

25	<u>The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators.</u>	N Engl J Med 1996 Oct;335(14):1001-9
26	<u>Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group.</u>	N Engl J Med 1999 Aug;341(6):410-8
27	<u>HDL cholesterol predicts coronary heart disease mortality in older persons.</u>	JAMA 1995 Aug;274(7):539-44
28	<u>Lipoprotein changes and reduction in the incidence of major coronary heart disease events in the Scandinavian Simvastatin Survival Study (4S).</u>	Circulation 1998 Apr;97(15):1453-60
29	<u>MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial.</u>	Lancet 2002 Jul;360(9326):7-22
30	<u>Effect of pravastatin on cardiovascular events in older patients with myocardial infarction and cholesterol levels in the average range. Results of the Cholesterol and Recurrent Events (CARE) trial.</u>	Ann Intern Med 1998 Nov;129(9):681-9
31	<u>The collaborative atorvastatin diabetes study: preliminary results.</u>	Int J Clin Pract 2005 Jan;59(1):121-3
32	<u>A comparison of the efficacy and tolerability of titrate-to-goal regimens of simvastatin and fluvastatin: a randomized, double-blind study in adult patients at moderate to high risk for cardiovascular disease.</u>	Clin Ther 2001 Mar;23(3):467-78
33	<u>Cholesterol-lowering therapy in women and elderly patients with myocardial infarction or angina pectoris: findings from the Scandinavian Simvastatin Survival Study (4S).</u>	Circulation 1997 Dec;96(12):4211-8
34	<u>Safety of low-density lipoprotein cholesterol reduction with atorvastatin versus simvastatin in a coronary heart disease population (the TARGET TANGIBLE trial).</u>	Am J Cardiol 1999 Jul;84(1):7-13
35	<u>Design & rationale of the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS).</u>	Am J Cardiol 1997 Aug;80(3):287-93
36	<u>Effects of low doses of simvastatin and atorvastatin on high-density lipoprotein cholesterol levels in patients with hypercholesterolemia.</u>	Clin Ther 2001 Jun;23(6):851-7
37	<u>Gemfibrozil for secondary prevention of cardiovascular events in mild to moderate chronic renal insufficiency.</u>	Kidney Int 2004 Sep;66(3):1123-30
38	<u>Reducing the risk of coronary events: evidence from the Scandinavian Simvastatin Survival Study (4S).</u>	Am J Cardiol 1995 Sep;76(9):64C-68C
39	<u>Effects of ezetimibe added to on-going statin therapy on the lipid profile of hypercholesterolemic patients with diabetes mellitus or metabolic syndrome.</u>	Curr Med Res Opin 2004 Sep;20(9):1437-45
40	<u>Effect of pravastatin on coronary disease events in subgroups defined by coronary risk factors: the Prospective Pravastatin Pooling Project.</u>	Circulation 2000 Oct;102(16):1893-900
41	<u>Cardiovascular events and their reduction with pravastatin in diabetic and glucose-intolerant myocardial infarction survivors with average cholesterol levels: subgroup analyses in the cholesterol and recurrent events (CARE) trial. The Care Investigators.</u>	Circulation 1998 Dec;98(23):2513-9
42	<u>Coaching patients with coronary heart disease to achieve the target cholesterol: a method to bridge the gap between evidence-based medicine and the "real world"--randomized controlled trial.</u>	J Clin Epidemiol 2002 Mar;55(3):245-52
43	<u>Design and baseline characteristics of the Incremental Decrease in End Points through Aggressive Lipid Lowering study.</u>	Am J Cardiol 2004 Sep;94(6):720-4
44	<u>Effect of pravastatin on cardiovascular events and mortality in 1516 women with coronary heart disease: results from the Long-Term Intervention with Pravastatin in Ischemic Disease (LIPID) study.</u>	Am Heart J 2003 Apr;145(4):643-51
45	<u>Efficacy and safety of pravastatin in the long-term treatment of elderly patients with hypercholesterolemia.</u>	Am J Med 1994 Jun;96(6):509-15
46	[Statin therapy for hypertensive patients]	Tidsskr Nor Laegeforen 2004 Jan;124(2):165-6
47	<u>The relationship between low-density lipoprotein cholesterol goal attainment and prevention of coronary heart disease--related events.</u>	J Cardiovasc Pharmacol Ther 2001 Apr;6(2):129-35
48	<u>Effects of simvastatin versus gemfibrozil on lipids and glucose control in patients with non-insulin-dependent diabetes mellitus. NIDDM Study Group.</u>	Clin Ther 1995 Mar-Apr;17(2):186-203
49	<u>Diabetes, plasma insulin, and cardiovascular disease: subgroup analysis from the Department of Veterans Affairs high-density lipoprotein intervention trial (VA-HIT).</u>	Arch Intern Med 2002 Dec 9-23;162(22):2597-604
50	<u>Cholesterol lowering with simvastatin improves prognosis of diabetic patients with coronary heart disease. A subgroup analysis of the Scandinavian Simvastatin Survival Study (4S).</u>	Diabetes Care 1997 Apr;20(4):614-20

図 4 j 高脂血症(05) 26～50位

その他(06) (糖尿病, 脳卒中, 複合領域ほか)

	Title	Journal
1	Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes.	N Engl J Med 2003 Jan;348(5):383-93
2	Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy.	N Engl J Med 2001 Sep;345(12):861-9
3	The effect of nisoldipine as compared with enalapril on cardiovascular outcomes in patients with non-insulin-dependent diabetes and hypertension.	N Engl J Med 1998 Mar;338(10):645-52
4	Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial.	Lancet 2004 Aug 21-27;364(9435):685-96
5	Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes.	N Engl J Med 2001 Sep;345(12):861-60
6	Effects of low dose ramipril on cardiovascular and renal outcomes in patients with type 2 diabetes and raised excretion of urinary albumin: randomised, double blind, placebo controlled trial (the DIABHYCAR study).	BMJ 2004 Feb;328(7438):495
7	A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women.	N Engl J Med 2005 Mar;352(13):1293-304
8	Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis.	N Engl J Med 2005 Jul;353(3):238-48
9	Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group.	BMJ 1998 Sep;317(7160):703-13
10	[Effect of losartan on renal and cardiovascular complications of patients with type 2 diabetes and nephropathy]	Ugeskr Laeger 2001 Oct;163(40):5514-9
11	Aspirin and ticlopidine for prevention of recurrent stroke in black patients: a randomized trial.	JAMA 2003 Jun;289(22):2947-57
12	Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol.	Lancet 2002 Mar;359(9311):995-1003
13	Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators.	Lancet 2000 Jan;355(9200):253-9
14	Effect of angiotensin-converting-enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: the Captopril Prevention Project (CAPPP) randomised trial.	Lancet 1999 Feb;353(9153):611-6
15	Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators.	N Engl J Med 2000 Jan;342(3):145-53
16	Outcome results of the Fosinopril Versus Amlodipine Cardiovascular Events Randomized Trial (FACET) in patients with hypertension and NIDDM.	Diabetes Care 1998 Apr;21(4):597-603
17	Trial of secondary prevention with atenolol after transient ischemic attack or nondisabling ischemic stroke. The Dutch TIA Trial Study Group.	Stroke 1993 Apr;24(4):543-8
18	The Study on Cognition and Prognosis in the Elderly (SCOPE): principal results of a randomized double-blind intervention trial.	J Hypertens 2003 May;21(5):875-86
19	Efficacy and safety of low-dose aspirin in polycythemia vera.	N Engl J Med 2004 Jan;350(2):114-24
20	A comparison of warfarin and aspirin for the prevention of recurrent ischemic stroke.	N Engl J Med 2001 Nov;345(20):1444-51
21	PROGRESS: Perindopril pROtection aGainst REcurrent Stroke Study: status in March 1997. PROGRESS Management Committee.	J Hum Hypertens 1998 Sep;12(9):627-9
22	New evidence on the prevention of cardiovascular events in hypertensive patients with type 2 diabetes.	J Cardiovasc Pharmacol 1998;32 Suppl 2(2):S18-23
23	Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group.	Lancet 1998 Sep;352(9131):837-53
24	Cardiovascular morbidity and mortality in patients with diabetes in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol.	Lancet 2002 Mar;359(9311):1004-10
25	The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes.	N Engl J Med 2001 Sep;345(12):870-8

図 4 k その他(06) (糖尿病, 脳卒中, 複合領域ほか) 1 ~ 2 5 位

25	The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes.	N Engl J Med 2001 Sep;345(12):870-8
26	Cardiovascular outcomes in the Irbesartan Diabetic Nephropathy Trial of patients with type 2 diabetes and overt nephropathy.	Ann Intern Med 2003 Apr;138(7):542-9
27	Vitamin E supplementation and cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators.	N Engl J Med 2000 Jan;342(3):154-60
28	Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group.	Lancet 1998 Jun;351(9118):1755-62
29	Effect of ramipril vs amlodipine on renal outcomes in hypertensive nephrosclerosis: a randomized controlled trial.	JAMA 2001 Jun;285(21):2719-28
30	Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial.	Lancet 2004 Jul 24-30;364(9431):331-7
31	Effects of cholesterol-lowering with simvastatin on stroke and other major vascular events in 20536 people with cerebrovascular disease or other high-risk conditions.	Lancet 2004 Mar;363(9411):757-67
32	Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack.	Lancet 2001 Sep;358(9287):1033-41
33	Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. Analysis of pooled data from five randomized controlled trials.	Arch Intern Med 1994 Jul;154(13):1449-57
34	Primary prevention of cardiovascular events with low-dose aspirin and vitamin E in type 2 diabetic patients: results of the Primary Prevention Project (PPP) trial.	Diabetes Care 2003 Dec;26(12):3264-72
35	Randomised trial of effects of calcium antagonists compared with diuretics and beta-blockers on cardiovascular morbidity and mortality in hypertension: the Nordic Diltiazem (NORDIL) study.	Lancet 2000 Jul;356(9227):359-65
36	Antiplatelet therapy for preventing stroke in patients with nonrheumatic atrial fibrillation and a history of stroke or transient ischemic attacks.	Cochrane Database Syst Rev 2000;(2):CD000186
37	Effects of losartan or atenolol in hypertensive patients without clinically evident vascular disease: a substudy of the LIFE randomized trial.	Ann Intern Med 2003 Aug;139(3):169-77
38	A clinical trial in type 2 diabetic nephropathy.	Am J Kidney Dis 2001 Oct;38(4 Suppl 1):S191-4
39	Comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis.	N Engl J Med 2005 Mar;352(13):1305-16
40	Dipyridamole for preventing stroke and other vascular events in patients with vascular disease.	Cochrane Database Syst Rev 2003;(1):CD001820
41	Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction.	N Engl J Med 2004 Sep;351(13):1285-95
42	Effects of low-dose angiotensin II receptor blocker candesartan on cardiovascular events in patients with coronary artery disease.	Am Heart J 2003 Dec;146(6):E20
43	Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators.	Lancet 1997 Sep;350(9080):757-64
44	Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial--Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial.	Lancet 2003 Apr;361(9364):1149-58
45	Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity the Swedish Trial in Old Patients with Hypertension-2 study.	Lancet 1999 Nov;354(9192):1751-6
46	Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial--Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial.	Drugs 2004;64 Suppl 2 0:43-60
47	PROGRESS (perindopril protection against recurrent stroke study): rationale and design. PROGRESS Management Committee [corrected].	J Hypertens 1995 Dec;13(12 Pt 2):1869-73
48	Morbidity and mortality in patients randomised to double-blind treatment with a long-acting calcium-channel blocker or diuretic in the International Nifedipine GITS study: Intervention as a Goal in Hypertension Treatment (INSIGHT).	Lancet 2000 Jul;356(9227):366-72
49	PROGRESS--perindopril protection against recurrent stroke study: status in July 1996. PROGRESS Management Committee.	J Hypertens Suppl 1996 Dec;14(6):S47-51
50	A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). CAPRIE Steering Committee.	Lancet 1996 Nov;348(9038):1329-39

図 4 L その他(06) (糖尿病, 脳卒中, 複合領域ほか) 26 ~ 50位

メタアナリシス (07)

	Title	Journal
1	<u>Intravenous glycoprotein IIb/IIIa receptor antagonists reduce mortality after percutaneous coronary interventions.</u>	J Am Coll Cardiol 2003 Jan;41(1):26-32
2	<u>Early vs late administration of glycoprotein IIb/IIIa inhibitors in primary percutaneous coronary intervention of acute ST-segment elevation myocardial infarction: a meta-analysis.</u>	JAMA 2004 Jul;292(3):362-6
3	<u>Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials.</u>	Lancet 2002 Jan;359(9302):189-98
4	<u>Health outcomes associated with calcium antagonists compared with other first-line antihypertensive therapies: a meta-analysis of randomised controlled trials.</u>	Lancet 2000 Dec;356(9246):1949-54
5	<u>Health outcomes associated with various antihypertensive therapies used as first-line agents: a network meta-analysis.</u>	JAMA 2003 May;289(19):2534-44
6	<u>Direct thrombin inhibitors in acute coronary syndromes: principal results of a meta-analysis based on individual patients' data.</u>	Lancet 2002 Jan;359(9303):294-302
7	<u>Improved clinical outcomes with abciximab therapy in acute myocardial infarction: a systematic overview of randomized clinical trials.</u>	Am Heart J 2004 Mar;147(3):457-62
8	<u>Effect of angiotensin converting enzyme inhibition on sudden cardiac death in patients following acute myocardial infarction. A meta-analysis of randomized clinical trials.</u>	J Am Coll Cardiol 1999 Mar;33(3):598-604
9	<u>Clinical outcomes of therapeutic agents that block the platelet glycoprotein IIb/IIIa integrin in ischemic heart disease.</u>	Circulation 1998 Dec 22-29;98(25):2829-35
10	<u>Meta-analysis of survival with platelet glycoprotein IIb/IIIa antagonists for percutaneous coronary interventions.</u>	Am J Cardiol 2003 Sep;92(6):651-5
11	<u>Use of statins in primary and secondary prevention of coronary heart disease and ischemic stroke. Meta-analysis of randomized trials.</u>	Int J Clin Pharmacol Ther 2003 Dec;41(12):567-77
12	<u>[The clinical use of the GPIIb/IIIa inhibitors eptifibatid and tirofiban in the treatment of acute coronary syndromes of the "non-ST elevation" type]</u>	Ital Heart J Suppl 2000 Feb;1(2):202-11
13	<u>Implantable defibrillators for the prevention of mortality in patients with nonischemic cardiomyopathy: a meta-analysis of randomized controlled trials.</u>	JAMA 2004 Dec;292(23):2874-9
14	<u>Platelet glycoprotein IIb/IIIa inhibitors reduce mortality in diabetic patients with non-ST-segment-elevation acute coronary syndromes.</u>	Circulation 2001 Dec;104(23):2767-71
15	<u>Effect of statins on risk of coronary disease: a meta-analysis of randomized controlled trials.</u>	JAMA 1999 Dec 22-29;282(24):2340-6
16	<u>Effect of prophylactic amiodarone on mortality after acute myocardial infarction and in congestive heart failure: meta-analysis of individual data from 6500 patients in randomized trials. Amiodarone Trials Meta-Analysis Investigators.</u>	Lancet 1997 Nov;350(9089):1417-24
17	<u>Efficacy and safety of abciximab on acute myocardial infarction treated with percutaneous coronary interventions: a meta-analysis of randomized, controlled trials.</u>	Am Heart J 2004 Dec;148(6):937-43
18	<u>The failure of orally administered glycoprotein IIb/IIIa inhibitors to prevent recurrent cardiac events.</u>	Am J Med 2002 Jun;112(8):647-58
19	<u>Health outcomes associated with antihypertensive therapies used as first-line agents. A systematic review and meta-analysis.</u>	JAMA 1997 Mar;277(9):739-45
20	<u>Increased mortality with oral platelet glycoprotein IIb/IIIa antagonists: a meta-analysis of phase III multicenter randomized trials.</u>	Circulation 2001 Jan;103(2):201-6
21	<u>Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. Blood Pressure Lowering Treatment Trialists' Collaboration.</u>	Lancet 2000 Dec;356(9246):1955-64
22	<u>Warfarin plus aspirin after myocardial infarction or the acute coronary syndrome: meta-analysis with estimates of risk and benefit.</u>	Ann Intern Med 2005 Aug;143(4):241-50
23	<u>Routine vs selective invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials.</u>	JAMA 2005 Jun;293(23):2908-17
24	<u>Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction: a systematic overview of data from individual patients. ACE-Inhibitor Myocardial Infarction Collaborative Group.</u>	Lancet 2000 May;355(9215):1575-81
25	<u>Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials.</u>	JAMA 1995 May;273(18):1450-6

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25	<u>Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials.</u>	JAMA 1995 May;273 (18):1450-6
26	<u>Effect of beta-blockade on mortality in patients with heart failure: a meta-analysis of randomized clinical trials.</u>	J Am Coll Cardiol 1997 Jul;30(1):27-34
27	<u>Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials.</u>	Lancet 2003 Nov;362 (9395):1527-35
28	<u>Effect of HMGcoA reductase inhibitors on stroke. A meta-analysis of randomized, controlled trials.</u>	Ann Intern Med 1998 Jan;128(2):89-95
29	<u>Clinical outcomes in statin treatment trials: a meta-analysis.</u>	Arch Intern Med 1999 Aug 9-23;159(15):1793-802
30	<u>Current evidence supporting the role of diuretics in heart failure: a meta analysis of randomised controlled trials.</u>	Int J Cardiol 2002 Feb;82 (2):149-58
31	<u>Effects of antibiotic therapy on outcomes of patients with coronary artery disease: a meta-analysis of randomized controlled trials.</u>	JAMA 2005 Jun;293 (21):2641-7
32	<u>Effect of glycoprotein IIb/IIIa inhibitors on the individual components of composite endpoints used in clinical trials of unstable angina and non-Q-wave myocardial infarction.</u>	Cardiovasc Drugs Ther 2000 Jun;14(3):253-8
33	<u>Platelet glycoprotein IIb/IIIa blockers for percutaneous coronary revascularization, and unstable angina and non-ST-segment elevation myocardial infarction.</u>	Cochrane Database Syst Rev 2001;(4):CD002130
34	<u>Cardiac resynchronization and death from progressive heart failure: a meta-analysis of randomized controlled trials.</u>	JAMA 2003 Feb;289 (6):730-40
35	[Does statin therapy reduce the risk of stroke? A meta-analysis]	Ann Med Interne (Paris) 2001 Apr;152(3):188-93
36	<u>Cardiovascular protection and blood pressure reduction: a meta-analysis.</u>	Lancet 2001 Oct;358 (9290):1305-15
37	<u>Transfer for primary angioplasty versus immediate thrombolysis in acute myocardial infarction: a meta-analysis.</u>	Circulation 2003 Oct;108 (15):1809-14
38	<u>Lack of benefit from intravenous platelet glycoprotein IIb/IIIa receptor inhibition as adjunctive treatment for percutaneous interventions of aortocoronary bypass grafts: a pooled analysis of five randomized clinical trials.</u>	Circulation 2002 Dec;106 (24):3063-7
39	<u>Effects of acadesine on myocardial infarction, stroke, and death following surgery. A meta-analysis of the 5 international randomized trials. The Multicenter Study of Perioperative Ischemia (McSPI) Research Group.</u>	JAMA 1997 Jan 22-29;277(4):325-32
40	<u>Risks and benefits of glycoprotein IIb/IIIa antagonists in acute coronary syndrome.</u>	Ann Pharmacother 2001 Apr;35(4):472-9
41	<u>Effect of glycoprotein IIb/IIIa receptor blocker abciximab on outcome in patients with acute coronary syndromes without early coronary revascularisation: the GUSTO IV-ACS randomised trial.</u>	Lancet 2001 Jun;357 (9272):1915-24
42	<u>Primary stenting versus primary balloon angioplasty for treating acute myocardial infarction.</u>	Cochrane Database Syst Rev 2005;(2):CD005313
43	<u>Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review.</u>	JAMA 1997 Dec;278 (23):2093-8
44	<u>Safety outcomes in meta-analyses of phase 2 vs phase 3 randomized trials: Intracranial hemorrhage in trials of bolus thrombolytic therapy.</u>	JAMA 2001 Jan 24-31;285(4):444-50
45	<u>Thrombolysis for acute ischaemic stroke.</u>	Cochrane Database Syst Rev 2003;(3):CD000213
46	<u>Angioplasty and stents in coronary artery disease: a systematic review and meta-analysis.</u>	Scand Cardiovasc J 2004 Aug;38(4):200-10
47	<u>Cholesterol lowering with statin drugs, risk of stroke, and total mortality. An overview of randomized trials.</u>	JAMA 1997 Jul 23-30;278(4):313-21
48	<u>Effect of smoking status and abciximab use on outcome after percutaneous coronary revascularization: Pooled analysis from EPIC, EPILOG, and EPISTENT.</u>	Am Heart J 2001 Apr;141 (4):599-602
49	<u>Clinical outcomes of bivalirudin for ischemic heart disease.</u>	Circulation 1999 Nov;100 (20):2049-53
50	<u>Amiodarone prophylaxis reduces major cardiovascular morbidity and length of stay after cardiac surgery: a meta-analysis.</u>	Ann Intern Med 2005 Sep;143(5):327-36

図 4 n メタアナリシス (07) 26 ~ 50 位

	Title	Journal
1	Characteristics of 9194 patients with left ventricular hypertrophy: the LIFE study. Losartan Intervention For Endpoint Reduction in Hypertension.	Hypertension 1998 Dec;32(6):989-97
2	Trends in the incidence of outcomes defining acquired immunodeficiency syndrome (AIDS) in the Multicenter AIDS Cohort Study: 1985-1991.	Am J Epidemiol 1993 Feb;137(4):423-38
3	Impaired glucose tolerance in obesity is associated with insensitivity to insulin in multiple aspects of metabolism as assessed by a low dose incremental insulin infusion technique.	Diabet Med 1991 Oct;8(8):718-25
4	The independent effect of type 2 diabetes mellitus on ischemic heart disease, stroke, and death: a population-based study of 13,000 men and women with 20 years of follow-up.	Arch Intern Med 2004 Jul;164(13):1422-6
5	The Losartan Intervention For Endpoint reduction (LIFE) in Hypertension study: rationale, design, and methods. The LIFE Study Group.	Am J Hypertens 1997 Jul;10(7 Pt 1):705-13
6	Regression of electrocardiographic left ventricular hypertrophy by losartan versus atenolol: The Losartan Intervention for Endpoint reduction in Hypertension (LIFE) Study.	Circulation 2003 Aug;108(6):684-90
7	Regression of electrocardiographic left ventricular hypertrophy during antihypertensive treatment and the prediction of major cardiovascular events.	JAMA 2004 Nov;292(19):2343-9
8	Baseline characteristics in relation to electrocardiographic left ventricular hypertrophy in hypertensive patients: the Losartan intervention for endpoint reduction (LIFE) in hypertension study. The Life Study Investigators.	Hypertension 2000 Nov;36(5):766-73
9	Population impact of losartan use on stroke in the European Union (EU): projections from the Losartan Intervention For Endpoint reduction in hypertension (LIFE) study.	J Hum Hypertens 2004 Jun;18(6):367-73
10	Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol.	Lancet 2002 Mar;359(9311):995-1003
11	Effects of losartan on cardiovascular morbidity and mortality in patients with isolated systolic hypertension and left ventricular hypertrophy: a Losartan Intervention for Endpoint Reduction (LIFE) substudy.	JAMA 2002 Sep;288(12):1491-8
12	Relation of QT interval and QT dispersion to regression of echocardiographic and electrocardiographic left ventricular hypertrophy in hypertensive patients: the Losartan Intervention For Endpoint Reduction (LIFE) study.	Am Heart J 2003 May;145(5):919-25
13	Cardiovascular morbidity and mortality in patients with diabetes in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol.	Lancet 2002 Mar;359(9311):1004-10
14	Effects of losartan or atenolol in hypertensive patients without clinically evident vascular disease: a substudy of the LIFE randomized trial.	Ann Intern Med 2003 Aug;139(3):169-77
15	Progressive hypertrophy regression with sustained pressure reduction in hypertension: the Losartan Intervention For Endpoint Reduction study.	J Hypertens 2002 Jul;20(7):1445-50
16	Relation of echocardiographic left ventricular mass and hypertrophy to persistent electrocardiographic left ventricular hypertrophy in hypertensive patients: the LIFE Study.	Am J Hypertens 2001 Aug;14(8 Pt 1):775-82
17	Regression of hypertensive left ventricular hypertrophy by losartan compared with atenolol: the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) trial.	Circulation 2004 Sep;110(11):1456-62
18	The Effect of Losartan Versus Atenolol on Cardiovascular Morbidity and Mortality in Patients With Hypertension Taking Aspirin The Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) Study.	J Am Coll Cardiol 2005 Sep;46(5):770-5
19	Lowering of blood pressure and predictors of response in patients with left ventricular hypertrophy: the LIFE study. Losartan Intervention For Endpoint.	Am J Hypertens 2000 Aug;13(8):899-906
20	QRS duration and QT interval predict mortality in hypertensive patients with left ventricular hypertrophy: the Losartan Intervention for Endpoint Reduction in Hypertension Study.	Hypertension 2004 May;43(5):1029-34
21	Risk of new-onset diabetes in the Losartan Intervention For Endpoint reduction in hypertension study.	J Hypertens 2002 Sep;20(9):1879-86
22	Use of losartan in diabetic patients in the primary care setting: review of the results in LIFE and RENAAL.	Curr Med Res Opin 2004 Dec;20(12):1909-17
23	The stroke volume/pulse pressure ratio predicts coronary heart disease mortality in a population of elderly men.	J Hypertens 2004 May;22(5):899-905
24	Cardiovascular morbidity and mortality in hypertensive patients with a history of atrial fibrillation: The Losartan Intervention For End Point Reduction in Hypertension (LIFE) study.	J Am Coll Cardiol 2005 Mar;45(5):705-11
25	The effects of losartan compared to atenolol on stroke in patients with isolated systolic hypertension and left ventricular hypertrophy. The LIFE study.	J Clin Hypertens (Greenwich) 2005 Mar;7(3):152-8

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25	The effects of losartan compared to atenolol on stroke in patients with isolated systolic hypertension and left ventricular hypertrophy. The LIFE study.	J Clin Hypertens (Greenwich) 2005 Mar;7(3):152-8
26	Prognostic value of a new electrocardiographic method for diagnosis of left ventricular hypertrophy in essential hypertension.	J Am Coll Cardiol 1998 Feb;31(2):383-90
27	Losartan benefits over atenolol in non-smoking hypertensive patients with left ventricular hypertrophy: the LIFE study.	Blood Press 2004;13(6):376-84
28	Relationship of the electrocardiographic strain pattern to left ventricular structure and function in hypertensive patients: the LIFE study. Losartan Intervention For End point.	J Am Coll Cardiol 2001 Aug;38(2):514-20
29	[The effect of losartan versus atenolol on cardiovascular morbidity and mortality in patients with hypertension and ECG-verified left ventricular hypertrophy in the LIFE-study]	Ugeskr Laeger 2003 Jan;165(5):456-9
30	Electrocardiographic strain pattern and prediction of cardiovascular morbidity and mortality in hypertensive patients.	Hypertension 2004 Jul;44(1):48-54
31	Cardiovascular risk reduction in hypertensive black patients with left ventricular hypertrophy: the LIFE study.	J Am Coll Cardiol 2004 Mar;43(6):1047-55
32	Changes in survival after acquired immunodeficiency syndrome (AIDS): 1984-1991.	Am J Epidemiol 1993 Dec;138(11):952-64
33	Body mass index and mortality from cardiovascular disease among Japanese men and women: the JACC study.	Stroke 2005 Jul;36(7):1377-82
34	Improved cardiovascular risk stratification by a simple ECG index in hypertension.	Am J Hypertens 2003 Aug;16(8):646-52
35	Cost effectiveness of losartan in patients with hypertension and LVH: an economic evaluation for Sweden of the LIFE trial.	J Hypertens 2005 Jul;23(7):1425-31
36	The prognostic characteristics of hypertensive left ventricular hypertrophy in a population with low prevalence of hypertension and low plasma cholesterol.	Chin Med Sci J 1993 Dec;8(4):197-202
37	Stroke reduction in hypertensive adults with cardiac hypertrophy randomized to losartan versus atenolol: the Losartan Intervention For Endpoint reduction in hypertension study.	Hypertension 2005 Jan;45(1):46-52
38	Long-term plasma catecholamines in patients with hypertension and left ventricular hypertrophy treated with losartan or atenolol: ICARUS, a LIFE substudy.	J Hum Hypertens 2004 Jun;18(6):375-80
39	The impact of serum uric acid on cardiovascular outcomes in the LIFE study.	Kidney Int 2004 Mar;65(3):1041-9
40	[Treatment of hypertension in patients with left ventricular hypertrophy]	Tidsskr Nor Laegeforen 2004 Mar;124(6):788-91
41	Diabetes mellitus, impaired glucose tolerance, and hyperinsulinemia in an elderly population. The Rotterdam Study.	Am J Epidemiol 1997 Jan;145(1):24-32
42	The ischemic electrocardiogram: a harbinger for ischemic heart disease independent of the blood pressure level. The Copenhagen City Heart Study.	Eur J Epidemiol 2005;20(4):301-9
43	Body weight change, all-cause mortality, and cause-specific mortality in the Multiple Risk Factor Intervention Trial.	Ann Intern Med 1993 Oct;119(7 Pt 2):749-57
44	Increased prevalence of left ventricular hypertrophy in hypertensive women with type 2 diabetes mellitus.	Cardiovasc Diabetol 2003 Nov;2(0):14
45	Risk factors for the development of type II diabetes among men enrolled in the usual care group of the Multiple Risk Factor Intervention Trial.	Diabetes Care 1993 Oct;16(10):1331-9
46	Angiotensin II receptor blockade reduces new-onset atrial fibrillation and subsequent stroke compared to atenolol: the Losartan Intervention For End Point Reduction in Hypertension (LIFE) study.	J Am Coll Cardiol 2005 Mar;45(5):712-9
47	Hypertension as a risk factor for cardiovascular morbidity and mortality in an elderly German population; the prospective STEPHY II study. Starnberg Study on Epidemiology of Parkinsonism and Hypertension in the Elderly.	Eur Heart J 1999 Dec;20(23):1752-6
48	Impact of atrial fibrillation on the risk of death: the Framingham Heart Study.	Circulation 1998 Sep;98(10):946-52
49	Left ventricular hypertrophy as a predictor of coronary heart disease mortality and the effect of hypertension.	Am Heart J 2000 Dec;140(6):848-56
50	Echocardiographic and electrocardiographic diagnoses of left ventricular hypertrophy predict mortality independently of each other in a population of elderly men.	Circulation 2001 May;103(19):2346-51

図 4 q 疫 学(09) 2 6 ~ 5 0 位

その他(10) (選択的 COX-2 阻害薬)

	Title	Journal
1	Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (TARGET), reduction in ulcer complications: randomised controlled trial.	Lancet 2004 Aug 21-27;364(9435):665-74
2	Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial.	N Engl J Med 2005 Mar;352(11):1092-102
3	Risk of cardiovascular events and rofecoxib: cumulative meta-analysis.	Lancet 2004 Dec 4-10;364(9450):2021-9
4	Cardiovascular risk associated with celecoxib in a clinical trial for colorectal adenoma prevention.	N Engl J Med 2005 Mar;352(11):1071-80
5	Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (TARGET), cardiovascular outcomes: randomised controlled trial.	Lancet 2004 Aug 21-27;364(9435):675-84
6	Risk of cardiovascular events associated with selective COX-2 inhibitors.	JAMA 2001 Aug 22-29;286(8):954-9
7	Complications of the COX-2 inhibitors parecoxib and valdecoxib after cardiac surgery.	N Engl J Med 2005 Mar;352(11):1081-91
8	Cardiovascular thrombotic events in arthritis trials of the cyclooxygenase-2 inhibitor celecoxib.	Am J Cardiol 2003 Aug;92(4):411-8
9	Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. VIGOR Study Group.	N Engl J Med 2000 Nov;343(21):1520-8, 2 p following 1528
10	Therapeutic arthritis research and gastrointestinal event trial of lumiracoxib - study design and patient demographics.	Aliment Pharmacol Ther 2004 Jul;20(1):51-63
11	Cardiovascular thrombotic events in controlled, clinical trials of rofecoxib.	Circulation 2001 Nov;104(19):2280-8
12	Selective cyclooxygenase-2 inhibition and cardiovascular effects: an observational study of a Medicaid population.	Arch Intern Med 2005 Jan;165(2):181-6
13	Gastrointestinal tolerability and effectiveness of rofecoxib versus naproxen in the treatment of osteoarthritis: a randomized, controlled trial.	Ann Intern Med 2003 Oct;139(7):539-46
14	Rofecoxib for rheumatoid arthritis.	Cochrane Database Syst Rev 2005;(1):CD003685
15	Risk of myocardial infarction in patients taking cyclo-oxygenase-2 inhibitors or conventional non-steroidal anti-inflammatory drugs: population based nested case-control analysis.	BMJ 2005 Jun;330(7504):1366
16	Rofecoxib for osteoarthritis.	Cochrane Database Syst Rev 2005;(1):CD005115
17	A comparison of reported gastrointestinal and thromboembolic events between rofecoxib and celecoxib using observational data.	Drug Saf 2005;28(9):803-16
18	Comparison of thromboembolic events in patients treated with celecoxib, a cyclooxygenase-2 specific inhibitor, versus ibuprofen or diclofenac.	Am J Cardiol 2002 Feb;89(4):425-30
19	Rofecoxib for the treatment of rheumatoid arthritis.	Cochrane Database Syst Rev 2002;(3):CD003685
20	Incidence of thrombotic cardiovascular events in patients taking celecoxib compared with those taking rofecoxib: interim results from the New Zealand Intensive Medicines Monitoring Programme.	Drug Saf 2005;28(5):435-42
21	Effect of selective cyclooxygenase 2 inhibitors and naproxen on short-term risk of acute myocardial infarction in the elderly.	Arch Intern Med 2003 Feb;163(4):481-6
22	A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women.	N Engl J Med 2005 Mar;352(13):1293-304
23	The gastrointestinal safety of the COX-2 selective inhibitor etoricoxib assessed by both endoscopy and analysis of upper gastrointestinal events.	Am J Gastroenterol 2003 Aug;98(8):1725-33
24	Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators.	N Engl J Med 2000 Jan;342(3):145-53
25	Vitamin E supplementation and cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators.	N Engl J Med 2000 Jan;342(3):154-60

図 4 r その他(10) (選択的 COX-2 阻害薬) 1 ~ 2 5 位

26	Patients exposed to rofecoxib and celecoxib have different odds of nonfatal myocardial infarction.	Ann Intern Med 2005 Feb;142(3):157-64
27	Incidence of gastroduodenal ulcers in patients with rheumatoid arthritis after 12 weeks of rofecoxib, naproxen, or placebo: a multicentre, randomised, double blind study.	Gut 2003 Jun;52(6):820-6
28	Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (the EUROPA study).	Lancet 2003 Sep;362 (9386):782-8
29	Single dose oral rofecoxib for postoperative pain.	Cochrane Database Syst Rev 2005;(1):CD004604
30	Efficacy and safety of low-dose aspirin in polycythemia vera.	N Engl J Med 2004 Jan;350(2):114-24
31	Angiotensin-converting-enzyme inhibition in stable coronary artery disease.	N Engl J Med 2004 Nov;351(20):2058-68
32	Final report on the aspirin component of the ongoing Physicians' Health Study. Steering Committee of the Physicians' Health Study Research Group.	N Engl J Med 1989 Jul;321(3):129-35
33	Reduced incidence of gastroduodenal ulcers associated with lumiracoxib compared with ibuprofen in patients with rheumatoid arthritis.	Aliment Pharmacol Ther 2004 Jun;19(11):1189-98
34	Relationship between selective cyclooxygenase-2 inhibitors and acute myocardial infarction in older adults.	Circulation 2004 May;109 (17):2068-73
35	Oral ximelagatran for secondary prophylaxis after myocardial infarction: the ESTEEM randomised controlled trial.	Lancet 2003 Sep;362 (9386):789-97
36	Risk of acute myocardial infarction and sudden cardiac death in patients treated with cyclo-oxygenase 2 selective and non-selective non-steroidal anti-inflammatory drugs: nested case-control study.	Lancet 2005 Feb 5-11;365(9458):475-81
37	The Effects of cyclooxygenase-2 inhibitors and nonsteroidal anti-inflammatory therapy on 24-hour blood pressure in patients with hypertension, osteoarthritis, and type 2 diabetes mellitus.	Arch Intern Med 2005 Jan;165(2):161-8
38	Serious lower gastrointestinal clinical events with nonselective NSAID or coxib use.	Gastroenterology 2003 Feb;124(2):288-92
39	Rofecoxib for the treatment of rheumatoid arthritis.	Cochrane Database Syst Rev 2002;(2):CD003685
40	The upper gastrointestinal safety of rofecoxib vs. NSAIDs: an updated combined analysis.	Curr Med Res Opin 2004 Oct;20(10):1539-48
41	Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis.	N Engl J Med 2005 Jul;353(3):238-48
42	Nonsteroidal anti-inflammatory drugs and aspirin for the prevention of colorectal adenomas and cancer: a systematic review.	Dis Colon Rectum 2004 May;47(5):665-73
43	Cyclo-oxygenase-2 inhibitors versus non-selective non-steroidal anti-inflammatory drugs and congestive heart failure outcomes in elderly patients: a population-based cohort study.	Lancet 2004 May;363 (9423):1751-6
44	Adverse events associated with rofecoxib therapy: results of a large study in community-derived osteoarthritic patients.	Drug Saf 2003;26(1):49-54
45	Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both.	N Engl J Med 2003 Nov;349(20):1893-906
46	Effect of angiotensin-converting-enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: the Captopril Prevention Project (CAPPP) randomised trial.	Lancet 1999 Feb;353 (9153):611-6
47	Gastrointestinal tolerability of the selective cyclooxygenase-2 (COX-2) inhibitor rofecoxib compared with nonselective COX-1 and COX-2 inhibitors in osteoarthritis.	Arch Intern Med 2000 Oct;160(19):2998-3003
48	The effectiveness of five strategies for the prevention of gastrointestinal toxicity induced by non-steroidal anti-inflammatory drugs: systematic review.	BMJ 2004 Oct;329 (7472):948
49	Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. Collaborative Group of the Primary Prevention Project.	Lancet 2001 Jan;357 (9250):89-95
50	The cyclooxygenase-2-selective inhibitors rofecoxib and celecoxib prevent colorectal neoplasia occurrence and recurrence.	Gastroenterology 2003 Aug;125(2):404-12

図 4 s その他(10) (選択的 COX-2 阻害薬) 26 ~ 50 位

表 1 虚血性心疾患の教師データを細分類したことの効果。

	薬 (58)	*	ステント (22)	*	手術 (5)	*
1	A clinical trial comparing primary coronary angioplasty with tissue plasminogen activator for acute myocardial infarction. The Global Use of Strategies to Open Occluded Coronary Arteries in Acute Coronary Syndromes (GUSTO IIb) Angioplasty Substudy Investigators	10	Coronary-artery stenting compared with balloon angioplasty for restenosis after initial balloon angioplasty. Restenosis Stent Study Group.	21	A randomized study of coronary angioplasty compared with bypass surgery in patients with symptomatic multivessel coronary disease. German Angioplasty Bypass Surgery Investigation (GABI)	-
2	Inhibition of platelet glycoprotein IIb/IIIa with eptifibatid in patients with acute coronary syndromes. The PURSUIT Trial Investigators. Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy.	30	Stent placement compared with balloon angioplasty for small coronary arteries: in-hospital and 6-month clinical and angiographic results.	107	A randomized trial comparing coronary angioplasty with coronary bypass surgery. Emory Angioplasty versus Surgery Trial (EAST)	100
3	Effect of nicorandil on coronary events in patients with stable angina: the Impact Of Nicorandil in Angina (IONA) randomised trial.	48	Randomized comparison of coronary stent implantation and balloon angioplasty in the treatment of de novo coronary artery lesions (START): a four-year follow-up.	7	A multi-centre randomised controlled trial of minimally invasive direct coronary bypass grafting versus percutaneous transluminal coronary angioplasty with stenting for proximal stenosis of the left anterior descending coronary artery.	-
4	Long-term benefit of primary angioplasty as compared with thrombolytic therapy for acute myocardial infarction.	17	Latin American randomized trial of balloon angioplasty vs coronary stenting for small vessels (LASMAL): immediate and long-term results.	13	Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. The Bypass Angioplasty Revascularization Investigation (BARI)	-

					Investigators.	
5	Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study.	2 5	A randomized trial comparing stenting with balloon angioplasty in small vessels in patients with symptomatic coronary artery disease. ISAR-SMART Study Investigators. Intracoronary Stenting or Angioplasty for Restenosis Reduction in Small Arteries.	3	Three-year outcome after coronary stenting versus bypass surgery for the treatment of multivessel disease.	-

メタ分析文獻数: 34									
1.5 cardiovascular									1
1.2 event									3
1.0 placebo									1
1.0 group									4
1.0 risk									3
1.0 patient									1
0.9 Cholesterol									6
0.9 Coronary_Disease									4
0.9 percent									1
0.9 women									6
0.8 level									4
0.8 CHD									9
0.8 year									6
0.8 atorvastatin									9
0.8 effect									6
0.7 Myocardial_Infarction									9
0.7 mean									6
0.7 trial									9
0.7 pressure									9
0.7 Coronary_Atherosclerosis									13
0.7 study									9
0.7 Estrogens									13
0.6 coronary									9
0.6 95									13
0.6 primary									9
0.6 progression									13
0.6 endpoint									9
0.6 therapy									13
0.6 death									9
0.6 stable									13
0.6 blood									9
0.6 treatment									13

1									Intensive lipid lowering with atorvastatin in patients with stable coronary disease. [15756765]
1									Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group. [10436259]
1									Aggressive lipid-lowering therapy compared with angioplasty in stable coronary artery disease. Atorvastatin versus Revascularization Treatment Investigators. [10395630]
1									Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study: a randomized controlled trial. [1127825]
1									Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. [2686036]
1									Simvastatin and niacin, antioxidant vitamins, or the combination for the prevention of coronary disease. [11757504]
1									Effects of estrogen replacement on the progression of coronary-artery atherosclerosis. [10954759]
1									Hormone therapy and the progression of coronary-artery atherosclerosis in postmenopausal women. [12904518]
1									Estrogen plus progestin and the risk of coronary heart disease. [12904517]
1									Effect of antihypertensive agents on cardiovascular events in patients with coronary disease and normal blood pressure: the CAMELOT study: a randomized controlled trial. [15536108]
1									Effect of amlodipine on the progression of atherosclerosis and the occurrence of clinical events. PREVENT Investigators. [11004140]
1									Effects of low-dose angiotensin II receptor blocker candesartan on cardiovascular events in patients with coronary artery disease. [14661009]
1									Effect of trapidil on cardiovascular events in patients with coronary artery disease (results from the Japan Multicenter Investigation for Cardiovascular Diseases-Mochida [JMID-M]). [14518877]
1									Clinical characteristics and mortality of patients screened for entry into the Trandolapril Cardiac Evaluation (TRACE) study. [7933993]
1									The TRAndolapril Cardiac Evaluation (TRACE) study: rationale, design, and baseline characteristics of the screened population. The Trace Study Group. [8166055]
1									A clinical trial of the angiotensin-converting-enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. Trandolapril Cardiac Evaluation (TRACE) Study Group. [7477219]
1									Angiotensin-converting-enzyme inhibition in stable coronary artery disease. [15531767]
1									Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: the CAPRICORN randomised trial. [11356434]
1									Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (the EUROPA study). [13678872]
1									Effect of long-acting nifedipine on mortality and cardiovascular morbidity in patients with stable angina requiring treatment (ACTION trial): randomised controlled trial. [15351192]
1									Comparison of nifedipine retard with angiotensin converting enzyme inhibitors in Japanese hypertensive patients with coronary artery disease: the Japan Multicenter Investigation for Cardiovascular Diseases-B (JMID-B) randomized trial. [15080377]
1									Effects of pravastatin in 3260 patients with unstable angina: results from the LIPID study. [11130382]
1									Effects of physiologic pacing versus ventricular pacing on the risk of stroke and death due to cardiovascular causes. Canadian Trial of Physiologic Pacing Investigators. [10805823]
1									Comparison of the effects of beta blockers and calcium antagonists on cardiovascular events after acute myocardial infarction in Japanese subjects. [15061437]
1									Oestrogen therapy for prevention of reinfarction in postmenopausal women: a randomised placebo controlled trial. [12504395]
1									Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial.
1									Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. Collaborative Group of the Primary Prevention Project. [11197445]
1									Determination of who may derive most benefit from aspirin in primary prevention: subgroup results from a randomised controlled trial. [10875825]
1									Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico. [10465168]
1									Randomised double-blind trial of fixed low-dose warfarin with aspirin after myocardial infarction. Coumadin Aspirin Reinfarction Study (CARS) Investigators. [9259652]
1									Blood pressure and risk of secondary cardiovascular events in women: the Women's Antioxidant Cardiovascular Study (WACS). [15023883]
1									MRC/BHF Heart Protection Study of antioxidant vitamin supplementation in 20,536 high-risk individuals: a randomised placebo-controlled trial. [12114037]
1									The effect of vitamin therapy on the progression of coronary artery atherosclerosis varies by haptoglobin type in postmenopausal women. [15047650]
1									The microsomal triglyceride transfer protein gene-493T variant lowers cholesterol but increases the risk of coronary heart disease. [15136504]

図5 (b) 第2クラス

メンバー文献数: 26 特徴的な語: 1.1 patient 1.0 LEPR 1.0 group 0.9 risk 0.9 type 0.8 pressure 0.8 control 0.8 blood 0.8 year 0.8 renal 0.8 percent 0.7 cardiovascular 0.7 Hg 0.7 hypertension 0.7 compare 0.7 Disease 0.6 level 0.6 95 0.6 serum 0.6 effect 0.6 placebo 0.6 treatment 0.6 primary 0.6 Ramipril 0.6 end 0.6 Amlodipine		1	Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. [11565518]	
		3 (1:1:1)	The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. [11565519]	
		5 (3:1:1)	Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. [10639539]	
		8 (5:1:1:1)	Effects of low dose ramipril on cardiovascular and renal outcomes in patients with type 2 diabetes and raised excretion of urinary albumin: randomised, double blind, placebo controlled trial (the DIABHYCAR study). [14960504]	
		1	Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. [12565541]	
		1	Effect of ramipril vs amlodipine on renal outcomes in hypertensive nephrosclerosis: a randomized controlled trial. [11386927]	
		1	The effect of nisoldipine as compared with enalapril on cardiovascular outcomes in patients with non-insulin-dependent diabetes and hypertension. [8466993]	
		1	Angiotensin-receptor blockade versus converting-enzyme inhibition in type 2 diabetes and nephropathy. [15516696]	
		18 (8:3:2:1:1:1:1)	2 (1:1)	Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. [9732337]
		3 (2:1)	1	Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. UK Prospective Diabetes Study Group. [9732338]
	20 (18:2)		1	Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. [9742976]
	23 (20:1:1:1)		2 (1:1)	1 Postmenopausal hormone therapy and risk of stroke: The Heart and Estrogen/progestin Replacement Study (HERS). [11156873]
			1	1 A clinical trial of estrogen-replacement therapy after ischemic stroke. [11680444]
			1	Combination treatment of angiotensin-II receptor blocker and angiotensin-converting-enzyme inhibitor in non-diabetic renal disease (COOPERATE): a randomised controlled trial. [12531578]
			1	Renoprotective effect of losartan in comparison to amlodipine in patients with chronic kidney disease and hypertension—a report of the Japanese Losartan Therapy Intended for the Global Renal Protection in Hypertensive Patients (JLIGHT) study. [1505252]
			1	Reduction of stroke incidence after myocardial infarction with pravastatin: the Cholesterol and Recurrent Events (CARE) study. The Care Investigators. [9692586]
			1	Outcome results of the Fosinopril Versus Amlodipine Cardiovascular Events Randomized Trial (FACET) in patients with hypertension and NIDDM. [9571349]
			1	Randomized, double-blind, placebo-controlled, international trial of the oral IIb/IIIa antagonist tirofiban in coronary and cerebrovascular disease. [12874182]
		2 (1:1)	1	Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. [15325633]
			1	Effect of fluvastatin on cardiac outcomes in renal transplant recipients: a multicentre, randomised, placebo-controlled trial. [12814712]
			1	Everolimus for the prevention of allograft rejection and vasculopathy in cardiac-transplant recipients. [12944570]
			1	Serum uric acid and cardiovascular mortality: the NHANES I epidemiologic follow-up study, 1971-1992. National Health and Nutrition Examination Survey. [10815083]
			1	Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. [11136953]
		1	Baseline characteristics of participants in phase I of the Trials of Hypertension Prevention. [1342280]	
		1	Alcohol consumption and breast cancer oestrogen and progesterone receptor status. [10098777]	
		1	N-Acetylcysteine versus lenalidopam mesylate to prevent contrast agent-associated nephrotoxicity. [15312855]	
メンバー文献数: 12 特徴的な語: 1.0 Aspirin 1.4 patient 1.4 stroke 1.4 ischaemic 1.2 recurrent 1.0 Warfarin 0.9 randomised 0.9 treatment 0.9 prevention 0.9 superior 0.8 risk 0.8 acute		1	Tinzaparin in acute ischaemic stroke (TAIST): a randomised aspirin-controlled trial. [11551576]	
		2 (1:1)	1	Low molecular-weight heparin versus aspirin in patients with acute ischaemic stroke and atrial fibrillation: a double-blind randomised study. HAEST Study Group. Heparin in Acute Embolic Stroke Trial. [10770301]
		4 (2:1:1)	1	Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial. [15276392]
		8 (4:3:1)	1	Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack. [11589932]
			1	A comparison of warfarin and aspirin for the prevention of recurrent ischemic stroke. [11794192]
		3 (1:1:1)	1	Long-term, low-intensity warfarin therapy for the prevention of recurrent venous thromboembolism. [12601075]
			1	Aspirin and ticlopidine for prevention of recurrent stroke in black patients: a randomized trial. [12799402]
			1	Efficacy of oral anticoagulants compared with aspirin after infrainguinal bypass surgery (The Dutch Bypass Oral Anticoagulants or Aspirin Study): a randomised trial. [10665553]
			1	Too little aspirin for secondary prevention after acute myocardial infarction in patients at high risk for cardiovascular events: Results from the MITRA study. [15309001]
			1	The ACCESS Study: evaluation of Acute Candesartan Cilixetil Therapy in Stroke Survivors. [12817109]
		1	Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. [15136594]	
		1	Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomized trial. [12086780]	

図6 (糖尿病, 脳卒中, 複合領域ほか) の
教師データのクラスタリング結果
緑: 脳 ピンク: 腎

D. 考察

連想検索による Pubmed データの分類の結果

図4gは「高血圧」に関する教師データ20文献を連想検索の種文書として与え、連想検索結果の上位を示したものである。灰色でハッチングがかかっているものは教師データとして用いたもので、それ以外が新たに引きあがった文献ということになる。上位に来ている文献はいずれも関連性の非常に高い文献であると判断される。

教師データが均一性と検索結果には相関があり、均一性が高いほど良い結果が得られている。高血圧の場合は均一性が比較的高いと判断される。

虚血性心疾患の場合には教師データ数が115件と多いこともあり、均一性が相対的に低いと考えられ、あらためて、「薬」「ステント」「手術」の3つのカテゴリに細分類を行って、各サブカテゴリごとに連想検索を実施した。

表1は各サブカテゴリの連想順位上位5位を示したものである。(検索結果から教師データは除いている。)

細分類を行わなかった場合との対比が分かるように、各文献の右となりに、全体を一枚岩で検索を行った場合の結果における順位を示している。例えば一番左上隅の文献は教師データ115件全部を使って検索した場合には10位で検索され、薬に限った58件の教師データから検索した場合には1位となったことを示している。

ほとんどの場合に、全体での順位よりもサブカテゴリでの順位の方が上位になっており、細分類により、よりシャープな検索結果が得られていることが分かる。

教師データの自動分類(クラスタリング)の結果

このように教師データが多くなり、均質性が低くなってきた場合には細分類を行うことが有効であるが、それを人手で行うことはコストが高い。そのため機械的な分類手法を適用して分類の

下準備を行うことはその後で人手で分類するにしても時間の短縮など大きなコスト削減効果が期待される。このような観点から虚血性心疾患の教師データの自動分類(クラスタリング)を実施した。クラスタリングに用いた手法は文書間距離に基づくボトムアップクラスタリングである。距離の近い文書から順にクラスタを形成し。クラスタ同士の距離はクラスタの重心に相当するベクトルを用いた。

図5は虚血性心疾患に関する教師データのクラスタリング結果である。図が大きいためトップレベルの3クラスタで分けて示した。図が小さく見づらいがグレーの部分が右から左にボトムアップにクラスタが形成される様を示している。

末端ノードに相当する文献に色を付けているのは、先に人間の判断で「薬(ピンク)」「ステント(緑)」「手術(青)」と分類したものである。

自動クラスタリングの結果とこの色分けがより符合しているほど好ましい。結果としては完全ではないもののかなり良い符合を示している。第3クラスタは「薬」のみとなっており、第2クラスタも1つのステントと例外的なもの(オレンジ、くすんだ緑、茶色)を除いて残りは「薬」となっている。

第1クラスタはこれらに比べると均質とは言えないが、主に「ステント」で構成され、「薬」が一部小さなサブカテゴリを示している。

問題となる点としては、「手術」の青が分散していることである。この分類は単語の分布のみではうまく特徴を捉えられないカテゴリであると考えられる。

次の図6は同様に、その他の項目(糖尿病、脳卒中、複合領域ほか)の教師データを機械的にクラスタリングした結果である。さきほどと同様人間の目を見た判断により色分けがなされており、ピンク色は[脳]関係、緑色は[腎]関係と判断された文献である。今回はトップクラスタが2つになっており、第2クラスタは[脳]のみ、また第1クラスタは緑色の[腎]がドミナントで、若干[脳]が混ざるといった結果となった。

この場合にも機械的なクラスタリングの結果と人間の判断による分類は比較的良く符号していると言えるだろう。

E. 結論

医療安全の実現のためには、科学的証拠に基づいた医療、すなわち EBM の実践が重要である。EBM の基本は文献情報であるが、年々加速度的に文献情報は増えており、その中から自分が課題に適合した文献を検索してこることは難しく成りつつある。本研究に於いて、少数の教師データ(教師文献データ)を用いて、数十万件の既存の Pubmed データから類似した文献を自動的に検索してこることが可能であることを示すことができた。

これは膨大な文献情報から個々の課題に対応した文献を自動的に抽出し、EBM 実現の基礎資料とすることの可能性を示唆するものである。

また、文献抽出の自動化に向けた試みとして、教師データの分類をクラスタリングにより行えることを示せた。

一方で、教師データをより洗練することにより、よりよい結果が得られたことや、クラスタリングの結果も完全に人間の判断と一致しているわけではないことから、現時点では全自動で行えるわけではなく、今後のテキスト処理技術の改善が期待される。

F. 健康危険情報

特になし

G. 研究発表

1. 論文発表

特になし

2. 学会発表

東京大学臨床展開研究シンポジウムにおいて、ポスター発表を行った(2007年3月2日)

H. 知的財産権の出願・登録状況

1. 特許取得

特になし

2. 実用新案登録

特になし

3. その他

特になし

Ⅲ.研究成果の刊行に関する一覧表

雑誌

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IV.参考資料 1