Additional file 2: Baseline characteristics of included studies

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Albert et al, 2001 a	Pravastatin 40 mg/d (n=1014) Placebo (n=999)	PRINCE	23 wks	Random, double blind, placebo controlled, community based trial. Primary prevention study.6 mth washout of statins before entry. Assessed at baseline, 12 & 24 wks. Lipids measured at a CDC standardised central laboratory.	LDL >130 mg/dL (3.5 mmol/L)	Men and women with no prior history of cardiovascular disease Not using statins for >6 mths, no contraindication to statin use. Mean age 57 yrs ± 12 (entry >18 yrs) 44% women 49% never smoker, 15% current smoker 86% Caucasian Mean BMI 29 Kg/m2 Diabetes mellitus 11% Oestrogen use 38% Aspirin use 28%	R 1 DB 1 W 0
Arntz et al, 1999	Pravastatin 20 mg once daily (n= 58) Bezafibrate 400 mg daily (n= 38) Dose doubled if LDL was >190 mg/dL after 6 wks		12 wks	Random, double blind (double dummy), multicentre, parallel group. Six wk placebo washout & low fat/cholesterol diet before randomisation.		Primary hypercholesteroleamia types Iia (65) & Ib (31) Mean age 52 yrs (20-68) Mean weight 71-72 Kg Male:female: 48/48	R 1 DB 2 W 0
Bak et al, 1998	Pravastatin 20 mg + Step 1 diet: (n= 54) Pravastatin 20 mg + Step 2 diet: (n= 55) Placebo + Step 1diet (n= 53) Placebo + Step 2 diet (n= 53)		6 mths	Random, double blind, parallel group. 4 wk dietary run-in (Step 1. Then randomised to either Step 1 or Step 2 diet and to active or placebo). Compliance assessed by tablet count. & food diaries Lipid assessments at 0. 4. 6 & 12 mths. Blood samples were analysed in blinded manner. Cholesterol & triglycerides were assayed enzymatically. HDL measured after precipitation with phosphowolfram/phosphotungistic acid & 2 mmol/L manganese chloride. LDL concentration measured by Friedewald technique.	Total cholesterol ≥6.5 and ≤8.0 mmol/L Triglycerides <4.0 mmol/L	Moderate, primary hypercholesterolaemia Mean age 55 yrs (40-70) Mean BMI: 27 kg/m2 Mean weight:79-84 Kg Systolic BP:135 Diastolic BP: 83 Smoker:3 3% (except Step 2 diet with pravastatin (not stated)). Excluded: impaired renal / hepatic function, any unstable medical condition, history of alcohol or drug abuse, ever use of lipid lowering drugs, use of hormones, fish oil preparations, immunosuppressive drugs, vasodilators, anticoagulants.	R 2 Db 2 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Beigel et al, 1993	Pravastatin 20 mg (evening) (n= 38) Placebo (n=39) Dose doubled in 6 pts after 13 wks because total cholesterol >200 mg/dL & reduction from baseline was <15%		26 wks	Random, double blind, parallel group, multicentre, Israeli study, placebo control. Minimum 6 wk dietary stabilisation (AHA). Compliance by tablet count & patient interview. Assessments at 0, 6, 13 & 26 wks. LDL cholesterol measured using Friedewald technique.	Total cholesterol between 200-300 mg/dL Triglycerides <350 mg/dL	Primary hypercholesterolaemia & 2 risk factors (male sex, current smoker, hypertension, family history of MI or angina before age 55, history of CAD). Mean age yrs (20-69) Mean weight: 72 Kg CAD risk factors: Current smoker: 16% Hypertension: 39% Previous MI: 43% Angina: 30% Family history of CAD: 34% Excluded: Premenopausal women, alcohol or drug abuse, any acute medical condition within 3 mths, poorly controlled congestive heart failure, unstable angina, type I, III, IV or V hyperlipidaemia, obesity, liver, kidney or pancreatic disease. disallowed drugs: antacids, corticosteroids, sex hormones, immunosuppressive / hypolipidaemic agents.	R 1 DB 1 W 1
Bertolini et al, 1997	Atorvastatin 10 mg (n= 227) Pravastatin 20 mg (n= 78) Once in the evening Initial dose was doubled at wk 16 if LDL goals not met at wk 4 & 10 By wk 52 daily dose taken: Atorv 10 mg 76% Atorv20 mg 24% Prav 20 mg 36% Prav 40 mg 64%		52 wks	Random, double blind, parallel groups, active control, multicentre, European study. 4 wk washout of all lipid lowering drugs (6 mths if probucol) with 6 wks dietary stabilisation (e.g. NCEP step I). Assessed at baseline then at wks 16 & 52. Unbalanced randomisation. Lipid analysis was conducted in a central laboratory in France. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation & LDL using Friedewald formula. Last observation carried forward for all patients with missing data	LDL > 4.1 & ≤ 6.5 mmol/L Triglycerides ≤ 4.5 mmol/L	Men & women (54%) with primary hyperchoelsterolaemia. Mean age 56 yrs 73% Frederickson Type IIa Mean BMI 26 kg/m2 Excluded: hypothyroidism, hypertension, diabetes mellitus, other metabolic/endocrine disease, active liver, hepatic or renal dysfunction, ≥14 alcoholic drinks/wk, concurrent use of other lipid lowering agents	R 1 DB 2 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Bestehorn et al, 1997	Simvastatin 20 mg (n= 129) Placebo (n= 125) Once daily Dose doubled after 6 wks if LDL >90 mg/dL. After 12 wks an ion exchange resin was added if LDL> 120 mg/dL with simvastatin (>250 mg/dL with placebo)		30 mths	Random, double blind, active control, parallel groups, multicentre (European). Dietary stabilisation on lipid-lowering AHA step I diet & washout of lipid - lowering drugs for 12 wks before randomisation. Assessed at baseline & then at 4 wk intervals. Investigators were blind to drug & lipid levels when the central laboratory informed them of need for dose change. Assessed at baseline & at regular intervals throughout the study. Total cholesterol, HDL & triglycerides were measured enzymatically, LDL using Friedewald formula.	Total cholesterol between 207 & 350 mg/dL Triglycerides between <350 mg/dL	Men with CAD & hypercholesterolaemia Mean age 49 yrs (30-55) Mean weight 80 Kg Family history of CAD 46% Smoker 84% BP 80/123 mm Hg Fasting serum glucose 90 mg/dL Excluded: No details provided	R 1 DB 1 W 1
Betteridge et al,1999	Treatments given orally, once daily in the evening Cerivastatin 0.025 mg (n=193) Cerivastatin 0.05 mg (n= 187) Cerivastatin 0.1 mg (n= 190) Cerivastatin 0.2 mg (n= 191) Placebo (n= 187) Simvastatin 20 mg (n= 183)		12 wks	Random, double blind, multicentre (12 countries), placebo control, international. 4-wk dietary stabilisation (AHA step I), 6 wk single blind placebo run-in before randomisation. LDL derived using Friedewald formula.		Men(52%) & women with uncomplicated primary hypercholesterolaemia Mean age 55 yrs (21-75) Mean weight 74 kg Excluded: homozygous familial hyperchoelsterolaemia, MI, stroke, bypass surgery within 6 mths, diabetes mellitus, significant renal, hepatic, neuromuscular or ophthalmic abnormalities.	R 1 DB 1 W0

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Bevilacqua et al, 1997	Fluvastatin 40 mg (n= 25) Placebo (n= 23) Once daily		20 wks	Random, double blind, placebo control, multicentre, parallel group. 4 wk placebo run-in and dietary stabilisation (isocaloric diet) before randomisation to study treatment. Assessed at baseline, 4, 8, 12 and 20 wks. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation, LDL using Friedewald formula.	Triglycerides >300 mg/dL	Men and postmenopausal women (not on oestrogen therapy) with coronary artery disease Mean age 59 yrs ± 7 Mean BMI 25 kg /m2 Previous MI 48% placebo, 60% fluvastatin Angina pectoris 14% Nitrates 26% placebo, 4% fluvastatin Beta-blockers 23% ACE inhibitors 25% Calcium channel antagonists 30% placebo, 24% fluvastatin Diuretics 13% placebo, 20% fluvastatin Excluded: secondary hyperchoelsterolaemia, liver or renal pathology, obesity, smokers.	R 1 DB 1 W 1
Blankenhorn et al, 1993	Lovastatin 80 mg (n= 123) 40 mg given twice daily Placebo (n= 124) Mean daily dose taken 73 mg		2 yrs	Random, double blind, placebo control, two-centre (USA), parallel groups. Cholesterol lowering dietary run-in before randomisation to treatment for 2 yrs. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation & LDL using Friedewald formula. Assessed at baseline & 2 yrs for lipids.	Total cholesterol between 4.91 & 7.63 mmol/L Triglycerides between 190 & 295 mg/dL	Elevated total cholesterol & CAD on angiography with ≥2 artery segments & 1 narrowed by >50% stenosis & unaltered percutaneous transluminal coronary angioplasty. 91% men Mean age 58 yrs (37-67) Mean systolic/diastolic BP 125/80 mm Hg Mean blood glucose 94 mg/dL % ideal body weight 122 80% current or former smoker Hypertension 46% Angina pectoris 41% Previous MI 63% Previous coronary bypass surgery 19% Previous angioplasty 13% concomitant medications: beta-blockers, calcium channel antagonists, angiotensin converting enzyme inhibitors, diuretics, aspirin	R 1 DB 1 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Bradford et al, 1991	Lovastatin 20 mg once in evening (n = 1642) Lovastatin 40 mg once in evening (n = 1645) Lovastatin 40 mg daily (as 2 doses) (n = 1646) Lovastatin 80 mg daily (as 2 doses) (n = 1649) Placebo (n = 1663)	EXCEL	48 wks	Random, double blind, multicentre (USA), parallel groups, placebo control. 4-6 wk dietary stabilisation (AHA or stricter diet), then 48 wks diet & study treatment. Assessed at baseline & then at 6 wiks intervals. Total cholesterol measured enzymatically, HDL by precipitation & LDL using Friedewald formula. Central laboratory conducted analyses. NB: CDC lipid standardisation program noted fixed high bias for total cholesterol levels (+^%). To correct this the instrument was recalibrated & readings corrected for samples analysed before recalibration.	Total cholesterol between 6.21 & 7.6 mmol/L Triglycerides <3.95 mmol/L	Men (58%) & women with moderate hypercholesterolaemia Mean age 57 yrs, >60 yrs 42% White 91%, Black 5% Current smoker 18% ≥30% overweight 17% >7 units alcohol/wk 13% Cardiovascular & associated disease 57% Hypertension 39% CAD 30%, Stroke 3%, Diabetes 1% Peripheral vascular disease 3% CAD or >2 risk factors (NCEP classification) 62% concomitant medications: Beta-blockers 21%, Calcium antagonists 15% Diuretics 12%, ACE inhibitors 7%, Alpha-blockers 1% Excluded: premenopausal women, patients taking other lipid lowering drugs, secondary hypercholesterolaemia, .	R 1 DB 2 W 1
Brown et al 2001 (Abstract)	Rosuvastatin 5 mg (n=123) Rosuvastatin 10 mg (n=116) Pravastatin 20 mg (n=118) Simvastatin 20 mg (n=120)		12 wks then 40 wk dose titration	Random, double blind, active control. 6 week dietary lead-in. Randomised to once daily treatment.40 wk dose titration period in which doses could be doubled to meet LDL goals. Analysis of drop-outs was handled by last observation carried forward. Daily doses were rosuvastatin 5-80 mg or 10-80 mg, pravastatin 20-40 mg and simvastatin 20-80 mg during dose titration up to 52 weeks	LDL ≥4.14 and <6.5 mmol/L triglycerides <4.52 mmol/L	Primary hypercholesterolaemia Age≥18 yrs (mean 58-60); 35-40% over 65 yrs Male/female ratio (%): 40:60 Mean weight 80 Kg Mean BMI 28 Caucasian 80-85%	R 1 DB 1 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Byington et al, 1995	Pravastatin 20 mg/day (n= 75) Placebo (n= 76) Once daily evening. Dose doubled if LDL >2.84 mmol/L & decreased to 10 mg if LDL was <2.33 mmol/L Number on different doses: 10 mg 4% 20 mg 23.5% 40 mg 72.5%	PLAC II	3 yrs	Random, double blind, single centre, placebo control, parallel group. Diet resistant lipid levels. Randomisation to pravastatin or placebo with increasing dose if lipids remained high. Assessed at baseline, at 1 mth intervals for 3 mths, & then at 3 mth intervals. Lipids measured at CDC standardised lipid laboratory.	LDL between 60th & 90th percentiles for age & sex Triglycerides <9.05 mmol/L	CAD (previous MI or evidence >50% stenosis with >1 extracranial carotid lesion with an IMT ≥1.3 mm). Mean age 63 yrs 85% men Excluded: secondary hyperlipidaemia, recent MI, severe or unstable angina pectoris, uncontrolled CHF or hypertension, significant gastrointestinal disease, surgery interfering with drug absorption, drugs including corticosteroids, androgens, lipid lowering agents, antacids with aluminium.	R 1 DB 2 W 1
Celis et al, 1994	Pravastatin (n= 25) Placebo (n= 25) Dose increased from 10 mg to 20 mg at end of mth 1 & to 40 mg at end of mth 2. Pts remained on 40 mg daily.		6 mths	Random, double blind, placebo control, parallel group. 1 mth diet, washout of lipid altering drugs & single blind placebo run-in. Then randomisation to study treatment for 6 mths. Compliance was by tablet count. Assessed at baseline, 1, 2, 3 & 6 mths. Dose of pravastatin was increased at 1mth to 20 mg, at 2 mths to 40 mg daily unless plasma cholesterol was <150 mg/dL. Cholesterol & triglycerides were measured using enzymatic methods, HDL by precipitation using sodium phosphotungstate MgCl2 & LDL by the Friedewald technique.	Total cholesterol between 250-400 mg/dl after 1 mth dietary control	Hypercholesterolaemia, in good health & well controlled BP (Diastolic BP <100 mmHg) Mean age 58 yrs (18-70) Male/female: approx 50% each Mean weight 75 Kg Mean systolic BP 155 mmHg Mean diastolic BP 90 mmHg	R 1 DB 1 W 1
Chan et al, 1996	Simvastatin 10 mg (n=38) Placebo (n=38) Once daily evening		12 mths	Random, double blind, placebo control, parallel group. 1 mth dietary stabilisation (AHA Step 1 diet) & washout of lipid altering drugs with single blind placebo run-in before randomisation to study treatment for 12 wks Assessed at monthly . Compliance by tablet count. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation, & LDL by Friedewald technique.	Total plasma cholesterol ≥6.47 mmol/L Triglyceride <3.39 mmol/L	Elderly patients with primary hypercholesterolaemia & hypertension Male/female: 50% each Mean age 75 yrs ± 6 Mean BMI 24 kg/m2 Mean systolic BP 138 ± 8 Mean diastolic BP 83 ± 5 Number on beta-blockers , ACE inhibitors, diuretics, calcium channel blockers: Monotherapy 38 Combination therapy 38	R 1 Db 2 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Chan et al, 1996	Pravastatin 15 mg (n= 48) Placebo (n= 48) Once in evening		12 mths	Random, double blind, placebo control, parallel group. 3 mth dietary stabilisation (AHA Step 1 diet), washout of lipid altering drugs & single blind placebo run-in before randomisation to study treatment for 2 mths. Assessed at mth 1 & 2 then every 2 mths. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation, & LDL by Friedewald technique.	Total plasma cholesterol ≥6.47 mmol/L Triglyceride <3.39 mmol/L	Elderly patients with primary hypercholesterolaemia & hypertension Mean age 77 yrs ± 10 Mean BMI 23 kg/m2 Mean systolic BP 140 ± 10, Mean diastolic BP 80 ± 9 Number on other drugs: Beta-blockers 19. ACE inhibitors 29 Diuretics 24, Calcium channel blockers 19 Other antihypertensives 9 Monotherapy 47, Ditherapy 39, Tritherapy 10	R 1 Db 2 W
Chan et al, 1996b	Pravastatin 10 mg (n= 25) Placebo (n=25) Once daily evening		20 wks	Random, double blind, placebo control, parallel group. 3 mth dietary stabilisation (AHA Step 1 diet), 2 mth washout of lipid altering drugs & 1 mth single blind placebo run-in before randomisation to study treatment. Assessed at baseline, 4, 8, 12 & 20 wks. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation, & LDL by Friedewald technique.	Total plasma cholesterol ≥6.47 mmol/L Triglyceride <3.39 mmol/L	Elderly patients with primary hypercholesterolaemia & otherwise healthy Male/female: approx 50% each Mean age 73 yrs ± 6 Mean BMI 23kg/m2 Mean systolic BP 133 Mean diastolic BP 83 ± 5 Number on beta-blockers , ACE inhibitors, diuretics, calcium channel blockers: Monotherapy 38 Combination therapy 38 Excluded type III, IV or V hyperlipoproteinaemia, diabetes, renal or hepatic impairment.	R 1 Db 2 W 1
Chan et al, 1995	Pravastatin 10 mg (n= 30) Placebo (n= 30)		6 mths	Random, double blind, parallel groups, placebo control. Washout of lipid lowering drugs with single blind placebo run-in & AHA step I diet for ≥4 wks. Antihypertensives continued at fixed doses. Assessed at baseline, then at monthly intervals for 6 mths. Compliance by tablet count. Total cholesterol & triglycerides measured using Monarch Autoanalyzer system, HDL by precipitation & LDL using Friedewald formula.	Total cholesterol between 250 mg/dL & 400 mg/dL	Elderly (>65 yrs) men & women with hypertension & primary hypercholesterolaemia No other cardiovascular risk factors Mean age 75 yrs Mean BMI 24 kg/m2 Mean BP 148/88 Antihypertensive monotherapy: 68% Antihypertensive combination therapy: 32%	R 1 DB 1 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Crepaldi et al, 1991	Pravastatin (n= 193) 40 mg/day evening		24 wks	Random, double blind, double dummy, active control, parallel group, multicentre (Italian), placebo control. 8 wk dietary stabilisation with single blind placebo run-in. Compliance by tablet count. Assessed at baseline & then every 4 wks for 24 wks. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation & LDL using the Friedewald method.	Total cholesterol between 7.25 & 11.6 mmol/L Triglycerides <2.82 mmol/L for familial or <1.32 for polygenic hypercholesterolaemia	Type Iia hypercholesterolaemia Mean age 53 ± 12 Men & women 50% each) Mean BMI 25 kg/m2 Excluded: homozygous familial hypercholesterolaemia, familial hypertriglyceriidaemia, familial chylomicronaemia, disbetalipoproteinaemia, obesity, abnormal liver or renal function, recent MI or coronary bypass surgery, organ transplant, major gastrointestinal disease, cholelithiasis, premenopausal women unless sterilised, use of hormones or lipid altering drugs.	R 1 DB 2 W 1
D'Agostino et al, 1992	Lovastatin evening (n= 52) Initial 20 mg dose wasdoubled after 6 wks if LDL > 160 mg/dL in stratum I or >130 mg/dL in stratum II Gemfibrozil 1200 mg/day given as 600 mg twice (n= 52) Dose remained constant		18 wks	Random, double blind, active control, multicentre (7), parallel group. 4-6 wk placebo run-in & dietary stabilisation. Randomisation to study treatment & split by baseline cholesterol: stratum I total >240 & LDL >190 mg/dL without CAD or CAD risk factors; stratum II total >240 & LDL >160 mg/dL plus CAD or 2 CAD risk factors. Assessed at baseline, 6,12 & 18 wks. Lipids were measured in a central laboratory using standard methods.	Total cholesterol > 240 mg/dL LDL > 160 mg/dL	Primary hypercholesterolaemia Mean age 56 yrs ± 14 (range 24-78) 58% men CAD 24% Hypertension 37% gemfibrozil, 56% lovastatin Family history of CAD 40% Smoker (>10/day) 7% gemfibrozil, 6% lovastatin diabetes mellitus 0% gemfibrozil, 2% lovastatin History of cerebrovascular / occlusive peripheral vascular disease 4% Excluded: hypersensitivity to components of study drugs, premenopausal unless sterilised, severe obesity, active liver disease, severe renal dysfunction, gallbladder disease, untreated hypothyroidism, secondary hypercholesterolaemia, poor mental function, substance abuse, immunosuppressive drugs, concurrent lipid lowering drugs, anticoagulants.	R 1 DB 1 W 1
Dart et al, 1997	Atorvastatin 10 mg (n=132) Dose doubled of LDL target not reached at wk 10 (64/132) Simvastatin 10 mg (n=45) Dose doubled of LDL target not reached at wk 10 (28/45) Completed 95%	SmAC	52 wks	Random, double blind, active control, parallel group, multicentre (Australian). Lipid values of randomised patients were blinded to the investigators & study sponsor. 6 wk dietary stabilisation (NCEP step 1 diet) with placebo run-in. Randomised 3:1 to atorvastatin. Dose doubled at 16 wks if target LDL of <3.36 mmol/L at wk 10. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation & LDL using the Friedewald method.	LDL between 3.8 & 7.8 mmol/L Triglycerides <4.5 mmol/L	Elevated LDL cholesterol. Median age 57 yrs (SEM 0.8) - inclusion criteria 18-80 yrs. Mean BMI 26 Kg/M2 94 men/83 women 98% white Excluded: hyperlipoproteinaemia secondary to uncontrolled hypothyroidism, nephrotic syndrome, renal or hepatic impairment, uncontrolled diabetes mellitus, uncontrolled hypertension, drug or alcohol abuse, use of lipid altering drugs, immunosuppressive agents, drugs associated with rhabdomyolosis in combination with statins, significant coronary abnormality.	R 2 Db 2 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Davidson et al, 1991	Pravastatin 40 mg (n=26) Placebo (n= 27) Probucol 1000 mg (n= 29) Pravastatin + probucol (n= 29) Probucol 500 mg given twice daily All other treatments given once daily evening		16 wks	Random, double blind, placebo & active control, parallel groups, multicentre (USA). 8 wks dietary stabilisation & placebo run-in with washout of all lipid lowering agents before randomisation. AHA step I diet or equivalent. Compliance assessed by tablet count and dietary counselling. Assessed at baseline, then at 2, 4, 8, 12 & 16 wks. Lipids analysed at a central laboratory. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation & LDL using Friedewald formula.	LDL > 3.88 mmol/L or in ≥75th percentile for age & sex	Men & women with primary hypercholesterolaemia Mean age 54 yrs (included 21-75) 55% Caucasian Diagnosis heterozygous familial 31% Polygenic 35% Familial combined 31% Other 3% Excluded: women of child bearing potential, homozygous familial hypercholesterolaemia, type I, III, IV or V hyperlipoproteinaemia, significant metabolic disease, renal or hepatic impairment, endocrine or cardiovascular disease, use of oestrogens (except HT), androgens or study drugs.	R 1 DB 1 W 1
Davidson et al, 1997	Atorvastatin 10 mg (n= 707) Lovastatin 20 mg (n= 191) Placebo (n=133) - cannot use placebo data as no baseline lipids provided		16 wks	Random, double blind, placebo & active control, multicentre. 6 wk dietary stabilisation, 4 wk washout of lipid altering agents, (6 mths for probucol) before randomisation to double blind study treatment. After 16 wks data uncontaminated and double blind (blinding broken after this and placebo patients reassigned to active). Food diaries and tablet counts for compliance. Cholesterol & triglycerides were measured enzymatically HDL by precipitation & LDL using Friedewald formula. Assessed at baseline & 16 wks.	LDL >4.14 mmol/L Triglycerides <4.52 mol/L	Men & women with primary hyperchoelsterolaemia Mean age 59 yrs (18-80) Mean BMI 27 Kg/m2 58% men 92% white Frederickson type Iia (66%), Iib (34%) Familial hypercholesterolaemia 14%, familial combined 4%, neither 44% Risk status: <2 risk factors 51% ≥2 risk factors 33% CHD 15% Excluded previous MI, stroke & angina, renal or hepatic impairment, uncontrolled diabetes, other unstable conditions, use of immunosuppressive agents, drugs known to affect lipid levels.	R 1 DB 1 W 1
Davidson et al. 2001 Now published as [Davidson et al, 2002]	Rosuvastatin 5 mg (n=129) Rosuvastatin 10 mg (n=130) Placebo (n=132) Atorvastatin 10 mg (n=128)		12 weeks	Random, double blind, active control. 6 week dietary lead-in. Randomised to once daily treatment.40 wk dose titration period in which doses could be doubled to meet LDL goals. Analysis of drop-outs was handled by last observation carried forward.	LDL ≥4.14 and <6.5 mmol/L triglycerides <4.52 mmol/L	Primary hypercholesterolaemia Age≥18 yrs (mean 57); 24-33% over 65 yrs Male: 40-50% Mean BMI 29 Caucasian 80-87%	R 1 DB 1 W1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Dobs et al, 2000	Simvastatin 20 mg (n= 40) Simvastatin 40 mg: (n= 41) Pravastatin 40 mg (n= 39) Placebo (n= 39)		24 wks	Random, double blind, parallel groups, multicentre, USA, active & placebo control. Six wk placebo run-in and dietary stabilisation before randomisation. Assessed at baseline, then at 6 wk intervals. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation & LDL using Friedewald formula.	LDL between 145 & 240 mg/dL	Type Iia or b hyperchoelsterolaemia Mean age 41 yrs (26 to 55) 83% Caucasian Excluded: secondary hypercholesterolaemia, types I, III, IV or V hyperlipidaemia, homozygous familial hypercholesterolaemia, uncontrolled hypertension, diabetes mellitus, active liver disease, MI or angioplasty or bypass surgery or angina within 4_mths of screening, use of lipid lowering agents within 6 wks (6 mths for probucol), androgenic or antiandrogenic agents.	R 2 DB 2 W 1
Farnier & the Cerivastatin Study Group, 1998	Cerivastatin 0.1 mg (n=166) 0.2 mg (n=171) 0.3 mg (175) Gemfibrozil 1200 mg (n=160) Placebo (n=79)	RIGHT	16 wk	Random, double blind, placebo control.4 wk dietary stabilisation & washout of lipid-lowering agents. 6 wk single blind placebo run-in. Then randomised to study treatment for 16 wk. Assessments at baseline & 16 wk.	LDL >160 mg/dL Triglycerides 200-500 mg/dL	Mixed hyperlipidaemia Male or female (postmenopausal or surgically sterilised women). Age 18-80 yrs (mean 54) Mean BMI 27-28 Male/female (%) 60/40 to 70/30 No history of angioplasty, MI, diabetes, uncontrolled hypertension, renal impairment, coronary artery bypass graft within 6 mths. Concomitant treatment with corticosteroids, anticoagulants, other lipid-lowering agents not permitted in the study.	R 1 DB 1 W 1
Farnier et al, 1992	Simvastatin 10-40 mg daily (n= 82) Dose doubled from 10 mg after 6 wks & to 40 mg after 12 wks if total cholesterol >5.2 mmol/L Doses taken at wk 18: 10 mg 11/82 20 mg 20/82 40 mg 51/82 Ciprofibrate 100 mg daily (n= 82) Dose maintained throughout		18 wks	Random, double blind, multicentre (France), parallel groups. Dietary stabilisation (AHA step I) before & throughout the study. 8 wk washout of lipid altering drugs including 4 wk placebo run-in before randomisation to study treatment for 18 wks. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation & LDL using Friedewald formula.	Total cholesterol ≥6.45 mmol/L Triglyceride ≤4.00 mmol/L	Primary hypercholesterolaemia mean age 51 yrs (20-69) 68% men Total cholesterol >7.8 mmol/L 52% Total triglycerides >1.7 mmol/L 40% No patients had previously used probucol. Excluded: diabetes mellitus, liver or biliary disease, ileal bypass, unstable angina, coronary bypass surgery or MI within 4 mths, severe hypertension, hypothyroidism, premenopausal women, substance abuse, use of corticosteroids, cyclosporin, barbiturates, cimetidine, anticonvulsants, theophylline, antacids or investigational drugs.	R 1 DB 2 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Fogari et al, 1997	Pravastatin 20 mg (n=106) Once daily Acipimpox 750 (n=106) 250 mg given 3 x daily		3 mths	Random, double blind (double dummy), active control, crossover, Italy. 8 wks dietary stabilisation & placebo washout. Randomisation to study treatment for 3 mths then 1 mth washout before crossover to other treatment for 3 mths. compliance by tablet count. Total cholesterol, HDL & triglycerides measured enzymatically. LDL measured using Friedewald method.	Total cholesterol > 200 mg/dL Triglycerides between 200 & 350 mg/dL	Men with combined hyperlipidaemia. Age 18-60 yrs (mean not provided) Mean weight 77 Kg Mean blood glucose 97 mg/dL Smoker: 35/106 men (33%) No concomitant medication known to affect lipids allowed Excluded: MI within 3 mths, endocrinal or debilitating diseases.	R 1 DB 1 W 1
Frederiksen et la, 1993	Pravastatin 20 mg (n= 110) Pravastatin 40 mg (n=67) Both groups analysed together Placebo (n= 96)		26 wks	Random, double blind, placebo control, multicentre, Danish, parallel group. Patients in hospital or in community.	Total cholesterol 6-8 mmol/L LDL ≥ 4.0 mmol/L Triglycerides <5.0 mmol/L	Patients with primary hypercholesterolaemia Age 20-69 yrs Excluded: premenopausal women, secondary hyperlipidaemia, endocrine diseases, obesity. Medication not allowed: corticosteroids, antacids, hormonal treatments, lipid altering drugs, immunosuppressive agents beta-blockers, thiazides.	R 1 Db 1 W 1
Frohlich et al, 1993	Lovastatin Stratum I (n= 77) Lovastatin StratumII (n= 72) 20 / 40/ 80mg daily Simvastatin Stratum I (n= 74) Simvastatin Stratum II (n= 75) 10 / 20 / 40 mg daily Dose doubled if total cholesterol >5.2 at 6 and 12 wks		18 wks	Random, double blind, parallel group, multicentre, Canadian, active control. 6 wk washout of lipid altering drugs. Dietary stabilisation (AHA step I or II) & 4 wk placebo run-in. Randomisation to 18 wks active treatment. Assessed at baseline, 6, 12 & 18 wks. Dose was doubled at 6 & 12 wks if total cholesterol was ≥5.2 mmol/L. Compliance by tablet count. Patients were randomised into 2 strata: Stratum I: Total cholesterol between 6.2-7.8 mmol/L Stratum II: Total cholesterol >7.8 mmol/L	Total cholesterol >6.2 mmol/L Triglycerides ≤4.0 mmol/L	Primary hypercholesterolaemia Mean age 51 yrs (21-71) 35% male, 65% female Mean BMI 26 Kg/m2 Smoker 15%, Caucasian 95% 1-10 units alcohol/wk 60% Peripheral atherosclerosis 9% Previous MI 21%, Hypertension 20% Angina pectoris 15-20% Aortocoronary bypass about 10% Other vascular surgery 5-15% Medications allowed: Beta-blockers, diuretics, corticosteroids, HRT at same dose throughout the study. Excluded: secondary hypercholesterolaemia, total cholesterol:HDL ration <4.0, insulin & unstable noninsulin dependant diabetes, impaired hepatic/renal function, recent hepatitis or biliary disease, MI or coronary bypass surgery within 2 mths, vasospastic angina or other serious cardiovascular disease, alcohol or drug abuse, obesity, premenopausal women. Medications not allowed: cimetidine, antacids, immunosuppressive agents.	R 1 Db 1 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Giannini et al, 1994	Pravastatin (n=not stated, assume 24) Dose increased from 10 mg to 20 mg to 60 mg/day Lovastatin (n=not stated, assume 24)			Random, double blind, active control, Brazilian, parallel group. 3 mths dietary stabilisation (AHA). 7 wk placebo run-in then randomisation to lovastatin 20 mg/day or pravastatin 10 mg/day for 6 wks. Doses double at 6 wks then again at 12 wks	Total cholesterol >240 mg/dL LDL >160 mg/L Triglycerides <300 mg/dL	Hypercholesterolaemia Aged 30-70 yrs No lipid-altering drugs for 6 wks or probucol for 4 mths Excluded: fertile women, diabetics.	R 1 DB 1 W 1
Greten et al, 1994	Fluvastatin 40 mg daily (n= 64) Bezfibrate 400 mg daily (n= 67)		12 wks	Random, double blind, active control, multicentre, German. 8 wks dietary stabilisation (AHA) & 6 wk placebo run-in. Randomisation to fluvastatin or bezfibrate once daily. Compliance by tablet count. Assessed at baseline & 3 wk intervals. Total cholesterol & triglycerides measured enzymatically. HDL by precipitation, LDL by Friedewald formula.	LDL >160 mg/dL Triglycerides <300 mg/dL	Primary hypercholesterolaemia (women 57%) Type of hypercholesterolaemia: Familial heterozygous 37% Familial combined 5%F vs 15%B Polygenic 54% Mean age 52 yrs (18-75) Mean weight 70 Kg Mean BMI 25 Kg/m2 Smokers 25% F vs 39% B White 91% Hypertension 18% CAD 24%	R 1 DB 1 W 1
Guillen et al, 1995	Pravastatin 10 mg (n= 76 analysed) Placebo (n= 74 analysed) Dose doubled if LDL targets not reached after 10-12 wks		26 wks	Random, double blind, placebo control, multicentre. 4-6 wks dietary stabilisation & 8 wk washout of lipid altering drugs. Randomisation to study treatment once daily. After 10/12 wks dose doubled if LDL dropped by <15% or remained >200 mg/dL. Compliance by tablet count. Assessed at baseline & 3 wk intervals. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation, LDL by Friedewald formula.	Total cholesterol between 200 & 260 mg/dL LDL >130 mg/dL Triglycerides <300 mg/dL	≥2 CAD risk factors & borderline / moderate hypercholesterolaemia. Included a few patients with angina pectoris or previous MI. Mean age 48 yrs (21-69) Mean weight 65 Kg Mean BMI 26 kg/m2 Mean systolic BP 122 mm Hg Mean diastolic BP 80 mm Hg Excluded: homozygous familial hypercholesterolaemia, type I, III, IV or V hyperlipidaemia, secondary hyperlipidaemia, chronic pancreatitis, extreme obesity, hypothyroidism, any acute medical condition or surgery within 3 mth, premenopausal women, previous substance abuse, hepatic or renal disease, unstable angina pectoris, uncontrolled congestive heart failure, uncontrolled hypertension. Drugs not allowed: lipid altering drugs, immunosuppressive agents, steroids (except HRT).	R 1 DB 1 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Haffner et al, 1995	Simvastatin 10 mg in evening (n= 88) Simvastatin 20 mg in morning (n= 83) Simvastatin 20 mg in evening (n= 86) Placebo (n= 86)		24 wks	Random, double blind, placebo control, parallel group, multicentre, USA. Min 6 wks on lipid lowering diet with placebo run-in before randomisation. Assessed at baseline then at 6 wk intervals for 24 wks. Lipid analysis at a central laboratory. Cholesterol & triglycerides measured enzymatically, HDL by precipitation, & LDL using Friedewald formula.	LDL>190 mg/dL if <2 risk factors, or ≥160 mg/dL with ≥2 risk factors for CHD Triglycerides <350 mg/dL	Men (57%) & women with primary hyperchoelsterolaemia Aged 18-82 yrs Met NCEP criteria for pharmacological treatment Beta-blockers, diuretics, corticosteroids, continuous oestrogen therapy were allowed at constant doses. Excluded: MI, coronary bypass surgery or angioplasty within 3 mths, unstable angina, cardiac or renal failure, nephrotic syndrome, hepatic disease, diabetes mellitus, secondary hyperchoelsterolaemia, hyperlipidaemia type III, premenopausal women of child bearing potential, treatment within 6 wks of any lipid lowering agent (or 6 mths for probucol), use of immunosuppressive drugs.	R 1 DB 2 W 1
Hagen et al, 1994	Fluvastatin 20/40 mg (n= 100) 20 mg dose doubled after 6 wks on treatment Cholestyramine 4/8 g (n=48) 4 g dose doubled after 1 wk on treatment		12 wks	Random, double blind, double dummy, active control, parallel group. 8 wks stabilisation on lipid-lowering diet, 6 wks single blind placebo washout , then randomisation to study treatment for 12 wks. Compliance by tablet count & diet diaries LDL measured by Friedewald method, HDL by precipitation, total cholesterol & triglycerides enzymatically. Assessed at baseline & 6 wk intervals.	LDL ≥4.9 mmol/L Triglycerides <3.15 mmol/L Patients with CHD or ≥2 risk factors were included if LDL >4.1 mmol/L	Primary hypercholesterolaemia Excluded MI within 6 mths, unstable angina, diabetes, drugs which affect efficacy or safety of statins, renal, liver or thyroid disease, substance abuse, obesity. CHD 21% No other data provided on patient characteristics	R 1 Db 2 W 1
Hunninghake et al, 1990 Efficacy and safety of pravastatin	Pravastatin 10 mg (n=65) Pravastatin 20 mg (n=56) Pravastatin 40 mg (n=59) Placebo (n=88)		12 wk	Random, double blind, placebo control, parallel group. Low fat, low cholesterol diet (Lipid Research Clinical Coronary Primary Prevention Trial diet or the AHA step I diet) for 3 wks followed by nutritional monitoring to determine compliance. Placebo run-in phase with plasma lipids measure at least 3 times at 7 day intervals. Randomisation to pravastatin 5 mg, 10 mg, 20 mg or placebo given twice daily for 12 wk. Clofibrate and probucol were withdrawn 12 wk & lipid-lowering drugs 6 wk before study entry. Main assessments at baseline & 12 wk, with interim laboratory & history.	Mean of 3 readings had to be: LDL >150 mg/dL (3.88 mmol/L) Triglyceride <250 mg/dL (2.82 mmol/L)	306 patients (231 men, 75 women) with hypercholesterolaemia were randomised. Type of hypercholesterolaemia: 162 familial; 79 polygenic; 27 familial combined. Age 21-70 (mean 46-53) yrs Mean weight: 75-78 Kg. Excluded were: Type III, IV or V hyperlipoproteinemia, patients with diabetes mellitus (NIDDM fasting blood glucose >7.8 mmol/L), uncontrolled hypertension, MI within 6 months, severe or unstable angina, uncompensated heart failure, significant renal or hepatic disease, excessive obesity, or subjects consuming more than 10 units of alcohol per week.	R 1 Db 2 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Isaacsohn et al, 2001	Cerivastatin 0.4 mg (n= 195) Cerivastatin 0.8 mg (n= 776) Pravastatin 40 mg: (n= 199) All pravastatin pateints received placebo for 8 wks & then took pravastatin for 46 wks		52 wks	Random, double blind, placebo/ active control, parallel group, multicentre, USA & Canada. 10 wk single blind placebo run in & dietary stabilisation (AHA step I). Randomised 4:1:1 to cerivastatin or placebo/ pravastatin. Active pravastatin given for 46 wks. Groups remained double blind. After 24 wks investigators who were not blinded to LDL levels were allowed to give open label bile acid resin if LDL remained above 160 mg/dL (or 130 if CAD present with ≥2 risk factors). Assessed at baseline then every 2 wks for 2 mths, then monthly for 4 mths, & then at 32, 40 & 52 wks. Adverse events were recorded using the COSTART criteria	LDL ≥130 mg/dL depending on CAD risk factors Triglycerides ≤400 mg/dL	Primary hypercholesterolaemia with or without CAD or risk factors Mean age 56 yrs ± SD 10 Mean weight 81 Kg 64% male 93% Caucasian 14% smokers Duration of hyperlipidaemia 9.3 yrs Family history of hyperlipidaemia 45% Family history of CAD 57%	R 1 Db 1 W 1
Jacobson et al, 1995	Pravastatin 20 mg evening (n=182) Placebo (n= 63)		12 wks	Random, double blind, multicentre, American, placebo control. 4 wks dietary stabilisation (AHA step I) & placebo run-in. Compliance by tablet count. Assessed at baseline, 6 & 12 wks. Total cholesterol & triglycerides measure enzymatically, HDL by precipitation, LDL by Friedewald method. Adverse events categorised according to COSTART dictionary.	LDL >4.9 mmol/L or >4.1 if history of CAD or 2 risk factors Triglycerides <4.5 mmol/L	Primary hyperchoelsterolaemia, 62% male African American men & women Age 18-75 yrs, mean 56 BMI 28 kg/m2 Systolic BP 134, Diastolic BP 83 mm Hg CAD 3%, >2 risk factors for CAD (NCEP) 76% NIDDM 8% Medications: Previous lipid-lowering 4% Prav vs 11% Plac Antihypertensives 47% vs 54% (calcium channel blockers 66% vs 82%). Constant doses of thiazide diuretics, beta-blockers, allowed. Excluded: type I, III, IV or V hyperlipoproteinaemia, homozygous familial hyperchoelsterolaemia, secondary hyperlipidaemia, poorly controlled diabetes, BP > 160/100 mm Hg, congestive heart failure, MI, stroke, TIA or unstable angina within 6 mths, major renal or hepatic disease, drugs known to interfere with drug absorption, >14 units alcohol/wk. Probucol & other lipid altering drugs disallowed 12 wks before study entry. Anticoagulants, oestrogens, fish oil preparations, corticosteroids, immunosuppressive drugs, antacids disallowed.	R 1 DB 2 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Jacotot et al, 1995b	Fluvastatin evening (n= 68) 40 mg for 4 wks then 80 mg/day (high dose given 2x daily) Pravastatin evening (n= 66) 20 mg for 4 wks then 40 mg/day (once daily)		16 wks	Random, double blind, active control, parallel group. Lipid lowering diet for 8 wks, 6 wk placebo run-in before randomisation. Cholesterol & triglycerides measured using standard methods, LDL by Friedewald method.	LDL ≥160 mg/dL Triglycerides ≤400 mg/dL	Primary hypercholesterolaemia Male (65%) or females(35%) Mean age 50 yrs (21-76) Excluded: homozygous familial hypercholesterolaemia, hyperlipidaemia types I, III, IV or V, impaired renal or hepatic function.	R 1 DB 1 W 1
Joukhadar et al, 2001	Atorvastatin 10 mg (n= 33) Simvastatin 40 mg (n= 33) Pravastatin 40 mg (n= 33)		12 wks	Random, double blind, active control, parallel group. Lipid lowering diet for 8 wks, 6 wk placebo run-in before randomisation. Compliance by pill count. Lipids measured using standard methods. Last observation carried forward for missing values.	Total cholesterol between 5.2 & 9.1 mmol/L Triglycerides <2.9 mmol/L	Primary hypercholesterolaemia Mean age 55 yrs (35-75) Mean BMI 24 Kg/m2 60% male Using HRT 12% Systolic BP 137 mm Hg diastolic BP 83 mm Hg Smoker 35 (mean 20 cigarettes/day) Excluded: BMI >32, unstable CHD, diabetes, impaired hepatic or renal function, secondary hyperchoelsterolaemia, >40 g ethanol/day, BP >160/100 mm Hg, lipid altering drugs, antacids, immunosuppressive agents, anti-inflammatory or antihypertensive drugs, thyroid disease, pregnancy/lactation, major illness (e.g. cancer), drugs known to affect haemostatic parameters.	R 1 DB 2 W 1
Jukema et al, 1995	Pravastatin 40 mg (n=450) Placebo (n=434) Once daily (evening)	REGRESS	2 yrs	Random, double blind, multicentre (Netherlands), placebo control. Eligible patients were catheterised by an angiographer using standard techniques. Dietary stabilisation & monitoring of compliance & smoking habits for the study duration. Assessed at baseline, 2, 4, 6, 12, 18 & 24 mths. Serum total cholesterol, HDL, LDL and triglycerides were measured enzymatically, HDL by precipitation & LDL using Fridewald formula.	Total cholesterol 4.0 to 8.0 mmol/L Triglycerides <4.0 mmol/L	Symptomatic CAD with ≥50% stenosis in a major coronary vessel Mean age 56 yrs ± 8 Mean BMI 26 kg/m2 Mean BP 135/81 mm Hg Familial heart disease 49% Hypertension 25% & 31% Diabetes 0.2% Smoker: current 28%, ever 88% Mean BP 134/81 mm Hg ≥2 stenosed (>50%) arteries 60% Previous MI 50% & 45% Previous PTCA 6% Excluded: MI within 8 wks, previous angioplasty, or coronary artery bypass, other life threatening illness, using lipid altering drugs, significant metabolic disease.	R1 DB 1 W 0

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Keech et al, 1994	Simvastatin 20 mg (n= 208) Simvastatin 40 mg (n= 206) Placebo (n= 207) Once daily	Oxford cholesterol study	3-5 yrs Median follow-up 3.4 yrs	Random, double blind, placebo control, parallel group, multicentre, mortality study. Single blind placebo run-in with AHA step I diet and advice on risk factor modification before randomisation. Assessed at baseline, 8 wks then at 12 wk intervals for 1 yr, then at 24 wk intervals. Compliance by tablet count & questioning. Compliance was 82% at end of yr 2 an 78% by end of year 3. About half of noncompliant patients took some medication and turned up for follow-up visits	Total blood cholesterol >3.5 mmol/L	At average risk of CHD Age ≥40 yrs, mean 63 ± 7.5, 85% men Mean weight 78 ± 12 kg, Mean BMI 26 ± 3.3 kg/m2 Mean BP 134/77 mm Hg Current smoker 14% Previous MI 62%, Angina 66%, Any CHD 82% Stroke 9%, TIA 16%, Peripheral vascular disease 10% Treated diabetes 3%, Treated hypertension 36% Concurrent medication: Beta-blockers 40%, Aspirin / antiplatelets 46%, Calcium antagonists 27%, Diuretics 26% ACE inhibitors 5%, Oral hypoglycaemics / insulin 3%, Fibrates 4%, Anticoagulants 4%, Nitrates 28% Excluded: statins contraindicated, MI, unstable angina or stroke within 6 mths, other important life threatening condition, use of cyclosporin, child bearing potential, substance abuse, psychiatric or physical disability which may affect compliance etc, low risk of cardiac events.	R 2 DB 1 W 1
LaRosa et al, 1994	Lovastatin 20 mg (n= 144; M=27, F=107) Lovastatin 40 mg (n= 145; M=34, F=111) Placebo (n= 142; M=54, F=88) Once daily in evening	CRISP	48 wks	Random, double blind, multicentre, USA, parallel group, placebo control. NCEP step I diet & 4-8 wks placebo run-in before randomisation. Compliance monitored using food-frequency questionnaire & by pill count. Lipid parameters were measured at baseline then at regular intervals. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation & LDL using the Friedewald formula.	LDL > 4.1 mmol/L & < 5.7 mmol/L	Elderly (>65 yrs) men & women with hyperchoelsterolaemia 71% women, 21% African Americans Mean age 71 yrs Mean BP: 134/75, Hypertensive 40% Mean weight 71 kg, Mean BMI 26 kg/m2 Obese 22% Smoker: current 6%, never smoked 57%, ex 37% Evidence of CHD 17% Use aspirin 28% Use antihypertensives 32% Excluded: uncontrolled hypertension, recent significant cardiovascular disease, insulin dependent diabetes, current use of lipid lowering agents, hypothyroidism, life-limiting disease.	R 1 DB 1 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Lecerf 1993	Simvastatin 10-40 mg daily daily (evening). (n=67) Gemfibrozil 900 mg once daily (evening) (n=69)		18 wks	Random, double blind, multicentre. 4 wk placebo run-in. 3 months diet. Dose of simvastatin was doubled after 6 wks & again after 12 wks if cholesterol >5.6 mmol/L. Use of barbiturates, anticonvulsants, theophylline, cimetidine and corticosteroids was not allowed. Cholesterol & triglycerides were measured using enzymatic techniques. there were no differences between groups for age, sex, plasma lipids or ischaemic disease. By week 18 63.6% of patients took simvastatin 40 mg 24% took 20 mg & 12.2% took 10 mg daily/	Total cholesterol >6.45 mmol/L	Primary hypercholesterolaemia. 107 men, 29 women. Age 26-78 years, mean 53	R=1 DB=1 W=1
Leichleitner et al, 1995	Simvastatin 10/20 mg daily (n= 32) Bezafibrate 600 mg/day (n= 31)		12 wks	Random, double blind, active control, parallel groups, multicentre, German. 4 wk placebo run-in with dietary counselling before randomisation to study treatment. Assessed at baseline & periodic intervals throughout the study	Total cholesterol >240 mg/dL LDL >195 mg/dL	Primary hypercholesterolaemia	R 1 DB 1 W 0
Leiter et al, 1999	Cerivastatin 0.05-0.3 mg/day (n= 260) Simvastatin 5-40 mg/day (n= 127) Once daily Lowest dose for 8 wks, then titrated up at 0.1 mg/day or 10 mg/day if LDL >3.36 mmol/L. Further titration at wks 16 & 24 if needed. Mean dose at end-point: Ceriv0.24 mg/day Simv 21.7 mg/day		32 wks	Random, double blind, parallel group, multicentre, Canadian, active control.10 wk dietary stabilisation (AHA step I) including 6 wks single blind placebo run-in. Then randomisation to double blind treatment for 32 wks (short-term stage). Also long-term stage but only 153 patients so excluded.	LDL >4.13 mmol/L Triglycerides ≤3.95 mmol/L	Primary hypercholesterolaemia Men (61%) or women Mean age 53 yrs (18-75) 94% Caucasian mean weight 76 kg Current smoker 15%, ex-smoker 50% Family history of hyperlipidaemia(58%) and CAD (70%) Drugs allowed: stable doses of diuretics, beta-blockers, oestrogen or thyroxine. Excluded homozygous familial hypercholesterolaemia, premenopausal women, MI, unstable angina, TIA, cerebrovascular accident, uncontrolled hypertension within 3 mths, diabetes mellitus, other endocrine disease, chronic liver disease, significant ophthalmologic abnormalities, disorders which impair drug absorption, use of any lipid altering drugs or fish oil preparations, corticosteroids, androgens, immunosuppressive agents, drug/alcohol abuse, >40% over ideal body weight, use of study drug within 30 days.	R 1 DB 1 W 0

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Lijnen et al, 1996	Pravastatin (n= 25) Placebo (n= 25) Once daily, evening Dose titrated from 10 mg to 20 mg to 40 mg at 4 wk intervals. Only 1 pt did not titrate up from 20 mg		6 mths	Random, double blind, placebo control, parallel groups. At least 4 wk washout of lipid altering drugs, then 4 wk placebo run-in & dietary stabilisation. Randomisation to study treatment; dose increased with time. Total cholesterol, LDL & triglycerides measured enzymatically, HDL by precipitation. Assessed at baseline & then at 2, 3, & 6 mths.	Total cholesterol >6.48 & <10.4 mmol/L	Hypercholesterolaemia Men & women Concomitant medications: Beta-blockers, diuretics, calcium channel blockers, antihypertensives, angiotensin converting enzyme at unchanged doses. Excluded: premenopausal women, uncontrolled hypertension, secondary hyperchoelsterolaemia, impaired hepatic or renal function, biliary disease including gall stones, history of CHD, signs of myopathy, serum creatinine >177 umol/L.	R 1 DB 1 W 0
Lintott et al, 1993	Simvastatin(n= 24) Pravastatin (n= 24) Dose titration up from 10 mg to 40 mg daily Dose /day by wk 18: Sim 10 mg 3/24 Sim 20 mg 3/24 Sim 40 mg 18/24 Prav 10 mg 1/24 Prav 20 mg 0/24 Prav 40 mg 22/24		18 wks	Random, double blind, double dummy, active control, parallel groups. Lipid lowering diet, 6 wk washout of lipid lowering agents & placebo run-in before randomisation to study treatment for 18 wks. Dose titration allowed if LDL >3.4 mmol/L after 6 wks & 12 wks. Assessments at baseline & then 6 wk intervals. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation & LDL calculated as cholesterol in the density fraction >1.006 g/dL less HDL cholesterol..	LDL ≥4.0 mmol/L Triglyceride <4.5 mmol/L	Primary hypercholesterolaemia Ratio male:Female = 2:1 Mean age 53 yrs Mean BMI 25 kg/m2 Heterozygous familial hypercholesterolaemia 69% Evident CAD 54% Excluded: combined hyperlipidaemia or hypertriglyceridaemia, impaired renal or hepatic function, secondary hyperlipidaemia, coronary event within 3 mths.	R 1 DB 2 W 1
Lovastatin Pravastatin Study Group 1990	Lovastatin (n= 339) 20 mg/day for 6 wks, then 40 mg for 6 wks & 80 for last 6 wks Pravastatin (n=333) 10 mg/day for 6 wks, then 20 mg for 6 wks & 40 for last 6 wks		18 wks	Random, double blind, parallel group, multicentre (16 countries), active control. Dietary stabilisation (AHA or comparable) & 7 wk placebo run-in before randomisation. Assessed at baseline, 6, 12 & 18 wks. 2 central laboratories determined cholesterol etc & used similar techniques. **NB:** if total cholesterol <3.1 mmol/L during treatment, patient was unblinded & back titrated to previous dose for rest of the study. No patients were back titrated & none fell below safety level of 3.1 mmol/L for total	Total cholesterol >6.5 mmol/L LDL > 4.1 mmol/L Triglyceride < 3.42 mmol/L	Primary hypercholesterolaemia. Mean age 54 yrs (26-71) Male 53%, female 47% Excluded: age <25 or >75 yrs, secondary hypercholesterolaemia, fertile women, diabetes mellitus.	R 1 DB 1 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Lye et al, 1998	Fluvastatin 40 mg once daily (n= 33) Placebo (n= 36)		12 wks	Random, double blind, double dummy, placebo control, parallel groups, multicentre, UK. Lipid lowering diet, 8 wk washout of lipid lowering agents before randomisation to study treatment for 12 wks. Dose titration allowed if LDL >3.4 mmol/L after 6 wks & 12 wks. Assessments at baseline, 6, 11 & 12 wks. Compliance by pill count. Adverse events were assigned standard codes. Cholesterol was measured using oxidase/phosphatidic acid phosphatase method, triglycerides measured enzymatically, HDL by precipitation.	LDL ≥4.1 mmol/L Triglyceride <4.0 mmol/L	Elderly (>60 yrs) patients with hypercholesterolaemia (type Iia, Iib, IV). Mean age 69 yrs (60-84) Mean BMI 26 kg/m2 40% men, 60% women 100% white Smoker 15%, former smoker 42% 64% cardiovascular abnormalities Family history of cardiovascular disease 49% Excluded: type III or V hypercholesterolaemia, renal, hepatic, biliary or gastrointestinal or impairment, MI within 3 mths, pancreatitis, gall bladder disease, congestive heart failure, severe unstable angina pectoris or hypertension, confounders of lipid altering treatment, BMI <35, fasting glucose >7.8 mmol/L. Concomitant medications: cardiovascular drugs & antihypertensives, analgesics, gastrointestinal drugs, diuretics.	R 1 DB 1 W 1
MAAS investigators, 1994	Simvastatin 20 mg (n= 193) Placebo (n= 188) Once daily evening	MAAS	4 yrs	Random, double blind, multicentre, parallel group, placebo control. Cholesterol & triglycerides were measured using standard techniques at a central laboratory. LDL derived using Friedewald formula.	Total cholesterol between 5,5-8.0 mmol/L Triglycerides < 4.0 mmol/L	Recent coronary angiography Mean age yrs (30-70) Excluded: MI or unstable angina within 6 wks, previous coronary artery bypass surgery, percutaneous coronary angioplasty or major surgery within 3 mths, congestive heart failure, diastolic BP >100 mm Hg, fasting glucose >7.8 mmol/L, use of lipid lowering drugs, steroids or oestrogen within 6 wks. Allowed anticoagulants, antiplatelet drugs & other drugs except lipid-lowering treatments.	R 1 DB 1 W 0
MacMahon et al, 1998	Pravastatin 40 mg/day Placebo (n= not stated, assumed equal split; 261) Once daily evening	Substudy of LIPID	4 yrs but with 3 yr lipid data	Random, double blind, multicentre (Australia/New Zealand), parallel group. 8 wk single blind placebo run-in & dietary stabilisation before randomisation. Diet maintained throughout. Assessments at baseline, 1 yr & 3 yrs for all lipids.	Total cholesterol between 4.0 & 7.0 mmol/L Triglycerides < 5.0 mmol/L	Acute MI or unstable angina within 3-36 mths. Average cholesterol levels, but mean ± 2x SD is >5.0 mmol/L. Mean age 61 yrs 88% men 75% previous MI 5% diabetic	R 1 DB 1 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Maggi et al, 1994	Simvastatin 20 mg/day (n =20) Placebo (n =20) Bezfibrate 400 mg (n=21)		6 mths	Random, double blind placebo control, parallel groups. AHA diet before randomisation to double blind treatment for 6 mths. Periodic assessments after baseline.	Total cholesterol >5.0 mmol/L	Type Iia & Iib hypercholesterolaemia Mean age yrs (35=70) Excluded: secondary hypercholesterolaemia.	R 1 DB 1 W 1
Mercuri et al, 1996	Pravastatin 40 mg once daily (n= 151) Placebo (n= 154)	CAIUS	3 yrs	Random, double blind, placebo control, multicentre (Italy), parallel group. Single blind placebo run-in & low-fat diet (European Atherosclerosis Society) before randomisation. Assessed at baseline & then at 3 mth intervals. Compliance by pill count. No details of lipid measurement techniques.	LDL between 3.88 & 6.47 mmol/L triglycerides <2.82 mmol/L	Moderately elevated LDL, free of symptoms or signs of CAD & ≥ 1 carotid artery lesion on ultrasound. Men 53% & women 47% Mean age 55 yrs (45-65) Current smoker 24% Mean BP 133/81 mm Hg Mean BMI 24.7 Kg2 Family history CHD 45% Excluded: liver abnormalities, serious medical conditions, use of lipid altering drugs, anticoagulants, calcium antagonists.	R 1 DB 2 W 1
Morgan et al, 1990	Simvastatin 10-40 mg (n=25) Placebo (n=25) Initial 10 mg/day dose given once in evening for 6 wks. Doubled at 6 & 10 wks if total cholesterol >4.5 mmol/L Dose increases: 10 mg 3/24 20 mg 6/24 40 mg 15/24		18 wks	Random, double blind. 3 mths on lipdf lowering diet before randomisation to study treatment. Antihypertensives were continued. Assessments at baseline, & regular intervals hroughout. Patients encouraged to report adverse events.	Total cholesterol >5.5 <7.5 mmol/L	Men & women with hypertension Diastolic BP greater than 100 mm Hg before antihypertensive therapy & controlled to under 95 mm Hg with drugs or diet pre-study.	R 1 DB 1 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Morris et al, 1996	Pravastatin (n= 45) Placebo (n= 53)		26 wks	Random, double blind, placebo control, parallel groups. 6 wks dietary advice, smoking cessation, exercise and stress reduction. Randomisation to study treatment for 26 wks. Assessed at baseline, 6, 13 & 26 wks. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation, LDL using Friedewald formula.	Total cholesterol between 5.2 & 6.7 mmol/L Triglycerides <4.0 mmol/L	Moderate primary hypercholesterolaemia plus≥2 risk factors Mean age 51 yrs (18-70) Mean BMI 29.5 Kg/m2 95% male Mean systolic BP 130 mm Hg Previous MI 13% Angina 9% Family history of IHD 43% Smoker 27% Hypertension 50%	R 1 DB 1 W 1
MRC/BHF Heart Protection Study Collaborative Group, 2001	Simvastatin 40 mg (n=10269) Placebo (n=10267) Once daily evening	Heart Protection Study	36 mths	Random, double blind, multicentre UK), parallel group, placebo control. Four wk placebo run-in & low fat/cholesterol diet before randomisation. Compliance was recorded. Assessed at baseline, at 4, 8, & 12 mths & then at 6 mth intervals.	Total plasma cholesterol ≥3.5 mmol/L	Men & women aged 40-80 yrs History of MI or other CHD, occlusive disease of noncoronary arteries, diabetes or untreated hypertension. 41% previous MI, 24% other CHD 35% no history of CHD 29% diabetes, 41% hypertension Other medications: Aspirin, other antiplatelets 63%, Anticoagulants 5% Nitrates 31%, Beta-blockers 16%, Calcium antagonists 18%, ACE inhibitor 8% Excluded: chronic liver disease or renal impairment, use of cyclosporin, fibrates, statins, or high dose niacin, child bearing potential, no other predominant medical problem (e.g. substance abuse).	R 2 DB 1 W 1
Olson et al, 2001	Fluvastatin 40 mg once daily (Immediate release; IR) (n= 174) Fluvastatin 40 mg twice daily (Immediate release; IR) (n=175)		24 wks	Random, double blind, double dummy, active control, multicentre (European), parallel group. Dietary stabilisation (European Atherosclerosis Society or NCEP) & placebo run-in & washout of lipid altering agents for 4 wks before randomisation. Assessed at baseline, 2, 4, 8, 12, 16, 20 & 24 wks. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation & LDL using Friedewald formula.	LDL >160 mg/dL Triglycerides <400 mg/dL	Men & women with primary hypercholesterolaemia (type IIa or IIb) Mean age 56 yrs (20-78) Mainly Caucasian Mean BMI26 kg/m2 CHD 54% Previous HMG CoA reductase inhibitor 42% Excluded: women likely to conceive, homozygous familial hypercholesterolaemia, type I, III, IV or V hyperlipidaemia, secondary hyperlipoproteinaemia, liver or renal impairment, MI or major surgery or angioplasty within 6 mths, unstable angina or congestive heart failure, uncontrolled hypertension, history of muscle disease.	R 1 DB 2 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Olson et al. 2001 (Abstract)	Rosuvastatin 5 mg (n=138) Rosuvastatin 10 mg (n=134) Atorvastatin 10 mg (n=140)		12 wks then 40 wk dose titration	Random, double blind, active control. 6 week dietary lead-in. Randomised to once daily treatment.40 wk dose titration period in which doses could be doubled to meet LDL goals. Analysis of drop-outs was handled by last observation carried forward. Daily doses were rosuvastatin 5-80 mg or 10-80 mg, and atorvastatin 10-80 mg during dose titration up to 52 weeks	LDL ≥4.14 and <6.5 mmol/L triglycerides <4.52 mmol/L	Primary hypercholesterolaemia Age≥18 yrs (mean 57); 27-33% over 65 yrs Male: 52-60%% Mean weight 77 Kg Mean BMI 26 Caucasian 99-100%	R 1 DB 1 W 1
Ose et al, 1999	Cerivastatin 0.2 mg (n=162) Cerivastatin 0.4 mg (n=332) Given once daily (bed time)		24 wks	Random, double blind, dose comparison, parallel groups, multicentre (multinational). 6 wk washout of all lipid altering drugs & placebo run-in before randomisation to 24 wks active treatment. AHA step I diet or its equivalent, food diaries & fat intake/activity questionnaire. Assessed at baseline then at 2, 4 , 8, 12, 16, 20 & 24 wks. LDL derived using Friedewald formula	LDL ≥160 mg/dL (4.12 mmol/L)	Men & women with primary hypercholesterolaemia & either history of CHD or ≥2 risk factors Mean age 56 yrs (18-75) 65% men Mean BMI 26 kg/m2 Excluded: previous MI, unstable angina, stroke, transient ischaemia, uncontrolled hypertension, endocrine disorder (e.g. diabetes) clinially significant ophthalmic abnormality, malignancy, homozygous familial hyperchoelsterolaemia, BMI >30 kg/m2, substance abuse, use of lipid lowering agents & probucol within 6 mths, hypoglycaemics, corticosteroids, erythromycin, oral anticoagulants, androgens, immunosuppressants.	R 1 DB 1 W 1
Ose et al, 2000	Simvastatin 40 mg (n= 436) Simvastatin 80 mg (n= 669)		24 wks	Results from two trials presented together. Random, double blind, dose assessment parallel groups. AHA step I diet & 4 wk placebo run-in. 6 wk washout of lipid lowering agents before randomisation to 24 wk double blind treatment with 24 wk blinded extension. Assessed at baseline then at 12, 18, & 24 wks. Lipids analysed in a central laboratory. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation & LDL using Friedewald formula.	LDL > 4.2 mmol/L Triglycerides <4.0 mmol/L	Men & women with hypercholesterolaemia Mean age 53 yrs (21-71) 56% men, 44% women 87% Caucasian Hypertension 22% Coronary vascular surgery 11% MI 10% CAD 7% Angina pectoris 6% Excluded: use of immunosuppressants, systemic azoles antifungal agents, anticoagulants, women of child bearing potential	R 2 DB 1 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Paoletti et al, 2001	Rosuvastatin 5 mg (n=120) Rosuvastatin 10 mg (n= 115) Pravastatin 20 mg (n= 137) Simvastatin 20 mg (n= 120)		12 wks	Random, double blind, active control, parallel groups, multicentre. 6 wk dietary stabilisation (NCEP step 1) & washout of cholesterol lowering drugs. Randomisation to treatment (evening) for 12 wks. Assessed at baseline, 2, 6, 10 & 12 wks. Compliance with diet rated using Eating Pattern Assessment Tool, tablets by pill count. Total cholesterol , HDL & triglycerides measured enzymatically,LDL using Friedewald formula. Last observation carried forward for missing data	LDL > 4.14 & < 6.5 mmol/L Triglycerides ≤ 4.52 mmol/L	Hypercholesterolaemia Mean age 57-60 yrs (>18 inclusion) >98% Caucasian female: 49-57% Mean weight 72-75 Kg Mean BMI 26-27 Kg/m2 Excluded: active arterial disease within 3 mths, familial hypercholesterolaemia, uncontrolled hypertension, active liver / hepatic dysfunction, fasting glucose >9.9 mmol/L, previous substance abuse, use of cyclic hormonal therapy.	R 1 DB 1 W 1
Pauciullo et al, 2000	Fluvastatin 40 mg (n= 80) Evening Bezfibrate 400 mg (n= 86) Given twice daily			Random, double blind, double dummy, active control, parallel groups, multicentre, Italy. 8 wk dietary stabilisation (European Atherosclerosis Society), washout of cholesterol lowering drugs & placebo run-in. Randomisation to treatment for 24 wks. Assessed at baseline, then at 4wk intervals. Compliance by pill count. Lipids were measured using standard techniques, LDL using Friedewald formula. Last observation carried forward.	LDL between 135 & 250 mg/dL Triglycerides between 180 & 400 mg/dL	Mixed hyperlipidaemia & CAD (stable angina for ≥4 mths, previous MI or coronary vascularisation procedure). Males & females; 75% male Mean age 55 yrs ± 9 Mean BMI 26 Kg/m2 Family history of CVD 53% CAD 50% Smoker 23%, ex-smoker 45% Systolic BP 134 mm Hg, Diastolic BP 81 mm Hg Angina 55%, History of MI 51% Coronary revascularisation 30% 60% were on a lipid lowering diet previously 54% took lipid altering drugs before study entry Excluded: type I, II, IV or V hyperlipidaemia, secondary hyperlipidaemia, diabetes mellitus, nephrotic syndrome, hepatobiliary disease, alcoholism, chronic pancreatitis, autoimmune disease, hyperthyroidism, congestive heart failure, unstable angina, MI, stroke or coronary revascularisation within 4 mths, uncontrolled hypertension, BMI >30 kg/m2, drugs which may confound lipid altering.	R 1 DB 1 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Pedersen, 1998	Simvastatin 20 mg mg/day (n=2221) Placebo (n=2223) Titration to 40 mg at 12 or 24 wk in patients who did not reach target total cholesterol of 3.0-5.2 mmol/L after 6-12 wk Daily dose taken: 10 mg 2 pts (0.1%) 20 mg 62.9% 40 mg 37%	4S	Median 5.4 yrs	Random, double blind, placebo control, multicentre, Scandinavian. 2 month dietary control before randomisation. Clinical assessments at baseline, 6 & 18 wk, 6 mths & every 6 mths after. Mean follow up was 5.4 yrs (range 4.9 to 6.3. Cholesterol levels were measured enzymatically. End-point events classified by committee	Total cholesterol between 5.5 and 8.0 mmol/L Triglyceride <2.5 mmol/L	Men (80%) or women (20%) with coronary heart disease. History of MI or angina. Age 35-70 yrs (mean 59) Concomitant drugs: aspirin 37% Beta-blockers 57% Calcium antagonists: 30% Thiazides 6% Warfarin 2% Isosorbide mono/dinitrate 32% Fish oil 13% Excluded: secondary hypercholesterolaemia, fertile premenopausal women, unstable angina, tendon xanthomata, planned coronary artery bypass surgery or angioplasty, Mi within 6 mths, antiarrhythmic therapy, diuretics, vasodilators, persistent atrial fibrillation, cardiomegaly, stroke, impaired renal or hepatic function, partial ileal bypass, substance abuse, poor mental function, other serious disease, use of investigational drug, hypersensitivity to statins.	R 1 DB 1 W 1
Pitt et al, 1993	Pravastatin 40 mg (n=206) Placebo (n= 202) Once daily in evening Mean daily dose 39 mg	PLAC I	3 yrs	Random, double blind, placebo control, multicentre, parallel group. Dietary advice and AHA step I diet for >4 wks before randomisation. Assessed at baseline then at 6 wk intervals for 18 mths, then every 12 wks afterwards.	LDL cholesterol >130 mg/dL & <190 mg/dL 3.36 to 4.91 mmol/L) Triglycerides ≤350 mg/dL	Patients with moderate hypercholesterolaemia & presence of ≥1 stenosis (≥50%) in a major vessel confirmed by angiography. Mean age 57 yrs (33-75) 88% Caucasian 77.5% men Excluded: life threatening illness other than CAD, women of child bearing potential, age > 75 yrs, secondary hyperlipidaemia, diabetes mellitus, congestive heart failure with ejection fraction <30%, significant hepatic or renal disease, cerebrovascular disease, GI disease, >3 units of alcohol/day, chronic pancreatitis, systemic lupus erythematosus, hypersensitivity to statins.	R 1 DB 1 W 1
Reigger et al, 1999	Fluvastatin 40 mg (n=187) 85 pts had dose doubled Placebo (n=178)		52 wk	Random, double blind, multicentre, lipid values were observer blind from randomisation onwards. 10 week run-in: 4 wk on cholesterol lowering diet (European Atherosclerosis Society guidelines). 6 wk on fluvastatin 40 mg & then randomisation to double blind fluvastatin or placebo once daily. If LDL decreased ≤30% treatment was given twice daily. Assessments at baseline then at 6, 8, 12, 16, 20, 28, 36, 44 & 52 wk.	LDL >160 mg/dL Triglycerides ≤300 mg/dL	Male & females with hyperlipidaemia. and stable symptomatic coronary heart disease after 4 wk on a lowering-lowering diet. Age 40-70 years (mean 59) Mean weight 76 Kg Smokers 9-10% Previous lipid-lowering therapy 22% Consumption of anti-anginal medication was recorded & food diaries. Other lipid altering drugs were prohibited .	R 1 DB 2 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Ritter et al, 1993	Pravastatin 20 mg (n= 79) Evening Dose doubled at 14 wks if total cholesterol not reduced by 15% or above 5.2 mmol/L (n= 12) Placebo (n=75) Dose doubled in 58 patients after 14 wks		26 wks	Random, double blind, multicentre, UK, parallel group, placebo control 6 wk dietary stabilisation, l lifestyle & smoking advice & placebo run-in before randomisation to study treatment for 26 wks. Assessed at baseline, 6, 13 & 26 wks. Lipids were measured using the same techniques throughout, LDL using the Friedewald formula. Compliance by tablet count.	Total cholesterol between 5.2 & 7.8 mmol/L Triglycerides <4.0 mmol/L	Elevated cholesterol & ≥2 risk factors for CAD (82% men) Mean age 54 yrs ± 1 Mean weight 74 Kg Mean systolic BP 135 mm Hg, diastolic BP 81 mm Hg Smoker 18% Hypertensive 46%, Family history of CHD 49% Previous MI 24%, Angina pectoris 25% Excluded: homozygous familial hypercholesterolaemia, secondary hypercholesterolaemia, type I, III, IV or V hyperlipidaemia, chronic pancreatitis, excessive obesity, pre-menopausal women unless sterilised, drugs which influence lipid altering, previous substance abuse, unstable angina pectoris, uncontrolled heart failure or hypertension, acute medical or surgical intervention within 3 mths. Excluded medications: corticosteroids, immunossuppressants, hormones except for replacement & other drugs which interfere with lipid altering	R 1 DB 1 W 1
Rubenfire et al, 1991	Pravastatin 20 mg (n= 57) Placebo (n= 25) Dose increased to 40 mg at end of wk 8 in all patients		16 wks	Random, double blind, multicentre, placebo control, parallel groups. 6-8 wk dietary stabilisation before randomisation to study treatment. Assessments were at baseline, 2, 4, 8, 10, 12 & 16 wks Compliance monitored by dietary records & tablet count. Cholesterol & triglycerides were measured using enzymatic methods, HDL by precipitation & LDL using Friedewald formula.	LDL >6.98 mmol/L (75th-90th percentile for age & sex) Triglyceride <2.82 mmol/L	Primary hypercholesterolaemia Male & female Mean age 501 yrs (27-75) White 85% Beta-blockers 20% Calcium channel blockers 5% Diuretics 7% Excluded: homozygous familial hypercholesterolaemia, type I, III, IV or V hyperlipidaemia, uncontrolled thyroid disease, hypertension or diabetes, excessive obesity, significant vascular events within 3 mths, excessive alcohol consumption, significant renal or hepatobiliary disease, treatment with lipid altering agents.	R1 DB 1 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Sacks et al, 1996	Pravastatin 40 mg (n= 2081) Placebo (n= 2078) Once daily, evening	CARE	5 yrs	Random, double blind, placebo control, parallel group, multicentre (Canada & USA). >4 wks NCEP step I diet before randomisation. Assessed at baseline, at 6 & 12 wks then quarterly for first yr, then at 6 mth intervals afterwards. Analyses conducted at a central laboratory. If LDL remained above 4.5 mmol/L step II diet was initiated with later cholestyramine if required. 6% of patients in each group took cholestyramine according to the protocol	Total plasma cholesterol <240 mg/dL LDL between 115 & 174 mg/dL Triglycerides <350 mg/dL	Men & postmenopausal women with previous MI (within 3-20 mths before study entry) and normal cholesterol levels Mean age 59 yrs ± 9 (included 21-75) 86% men 92% Caucasian Hypertension 43% Current smoker 21% Diabetes 14% Mean BMI 28 ± 4 kg/m2 Mean BP 129/79 concomitant medication: Aspirin 83%, Beta-blocker 40% Nitrates 33%, Calcium channel blocker 39% ACE inhibitor 14%, Diuretics 11% Excluded: symptomatic congestive heart failure, left ventricular ejection fraction <25%	R 1 DB 1 W 1
Saito et al, 1991	Simvastatin 2.5 mg in morning (n=30) Simvastatin 2.5 mg in evening (n=28) Simvastatin 5 mg in morning (n=32) Simvastatin 5 mg in evening (n=29) Placebo (n=31)		12 wks	Random, double blind, double dummy, placebo control. Subjects discontinued pre-study antihyperlipidaemic drugs. 4 wk placebo washout before randomisation to treatment once daily for 12 wk. Other lipid-altering drugs & alcohol (in the 24 hrs preceding tests) were prohibited. Assessments were at baseline & 4 wk intervals. Cholesterol & triglycerides were measured using enzymatic methods.	Serum cholesterol ≥220 mg/dL determined ≥2 times over 2 wk	Men or women with hyperlipidaemia, including familial hypercholesterolaemia. Age 18-65 yr Male:female ratio: 1:3 Excluded were subjects with liver or serious renal disease, recent MI, heart failure, secondary hyperlipidaemia, pregnant or breast feeding. Included familial heterozygous hyperchoelsterolaemia (15%)	R 1 DB 2 W 1
Salonen et al, 1995	Pravastatin 40 mg (n=223) Placebo (n=224)	KAPS	3 yr	Random, double blind, placebo control, single centre. 2.5 mth placebo run-in before randomisation to treatment given once daily for 3 yrs. Assessments at baseline & at 3 mth intervals. Cholesterol concentrations were measured enzymatically.	LDL ≥4.0 mmol/L Total cholesterol <7.5 mmol/L	Men only Mean age 57 (range 44-65) Current smoker 25-27% Diabetes 2-3% Prior MI 6-9% Hypertension 31-34%	R 1 DB 2 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Santinga et al, 1994	Pravastatin (n= 94) Placebo (n= 48)		16 wks	Random, double blind, double dummy, placebo control, parallel groups.7-14 wk dietary stabilisation (AHA step I) with 9 wk washout of lipid altering drugs. Then randomisation to treatment once daily for 12 wk. Other lipid-altering drugs & alcohol (in the 24 hrs preceding tests) were prohibited. Assessments were at baseline 2-6 wk intervals. Cholesterol & triglycerides were measured using enzymatic methods. Compliance with diet monitored using food records & with treatment by tablet count. Cholesterol & triglycerides were measured enzymatically, HDL by precipitation, LDL using Friedewald formula.	LDL >95th percentile for age & sex (165 mg/dL for men & >170 mg/dL for women) Triglycerides <250 mg/dL	Elderly men & women with primary (type II) hypercholesterolaemia Mean age 70 yrs (64-90) 67% women 75% white Excluded: homozygous familial hypercholesterolaemia, type I, III, IV or V hyperlipideamia, significant endocrine, renal, hepatic, metabolic, or cardiovascular disease. Disallowed modification: corticosteroids, thiazide, diuretics, beta-adrenergic blockers or other drugs which affect lipid parameters.	R 1 DB 1 W 1
Seed et al, 1999	Simvastatin 20 mg evening (n= 194) Pravastatin 40 mg evening (n= 193)		12 wks	Random, double blind, active control, parallel groups, multicentre (European). Dietary stabilisation on lipid-lowering AHA step I diet & washout of lipid - lowering drugs for 12 wks before randomisation. Assessed at baseline & then at 4 wk intervals. Total cholesterol, HDL & triglycerides were measured enzymatically, LDL using Friedewald formula.	Total cholesterol between 6.2 & 8.8 mmol/L LDL ≥4.9 mmol/L with CHD & ≤2 risk factors, or ≥4.1 with CHD & > 2 risk factors Triglycerides <4.5 mmol/L	Mild-moderate primary hypercholesterolaemia Men only Mean age 51 yrs (21-72) CHD 50% Excluded: secondary hypercholesterolaemia, type I, III, IV or V hyperlipidaemia, MI, coronary artery bypass surgery within 6 mths, unstable angina, active liver disease, peripheral vascular disease, persistent gastrointestinal disease, cerebrovascular incident with permanent sequelae, psychiatric, neuromuscular or sleep disorders,	R 1 DB 2 W 1
Sigurdsson et al, 1996	Simvastatin (n= 56) Fluvastatin (n= 57) Dose doubled at wk 10 if 6 wk reading of total cholesterol>5.2 mmol/L		16 wks	Random, double blind, double dummy, active control, parallel groups, multicentre, Nordic. 8 wk washout with dietary stabilisation, followed by 2 wk & placebo run-in. Randomisation to study treatment. Assessed at baseline, 6, 10 & 16 wks. Lipids were measured using identical procedures in a central laboratory. Last observation was carried forward for missing data.	Serum total cholesterol between 5.2 & 8.0 mmol/L Triglyceride ≤2.5 mmol/L	Moderate hypercholesterolaemia & IHD (92% men, 8% women) Mean age 60 yrs MI 10%, Angina 29% MI & angina 53% Intermittent claudication 12%, Diabetes 4% Hypertension 36%, TIA 1% Excluded: I or CVAi within 6 mths, unstable angina pectoris or hypertension, planned angioplasty, coronary bypass surgery within 6 mths, cardiac or renal failure, hepatic disease, partial ileal bypass, secondary hyperchoelsterolaemia, premenopausal women unless surgical sterilised, history of substance abuse, concomitant treatment with lipid altering agents.	R 1 DB 2 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Simvastatin Pravastatin Study Group, 1993	Simvastatin 10-40 mg (n= 275) Pravastatin 10-40 mg (n=275) Initial daily dose doubled after 6 wks & again after 12 wks if LDL remained >130 mg/dL Mean daily dose: Sim & Prav 27 mg/day. Number taking: Sim 10 mg 82 (30%) Sim 20 mg 60 (22%) Sim 40 mg 133 (48%) Prav 10 mg 39 (14%) Prav 20 mg 56 (20%) Prav 40 mg 180 (66%)		18 wks	Random, double blind, double dummy, multicentre (11 countries), parallel group, active control. 6 wk placebo run-in and dietary stabilisation, then randomised to study treatment for 18 wks. Cholesterol & triglycerides were measured using standard techniques in central laboratories. Drop-outs with at least one baseline & on treatment observation were included in analysis using last observation carried forward for all remaining assessments.	LDL ≥160 mg/dL (4.14 mmol/L) Triglycerides <400 mg/dL (4.5 mmol/L)	Primary hypercholesterolaemia Mean age 52 yrs Excluded: MI, coronary bypass surgery or angioplasty within 3 mths, unstable angina, cardiac, hepatic or renal failure, diabetes mellitus, secondary hypercholesterolaemia, type III hyperlipidaemia.	R 1 DB 2 W 1
Steinhagen-Thiessen, 1994	Simvastatin 5-10 mg (n= 143) Initial 5 mg dose increased to 10 mg after 6 wks Pravastatin 10 mg (n= 138) Dose remained constant throughout		12 wks	Random, double blind, parallel group, multicentre (France & Germany), active control. 10 wks on lipid lowering diet, 4 wk placebo run-in then randomised to study treatment for 12 wks. Assessed at baseline, then 6 & 12 wks. Total cholesterol & triglycerides were measured enzymatically, HDL by precipitation, & LDL using the Friedewald formula.	Total cholesterol between 5.7 & 7.3mmol/L LDL ≥ 3.4 mmol/L Triglycerides ≤ 4.0 mmol/L	Moderate primary hyperchoelsterolaemia All Caucasian 162 men, 119 women Median age 53 yrs (21-71) Excluded: Mi or coronary bypass surgery within 2 mths, unstable angina, ventricular ectopic beats >5/min, secondary hypercholesterolaemia, complete biliary obstruction, partial ileal bypass, impaired renal or hepatic function, diabetes mellitus, hypersensitivity to statins, use of immunosuppressants, or investigational drug, poor mental function. Corticosteroids, diuretics & beta-blockers were allowed at stable doses.	R 1 DB 2 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Steinmetz et al, 1996	Simvastatin 20 mg (n= 66) Micronised fenofibrate 200 mg (n= 67) Once daily		12 wks	Random, double blind, active control, parallel groups, multicentre (Germany). 8 wk washout of all lipid lowering agents, single blind placebo run-& European Atherosclerosis Society diet before randomisation. Assessed at baseline & 12 wks. Lipids analysed at central laboratory. LDL determined using Friedewald formula. .	Total cholesterol >250 mg/dL LDL between 180-300 mg/dL Triglycerides <500 mg/dL	Men (65%) & women with primary Type IIA or IIB hypercholesterolaemia. Mean age 51yrs (18-70) Duration of hyperlipidaemia 3.5 yrs Risk factors present 82% Systolic BP 132 mm Hg, Diastolic BP 83 mm Hg Mean weight 74 Kg Excluded: pregnancy or breast feeding women, familial hyperchoelsterolaemia, distal ileal bypass surgery, renal insufficiency or liver dysfunction, diseases of biliary tract, pancreatitis, diabetes mellitus, hypothyroidism, MI or coronary artery bypass surgery, previous use of probucol.	R 1 DB 1 W 1
Sweany et al, 1993	Simvastatin 10 mg (n=275) Pravastatin 10 mg (n=275) Evening Dose titration from 10 mg to 40 mg/day at 6 & 12 wks if LDL >130 mg/dL (3.4 mmol/L)		18 wks	Random, double blind, double dummy, active control, multicentre (31 centres in 11 countries), parallel group. AHA step I diet & placebo run-in for 6 wks. Randomisation to study treatment for 18 wks. Dose titrated. Assessed at baseline then at 6 wk intervals. Lipids were assessed in two laboratories using similar methods. HDL measured by precipitation.	LDL ≥160 mg/dL (4.14 mmol/L) Triglycerides <400 mg/dL (4.5 mmol/L)	Primary hypercholesterolaemia Men (61%) or women (39%) Mean age 52 yrs (18-71) Excluded: MI, coronary bypass surgery or angioplasty within 3 mths, unstable angina, secondary hyperchoelsterolaemia, type III hyperlipidaemia, cardiac or renal failure, hepatic disease, premenopausal women unless sterilised, use of lipid altering drugs within 6 wks or probucol within 6 mths, use of immunosuppressive drugs. Allowed medications at unchanged doses beta-blockers, diuretics, corticosteroids, oestrogen replacement.	R 1 DB 2 W 1
Teo et al, 1997	Simvastatin 10-40 mg (n= 230) Placebo (n= 230) Once daily evening Dose titration according to LDL levels Average daily dose: 28.5 mg ± 13.0	SCAT	3-5 yrs Average follow-up was 47.8 mths	Random, double blind, multicentre, placebo control, parallel group.4 wk single blind, placebo run-in with NCEP step I/II diet before randomisation. Assessed at baseline, monthly for 6 mths, at 9 & 12 mths, then at 6 mthly intervals. *Patients on placebo with persistently high TC>5.5 mmol/L were identified & reallocated to simvastatin in a double blind fashion Average compliance was 95%	Total serum cholesterol between 4.1 & 6.2 mmol/L HDL < 2.2 mmol/L Triglycerides < 4.0 mmol/L (& less than TC)	Age >21 yrs, mean 61 yrs 89% men Angina 54%, MI 70% Diabetes 11% Hypertension 36% Smoker: current 15%, previous 67%, never 18% Concomitant medication: Aspirin 90% Beta-blockers 47%nitrates 64% Calcium blockers 14% Excluded: contraindication to study drugs, coronary atherosclerosis in ≥3 major coronary artery segments, left ventricular ejection fraction >35%, coronary artery bypass surgery or angioplasty within 6 mths, other significant disease.	R 1 DB 1 W0

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
The Lovastatin Pravastatin Study Group, 1993	Lovastatin (n= 339) Pravastatin (n= 333) Dose titration from 20 mg to 80 mg/day (at 6 & 12 wks) in all patients		18 wks	Random, double blind, double dummy, active control, multicentre (16 countries), parallel group. AHA step I diet & placebo run-in for 7 wks. Randomisation to study treatment for 18 wks. Dose titrated regardless of cholesterol levels. Assessed at baseline then at 6 wk intervals. Centres used different techniques to isolate lipids.	Total cholesterol >6.5 mmol/L LDL >4.1 mmol/L Triglyceride <3.4 mmol/L (300 mg/dL)	Hypercholesterolaemia Mean age 54 yrs (26-71) 49% men Excluded: secondary hyperchoelsterolaemia, fertile women, diabetes mellitus.	R 1 DB 2 W 1
The Lovastatin Study Group, 1990	Lovastatin 40 mg morning (n= 49) Lovastatin 40 mg evening (n= 47) Lovastatin 40 mg twice daily (n= 48) Lovastatin 80 mg evening (n= 49) Probucol 500 mg given twice daily (n= 97). Daily dose 1000 mg		14 wks	Random, double blind, parallel group, multicentre, active control. 6 wk washout of all lipid altering drugs & dietary stabilisation (AHA). Regular visits to dietician. Single blind placebo run-in for 4 wks before randomisation Assessed at baseline, 6, 12 & 18 wks. Compliance assessed by tablet count. 2 central laboratories determined cholesterol etc & used similar techniques. NB: if total cholesterol <3.1 mmol/L during treatment, patient was unblinded & back titrated to previous dose for rest of the study.	Total cholesterol > 6.72 mmol/L LDL > 4.27 mmol/L Triglycerides < 3.95 mmol/L	Severe primary hypercholesterolaemia defined as total cholesterol > 6.72 mmol/L Mean age 50 yrs (23 to 69) 68% men High risk of MI, 72% had ischaemic heart disease Excluded: premenopausal women, more than 10 units of alcohol/wk, impaired hepatic or liver function, MI or coronary bypass surgery within 4 mths, diabetes mellitus or fasting glucose > 7.8 mmol/L	R 1 DB 1 W 1
The pravastatin multinational study group for cardiac risk patients, 1993	Pravastatin 20 mg evening (n= 530) Placebo (n= 532) Dose doubled at 13 wks if total cholesterol not reduced by 15% or above 5.2 mmol/L (n= 69; 31%)		26 wks	Random, double blind, placebo control, multicentre, international, parallel group. 8 wk washout of all lipid altering agents. 6 wk dietary stabilisation & placebo run-in before randomisation to study treatment for 26 wks. Assessed at baseline, then at 6, 13 & 26 wks. Lipids were measured using standard techniques, LDL using the Friedewald formula	Serum total cholesterol between 5.2 & 7.8 mmol/L	Hypercholesterolaemia & ≥2 additional risk factors for CAD. 82% had 2 or 3 risk factors for CAD 16% had 4 or 5 risk factors for CAD History of angina more prevalent in placebo group. Excluded: homozygous familial hyperchoelsterolaemia, types I, III, IV or V hyperlipidaemia, significant renal, hepatic or endocrine disease, substance abuse, obesity (>40% above ideal weight). Excluded medications: corticosteroids, immunosuppressive agents, investigational drugs, androgens, estrogens, progestins other than for replacement therapy.	R 1 DB 1 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Tikkanen et al, 1988	Lovastatin (n= 167) Evening Stratum I: (n=53) 20-40 mg/day Stratum II: n=114) 40-80 mg/day Number titrated to higher dose: Stratum I: 49 Stratum II: 106 Gemfibrozil (n= 167) Stratum I & II: 600 mg given twice daily Stratum I: (n= 56) Stratum II: (n= 111)		12 wks	Random, double blind, multicentre (Finnish), parallel group, active control. AHA step I diet for 4-6 wks & 4 wk placebo run-in before randomisation to study treatment. Segregation of patients by baseline total cholesterol: Stratum I 240-300 mg/dL, Stratum II >300 mg/dL. Dose of lovastatin was doubled after 6 wks if cholesterol was >200 mg/dL. Dose of gemfibrozil or matching placebo was constant. Assessed at baseline, 6, & 12 wks. Lipids measured at a central laboratory. Total cholesterol & triglycerides measured enzymatically, HDL by precipitation & LDL using Friedewald formula.	Total cholesterol > 240 mg/dL Triglycerides ≤350 mg/dL	Primary hypercholesterolaemia Mean age 52 yrs Men (45-56%) & women Mean BMI 26 kg/m2 CAD 36-50% Concomitant drugs: Beta-blockers 31-55% Diuretics 9-17% Sex steroids 2-4% Excluded: MI or coronary bypass surgery within 2 mths, other severe cardiovascular disease, diabetes mellitus, partial ileal bypass, liver or biliary disease, poor mental function, substance abuse, other investigational drug, corticosteroids, barbiturates, anticonvulsants, anticoagulants, quinidine, theophylline, cimetidine, regular antacids.	R 1 DB 1 W 0
Tikkanen et al, 1989	Simvastatin given once daily in the afternoon Simvastatin 5 mg (stratum I) (n= 68) Simvastatin 10 mg (stratum II) (n= 78) Dose was doubled after 6 wks if LDL >140 mg/dL Gemfibrozil 600 mg twice daily (n= 68) Stratum I: Gemfibrozil 600 mg twice daily (n=75) Stratum II: Daily dose 1200 mg Dose was unchanged throughout		12 wks	Random, double blind, active control, multicentre (9 countries in S America & Europe), parallel group. AHA diet & washout of all lipid altering drugs with placebo run-in for 4 wks. Randomisation to study treatment for 12 wks. Randomised into two strata: stratum I LDL <195 mg/dL, stratum II LDL >195 mg/dL. Assessed at baseline then at 6 & 12 wks.	Total cholesterol >240 mg/dL Triglycerides <350 mg/dL	Hypercholesterolaemia 93% white 64% men, 34% women Mean age 52 yrs (18-70) Prior use of lipid altering drugs 41% Took concomitant medications 50% Hypertension 34% CHD 28% Excluded: premenopausal women unless surgically sterilised, hyperlipoproteinaemia type I, III, IV or V, unstable angina, recent MI, coronary bypass surgery within 4 mths, severe ventricular arrhythmias, diabetes mellitus (blood glucose > 140 mg/dL), poor mental function, substance abuse, impaired liver function, gallstones, severe biliary disease, partial ileal bypass, any other condition posing a risk to the patient. Excluded medication: treatment with any investigational drug, barbiturates, corticosteroids, anticoagulants, theophylline, quinidine, cimetidine, regular antacids.	R 1 DB 2 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Valles et al, 1991	Lovastatin Group I 20 mg (n=44) Group II 40 mg (n=42) Given in evening Dose was doubled after 6 wks if total cholesterol > 200 mg/dL Gemfibrozil 1200 mg (600 mg given twice daily) (n= 96) Group I (n=43) Group II (n=53)		12 wks	Random, double blind, double dummy, parallel group, multicentre (Spanish), active control. 6 wks dietary stabilisation (AHA step I) & 4 wk placebo run-in before randomisation. Patients were randomised to lovastatin or placebo & data split according to baseline total cholesterol: Group I between 250 & 300 mg/dL and Group II - >300 mg/dL. Dose of lovastatin or matching placebo was doubled if total cholesterol was >200 mg/dL after 6 wks of double blind treatment. Assessed at baseline & 12 wks. Total cholesterol & triglycerides measured enzymatically, LDL using Friedewald formula, HDL by precipitation.	Total cholesterol between >250 mg/dL	Primary hypercholesterolaemia Men & women (50-70% split in different treatment groups) Mean age 52-54 yrs (18-70) CAD 30-36% Excluded: unstable angina, MI or coronary bypass surgery within 4 mths, diabetes mellitus, liver or biliary disease, partial ileal bypass, premenopausal women, substance abuse, use of corticosteroids, barbiturates, anticonvulsants, cimetidine, theophylline, regular use of antacids, any other study drug.	R 1 DB 2 W 1
Van Dam et al, 2001	Simvastatin 10 mg/day (n= 237) Fluvastatin 20 mg/day (n= 241) Initial dose doubled after 6 & 12 wks if LDL > than goal Pts whose dose was titrated up: Sim 64% vs Fluv 87%		18 wks	Random, double blind, double dummy, active control, parallel groups, multicentre (Netherlands). 6 wk washout of all lipid altering drugs including 2 wk placebo run-in before randomisation. LDL goal was ≤ 2.62 mmol/L in patients with CHD or other atherosclerotic disease, & ≤ 3.5 mmol/L in patients with multiple risk factors for CHD. Total cholesterol, HDL & triglycerides were measured using standard techniques, LDL using the Friedewald formula.	LDL ≤ 6.0 mmol/L Triglycerides < 4.5 mmol/L	Men (69%) & women with primary hypercholesterolaemia, 98% with other conditions (mainly cardiovascular) Mean age 56 yrs (20-70) Prior lipid-lowering therapy 13% Concomitant medications 89% Excluded: hypersensitivity to study drugs, pregnancy or lactation, active liver disease, hepatic dysfunction, homozygous familial or secondary hyperchoelsterolaemia, uncontrolled diabetes, substance abuse, MI, coronary bypass surgery or angioplasty within 3 mths, unstable angina or significant ventricular arrhythmia, use of drugs known to interact with study treatment or affect lipids, any other significant condition.	R 1 DB 2 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
Waters et al, 1994	Lovastatin 20 mg Evening (n= 165) Placebo Evening (n= 166) Dose doubled if LDL >130 mg/dL at wk 4 & again to 40 mg twice daily at wk 16. Dose reduced if LDL fell below 80 mg/dL Doses taken: 20 mg 91/165 40 mg 41/165 80 mg 33/165 Mean daily dose 36 mg		24 mths	Random, double blind, placebo control, parallel groups. Counselling & AHA step I diet. Randomised to once daily treatment for 24 mths. Compliance was monitored by tablet count & dietary records.If total cholesterol was >340 mg/dL special dietary counselling was given; if unchanged cholestyramine was added. Assessment at baseline & then at regular intervals. Measurement of lipid parameters was not described. NB: Cholestyramine was given to 7 patients on placebo for >1 mth & none on lovastatin.	Total cholesterol between 220 & 300 mg/dL Triglycerides <500 mg/dL	Coronary atherosclerosis on arteriogram (within 12 wks of entry) 85% men (mean age 52 yrs) 15% women (mean age 58 yrs) Previous MI 53% Hypertensive 40% Diabetes 14% Current smoker 27% Angina 66% Multivessel coronary disease 33% Concomitant drugs: Beta-blockers 50%, ACE inhibitors 5% Nifedipine 13%, Diltiazem 56%, Digitalis 4% Excluded: previous coronary bypass surgery, angioplasty within 6 mths, ejection fraction <40%, left main coronary artery stenosis >50%, 3-vessel disease & preseptal left anterior descending stenosis >70%, any coexisting severe illness, MI or unstable angina within 6 wks, concurrent lipid altering drugs, cyclosporin, anticoagulants, corticosteroids, cimetidine, elevated hepatic enzymes, impaired renal function, women of child bearing potential.	R 1 DB 1 W 0
Weir et al, 1996	Lovastatin 40 mg (n= 211) Evening meal Pravastatin 40 mg (n= 215) Bedtime		12 wks	Random, double blind, double dummy, parallel groups, active control, multicentre. 12 wk NCEP diet including 6 wk placebo run-in before randomisation to study treatment. Assessed at baseline & every 4 wks. Lipids assessed in a central laboratory. LDL determined using the Friedewald formula	Total cholesterol between 240 & 340 mg/dL LDL ≥160 mg/dL (if CAD present >190 mg/dL) Triglycerides <400 mg/dL	Primary hypercholesterolaemia (types Iia or Iib) Men only Mean age yrs (20-65) Definite CAD 14% ≥2 risk factors & definite CAD 85% ≥2 risk factors but no CAD 71% Severe obesity 30% Low risk status 15% Excluded: impaired renal or hepatic function, MI or coronary bypass surgery within 6 mths, previous cerebrovascular incident or peripheral vascular disease which interferes with normal function, treatment with any lipid altering drug within 6 wks of study entry (6 mths for probucol), history of depression, anxiety or other psychiatric or sleep disorder.	R 1 DB 1 W 1

Author 2	Treatments & daily dose (mg)	Study name	Duration of active treatment	Study methods	Fasting lipids after dietary stabilisation	Patient characteristics at baseline	Quality score
West of Scotland Coronary Prevention Study Group, 1992	Pravastatin 40 mg daily (n=3302) Placebo (n=3293) Once daily evening	WOSCOPS	5 yrs	Random, double blind, parallel group. Screening phase with 3 cholesterol assessments. Subjects meeting inclusion criteria were randomised. Assessment was at baseline, & 3 mth intervals.	Total cholesterol ≥6.5 mmol/L LDL >4.5 mmol/L	Men with moderate hypercholesterolaemia. Age 45-64 yrs, mean 55 BMI: mean 26.0±3.7 Kg/m2 Mean BP: systolic 136±17, diastolic 84±11. Stable hypertension 15% Diabetes mellitus 1% Angina pectoris (not hospitalised for 12 mths) 5% Intermittent claudication 3% Current smoker 44% Concomitant medication: Beta-blockers 7%, ACE inhibitors 1% Calcium channel blockers 4%, Nitrates 2% Aspirin/antiplatelet agent 3%	R 1 DB 1 W 1
Wiklund et al, 1993	Pravastatin 40 mg once in the evening (n= 71)		12 wks	Random, double blind, active & placebo control, parallel groups. 6-12 wk washout of lipid altering drugs, dietary stabilisation (≥2 wks) & single blind 3 wk placebo run-in, doses of thiazides & beta-adrenergic drugs were stabilised before randomisation. Assessed at baseline & 4 wk intervals. Lipids were measured enzymatically at several central laboratories.	Total cholesterol >6.0 mmol/L (or 90th percentile for age & sex) Triglycerides <4.0 mmol/L	Hypercholesterolaemia Mean age 53 yrs (21-78) Mean weight 77 Kg Mean systolic/diastolic BP 137/84 Excluded: homozygous familial hypercholesterolaemia, type I, III, IV & V hyperlipidaemia, significant cardiovascular, renal, hepatic, metabolic or gastrointestinal disease, except CHD, expected to limit life span by <5 yrs. Excluded medications: corticosteroids, oestrogens (except replacement), androgens, quinidine, coumarin anticoagulants, theophylline, barbiturates, aluminium-containing antacids, cyclosporin, fish oil preparations.	R 1 DB 1 W 1