | low-fat<br>versus<br>Mediterranean-style diets | First MI survivors | Parallel groups<br>open |



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# 4 ezetimibe

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

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# 5 Fibrates

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

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

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

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# 6 hormones

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

continued...

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

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# 7 niacin

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

continued...

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

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# 8 niacin (on top statin)

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

continued...

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

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# 9 other cholesterol lowering drugs

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

continued...

| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|---|
| **various drugs vs placebo** | | | |
| HARP , 1994<br>[NCT00000461]<br>n=40/39<br>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)<br>versus<br>placebo | normocholesterolaemic patients with coronary heart disease | Parallel groups<br>open |
| **various drugs vs usual care** | | | |
| SCRIP , 1994<br>[NCT00000508]<br>n=145/155<br>follow-up: 4.0 years | multifactor risk reduction (Various drugs)<br>versus<br>usual care | patients with angiographically defined coronary atherosclerosis | Parallel groups<br>open |

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# 10 Policosanol

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

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# 11 probucol

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

continued...

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

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# 12 resins

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

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# 13 statins

| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|---|
| **pravastatin vs control** | | | |
| MEGA , 2006<br>[NCT00211705]<br>n=3866/3966<br>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)<br>versus<br>control | patients with hypercholesterolaemia (total cholesterol 569698 mmol/L) and no history of coronary heart disease or stroke | Parallel groups<br>open, blind assessment<br>Japan |
| **Rosuvastatin vs control** | | | |
| ASTEROID *ongoing*<br>n=NA<br>follow-up: | - | - | |
| **simvastatin vs control** | | | |
| Hong , 2005<br>n=106/96<br>follow-up: 1 year | simvastatin<br>versus<br>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<br>open |
| **atorvastatin vs placebo** | | | |

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| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|---|
| SPARCL , 2006<br>[NCT00147602]<br>n=2365/2366<br>follow-up: 4.9y (median) | atorvastatin 80mg daily<br>versus<br>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<br>double blind |
| Deutsche Diabetes Dialyse Studie (4D) , 2005<br>n=619/636<br>follow-up: 4 y (median) | atorvastatin 20mg daily<br>versus<br>matching placebo | patients with type 2 diabetes mellitus on maintenance hemodialysis | Parallel groups<br>double blind |
| Strey , 2005<br>n=24/24<br>follow-up: 6 weeks | atorvastatin 40mg<br>versus<br>placebo | patients with stable, symptomatic heart failure (New York Heart Association Class II or III) and a left ventricular ejection fraction <40% | Cross over |
| ASCOT , 2003<br>n=5168/5137<br>follow-up: 3.3 years | atorvastatin 10mg/d<br>versus<br>placebo | hypertensive patients aged 40-79 years with at least three other cardiovascular risk factors | Parallel groups<br>double blind<br>UK et Scandinavie |
| ASPEN , 2006<br>n=1211/1199<br>follow-up: 4 year | atorvastatin 10mg<br>versus<br>placebo | subjects with type 2 diabetes and LDL cholesterol levels below contemporaryguideline targets | Parallel groups<br>double blind<br>14 countries |
| Mohler III , 2003<br>n=240/114<br>follow-up: 1 an | Atorvastatine: 10 mg/ jour ou 80 mg/ jour pendant 12 mois (groupes 1 et 2).<br>versus<br>placebo | Stade de la madie : II , stable pendant au moins 6 mois. | Parallel groups<br>Double aveugle |
| CARDS , 2004<br>[NCT00327418]<br>n=1429/1412<br>follow-up: 3.9 years | atorvastatin 10mg/d<br>versus<br>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<br>double blind<br>UK, Irelande |
| **cerivastatin vs placebo** | | | |
| Laufs , 2004<br>n=8/7<br>follow-up: mean 20 weeks | cerivastatin 0.4 mg<br>versus<br>placebo | patients with heart failure NYHA II-III caused by non-ischemic dilated cardiomyopathy | Parallel groups<br>double blind |
| **fluvastatin vs placebo** | | | |
| ALERT , 2003<br>n=1050/1052<br>follow-up: 5.1 years | fluvastatin<br>versus<br>placebo | renal transplant recipients with total cholesterol 4090 mmol/L. | Parallel groups<br>double blind |
| ALERT , 2003<br>n=1050/1052<br>follow-up: 5.1 years | fluvastatin 40 mg daily<br>versus<br>placebo | renal transplant recipients with total cholesterol 4.0-9.0 mmol/L | Parallel groups<br>double-blind<br>Belgium, Denmark, Finland, Germany, Norway, |

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| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|---|
| BCAPS , 2001<br>n=395/398<br>follow-up: 3.0 years | fluvastatin 40 mg once daily<br>versus<br>placebo | subjects who had carotid plaque but no symptoms of carotid artery disease | Factorial plan<br>double-blind<br>Sweden |
| FLARE , 1999<br>n=409/425<br>follow-up: 40 weeks | fluvastatin 40 mg twice daily<br>versus<br>placebo | successful coronary balloon angioplasty | Parallel groups<br>double blind |
| LCAS , 1997<br>n=164/157<br>follow-up: 2.5 years | fluvastatin 20 mg twice daily<br>versus<br>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<br>double-blind |
| LIPS , 2002<br>n=844/833<br>follow-up: 3.9 years | fluvastatin, 80 mg/d<br>versus<br>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<br>double blind<br>Europe, Canada, and Brazil |
| Riegger et al. , 1999<br>n=187/178<br>follow-up: 1.0 years | fluvastatin 40 mg (o.a.d. or b.i.d.)<br>versus<br>placebo | hyperlipidaemic patients with symptomatic, clinically-diagnosed (exercise-ECG) coronary heart disease | Parallel groups<br>double blind |
| **lovastatin vs placebo** | | | |
| ACAPS , 1994<br>[NCT00000469]<br>n=460/459<br>follow-up: 2.8 years | lovastatin 20mg daily<br>versus<br>placebo | men and women, 40 to 79 years old, with early carotid atherosclerosis and moderately elevated LDL cholesterol. | Factorial plan<br>double blind<br>USA |
| AFCAPS/TexCAPS , 1998<br>n=3304/3301<br>follow-up: 5.2 years | lovastatin 20-40 mg/d<br>versus<br>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<br>double blind<br>USA |
| CCAIT , 1994<br>n=165/166<br>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 <or = 130 mg/dL<br>versus<br>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<br>double-blind<br>Canada |
| CRISP 20mg , 1994<br>[NCT00000477]<br>n=NA<br>follow-up: 1 years | lovastatin 20mg daily<br>versus<br>placebo | elderly (mean 71y) with low-density lipoprotein cholesterol levels greater than 4.1 and less than 5.7 mmol/L | Parallel groups<br>double blind |
| CRISP 40mg , 1994<br>[NCT00000477]<br>n=NA<br>follow-up: 1 years | lovastatin 40 mg daily<br>versus<br>placebo | elderly (mean 71y) with low-density lipoprotein cholesterol levels greater than 4.1 and less than 5.7 mmol/L | Parallel groups<br>double blind |

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

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| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|---|
| PROSPER , 2002<br>n=2891/2913<br>follow-up: 3.2 years | pravastatin 40mg daily<br>versus<br>placebo | men and women aged 70-82 years with a history of, or risk factors for, vascular disease | Parallel groups<br>double blind<br>Ecosse, Irelande, Pays bas |
| REGRESS , 1995<br>n=450/435<br>follow-up: 2 years | pravastatin 40 mg daily<br>versus<br>placebo | symptomatic men with normal to moderately elevated serum cholesterol levels | Parallel groups<br>double blind<br>Netherlands |
| WOSCOPS , 1995<br>n=3302/3293<br>follow-up: 4.9 years | pravastatine 40 mg daily<br>versus<br>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<br>double blind<br>Scotland |
| **rosuvastatin vs placebo** | | | |
| AURORA , 2009<br>n=1391/1385<br>follow-up: 3.2 y mean (max 5.6y) | rosuvastatin 10 mg daily<br>versus<br>placebo | in patients with end-stage renal disease on hemodialysis | Parallel groups<br>double blind |
| HOPE 3 , 2016<br>[NCT00468923]<br>n=6361/6344<br>follow-up: | rosuvastatin 10 mg per day<br>versus<br>placebo | subjects who did not have cardiovascular disease and were at intermediate risk | Factorial plan<br>double-blind<br>21 countries |
| CORONA , 2007<br>[NCT00206310]<br>n=2514/2497<br>follow-up: 32.9 months median | rosuvastatin 10mg/d<br>versus<br>placebo | patients at least 60 years of age with NYHA class II, III, or IV ischemic, systolic heart failure | Parallel groups<br>double blind |
| Krum , 2007<br>n=40/46<br>follow-up: 6 months | rosuvastatine 40mg/d<br>versus<br>placebo | patients with systolic (LVEF<40% ) CHF of ischemic or nonischemic etiology | Parallel groups<br>double blind<br>Australia |
| GISSI-HF rosuvastatine , 2008<br><br>[NCT00336336]<br>n=2314/2317<br>follow-up: 3.9y median (IQR 3-4.4) | low-dose rosuvastatin 10 mg daily<br>versus<br>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 cholesterollowering therapy | Parallel groups<br>double blind<br>Italy |
| JUPITER , 2008<br>[NCT00239681]<br>n=8901/8901<br>follow-up: median 1.9 year | rosuvastatin 20 mg daily<br>versus<br>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<br>double blind<br>26 countries |
| METEOR , 2007<br>[NCT00225589]<br>n=702/282<br>follow-up: | rosuvastatin 40mg daily<br>versus<br>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<br>double-blind<br>USA, Europe |

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

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| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|---|
| GISSI Prevenzione , 2000<br>n=2138/2133<br>follow-up: 23 months (mean) | low-dose pravastatin regimen 20 mg daily<br>versus<br>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<br>open<br>Italy |
| **atorvastatin vs angioplasty** | | | |
| AVERT , 1999<br>n=164/177<br>follow-up: 1.5 years | atorvastatin 80 mg/d<br>versus<br>recommended percutaneous revascularization procedure(angioplasty) followed by usual care, whichcould 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<br>open<br>US, Europe |
| **simvastatin vs ezetimibe** | | | |
| Landmesser , 2005<br>n=10/10<br>follow-up: | simvastatin 10mg/d<br>versus<br>ezetimibe 10mg/d | patients with chronic heart failure | |

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# 14 statins high dose

| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|---|
| **atorvastatin high dose vs atorvastatin** | | | |
| TNT , 2005<br>[NCT00327691]<br>n=4995/5006<br>follow-up: 4.9 years | 80 mg of atorvastatin daily<br>versus<br>10 mg of atorvastatin daily | Chronic coronary artery disease LDL cholesterol <3.4 mmol/L | Parallel groups<br>double blind<br>14 countries |
| **atorvastatin high dose vs lovastatin** | | | |

continued...

| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|---|
| Vascular basis , 2005<br>n=197/103<br>follow-up: 1 year | atorvastatin (80 mg) with or without vitamin C and E<br>versus<br>low dose lovastatin (5 mg) | Chronic coronary artery disease | Parallel groups<br>double blind |
| **atorvastatin high dose vs pravastatin** | | | |
| PROVE-IT , 2004<br>n=2099/2063<br>follow-up: 2 years | atorvastatin 80 mg daily<br>versus<br>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<br>double blind<br>8 countries |
| REVERSAL , 2004<br>n=327/327<br>follow-up: 1.5 years | atorvastatin 80 mg daily<br>versus<br>Pravastatin(40 mg) | Chronic coronary artery disease | Parallel groups<br>double blind |
| SAGE , 2007<br>n=446/445<br>follow-up: 1 years | atorvastatin 80 mg daily<br>versus<br>pravastatin(40 mg) | Chronic coronary artery disease | Parallel groups<br>double blind |
| **atorvastatin high dose vs simvastatin** | | | |
| IDEAL , 2005<br>[NCT00159835]<br>n=4439/4449<br>follow-up: 4.8 years | atorvastatin 80mg daily<br>versus<br>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<br>open<br>Denmark, Finland, Iceland, Netherlands, Norway, Sweden |
| **simvastatin high dose vs simvastatin** | | | |
| SEARCH , 2010<br>[NCT00124072]<br>n=6031/6033<br>follow-up: 6.7 years (mean) | simvastatin 80 mg daily<br>versus<br>simvastatin 20mg daily | MI survivors | Parallel groups |



## References

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

# 15 strategy

| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|---|
| **aggressive treatment vs standard teatment** | | | |

continued...

| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|---|
| SANDS , 2008<br>[NCT00047424]<br>n=252/247<br>follow-up: 3 years | aggressive targets of LDL-C of 70 mg/dL or lower and SBP of 115 mm Hg or lower<br>versus<br>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<br>open<br>US |

## References

**SANDS, 2008:**

# 16 surgery

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



## References

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# 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.

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