Web Table 1: Randomized clinical trials of statins and risk of coronary heart disease (CHD) or mortality

Author and year (study acronym)	Study population	Exclusion criteria	Intervention groups	Primary outcome	Follow-up	Compliance
Primary prevention						
Furberg 1994 (ACAPS) (1)	919 asymptomatic men and women, 40 to 79 years old, with early carotid atherosclerosis as defined by B-mode ultrasonography and LDL cholesterol between the 60th and 90th percentiles, mean age 61.7 years and 51.5% male	History of MI, stroke, or angina	Lovastatin 20-40 mg/d or placebo	Angiographic measures	Mean 2.84 years	77% in both arms
Downs 1998 (AFCAPS/TexCAPS) (2)	5608 men and 997 women 45 to 73 years old with average TC and LDL-C and below-average HDL-C and had no prior history, signs, or symptoms of definite myocardial infarction, angina, claudication, CVA, or TIA	Uncontrolled HTN, secondary hyperlipidemia, or type 1 or type 2 DM that was either managed with insulin or associated with a glycohemoglobin >10%. a body weight of more than 50% greater than the desirable limit for height	Lovastatin (20-40 mg/d) or placebo in addition to a low–saturated fat, low-cholesterol diet	First acute major coronary event defined as fatal or nonfatal MI, unstable angina, or sudden cardiac death	Mean 5.2 years	71% in treatment arm and 63% in controls
ALLHAT-LLT 2002 (3)	Ambulatory persons (n=10355), aged 55 years or older, with LDL of 120 to 189 mg/dL (100 to 129 mg/dL if known CHD) and triglycerides lower than 350 mg/dL, mean age 66 years, 49% women, 38% black and 23% Hispanic, 14% had a history of CHD, and 35% had type 2 diabetes	Currently receiving lipid-lowering therapy, taking large doses of niacin, or taking Probucol in the last year; known to be intolerant of statins or to have significant liver or kidney disease (serum ALT >100 IU/L or serum creatinine >2.0 mg/dL or other contraindications for statin therapy; or had a known secondary cause of hyperlipidemia	Pravastatin 40 mg/d or usual care	All-cause mortality	Mean 4.8 years	71% in the control arm, 77% in treatment arm
Sever 2003 (ASCOT-LLA) (4)	19342 hypertensive patients (aged 40–79 years with at least three other CVD risk factors and fasting TC<6.5 mmol/L mainly white (95%) and male (81%), with a mean age of 63 years and	Previous MI, current treated angina, CeVD in the past 3 months, fasting TG> 4.5 mmol/L, CHF, uncontrolled arrhythmia or any other clinically important hematological or biochemical abnormality on screening	Atorvastatin 10 mg/d or placebo	Non-fatal MI and fatal CHD	Median 3.3 years	87% in treatment and 91% in control after 3 years

	at least 3 of the following: LVH, abnormalities on ECG, DM, PAD, previous stroke or TIA, male, aged 55 or older, microalbuminuria or proteinuria, smoking, cholesterol/HDL ≥ 6 or family history of premature CHD					
Knopp 2006 (ASPEN) (5)	2411 patients with type 2 DM for 3 years or more and low LDL (<3.6 mmol/L if history of MI or interventional procedure and < 4.1 mmol/L if not), TG<600 mg/dL, aged 40-75	Type 1 DM, MI, interventional procedure or episodes of unstable angina less than 3 months before screening, HbA1c>10%, active liver disease or hepatic dysfunction, severe renal disease, CHF treated with digoxin, CK>3 times upper limit, BP>160/100 mmHg, BMI >35 kg/m2, alcohol or drug abuse, hypersensitivity to study medication, current or planned pregnancy, placebo run-in compliance <80%, use of excluded medications	Atorvastatin 10 mg/d or placebo	CVD death or event	Median 4 years	67.5% in treatment arm and 57.6% in controls
Hedblad 2001 (BCAPS) (6)	793 men and women 49 to 70 years of age with plaque in the right carotid artery but with no symptoms of CAD, mean age 61.8, 41.5% male	History of MI, angina pectoris, or stroke within the preceding 3 months; history of surgical intervention in the right carotid artery; regular use of beta-blockers or statins; SBP>160 or DBP>95 mmHg; TC>8.0 mmol/L; hyperglycemia suspected to require insulin treatment; and conditions that in the opinion of the investigator rendered the subject unsuitable for the trial	Fluvastatin 40 mg/d or placebo	Angiographic measures	Mean 3 years	79% in treatment and 77% in placebo arm
Mercuri 1996 (CAIUS) (7)	305 patients with atherosclerosis and carotid intima media thickness and without history of CHD; 53% male and mean age 55 years with high baseline LDL (mean 181 mg/dL)	Persistent liver function abnormalities, other serious medical conditions and regular use of lipid-lowering agents, anticoagulants and calcium antagonists	Pravastatin 40 mg/d or placebo	Angiographic measures	3 years	
Colhoun 2004 (CARDS) (8)	2838 diabetes patients aged 40–75 years with no documented	Any past history of MI, angina, coronary vascular surgery, CVA, or severe PVD	Atorvastatin 10 mg/d or placebo	Acute CHD events	Median 3·9 years	85% in treatment and 91% in

	previous history of CVD, LDL ≤ 4.14 mmol/L, fasting TG ≤ 6.78 mmol/L, and at least one of the following: retinopathy, albuminuria, current smoking, or HTN	(defined as warranting surgery)				controls during 4 years
Sawayama 2002 (FAST) (9)	246 patients with TC ≥ 220 mg/dL aged 30-89, mean age 66.1 yrs and 31.3% male	TG ≥ 350 mg/dL, uncontrolled heart failure, recent (<6 months) MI; severe or unstable angina pectoris; hypothyroidism/hyperthyroidism or other endocrine diseases; secondary hyperlipidemia; uncontrolled DM; uncontrolled HTN; heavy drinking; obese patients on weight reduction programs; diseases that might interfere with drug absorption; any severe illness; and treatment with certain drugs, including corticosteroids, other lipid-lowering agents or antacids containing aluminum salts	Pravastatin 10 mg/d or diet alone	Major cardiovascular events	2 years	-
Anderssen 2005 (HYRIM) (10)	568 drug-treated hypertensive men aged 40–74 years with TC 4.5–8.0 mmol/L, TG < 4.5 mmol/L, BMI 25–35 kg/m2, and a sedentary lifestyle	Any symptomatic CVD (MI, angina pectoris, stroke), CHF, type 1 DM, history of coronary intervention, need for treatment with lipid-lowering medications other than the study drug, known or suspected impaired hepatic or renal function or malignancy, history of alcohol and/or drug abuse, vegetarian diet or diet comprising a high omega-3 fatty acid intake, and inability to perform physical exercise	Fluvastatin 40 mg/d or lifestyle in a 2 by 2 factorial design	Angiographic measures	4 years	-
Ridker 2008 (JUPITER) (11)	17802 patients including men over 50 and women over 60 without history of CVD and LDL<130 mg/dL and CRP > 2 mg/L and triglycerides < 500 mg/dL	Patients with previous or current use of lipid-lowering therapy, or postmenopausal HRT, evidence of hepatic dysfunction, high CK level, high creatinine level, DM, uncontrolled HTN, cancer within 5 years before enrollment, uncontrolled hypothyroidism, and a recent history of alcohol or drug abuse or	Rosuvastatin, 20 mg/d or matching placebo	First major cardiovascular event	Maximum 5 years; median 1.9 years	75% in both arms

		another medical condition that might compromise safety or the successful completion of the study				
Salonen 1995 (KAPS) (12)	447 men with 4.25 < LDL < 8 mmol/L and BMI < 32 kg/m^2 who after a 2.5 months run-in phase with placebo and dietary - advice still had LDL > 4 mmol/L, mean age 57 years	Liver enzymes (ALT, AST) exceeding 1.5 fold the laboratory upper limit	Pravastatin 40 mg/d or placebo	Angiographic measures	Max 3 years	92% in treatment and 93% in placebo
Nakamura 2006 (MEGA) (13)	7,832 hypercholesterolemic patients (total cholesterol 5.69 to 6.98 mmol/L) and no history of CHD, men and post-menopausal women aged 40-70	Familial hypercholesterolemia, history of angina, MI or bypass surgery or PCI, ECG abnormalities consistent with MI, history of PAD, stroke or TIA, congenital or rheumatic heart disease, chronic atrial fibrillation, current diagnosis of malignancy, severe liver or kidney disease, poorly controlled HTN or DM, secondary hyperlipidemia, current use of corticosteroids and other conditions at the discretion of the individual physician	Pravastatin 10-20 mg/d and diet vs diet alone	First occurrence of CHD	Mean 5.3 years	89% in treatment arm
Shepherd 1995 (WOSCOPS) (14)	6595 men, 45 to 64 years of age, with a mean plasma TC of 272 mg/dL	History of MI and non-fasting TC < 252 mg/dL, LDL < 155 mg/dL during second and third visits, major ECG abnormalities or arrhythmias or serious illness	Pravastatin 40 mg/d or placebo	non-fatal MI and fatal CHD	Mean 4.9 years	70.4% in treatment and 69.2% in controls at year 5
Secondary prevention						
Anonymous 1994 (4S) (15)	4444 patients 35 to 70 years old with angina pectoris or previous MI and TC of 5.5 to 8 mmol/L on a cholesterol lowering diet	Premenopausal women of childbearing potential, secondary hypercholesterolemia, unstable or Prinzmetal angina, tendon xantomata, planning coronary artery surgery or angioplasty, MI during the past 6 months, antiarrhythmic therapy, CHF requiring treatment with digitalis, diuretics or vasodilators, persistent atrial fibrillation, cardiomegaly, hemodynamically important valvular heart disease, history of completed stroke, impaired liver	Simvastatin (with dosage adjusted) or placebo	Coronary deaths	Median 5.4 years	90% in treatment and 87% in controls

		function, partial ileal bypass, history of drug or alcohol abuse, poor mental function, other serious disease, current treatment with another investigational drug or hypersensitivity to statins.				
Koren 2004 (ALLIANCE) (16)	2442 patients with CHD from managed care and Veteran Administration organization, >18 years old and LDL levels between 110 and 200 mg/dL if on lipid-lowering treatment and 130 and 250 mg/dL if not on treatment.	-	Atorvastatin titrated up to 80 mg/d or usual care	All-cause death	Median 4.5 years	-
Knopp 2006 (ASPEN) (5)	2411 patients with type 2 DM for 3 years or more and low LDL (<3.6 mmol/L if history of MI or interventional procedure and < 4.1 mmol/L if not), TG < 600 mg/dL, aged 40-75 years	Type 1 DM, MI, interventional procedure or episodes of unstable angina less than 3 months before screening, HbA1c>10%, active liver disease or hepatic dysfunction, severe renal disease, CHF treated with digoxin, CK > 3 times upper limit, BP > 160/100 mmHg, BMI > 35 kg/m2, alcohol or drug abuse, hypersensitivity to study medication, current or planned pregnancy, placebo run-in compliance <80%, use of excluded medications	Atorvastatin 10 mg/d or placebo	CVD death or event	Median 4 years	67.5% in treatment arm and 57.6% in controls
Yokoi 2005 (ATHEROMA) (17)	361 patients with age 40–69 years; TC of 195–265 mg/dL; and 1 stenosis of >25% in major coronary segments	ACS or previous CABG	Pravastatin 10-20 mg/d or diet alone	Angiographic measures	3 years	-
Flaker 1999 (CARE) (18)	4159 patients 21 to 75 years old who survived an MI (3 to 20 months before randomization), had a TC < 240 mg/dl (6.2 mmol/L), and LDL of 115 to 174 mg/dL (3.0 to 4.5 mmol/L) and fasting glucose levels of no more than 220 mg/dL, fasting TG of less than 350 mg/dL, LVEF no	-	Pravastatin 40 mg/d or placebo	CHD death or nonfatal MI	Median 5 years	-

	less than 25% and no symptomatic CHF					
Waters 1994 (CCAIT) (19)	331 patients with diffuse but not necessarily severe coronary atherosclerosis documented on a recent arteriogram and with fasting TC between 220 and 300 mg/dL, mean age 53, 81% male	Previous CABG; coronary angioplasty in the 6 months preceding the qualifying coronary arteriogram; LVEF < 40%; left main coronary artery stenosis > 50%; three-vessel disease with preseptal left anterior descending stenosis > 70%; any coexisting severe illness that would make repeat arteriography ethically unjustifiable; MI or unstable angina within 6 weeks before study entry or after the entry coronary arteriogram; a technically suboptimal coronary arteriogram; plasma TG>500 mg/dL; concurrent use of lipid-lowering drugs, cyclosporine, anticoagulants, corticosteroids, or Cimetidine; elevated hepatic enzymes or impaired renal function; and patients living too far away from the clinic or having any potential condition or problem that might hinder follow-up or compliance or present an unacceptable risk to the patient	Lovastatin 20 mg/d titrated to 40 mg/d if LDL>130 mg/dL at week 4	Angiographic end points	2 years	-
Colivicchi 2002 (20)	81 patients with unstable angina or non-Q-wave MI, angiographic evidence of severe CAD and evidence of symptomatic myocardial ischemia, LVEF > 35%, mean age 68 years in the control and 69 years in the treatment group, 59% male in the control and 58% in the treatment group	CHF, the need for continuous use of intravenous antianginal medications, and the presence of any major concurrent illness	Atorvastatin 80 mg/d or usual care	Recurrent ischemia or cardiac death	1 year	97.5% in the treatment arm
Ostadal 2010 (FACS) (21)	156 patients with ACS, 71% male in treatment and 65% male in placebo group; mean age 61 years in the treatment and 63 years in the placebo group	Concomitant active liver disease or persistent elevation of transaminases more than three times above the upper limit of normal, history of lipid lowering therapy < 30 days before index event,	Fluvastatin 80 mg/d or placebo	Major adverse cardiovascular event	1 year	75% in treatment and 22% in placebo group

		known allergy for Fluvastatin or any present additives in the drug, disability of oral drug administration, disability of follow-up, pregnancy or nursing, women of fertile age without effective contraception, suspicions of muscle disease like myositis, < 18 years old, CK ≥ 5 times of the upper limit of normal range with other casual explanation than presence of MI				
GISSI investigators 2000 (22)	4271 recent AMI patients with total cholesterol ≥ 200mg/dL	-	Pravastatin 20 mg/d or no treatment	CVD event or death	Mean 1.9 years	86.2% in treatment arm and 81% in controls
Heart Protection Study 2002 (23)	20536 adults aged 40-80 years at high risk of CAD due to either previous history of CAD, other occlusive arterial disease or DM or treated HTN at baseline	Chronic liver disease or abnormal liver function (ALT>67 IU/L), severe renal disease or renal impairment, inflammatory muscle disease or evidence of muscle problems, concurrent treatment with cyclosporine, fibrates, or high-dose niacin; child-bearing potential; severe heart failure; some life-threatening condition other than vascular disease or diabetes (eg, severe chronic airways disease or any cancer; or conditions that might limit long-term compliance (eg, severely disabling stroke, dementia, or psychiatric disorder)	Simvastatin 40 mg/d or matching placebo	Major vascular event	Mean 5 years	82% in treatment arm and 68% in controls at the end of follow-up
Anonymous 2002 (LIPID) (24)	9014 patients with previous MI or unstable angina and a baseline TC of 4·0–7·0 mmol/L, median age 62 years	-	Pravastatin 40 mg/d or placebo	Death from CHD	Mean 6 years	81% in treatment arm and 76% in controls
Serruys 2002 (LIPS) (25)	1677 patients undergoing a first successful PCI and had baseline total cholesterol between 135 and 270 mg/dL with fasting TG < 400 mg/dL	Sustained SBP > 180 mm Hg and DBP > 100 mm Hg despite medical therapy, LVEF < 30%, history of previous revascularization (PCI or CABG), severe valvular disease, idiopathic cardiomyopathy or congenital heart disease, severe renal dysfunction, obesity	Fluvastatin 40 mg twice daily or placebo	Cardiac death or non-fatal MI	Median 3.9 years	81% in the treatment and 76% in the control arm

		(BMI > 35 kg/m2), and the presence of malignant or other disease with a life expectancy of < 4 years				
Riegger 1999 (LiSA) (26)	365 patients aged 40-70 years with stable symptomatic CHD, TC > 250 mg/dL and LDL > 160 mg/dL and TG < 300 mg/dL after 4 weeks on a lipid-lowering diet. Mean age was 59.4 years in treatment and 60.2 in placebo group. 61.6% were male	PTCA or CABG, CHF (NYHA III and IV), hypersensitivity or intolerance to statins, therapy with nonregistered drugs or participation in other experimental studies within 3 months before the start of the trial; diseases and conditions which could influence the pharmacokinetics or pharmacodynamics of the trial medication, e.g. gastro-intestinal diseases; liver and kidney diseases; AST and ALT >120% of the upper limit of normal; g-glutamyl transferase (g-GT), alkaline phosphatase, bilirubin and creatinine above 150% of the upper limit of normal; pregnant or nursing women, women of child-bearing age not using adequate contraception; non-permitted concomitant medication; medication abuse, drug abuse, and/or alcohol abuse. likely to be non-compliant or not willing/able to appear for the check-up visits, refusing to give written consent	Fluvastatin 40 mg or placebo	Incidence of cardiac events	1 year	79.3% in both arms
Anonymous 1994 (MAAS) (27)	381 patients with CAD undergoing routine angiography and at least 2 atheromatous segments, TC between 5.5 and 8 mmol/L, 88% male in placebo and 89% in treatment group; mean age 54.9 in placebo and 55.6 in treatment arm.	Previous CABG, MI or unstable angina within 6 wks of angiogram, PTCA or major surgery within 3 months before angiogram, angiogram more than 60 days before randomization, CHF or EF < 30%, DBP > 100 mmHg despite treatment, FPG > 7.8mmol/L or DM requiring treatment other than diet, secondary hypercholesterolemia, use of lipid-lowering, steroid or estrogen within 6 weeks before randomization	Simvastatin 20 mg/d	Angiographic measures	Max 4 years	-
Blankenhorn 1993 (MARS) (28)	270 patients, 37 to 67 years old, with TC from 4.92 to 7.64 mmol/L (190 to 295 mg/dL) and	HTN (DBP > 115 mm Hg or, if the patient was receiving treatment, > 100 mm Hg), DM, and the use of lipid-lowering drugs within 2	Lovastatin 80 mg/d with back-titration if needed or	Angiographic measures	Mean 2.2 years	96% in the Lovastatin group and 95% in the

	angiographically defined CAD, mean age 58 and 91% male	months of randomization, premenopausal women (unless they had undergone surgical sterilization), candidates for CABG	placebo			placebo group
Nakagawa 2004 (PCS) (29)	329 patients with CAD and TC between 180 and 219 mg/dL, mean age 59 and 91% male in the treatment and 92% in the control arm	Stenosis ≥ 90% or < 25%, age ≥ 70 or < 20 years, MI or stroke within 1 month of angiography, severe hepatic dysfunction or renal disease, secondary hypercholesterolemia, pregnancy or breast feeding, allergy to pravastatin, long-term hospitalization, malignant disease	Pravastatin 10 mg/d or no dietary control	Angiographic measures	5 years	90% in both arms
Sato 2008 (OACIS-LIPID) (30)	353 patients with AMI who had TC of 200-250 mg/dL and TG < 300 mg/dL. mean age 63 years and 73% male in the treatment and 80% in the control arm	Receiving concurrent therapy with any statins or had a history of side-effects associated with any statin, evidence of life-threatening arrhythmia, severe chronic CHF, hepatic dysfunction, renal failure, CeVD, poorly controlled DM, pregnancy, lactation, age <20 yrs, and unable to take medication or absence of written informed consent, patients whom the doctors consider inappropriate for any other reason	Pravastatin 10 mg/d or no treatment	Cardiovascular events or revascularizatio n	9 months	-
Petronio 2005 (31)	71 patients undergoing elective coronary stenting with normal cholesterol levels, mean age 63years in the treatment and 60 years in the control arms, 72% male in the treatment and 77% in the control arms	Patients with ACS, DM, LVEF < 30%, ongoing statin or other lipid-lowering treatment, intolerance to statins, more lesions requiring revascularization, vessels < 2.75 mm, lesions > 20 mm, and chronic total occlusions dating > 1 month	Simvastatin 20 mg/d or no treatment	Angiographic measures	1 year	-
Furberg 1995 (PLAC I & II) (32)	559 CAD patients with moderately elevated levels of LDL cholesterol (130-189 mg/dL following diet stabilization)	-	Pravastatin or placebo	Death or coronary events	3 years	-
Shepherd 2002 (PROSPER) (33)	5804 men (n=2804) and women (n=3000) aged 70–82 years with a history of, or risk factors for, vascular disease with TC 4.0–9.0 mmol/L and TG < 6.0 mmol/L, 44% had history of vascular	Individuals with poor cognitive function (mini mental state examination score < 24)	Pravastatin 40 mg/d or placebo	Coronary death, non-fatal MI, and fatal or non-fatal stroke	Mean 3.2 years	94% in treatment arm and 90% in controls

	disease					
Jukema 1995 (REGRESS) (34)	885 male patients with TC between 4-8 mmol/L who were scheduled for coronary angiography, mean age 56.5 years in the treatment and 55.9 years in the control arm, 50% in the treatment arm had prior history of MI	Age ≥ 70 years; inability or unwillingness to consent to and undergo a repeat coronary cinearteriography; noncompliance. Enrollment in another study protocol that includes a coronary cineangiogram and experimental drug therapy; TG > 4.0 mmol/L; life-threatening illnesses other than CAD or a concurrent serious illness; use of lipid-lowering drugs ≤ 6 weeks before qualifying lipid measurement (≤12 weeks for fibrates or statin), history of poor response to other statins, immune disorder (systemic lupus, dysproteinemia, or major hypersensitivity or allergic disorders) or use of immunosuppressive therapy or corticosteroids; significant metabolic disease; significant gastrointestinal disease or surgery that might interfere with drug absorption; Excess ethanol consumption (>3 drinks/d)	Pravastatin 40 mg/d or placebo	Angiographic measures	2 years	-
Teo 2000 (SCAT) (35)	460 patients with age > 21 years, TC between 4.1 and 6.2 mmol/L, HDL < 2.2 mmol/L, and TG < 4 mmol/L and lower than TC, and angiographically detectable coronary atherosclerosis in 3 or more major coronary artery segments; and LVEF > 35%	Clear indications for or contraindications to study drugs, clinical instability, imminent need for intervention, other significant cardiac or systemic diseases, potential noncompliance, and inability to give informed consent	Simvastatin 10 mg/d titrated to 40 mg/d during the first 3 months or placebo	Angiographic end points	Mean 47.8 months	~95% on both arms
Amarenco 2006 (SPARCL) (36)	4731 patients who had stroke or TIA 1-6 months before entry, had LDL of 100-190 mg/dL and no known CHD	Atrial fibrillation, other cardiac sources of embolism and subarachnoid hemorrhage	Atorvastatin 80 mg/d or placebo	Major coronary and cardiovascular event	Median 4.9 years	75% in controls

Web Table 2: Observational studies on the effect of statins on coronary heart disease (CHD) or mortality

Author and year	Study population	Eligibility criteria	Comparison	Outcome	Follow-up	Adjustment	Method of adjustment
Primary prevention							
Seeger 2003, 2005 (37, 38)	Members of Fallon Community Health Plan who had a recorded LDL > 130 mg/dL) at any time between 1994 and 1998	Enrolled for at least 1 year, have LDL, TG, HDL levels all in the 6 months preceding cohort entry, no diagnosis of PAD, and not current statin user	Initiators vs. non-initiators of any statin (mostly Fluvastatin)	Fist MI	Maximum 6 years	52 variables including age, sex, smoking, LDL, HDL, TG, DM, HTN, health care utilization; one propensity model for each 1-year block	Propensity score matching
Smeeth 2009 (39)	5.5 million subjects in 303 general practices in the UK followed from Jan 1995 to Dec 2006 (The Health Improvement Network)	More than 12 months prior continuous registration, some contact within the 6 months prior to event, diagnosis of atherosclerosis before index date	Initiators vs. non-initiators of any statin matched by age, sex and practice	First MI	Median 4.4 years	Age, sex, practice (by matching), observation time in the THIN database, BMI, SES, consultation rate, prescribing rate, smoking status, drinking habits, DM, CHD, CeVD, PAD, other diseases and use of drugs	Cox proportional hazard model with adjustment for age, sex, propensity score and further adjustment for diagnosis of diseases or use of drugs after index date
Leeper 2007 (40)	6107 consecutive patients seen at the Palo Alto VA Medical Center in Palo Alto, California, or 1 of 7 affiliated community clinics between 1998 and 2004 with LDL < 60 mg/dL, mean age 65 years	Patients who had no prescription within 150 days of the low LDL value or who had history of CHD	Having or not having a statin prescription	All-cause mortality	Mean 2 years	Age, sex, creatinine greater than 1.5 mg/dL, LDL level, prior malignancy, IHD, prior MI, PAD, HTN, CHF, DM, stroke, COPD, alcohol dependence, ACE inhibitors/ARBs, beta-blockers	Cox proportional hazard model and propensity scores adjustment
Lemaitre 2002 (41)	1250 women and 664 men from the Cardiovascular Health Study, 65 years old or older	Patients who had an MI or stroke, received drugs to lower TC at baseline and those for whom no treatment was recommended based on 1993 NCEP guidelines.	Use or non-use of statins	All-cause mortality	Median 7.3 years	Sex, age, DM, and prevalent CVD (angina, CABG, angioplasty, carotid endarterectomy, or bypass procedure on a leg artery)	Cox proportional hazard model

		participants with missing TC values					
Gardette 2009 (42)	7722 French men from the Prospective Epidemiological Study of Myocardial Infarction (PRIME), aged 50 to 59 years at baseline	Treatment with statin plus fibrate, lipid lowering drugs other than statin or fibrate, no plasma lipid level assessment	Use or non-use of statins	All-cause mortality	Mean 9.6 years	Center, age, educational level, histories of CVD and severe chronic diseases, HTN, and DM; smoking habits, alcohol consumption, physical activity, waist circumference, and HDL and non–HDL cholesterol	Cox proportional hazard model
Secondary prevention							
Author and year	**Study population**	**Eligibility criteria**	**Comparison**	**Outcome**	**Follow-up**	**Adjustment**	**Method of adjustment**
Allen-Maycock 2002 (43)	7220 patients with angiographically defined significant CAD, mean age 65 years and 74% male	-	Having or not having a statin prescription on discharge	All-cause mortality	Mean 3.3 years	Age, gender, CHF, renal failure, DM, CABG, coronary anatomy, PCI, hypertension, previous stroke, smoking	Cox proportional hazard
Carrier 2009 (44)	6655 patients who underwent CABG in the Montreal Heart Institute between 1995 and 2007	Concomitant valve or other cardiac surgical procedures or re-operation	Use vs. non-use of any statins	Combined death or re-operation or PCI	Maximum 12 years	Age, sex, diabetes, hyperlipidemia, antiplatelet, beta-blockers, ACE-inhibitor	Cox proportional hazard
Christensen 2010 (45)	12,483 critically ill patients > 45 yrs of age with a first-time admission to one of three highly specialized ICUs within the Aarhus University Hospital network, Denmark	-	Use vs. non-use of any statins	All-cause mortality	Maximum 1 year	Age group, gender, medical/ surgical department, diagnosis, Charlson index score and alcoholism-related disease, surgery within seven days, current use of ACE-inhibitors, beta blockers and low-dose aspirin and marital status	Cox proportional hazard
Cook 2009 (46)	4232 patients selected retrospectively from the Nova Scotia Seniors Pharmacare Program; 65 year old or older,	-	User-initiator vs. non-user	All-cause mortality	Mean 28 months	Age, gender, region, TC, LDL, HDL, TG, DM, HTN, smoking, family history of CVD, previous PTCA/CABG/CHF/MI/cathet	Propensity score categories and multivariate Cox proportional hazard model

	discharged after a diagnosis of IHD, mean age 77.5 years, 48% male					erization/stroke/TIA, number of prescriptions in the past 6 months, year of entry into study, discharge diagnosis (unstable angina/MI), in-hospital procedures, on-discharge medications	
De Liefde 2008 (47)	2109 patients with symptoms of PVD, mean age 63 and 67% male, 20% had previous MI, 20% revascularization and 30% abnormal ECG	-	Baseline use vs. non-use of statins	Major cardiovascular events, all-cause mortality	Mean 5 years	Age, gender, current smoking at baseline, HTN, COPD, hypercholesterolemia, DM, history of CHF, previous CVD, renal failure, SBP at rest, and ankle-brachial index at rest	Cox proportional hazard model (Results were the same using propensity score analysis.)
De Luca 2006 (48)	1513 patients with ST elevation MI and primary angioplasty, mean age 61 years and 78% male	Presenting within 6 hours of symptoms	Statin users and non-users at discharge	All-cause mortality	At 1 year	Age, sex, DM, previous MI, PCI or CABG, hypercholesterolemia, smoking, HTN, anterior MI, Killip 1 class, multivessel disease, angiographic collateral, successful reperfusion, pre-procedural TIMI flow, use of intra-aortic balloon pump and therapy at discharge, including beta-blockers, ACE-inhibitors, nitrates and calcium antagonist	Propensity score
Fintel 2007 (49)	13715 patients from the PharMetrics database of commercially insured subjects in the US with a cardiac-related hospitalization in prior 12 months, less than 65 years old, not covered by Medicare risk, and with a previous diagnosis or treatment of lipid	Data on all health care utilizations, continuously eligible for drug benefits during follow-up	Use or non-use of statins	All-cause mortality	Up to 3 years	Sex, payer type, geographic region, pre-index presence of CHD comorbidities, presence of comorbidities during index hospitalization, preindex use of treatment for lipid disorders, concomitant medications for selected conditions, pre-index CHD event diagnosis, CHD event at index diagnosis, total pre-	Cox proportional hazard model after propensity score matching

	disorders, mean age 58.9 and 68.7% male					index health care costs, total index hospitalization costs, index hospitalization length of stay, and days of follow up	
Feringa 2009 (50)	1,693 patients aged 65 years or older who underwent non-cardiac vascular surgery, mean age 73 and 76% men, 36% had CAD and 49% abnormal ECG at baseline	-	Peri-operative use vs. non-use of statins	All-cause mortality	Median 8.2 years	Age, sex, HTN, hypercholesterolemia, smoking, COPD and propensity score	Cox proportional hazard model using propensity scores
Foody 2006 (51)	23,013 Medicare patients (> 65 years old) with a discharge diagnosis of AMI	Excluded patients who transferred to another hospital; left against medical advice; had a terminal illness, comorbid condition limiting statin use, a do-not-resuscitate order, or intolerance to stains; or resided outside the United States, also excluded patients who were on statins before admission, died during hospitalization or had an unknown date of death	Having vs. not having a discharge prescription for statins	All-cause mortality	3 years after discharge	Age, sex, race, history of HTN, DM, CHF, MI, PCI, CABG, dementia, smoking, heart rate, SBP, rales, location and type of MI, LV function, peak CK level, atrial fibrillation, stroke, shock, arrest, WBC, creatinine, glucose, physician specialty, type of hospital, medication use at discharge	Logistic regression using propensity scores
Furukawa 2008 (52)	9225 patients undergoing their first coronary revascularization in CREDO-Kyoto registry, mean age 67.1 and 70.5% male	Excluded patients with AMI within the first week of follow-up, malignant diseases and those who died in hospital or did not have precise information on discharge prescriptions	With or without statin prescription at discharge	CVD death	Median 3.5 years	Mode of revascularization, old-old age (≥ 75 years), sex, BMI, smoking, hypertension, DM, PAD, CeVD, atrial fibrillation, COPD, CKD, liver cirrhosis, anemia, unstable angina, prior MI, history of CHF, TC ≥ 220mg/dL) or TG ≥ 150mg/dL, left main coronary artery disease, proximal left anterior descending artery lesion and multivessel	Cox proportional hazard model using stepwise approach and propensity scores

						disease, and 7 potential risk reducing pharmacotherapies at hospital discharge: statins, ACE-inhibitor, ARBs, beta-blockers, antiplatelet drugs, nitrates and calcium-channel blockers	
Herrington 2002 (53)	2763 postmenopausal women, mean age 67.3 years with CHD, from the HERS trial of HRT	Women using other lipid-lowering agents at baseline	Use vs. non-use of any statin	CHD or non-fatal MI and all-cause mortality	Mean 5.7 years	Race, DM (according to self-report or fasting glucose >125 mg/dL), HTN (SBP ≥ 140 mmHg or DBP ≥ 90 mmHg), creatinine clearance ≥40 mL/min, LDL, HDL, prior MI, and CHF (New York Heart Association class I to III)	Cox proportional hazard
Hippisley-Cox 2005 (54)	13029 patients with first diagnosis of AMI within the General Practitioners' Research Database in the UK	Excluded patients whose diagnosis was made within the first three months of registration with the general practice (to minimize information bias), patients prescribed statins before the diagnosis of IHD, and patients whose first diagnosis was made after death (postmortem diagnosis)	Current-users vs. never-users of any statin	All-cause death	Median 5.3 years	Current use of aspirin, beta blockers, and ACE-inhibitors, comorbidity (MI, DM, HTN, CHF), smoking, BMI, and quintile of deprivation	Cox proportional hazard for the cohort analysis and conditional logistic regression for the nested case-control (matched on age, sex and year of diagnosis of IHD)
Karp 2007 (55)	38543 patients in Quebec, Canada discharged with a first diagnosis of AMI and linked information from drug claims database, mean age 67 years in men and 73 in women	Excluded if AMI was an in-hospital complication or a transfer from another hospital, length of stay less than 2 days, patient discharged to a long-term care institution, or moved out of province, or health care number was invalid	Continuous statin users vs. never-users	CVD death	Up to 7 years	Age, marital status, comorbidities, use of cardiac medications at baseline and use of statins in the year preceding the index hospitalization, in-hospital procedure performed, length of hospital stay, fiscal-calendar year, specialty of treating physician and type of hospital (teaching or rural)	Cox proportional hazard model

Kertai 2004 (56)	519 patients who underwent elective abdominal aortic repair and survived 30 days after surgery, mean age 68.7 years and 86% male	-	Baseline use vs. non-use of statins	All-cause mortality, CVD mortality	Median 4.7 years	Age, gender, beta-blockers, aspirin, angina, prior MI, heart failure, prior CVA, DM, COPD, renal function	Cox proportional hazard model adjusting for confounders and propensity score
Kubota 2008 (57)	575 consecutive Japanese patients who underwent PCI, 85% of the patients were non-obese males aged between 59 and 61 years, mean age 59.8 and 86% male	-	Having vs. not having a statin prescription after PCI	CVD death or all-cause mortality	Mean 11 years	Age, sex, BMI, smoking history, family history of CHD, TC, HDL, TG, HTN, DM, other medications, history of PCI or CABG, presentation of ACS, LVEF, vessel disease, protected left main trunk lesions, left anterior descending lesions, saphenous vein graft lesions, and procedural success (defined as residual stenosis of ≤ 50% after percutaneous coronary intervention)	Cox proportional hazard model
Kulik 2008 (58)	7503 Medicare patients ≥ 65 years of age who underwent CABG (1995–2003) , mean age 75.6 years and 35% male	Patients who died or were readmitted to hospital within 30 days of CABG. patients who were not active users of either drug benefit program, and patients who received prescriptions for Cerivastatin	Users and initiators of statins compared to non-users	CVD event	6 months	Age, sex, race, year of surgery, PVD, preoperative stroke, previous MI or ACS, DM, postoperative beta-blocker, clopidogrel, ACE-inhibitor or ARBs use, teaching hospital, hospital volume, and surgeon volume	Cox proportional hazard model
Leeper 2007 (40)	6107 consecutive patients seen at the Palo Alto VA Medical Center in Palo Alto, California, or 1 of 7 affiliated community clinics between 1998 and 2004 with LDL < 60 mg/dL, mean age 65 years and 43% with documented CHD	Patients who had no prescription within 150 days of the low LDL value	Having or not having a statin prescription	All-cause mortality	Mean 2 years	Age, sex, creatinine > 1.5 mg/dL, LDL level, Prior malignancy, IHD, prior MI, PAD, HTN, CHF, DM, stroke, COPD, alcohol dependence, ACE-inhibitors/ARBs, beta-blockers	Cox proportional hazard model and propensity scores adjustment

Muhlestein 2004 (59)	2924 patients from a catheterization registry between 1994 and 1996, who had significant CAD, with mean age 65 and 76% male	Lack of data on CRP or statin prescription	Having or not having a statin prescription on discharge	All-cause mortality	Mean 2.4 years	Age, sex, physician-reported DM, HTN and hyperlipidemia, reported family history active smokers or those with a 10 pack-year history, clinical presentation, coronary anatomy (as 1-, 2-, or 3 vessel disease). clinical interventions (medical therapy (only), PCI, CABG), history of stroke, MI, renal failure, and heart failure	Cox proportional hazard
Nagashima 2007 (60)	4075 patients with AMI treated at 17 hospitals in Japan from 1999 to 2004, mean age 63 and 73% male	TC > 400 mg/dL or patients died before discharge	Having or not having a statin prescription at discharge	CVD death	Median 4.1 years	Age, sex, SBP, DBP, BMI, heart rate, peak CK, CRP, creatinine, HTN, hyperlipidemia, smoking, CeVD, previous MI, number of diseased vessels, PCI and CABG during hospitalization, aspirin use, ACE-inhibitor or ARB use, beta-blocker use, nitrate use, and TC	Propensity score matching (1,404 patients included) and proportional hazard model
Schanzer 2008 (61)	1404 patients with critical limb ischemia who underwent lower extremity bypass grafting in a randomized trial (PREVENT III), 42% had prior CHD, mean age 68.5, 64% male	Aged 18 years or more who underwent bypass grafting with autogenous vein, not having claudication as an indication for graft	having a statin prescription at discharge	All-cause mortality	1 year	Age, sex, race, institutional setting, tobacco use, DM, HTN, CAD, prior CABG, CKD, prior infrainguinal bypass grafting, aspirin, beta-blocker, surgical characteristics	Cox proportional hazards model with backwards elimination and propensity score weighting
Schillinger 2004 (62)	515 patients with advanced peripheral arterial disease, mean age 69.5 and 58% male	-	Use vs. non-use of statins	MI or death	Median 1.75 years	Age, sex, BMI, LDL, hypertension, diabetes, smoking, history of MI, history of stroke, critical limb ischemia, Clopidogrel therapy	Cox proportional hazard model
Schneeweiss 2007 (63)	Seniors age 65 years and older enrolled in both	Subjects who had had a stroke, transitory ischemic	Having vs. not having a	All-cause mortality	Max 1-year	Age, sex, race, comorbidity score, alzheimer disease or	Cox proportional hazard model

	Medicare and the Pennsylvania Pharmaceutical Assistance Contract for the Elderly (PACE) programs between 1995 and 2002	attack, MI, arterial surgery, or amputation for vascular disease in the past 6 months were excluded, as were those with a hospitalization for CHF, arrhythmia, or atrial fibrillation in the past 6 months	statin prescription			other dementia, angina or use of nitrates, atrial fibrillation, cancer, CVD diagnoses, cardiovascular system symptoms, cataract, chest pain, COPD, complications of heart disease, conduction disorders, coronary atherosclerosis, depression, DM, DM medication, disorders of refraction and accommodation, fracture of hip, wrist, humerous, or spine, gait abnormalities, CHF, hyperlipidemia, hyperparathyroidism, HTN, hyperthyroidism, hypothyroidism, CHD, lupus, MI, osteoarthrosis, osteoporosis, palpitations, Parkinson disease, PVD, renal disease, rheumatoid arthritis, stroke, TIA, syncope, urinary tract infection, bone mineral density test, ECG, laboratory test, lipid test	
Sheng 2009 (64)	2759 patients in Tayside, Scotland, selected from primary practice database after being discharged from a hospitalization for MI	-	Having a prescription within 30 days of discharge	All-cause mortality and recurrent MI	-	Age, sex, social deprivation category, TC change, and use of drugs (ACE-inhibitors, anticoagulants, antiplatelet agents, alpha-blockers, beta-blockers, bronchodilators, calcium channel blockers, cardiac glycosides, diuretics, disease-modifying antirheumatic drugs, nitrates, and hypoglycaemic drugs) during the follow-up period	-

Stenestrand 2001 (65)	19599 patients with a first MI and less than 80 years old from the Swedish Regiser of Cardiac Intensive Care from 1995 to 1998, mean age 65.5 and 71% male	Patients with incomplete data or those who died before hospital discharge	Having or not having a statin prescription at discharge	All-cause mortality	Up to 1-year	42 covariates including age, sex, smoking, previous MI, previous PCI or CABG, history of DM, history of HTN, circulatory arrest, medication use, type and size of hospital, admission year, hospital's statin prescription rate	Cox proportional hazard adjusted for propensity scores
Ward 2005 (66)	446 patients who underwent infrainguinal vascular bypass surgery, mean age 67 and 51% men, 59% had CAD	Surgeries for which the indication was not atherosclerotic peripheral vascular disease (trauma, gunshot wound, congenital vascular malformation, or vascular infiltration of tumor)	Baseline use vs. non-use of statins	All-cause mortality	Mean 5.5 years	Age, CAD, beta-blocker use, ESRD, operative year, HTN, DM, and an operative indication of limb salvage	Cox proportional hazard model
Weiner 2008 (67)	4151 patients with history of MI and/or angina and total cholesterol >210 mg/dL in the General Practitioners' Research Database in UK, males 35-70 years old and females 45-70 years old, 63.2% male	AMI in the past 6 months, history of CVA, heart failure requiring treatment, impaired hepatic function, valvular heart disease, altered hemodynamics, history of drug or alcohol abuse, poor mental function, other serious disease	Initiator vs. non-initiator of any statins	Recurrent MI	Median 5.4 years	Age, sex, SBP, BMI, smoking, previous MI, angina and/or other IHD and/or nitrate therapy, prior coronary revascularization, TIA and/or other ischemic CeVD, DM, and/or DM treatment	Cox proportional hazard model (Results were the same using propensity score analysis)
Welten 2007 (68)	2126 patients who were referred for elective open infrarenal abdominal aortic surgery or lower limb arterial revascularization procedures, mean age 66 years and 76% male, 29% had MI, 26% revascularization and 17% angina pectoris at baseline	-	Perioperative use vs. non-use of statins	All-cause and CVD mortality	Mean 6 years	Age, sex, HTN, DM, smoking, hypercholesterolemia, COPD, BMI, type of surgery, history of MI, coronary, revascularization, heart failure, angina, CeVD, and year of operation	Cox proportional hazard model adjusting for confounders and propensity score

Zhang 2007 (69)	201102 individuals who used a Veteran Health Administration facility at least once in FY96 to FY98 and who had diabetes based on claims criterion	Patients who either had incomplete medication data files or that did not perform hemoglobin A1c tests using validated laboratory methodology	Having vs. not having a statin prescription	All-cause mortality	Up to 2-2.5 years	Age, sex, ethnicity, CHF, IHD, PVD, any mental health condition, HTN, hyperlipidemia, renal disease, ACE-inhibitor use, beta-blockers, calcium channel blockers, insulin, mean HbA1c, mean creatinine, mean TC, mean LDL, Charlson score, total inpatient days	Propensity score matched conditional logistic regression
Zhang 2009 (70)	3227 patients who underwent PCI and were taken from two rounds of the National Heart, Lung and Blood Institute Dynamic Registry. Mean age 63.8, 67% male	Patients with cardiogenic shock, in-hospital adverse events (including MI or CABG), liver disease, renal disease, alcoholism or drug abuse	Having vs. not having a statin prescription	All-cause mortality	1 year	Age, sex, race, enrollment wave, insurance, BMI, disease history, procedure indication, procedure circumstance, use of drug-eluting stent, LVEF, peri-procedural glycoprotein IIb/IIa inhibitor, single/double/triple vessel disease, number of lesions, medications at discharge	Propensity score adjusted Cox regression

Abbreviations:

ACE: angiotensin converting enzyme
ACS: Acute coronary syndrome
ALT: alanine aminotransferase
AMI: acute myocardial infarction
AMI: acute myocardial infarction
ARB: angiotensin II receptor blocker
AST: aspartate aminotransferase
BMI: body mass index
CABG: coronary artery bypass graft
CAD: coronary artery disease
CeVD: cerebrovascular disease
CHD: coronary heart disease
CHF: congestive heart failure
CK: creatine phosphokinase
CKD: chronic kidney disease
COPD: chronic obstructive pulmonary disease
CRF: chronic renal failure
CRP: C-reactive protein
CVA: Cerebrovascular accident
CVD: cardiovascular disease
DBP: diastolic blood pressure
DM: diabetes mellitus
ECG: electrocardiogram
ESRD: end-stage renal disease
HDL: high-density lipoprotein
HRT: hormone replacement therapy (post-menopausal)
HTN: hypertension
IFG: impaired fasting glucose
IHD: ischemic heart disease
LDL: low-density lipoprotein
LV: left ventricle
LVEF: left ventricular ejection fraction
LVH: left ventricular hypertrophy
MI: myocardial infarction
NYHA: New York Heart Association
PAD: peripheral arterial disease
PCI: percutaneous coronary intervention
PTCA: percutaneous transluminal coronary angioplasty
PVD : peripheral vascular disease
SBP: systolic blood pressure
SES: socioeconomic status
TG: (serum) triglycerides
TIA: transient ischemic attack
UK: United Kingdom
WBC: white blood cell count

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