CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Stroke Trials Reference List

A supplement to the Canadian Stroke Best Practice Recommendations

October 2015

The Canadian Stroke Best Practice Recommendations process includes a review of clinical trials related to each topic. Our groups have found it helpful to keep track of these through the following quick reference list. The first list is the acronyms and full name of the trial. This is followed by tables that provide high-level details of each trial for reference. They are listed on both tables in alphabetical order.

We update this list with each update of our stroke best practices. Please note, this list is not meant to be exhaustive, rather it reflects the trials considered as part of our update evidence reviews. If any trials are missing from the list that are relevant, kindly send a message with the information regarding the trial (name, authors, publication journal and year) to strokebestpractices@hsf.ca.

Stroke Trials Quick Reference List

Acronym	Title
ACAS	Asymptomatic Carotid Atherosclerosis Study
ACST	Asymptomatic Carotid Surgery Trial (5 year follow-up)
ACST-1	Asymptomatic Carotid Surgery Trial (10 year follow-up)
ACCESS	Acute Candesartan Cilexetil Therapy in Stroke Survivors Study
ACCOMPLISH	Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension
ACCORD	Action to Control Cardiovascular risk in Diabetes
ACTIVE	Atrial Fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W) (ACTIVE A) (ACTIVE I)
ADVANCE	Action in Diabetes and Vascular Disease: PreterAx and DiamicroN Modified-Release Controlled Evaluation
ALLHAT	Antihypertensive & Lipid Lowering Treatment to Prevent Heart Attack Trial
ALLHAT-LLT	Antihypertensive & Lipid Lowering Treatment to Prevent Heart Attack Trial-Lipid Lowering Component
ARISTOTLE	Apixaban for the Prevention of Stroke in Subjects With Atrial Fibrillation
ASPEN	Atorvastatin Study for the Prevention of Coronary Heart Disease Endpoints in Non-Insulin-Dependent Diabetes Mellitus
ATACH 1	Antihypertensive Treatment of Acute Cerebral Hemorrhage
ATLANTIS	Alteplase Thrombolysis in Ischemic Stroke
AVERROES	Apixaban Versus Acetylsalicyclic Acid to Prevent Stroke in Atrial Fibrillation Patients Who Have Failed or Unsuitable for Vitamin K Antagonist Treatment
AVERT	A Very Early Rehabilitation Trial
BAFTA	Birmingham Atrial Fibrillation Treatment of the Aged study
BRAT	The Barrow Ruptured Aneurysm Trial
CAPRIE	Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events trial
CARESS	Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis
CASES	Canadian Alteplase for Stroke Effectiveness Study
CAST/IST	Chinese Acute Stroke Trial/International Stroke Trial
CATCH	CT And MRI in the Triage of TIA and minor Cerebrovascular events to identify High risk patients
CATIS	China Antihypertensive Trial in Acute Ischemic Stroke
CAVATAS	Carotid and Vertebral Artery Transluminal Angioplasty Study

Acronym	Title
CHANCE	Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events
CHARISMA	Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance
CLAIR	Clopidogrel plus Aspirin versus Aspirin alone for Reducing embolization in Patients with Acute Symptomatic Cerebral or Carotid Artery Stenosis
CLOSURE I	Evaluation of the STARFlex Septal Closure System in Patients with a Stroke and/or Transient Ischemic Attack due to Presumed Paradoxical Embolism through a Patent Foramen Ovale
CLOTS I	Clots in Legs Or sTockings after Stroke
CLOTS 2	Clots in Legs Or sTockings after Stroke
CLOTS 3	Clots in Legs Or sTockings after Stroke
CONSCIOUS-1	Clazosentan to Overcome Neurological Ischemia and Infarct Occurring After Subarachnoid Hemorrhage
CONSCIOUS-2	Clazosentan to Overcome Neurological Ischemia and Infarct Occurring After Subarachnoid Hemorrhage
CONSCIOUS-3	Clazosentan to Overcome Neurological Ischemia and Infarct Occurring After Subarachnoid Hemorrhage
CORONA	Controlled Rosuvasatin Multinational Trial in Heart Failure
CREST	Carotid Revascularization Endarterectomy versus Stenting Trial
CRYSTAL-AF	Cryptogenic Stroke and Underlying Atrial Fibrillation
DECIMAL	Decompressive Craniectomy In Malignant Middle Cerebral Artery Infarcts
DESTINY I & II	Decompressive Surgery for the Treatment of Malignant Infarction of the MCA
EAFT	European Atrial Fibrillation Trial
EARLY	Early treatment with aspirin plus extended-release dipyridamole for transient ischaemic attack or ischaemic stroke within 24 hours of symptom onset
ECASS I	European Cooperative Acute Stroke Study I
ECASS II	European Cooperative Acute Stroke Study II
ECASS III	European Cooperative Acute Stroke Study III
ECLAT	EffiCiency and Safety of an eLectronic cigareTte (ECLAT)
ECST	European Carotid Surgery Trial
EMRACE	Event Monitor Belt for Recording Atrial Fibrillation after a Cerebral Ischemic Event
ENGAGE AF-TIMI 48	Effective Anitcoagulation with Factor Xa Next Generation in Atrial Fibrillation-Thrombolysis in Myocardial Infarction 48
ESCAPE	Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times
ESPRIT	European/Australian Stroke Prevention Reversible Ischemia Trial group
ESPS2	Second European Stroke Prevention Study
EVA-3S	Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis
EXPRESS	Effect of urgent treatment of transient ischemic attack and minor stroke on early Recurrent Stroke Study
EXTEND IA	Extending the Time for Thrombolysis in Emergency Neurological Deficits - Intra-Arterial
FAST	Factor Seven for Acute Hemorrhagic Stroke
FASTER	Fast Assessment of Stroke and transient ischemic attack to prevent Early Recurrence
FIELD	Fenofibrate Intervention and Event Lowering in Diabetes

Acronym	Title
FLAME	Fluoxetine for Motor Recovery after Acute Ischaemic Stroke
FOOD (1 & 2)	Feed or Ordinary Diet (parts 1 & 2- timing and method of feeding)
FOOD (3)	Feed or Ordinary Diet (part 3-oral supplementation)
GIST UK	Glucose in Stroke Trial
HAMLET	Hemicraniectomy After MCA infarction with Life-threatening Edema Trial
HOPE	Health Outcomes Prevention Study
HOT	Hypertension Optimal Treatment
HPS	Heart Protection Study
HYVET	Hypertension in the Very Elderly trial
ICSS	International Carotid Stenting Study
ICH ADAPT	Intracerebral Hemorrhage Acutely Decreasing Arterial Pressure Trial
IDEAL	Incremental Decrease in End Points Through Aggressive Lipid Lowering
IMAGES	Intravenous Magnesium Efficacy in Stroke Trial
IMS III	Interventional Management of Stroke III
INTERACT	The Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (I and II)
ISAT	International Subarachnoid Aneurysm Trial
IST-3	International Stroke Trial-3
ISTAPS	Effectiveness of a stepped primary care smoking cessation intervention
JUPITER	Justification for the Use of Statins in Prevention
LEAPS	Locomotor Experience Applied Post Stroke Trial
LIFE	Losartan Intervention for Endpoint Reduction Study
MATCH	Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients
MOSES	Morbidity & Mortality after Stroke
MR CLEAN	A Multi center Randomized Clinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands
MR RESCUE	Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy
NASCET	North American Symptomatic Carotid Endarterectomy Trial
NINDS	The National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Stroke Study
ONTARGET	The Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial
OXVASC	Oxford Vascular study
PAIS	Paracetamol (Acetaminophen) In Stroke (PAIS) trial
PC	Clinical Trial Comparing Percutaneous Closure of Patent Foramen Ovale Using the Amplatzer PRO Occluder with Medical Treatment in Patients with Cryptogenic Embolism
PHANTOM-S	Prehospital Acute Neurological Treatment and Optimization of Medical care in Stroke Study
PREDIMED	Prevention with Mediterranean Diet
PREVAIL	The efficacy and safety of enoxaparin versus unfractionated heparin for the prevention of venous thromboembolism after acute ischaemic stroke
PROACT II	Prolyse in Acute Cerebral Thromboembolism II
PROACTIVE	PROspective pioglitAzone Clinical Trial In macroVascular Events

Acronym	Title
PRoFESS	Prevention Regimen for Effectively avoiding Second Stroke
PROGRESS	The perindopril protection against recurrent stroke study
PROSPER	PRospective Study of Pravastatin in the Elderly at Risk
PROTECT	PROphylaxis of Thromboembolic Events by Certoparin Trial
RE-LY	Randomized Evaluation of Long-term Anticoagulation Therapy
REGARDS	Reasons for Geographic and Racial Differences in Stroke Study
RESPECT	Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment
REVASCAT	Randomized Trial of Revascularization with Solitaire FR Device versus Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting within Eight Hours of Symptom Onset
ROCKET AF	The Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation
SAFE	Screening for Atrial Fibrillation in the Elderly
SAMMPRIS	Stenting vs. Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis
SAPPHIRE	Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy
SCAST	Scandinavian Candesartan Acute Stroke Trial
SCOPE	The Study on COgnition and Prognosis in the Elderly
SEARCH	Study of the Effectiveness of Additional Reductions in Cholesterol & Homocycteine
SHEP	Systolic Hypertension in the Elderly trial
SIFA	Studio Italiano Fibrillazione Atriale
SPACE	Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy
SPARCL	Stroke Prevention by Aggressive Reduction in Cholesterol Levels trial
SPS3	Secondary Prevention of Small Subcortical Strokes
STASH	Simvastatin in Aneurysmal Subarachnoid Haemorrhage
STITCH	Simplified Treatment Intervention to Control Hypertension (I and II)
SWIFT	SOLITAIRE™ FR With the Intention For Thrombectomy (SWIFT) Study
SWIFT-PRIME	Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment
SYNTHESIS EXP	Intra-arterial Versus Systemic Thrombolysis for Acute Ischemic Stroke
TREVO-2	Thrombectomy REvascularization of Large Vessel Occlusions in Acute Ischemic Stroke
TNT	Treating to New Targets Trial
TRANSCEND	ONgoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial/Telmisartan Randomized AssessmeNT Study in ACE-INtolerant Subjects with Cardiovascular Disease
UKPDS	United Kingdom Prospective Diabetes Study 38
VECTORS	Very Early Constraint-Induced Movement during Stroke Rehabilitation

Stroke Trials Reference Table

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
ACAS	Asymptomatic Carotid Atherosclerosis Study	Walker MD, Marler JR, Goldstein M, Grady PA, Toole JF, Baker WH et al. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. JAMA 1995;273(18):1421-8.	Management of risk factors and aspirin use vs. management of risk factors, aspirin use and carotid endarterectomy (Carotid intervention)	For asymptomatic patients with ≥60% carotid artery stenosis, those who received surgery (CEA) in addition to aggressive management of risk factors had a 5.1% risk of stroke or death over 5 years compared to an 11.0% risk for those who did not receive surgery (aggregate risk reduction of 53%; 95% CI 22% to 72%).
ACST	Asymptomatic Carotid Surgery Trial	Halliday A, Mansfield A, Marro J, Peto C, Potter J, et al.; MRC Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group. Prevention of disabling and fatal strokes by successful carotid endartertectomy in patients without recent neurological symptoms: randomised controlled trial. Lancet 2004; 363: 1491- 1502	Immediate CEA vs. indefinite deferral of CEA in asymptomatic pts with substantial carotid narrowing *(Carotid intervention)*	In asymptomatic patients younger than 75 years with carotid diameter reduction about 70% or more on ultrasound, immediate CEA halved the net 5-year stroke risk from about 12% to about 6% (incl. 3% perioperative hazard). Half this 5-year benefit involved disabling or fatal strokes. But, outside trials, inappropriate selection of patients or poor surgery could obviate such benefits.
ACST-1	Asymptomatic Carotid Surgery Trial *(Long-term follow-up of ACST)*	Halliday A, Harrison M, Hayter E, Kong X, Mansfield A, Marro J, et al. 10-year stroke prevention after successful carotid endarterectomy for asymptomatic stenosis (ACST-1): a multicentre randomised trial. Lancet. 2010;376(9746):1074-84.	Immediate CEA vs. indefinite deferral of CEA in asymptomatic pts with substantial carotid narrowing *(Carotid intervention)*	In the long-term follow-up of ACST, the 10 year stroke risk was 13.4% for the immediate CEA group and 17.9% for those receiving an indefinite deferral of a carotid procedure (including perioperative events).
ACCESS	The Acute Candesartan Cilexetil Therapy in Stroke Survivors	Schrader J, Luders S, Kulschewski A, Berger J, Zidek W, Treib J, et al. The ACCESS Study: evaluation of Acute Candesartan Cilexetil Therapy in Stroke Survivors. Stroke; 2003;34(7):1699-703.	Candesaran cilexetil (Ageotensin II receptor agonist) vs. placebo *(Blood pressure management)*	The trial was stopped prematurely due to an imbalance in 12 month mortality and vascular events between the groups. The 12 month mortality for the cilexetil group was 2.9% vs 7.2% in the placebo group. Likewise, vascular events

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
				were higher in the placebo group (18.7% vs. 9.8%).
ACCOMPLISH	Avoiding Cardiovascular Events Through Combination Therapy in Patients Living With Systolic Hypertension	Jamerson K, Weber MA, Bakris GL, Dahlof B, Pitt B, Shi V, et al. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. The New England journal of medicine. 2008;359(23):2417-28	Benazepril plus amlodipine vs. Benazepril plus hyprochlorothiazide *(Blood pressure management)*	The trial was stopped prematurely. There was no significant difference in death from cardiovascular causes between the groups but there were significantly fewer fatal/non-fatal myocardial infarctions in the benazepril-amlodipine group.
ACCORD	Action to Control Cardiovascular risk in Diabetes	Cushman WC, Evans GW, Byington RP, Goff DC, Jr., Grimm RH, Culter JA et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. The New England journal of medicine. 2010;362(17):1575-85.	Intensive systolic blood pressure lowering therapy (<120mmHg) vs. standard systolic blood pressure lowering (<140mmHg) *(Blood pressure management)*	There were no significant differences in nonfatal MI, nonfatal stroke or death from cardiovascular causes but there were the number of fatal and non-fatal strokes were lower in the intensive therapy group.
ACTIVE W	Atrial Fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W)	ACTIVE Writing Group of the ACTIVE Investigators, Connolly S, Pogue J, Hart R, Pfeffer M, Hohnloser S et al. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial Fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial. Lancet 2006; 367(9526): 1903- 1912	Oral anticoagulation therapy vs. clopidogrel plus aspirin *(Antithrombotic therapy in atrial fibrillation)*	The study was stopped prematurely with clear evidence of superiority of anticoagulation therapy.
ACTIVE A	Atrial Fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events	Connolly SJ, Pogue J, Hart RG, Hohnloser SH, Pfeffer M, et al. Effect of clopidogrel added to aspirin in patients with atrial fibrillation. The New England journal of medicine. 2009;360(20):2066-78.	Aspirin and clopidogrel vs. aspirin and placebo *(Antithrombotic therapy in atrial fibrillation)*	Risk of stroke was significantly lower in patients receiving clopidogrel and aspirin vs. aspirin alone; however, major bleeding was significantly greater in patients receiving clopidogrel and aspirin vs. aspirin alone.
ACTIVE I	Atrial Fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events *(Parallel to ACTIVE A and ACTIVE W)*	Yusuf S, Healey JS, Pogue J, Chrolavicius S, Flather M, et al. Irbesartan in patients with atrial fibrillation. The New England journal of medicine. 2011;364(10):928-38.	Irbesartan vs. placebo *(Antithrombotic therapy in atrial fibrillation)*	There were no differences between groups for rates of stroke, myocardial infarction, death from vascular causes, or hospitalization for heart failure.

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
ADVANCE	Action in Diabetes and Vascular Disease: PreterAx and DiamicroN Modified-Release Controlled Evaluation	The ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. NEJM 2008; 358: 2560- 2572	Standard glucose control vs. intensive glucose control (defined as use of gliclazide – modified-release – plus other drugs as requited to achieve a glycated haemoglobin value of 6.5% or less. (*Diabetes management)*	Intensive control reduced the incidence of combined major macrovascular and microvascular events, as well as that of microvascular events.
ALLHAT	Antihypertensive & Lipid Lowering Treatment to Prevent Heart Attack Trial	Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA 2002;288(23):2981-97	Chlorthalidone vs, amlodipine vs. lisinopril *(Blood pressure management)*	There were no differences in combined fatal CHD or nonfatal myocardial infarction between groups. The risk of stroke was significantly greater with lisinopril vs. chlorthalidone and risk of heart failure was higher with amlodipine and lisinopril vs. chlorthalidone.
ALLHAT-LLT	Antihypertensive & Lipid Lowering Treatment to Prevent Heart Attack Trial-Lipid Lowering Component	Major outcomes in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin vs usual care: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT). JAMA 2002;288(23):2998-3007	Pravastatin vs. usual care *(Lipid management)*	There were no significant differences between groups for all-cause mortality or number of CHD events.
ARISTOTLE	Apixaban for the Prevention of Stroke in Subjects With Atrial Fibrillation	Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, et al. Apixaban versus warfarin in patients with atrial fibrillation. The New England journal of medicine. 2011;365(11):981-92	Apixaban vs. warfarin *(Antithrombotic therapy in atrial fibrillation)*	Rates of death, hemorrhagic stroke, and major bleeding were significantly lower in the apixaban group. There were no significant differences in the rate of ischemic or uncertain type of stroke between the groups.
ASPEN	Atorvastatin Study for the Prevention of Coronary Heart Disease Endpoints in Non-Insulin-Dependent Diabetes Mellitus	Knopp RH, d'Emden M, Smilde JG, et al. Efficacy and safety of atorvastatin in the prevention of cardiovascular end points in subjects with type 2 diabetes: the Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in non-insulin-dependent diabetes mellitus (ASPEN). Diabetes Care 2006;29:1478-85.	Atorvastatin vs. placebo *(Prevention-Diabetes management)*	Treatment with statin was not associated with significant reductions in fatal or non-fatal stroke risk in either primary or secondary prevention patients.
ATACH	Antihypertensive Treatment of Acute Cerebral Hemorrhage	Antihypertensive treatment of acute cerebral hemorrhage (ATACH): final	The objective was to determine the tolerability and	Aggressive systolic blood pressure (SBP) reduction to 110–140mm Hg

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
		results. Journal of Neurological Sciences 2009; 285: s98	safety of three escalating levels of antihypertensive treatment goals (170mmHg - 200mmHg, 140mmHg – 170 mmHg and 110mmHg – 140mmHg) for acute hypertension in subjects with supratentorial intracerebral hemorrhage (*Management of Subarachnoid and Intracerebral Hemorrhage).*	using intravenous nicardipine was well tolerated with low risk of hematoma expansion, neurological deterioration and in-hospital mortality. The results favor pharmacological reduction of SBP in acute ICH
ATLANTIS	Alteplase Thrombolysis in Ischemic Stroke	Clark WM, Wissman S, Albers GW, et al. Recombinant tissue-type plasminogen activator (Alteplase) for ischemic stroke 3 to 5 hours after symptom onset. The ATLANTIS Study: a randomized controlled trial. Alteplase Thrombolysis for Acute Noninterventional Therapy in Ischemic Stroke. JAMA 1999;282:2019-26	Intravenous alteplase vs. placebo (*Acute thrombolytic therapy)*	There was no difference between groups in the number of patients experiencing excellent neurological recovery (NIHSS of 0-1) at 90 days (33.8% vs. 32.0%, p=0.65).
AVERROES	Apixaban Versus Acetylsalicyclic Acid to Prevent Stroke in Atrial Fibrillation Patients Who Have Failed or Unsuitable for Vitamin K Antagonist Treatment	Connolly SJ, Eikelboom J, Joyner C, Diener HC, Hart R, Golitsyn S, et al. Apixaban in patients with atrial fibrillation. The New England journal of medicine. 2011;364(9):806-17.	Apixaban vs. aspirin *(Antithrombotic therapy in atrial fibrillation)*	The trial was stopped prematurely due to results in favor of apixaban. There were significantly greater stroke events or systemic embolism in the aspirin group compared to the apixaban group. Cases of major bleeding were not significantly different between the groups.
AVERT (feasibility study)	A Very Early Rehabilitation Trial	Bernhardt J, Dewey H, Thrift A, Collier J and Donnan G. A very early rehabilitation trial for stroke (AVERT) Phase II Safety and Feasibility. Stroke 2008;39;390-396	Standard care vs. standard care plus very early mobilization (*Mobilization)*	Very early mobilization of patients within 24 hours of acute stroke appears safe and feasible. Intervention efficacy and cost-effectiveness are currently being tested in a large randomized, controlled trial.
AVERT	A Very Early Rehabilitation Trial	The AVERT Trial Collaboration group. Efficacy and safety of very early mobilisation within 24 h of stroke onset (AVERT): a randomised controlled trial. *Lancet 2015;* 386(9988) *: 46-55.*	Standard care vs. standard care plus very early mobilization (*Mobilization)*	Assignment to the intervention group was associated with worse outcome (adjusted OR for mRS score of 0-2 at 90 days=0.73, 95%

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
				CI 0.59–0.90, p=0.04).
BAFTA	Birmingham Atrial Fibrillation Treatment of the Aged study	Mant J, Hobbs R, Fletcher K, Roalfe A, Fitzmaurice D, Lip GYH, Murray E, on behalf of the BAFTA investigators* and the Midland Research Practices Network (MidReC)* Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. Lancet 2007; 370: 493-503	Warfarin vs. aspirin in pts over the age of 75 with atrial fibrillation *(Antithrombotic therapy in atrial fibrillation)*	Fewer primary events in patients receiving warfarin were reported, suggesting that anticoagulation is beneficial for patients 75 years with atrial fibrillation.
BRAT	The Barrow Ruptured Aneurysm Trial	McDougall CG, Spetzler RF, Zabramski JM, et al. The Barrow Ruptured Aneurysm Trial. J Neurosurg 2012;116:135-44.	Aneurysm clipping vs. coil embolization, conducted within 24 hours	More patients in the surgical group had a poor outcome at 1 year.
CAPRIE	Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events trial	CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). Lancet 1996; 348 (9038): 1329- 1339	Clopidogrel vs. ASA *(Antiplatelet therapy)*	An 8.7% reduction in primary endpoint of ischemic stroke, MI or vascular death was indicated in favour of clopidogrel.
CARESS	Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis	Markus HS, Droste DW, Kaps M, et al. Dual antiplatelet therapy with clopidogrel and aspirin in symptomatic carotid stenosis evaluated using doppler embolic signal detection: the Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis (CARESS) trial. Circulation 2005;111:2233-40.	Dual clopidogrel plus aspirin vs. aspirin alone (*Antiplatelet therapy)*	There were significantly fewer patients with at least one microembolic signal on day 7 in the group treated with dual therapy and a non-significant reduction at day 2.
CASES	Canadian Alteplase for Stroke Effectiveness Study	Hill M, Buchan A, for the Canadian Alteplase for Stroke Effectiveness Study (CASES) Investigators. Thrombolysis for acute ischemic stroke: results of the Canadian alteplase for stroke effectiveness study. CMAJ 2005;172(10).	The objective was to assess the effectiveness of alteplase therapy for ischemic stroke *(Acute thrombolytic therapy)*	The rate of symptomatic intracranial hemorrhage was low. Stroke thrombolysis is a safe and effective therapy in actual practice
CAST/IST	Chinese Acute Stroke Trial/International Stroke Trial	Chen Z, Sandercock P, Pan H, Counsell C, Collins R, Liu L, Xie J, Warlow C and Peto R. Indications for early aspirin use in acute ischemic stroke: A combined analysis of 40 000	The objective was to assess the balance of benefits and risks of aspirin in particular categories of patients with acute stroke. (*Acute*	Early aspirin is of benefit for a wide range of patients, and its prompt use should be routinely considered for all patients with suspected acute ischemic stroke, mainly to

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
		randomized patients from the chinese acute stroke trial and the international stroke trial. Stroke 2000;31;1240	*management of TIA and minor stroke)*	reduce the risk of early recurrence.
CATCH	CT And MRI in the Triage of TIA and minor Cerebrovascular events to identify High risk patients	Coutts SB, Modi J, Patel SK, Aram H, Demchuk AM, Goyal M, et al. What causes disability after transient ischemic attack and minor stroke?: Results from the ct and mri in the triage of tia and minor cerebrovascular events to identify high risk patients (catch) study. Stroke 2012;43:3018-3022	Association between immediate CT/CTA imaging findings and recurrence of stroke at 90 days.	Immediate CT/CTA imaging findings (within 24 hours) were found to be predictive of recurrent stroke at 90 days.
CATIS	China Antihypertensive Trial in Acute Ischemic Stroke	He J, Zhang Y, Xu T, Zhao Q, et al. Effects of immediate blood pressure reduction on death and major disability in patients with acute ischemic stroke. JAMA 2014;311:479-489.	Antihypertensive therapy +/- during acute hospitalization	At 7 days post-randomization, mean systolic blood pressure was significantly lower among patients in the intervention group (137.3 vs. 146 mm, p<0.001).
CAVATAS	Carotid and Vertebral Artery Transluminal Angioplasty Study	Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial Lancet 2001;357:1729-1737.	Endovascular treatment with balloon angioplasty with or without stent insertion vs. carotid endarterectomy.	There were no differences between groups including death, disabling stroke, non-disabling stroke, death or disabling stroke, or death or any stroke within 30 days.
CHANCE	Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events	Wang Y, Wang Y, Zhao X, et al. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack. N Engl J Med 2013;369:11-19.	Clopidogrel plus aspirin vs. placebo plus aspirin. (*Antiplatelet therapy)*	Significantly fewer patients in the clopidogrel plus aspirin group experienced a stroke within 90 days.
CHARISMA	Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance	Bhatt DL, Fox KA, Hacke W, Berger PB, Black HR, Boden WE, et al.; CHARISMA Investigators. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. N Engl J Med 2006; 354(16): 1706-1717	Clopidogrel plus low-dose ASA vs. placebo plus low-dose ASA *(Antiplatelet therapy)*	Although there was a suggestion of benefit for patients with atherothrombosis, overall, clopidogrel plus ASA was not significantly more effective than ASA alone in reduction of stroke, MI or vascular death.
CLAIR	Clopidogrel plus Aspirin versus Aspirin alone for Reducing embolization in Patients with Acute Symptomatic Cerebral or Carotid Artery Stenosis	Wong KS, Chen C, Fu J, et al. Clopidogrel plus aspirin versus aspirin alone for reducing embolisation in patients with acute symptomatic cerebral or carotid artery stenosis (CLAIR study): a randomised, open-	Dual clopidogrel plus aspirin vs. aspirin alone (*Antiplatelet therapy)*	There were significantly fewer patients with at least one microembolic signal on day 2 in the group treated with combination therapy

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
		label, blinded-endpoint trial. Lancet Neurol 2010;9:489-97.		
CLOSURE I	Evaluation of the STARFlex Septal Closure System in Patients with a Stroke and/or Trransient Ischemic Attack due to Presumed Paradoxical Embolism through a Patent Foramen Ovale	Furlan AJ, Reisman M, Massaro J, et al., for the CLOSURE I Investigators. Closure or medical therapy for cryptogenic stroke with patent foramen ovale. N Engl J Med 2012;366:991-999.	PFO closure vs. medical therapy	As compared to medical therapy, PFO closure was not associated with a significant reduction in the composite outcome of stroke/TIA, death from neurologic cause, and 30-day all-cause mortality.
CLOTS I	Clots in Legs Or sTockings after Stroke	The CLOTS trials collaboration. Effectiveness of thigh-length graduated compression stockings to reduce the risk of deep vein thrombosis after stroke (CLOTS trial 1): a multicentre, randomised controlled trial. The Lancet 2009;6736(09)60941-7	Routine care plus thigh-length graduated compression stockings vs. routine care plus avoidance of graduated compression stockings (*Venous thrombo embolism prophylaxis*)	There was a non-significant absolute reduction in risk of DVT. Skin breaks, ulcers, blisters and skin necrosis were significantly more common in patient allocated to graduated compression stockings than in those allocated to avoid their use.
CLOTS 2	Clots in Legs Or sTockings after Stroke	The CLOTS Trials Collaboration. Thigh-length versus below-knee stockings for deep venous thrombosis prophylaxis after stroke: a randomized trial. (CLOTS 2) Ann Intern Med 2010;153:553-562.	Thigh-length compression stockings vs. below-knee stockings (*Venous thrombo embolism prophylaxis*)	At 30 days, there was a significant reduction in the incidence of proximal DVT associated with thigh-length GCS
CLOTS 3	Clots in Legs Or sTockings after Stroke	Dennis M, Sandercock P, Reid J, Graham C, Forbes J, Murray G. Effectiveness of intermittent pneumatic compression in reduction of risk of deep vein thrombosis in patients who have had a stroke (CLOTS 3): a multicentre randomised controlled trial. Lancet 2013;382:516-524.	Thigh length intermittent pneumatic compression (IPC) device vs. no IPC (*Venous thrombo embolism prophylaxis*)	The incidence of proximal DVT within 30 days was lower in the IPC group
CONSCIOUS-1	Clazosentan to Overcome Neurological Ischemia and Infarct Occurring After Subarachnoid Hemorrhage	MacDonald RL, Kassell NF, Mayer S, et al. Clazosentan to overcome neurological ischemia and infarction occurring after subarachnoid hemorrhage (CONSCIOUS-1): randomized, double-blind, placebo-	Escalating doses of clazosentan vs. placebo for the prevention of vasospasm secondary to subarachnoid hemorrhage	There was a significant reduction in the incidence of moderate or severe vasospasm associated with any dose of clazosentan within the first 14 days of treatment.

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
		controlled phase 2 dose-finding trial. Stroke 2008;39:3015-21.		
CONSCIOUS-2	Clazosentan to Overcome Neurological Ischemia and Infarct Occurring After Subarachnoid Hemorrhage	MacDonald RL, Higashida RT, Keller E, et al. Clazosentan, an endothelin receptor antagonist, in patients with aneurysmal subarachnoid haemorrhage undergoing surgical clipping: a randomised, double-blind, placebo-controlled phase 3 trial (CONSCIOUS-2). Lancet Neurol 2011;10:618-25.	5 mg/hr of clazosentan or placebo for the prevention of vasospasm secondary to subarachnoid hemorrhage	At 6 weeks, all-cause mortality and vasospasm-related morbidity were similar between groups
CONSCIOUS-3	Clazosentan to Overcome Neurological Ischemia and Infarct Occurring After Subarachnoid Hemorrhage	MacDonald RL, Higashida RT, Keller E, et al. Randomized trial of clazosentan in patients with aneurysmal subarachnoid hemorrhage undergoing endovascular coiling. Stroke 2012;43:1463-69.	5 or 15 mg/h clazosentan or placebo for 14 days for the prevention of vasospasm secondary to subarachnoid hemorrhage	The risk of all-cause mortality and vasospasm-related morbidity at 6 weeks was reduced significantly for patients in the 15 mg group
CREST	Carotid Revascularization Endarterectomy versus Stenting Trial	Brott TG, Hobson RW, 2nd, Howard G, Roubin GS, Clark WM, Brooks W, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. The N Engl J Med 2010;363(1):11-23	Carotid-artery stenting vs. carotid endarterectomy *(Carotid intervention)*	There were no significant differences in stroke, myocardial infarction or death between the two groups. The endarterectomy group had significantly lower rates of stroke or death at year 4. Periprocedural rates of stroke were significantly higher in the stenting group, and periprocedural rates of myocardial infarction higher in the endarterectomy group.
CRYSTAL-AF	Cryptogenic Stroke and Underlying Atrial Fibrillation	Sanna T, Diener HC, Passman RS, Di L, V, Bernstein RA, Morillo CA, Rymer MM, Thijs V, Rogers T, Beckers F, Lindborg K, Brachmann J: Cryptogenic stroke and underlying atrial fibrillation. N Engl J Med 2014;370:2478-2486.	ECG monitoring on a schedule at the discretion of their treating physician or long-term monitoring with an insertable cardiac monitor (ICM) using the Reveal® XT device *(Outpatient management of stroke and TIA)*	At 6 and 12 months, the rate of detection of AF was significantly higher among patients assigned to the ICM group
DECIMAL	Decompressive Craniectomy In	Vahedi, K., Vicaut, E., Mateo, J.,	Surgical decompression and	At 12 months, more patients in the

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
	Malignant Middle Cerebral Artery Infarcts	Kurtz, A., Orabi, M., Guichard, J. P. et al. Sequential-design, multicenter, randomized, controlled trial of early decompressive craniectomy in malignant middle cerebral artery infarction (DECIMAL Trial). Stroke 2007; 38: 2506-2517.	medical treatment following intracerebral hemorrhage *(hemicraniectomy)*	surgical arm had survived. There was no difference in functional outcome between groups.
DESTINY I & II	Decompressive Surgery for the Treatment of Malignant Infarction of the MCA	Juttler, E., Schwab, S., Schmiedek, P., Unterberg, A., Hennerici, M., Woitzik, J. et al. Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery (DESTINY): a randomized, controlled trial. *Stroke* 2007; *38,* 2518-2525.	Conservative treatment group vs. surgical intervention group with hemicraniectomy (diameter ≥12 cm and duroplasty) within 6 hours of group assignment (*hemicraniectomy)*	A significantly higher proportion of patients in the surgical group were alive and living without severe disability (mRS 0-4) at 6 months, although no patient in either group had mRS score of 0-2 at 6 or 12 months. More patients in the surgical arm were alive and had mRS scores of 0-3 at 6 months.
EARLY	Early treatment with aspirin plus extended-release dipyridamole for transient ischaemic attack or ischaemic stroke within 24 h of symptom onset	Dengler R, Diener HC, Schwartz A, et al. Early treatment with aspirin plus extended-release dipyridamole for transient ischaemic attack or ischaemic stroke within 24 h of symptom onset (EARLY trial): a randomised, open-label, blinded-endpoint trial. Lancet Neurol 2010;9:159-66.	Early vs. late initiation of Aspirin plus extended-release dipyridamole (*Antiplatelet therapy)*	There was no difference between groups in terms of the number patients who experienced a favourable outcome, as assessed by the TelemRS.
EAFT	European Atrial Fibrillation Trial	Secondary prevention in non-rheumatic atrial fibrillation after transient ischaemic attack or minor stroke. EAFT (European Atrial Fibrillation Trial) Study Group. Lancet. 1993;342(8882):1255-62.	Warfarin vs. aspirin (*Antithrombotic therapy in atrial fibrillation)*	Combined results showed that anticoagulants were significantly more effective than antiplatelet therapy for the prevention of all ischemic vascular events and for the prevention of stroke recurrence. Major extracranial bleeding complications occurred more often in pts on anticoagulants, but the absolute difference was small.
ECASS I	European Cooperative Acute Stroke Study I	Hacke W, Kaste M, Fieschi C, et al. Intravenous thrombolysis with recombinant tissue plasminogen	Intravenous alteplase vs. placebo (*Acute thrombolytic therapy)*	There was no difference in the median Barthel Index scores or Scandinavian Stroke Scale scores

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
		activator for acute hemispheric stroke. The European Cooperative Acute Stroke Study (ECASS). JAMA 1995;274:1017-25		between groups, but patients in the alteplase group had significantly higher combined scores.
ECASS II	European Cooperative Acute Stroke Study II	Hacke W, Kaste M, Fieschi C, et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). Second European-Australasian Acute Stroke Study Investigators. Lancet 1998;352:1245-51	Intravenous alteplase vs. placebo (*Acute thrombolytic therapy)*	There was no significant difference in the percentages of patients with mRS<2 at 90 days.
ECASS III	European Cooperative Acute Stroke Study III	Bluhmki E, Chamorro A, Davalos A, Machnig T, Sauce C, Wahlgren N, Wardlaw J and Hacke W. Stroke treatment with alteplase given 3.0-4.5 h after onset of acute ischaemic stroke (ECASS III): additional outcomes and subgroup analysis of a randomised controlled trial. Lancet Neurol 2009;8:109-102	Intravenous alteplase vs. placebo (*Acute thrombolytic therapy)*	The results support the use of alteplase up to 4·5 h after the onset of stroke symptoms across a broad range of subgroups of patients who meet the requirements of the European product label but miss the approved treatment window of 0–3h.
ECLAT	EffiCiency and Safety of an eLectronic cigareTte	Caponnetto P, Campagna D, Cibella F, Morjaria JB, Caruso M, Russo C, Polosa R: EffiCiency and Safety of an eLectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: a prospective 12-month randomized control design study. *PLoS One* 2013;8:e66317.	Different doses and duration of use associated with nicotine-replacement cartridges used in electronic cigarettes (7.2 mg/cartridge x 12 weeks vs. 7.2 mg for 6 weeks then 5.4 mg/cartridge vs. 0 mg nicotine x 12 weeks). *(Smoking cessation)*	Nicotine containing cartridges were more effective in reducing the use of conventional cigarettes for up to 1 year.
ECST	European Carotid Surgery Trial	Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). Lancet 1998;351(9113):1379-87	Carotid enarterectomy vs. delayed surgery indefinitely *(Carotid intervention)*	The NNT with surgery to avoid one disabling stroke was 18; 9 surgeries to avoid one death or major stroke. The benefits of surgery are greater for those with higher levels of stenosis (>80%).
EMBRACE	Event Monitor Belt for Recording Atrial Fibrillation (AF) after a Cerebral Ischemic Event	Gladstone DJ, Spring M, Dorian P, Panzov V, Thorpe KE, Hall J, Vaid H, O'Donnell M, Laupacis A, Cote R, Sharma M, Blakely JA, Shuaib A, Hachinski V, Coutts SB, Sahlas DJ,	Ambulatory ECG monitoring with a 30-day event-triggered loop recorder or additional 24-hour Holter monitoring	Episodes of AF lasting longer than 30 seconds and 2.5 minutes were detected more frequently in patients receiving enhanced

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
		Teal P, Yip S, Spence JD, Buck B, Verreault S, Casaubon LK, Penn A, Selchen D, Jin A, Howse D, Mehdiratta M, Boyle K, Aviv R, Kapral MK, Mamdani M: Atrial fibrillation in patients with cryptogenic stroke. N Engl J Med 2014;370:2467-2477.	*(Outpatient management of stroke and TIA)*	monitoring.
ENGAGE AF-TIMI 48	Effective Anitcoagulation with Factor Xa Next Generation in Atrial Fibrillation-Thrombolysis in Myocardial Infarction 48	Giugliano RP, Ruff CT, Braunwald E, et al. for the ENGAGE AF-TIMI 48 investigators. Edoxaban versus warfarin in patients with atrial fibrillation. N Engl J M;2013, 369:2093-2104.	Edoxaban (high and low-dose) vs. warfarin (*Antithrombotic therapy)*	Both high-dose and low-dose edoxaban were found to be non-inferior to warfarin in terms of preventing stroke and systemic embolic events and were associated with significantly lower rates of major bleeding events.
ESCAPE	Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times	Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J et al. Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke. N Engl J Med 2015;372:1019-1030.	Endovascular mechanical thrombectomy or endovascular delivery of t-PA (intervention) vs. best medical management +/- tPA (control group). *(Endovascular therapy)*	The odds of improvement in mRS score by 1 point were significantly higher among patients in the intervention group (adj OR=3.2, 95% CI 2.0-4.7).
ESPRIT	European/Australian Stroke Prevention Reversible Ischemia Trial	ESPRIT Study Group, Halkes PH, van Gijn J, Kappelle LJ, Koudstaal PJ, Algra A. Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial. Lancet 2006; 367(9523): 1665-167.	ASA with dipyridamole vs. ASA without dipyridamole within six months of a TIA or minor stroke of arterial origin *(Antiplatelet therapy)*	Primary outcome events rose 16% in patients taking ASA alone vs. 13% in patients on combination treatment. When ESPRIT data was combined with data from previous meta-analysis, it was determined that patients receiving combination therapy discontinued trial medication more often than those on ASA alone. 104 patients would need to be treated with combination therapy each year to prevent one vascular death, non-fatal MI or non-fatal stroke.
ESPS2	European Stroke Prevention Study-2	Diener HC, Cunha L, Forbes C, Sivenius J, Smets P, Lowenthal A. European Stroke Prevention Study. 2. Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. J Nuerol Sci 1996;143(1-2):1-13.	Acetylsalicylic acid (ASA) vs. dipyridamole, vs. ASA plus dipyridamole vs. placebo *(Antiplatelet therapy)*	Significant reduction in stroke risk with ASA, dipyridamole and combination therapy compared to placebo. No significant effect of any on rates of death. ASA had

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
				significantly higher rates of bleeding vs. the placebo and dipyridamole groups.
EVA-3S	Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis	Mas JL, Trinquart L, Leys D, Albucher JF, Rousseau H, Viguier A, et al. Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S) trial: results up to 4 years from a randomised, multicentre trial. Lancet Neurol 2008;7(10):885-92.	Stenting vs. endarterectomy *(Carotid intervention)*	Trial was stopped prematurely due to imbalanced endpoints in factor of endarterectomy. Incidence of stroke or death was significantly greater in the stenting group, as was the incidence of disabling stroke or death. Non-significant increases in local and systemic complications were found in the endarterectomy group.
EXCITE	The Extremity Constraint Induced Therapy Evaluation Trial	Wolf SL, Winstein CJ, Miller JP et al. Effect of constraint-induced movement therapy on upper extremity function 3 to 9 months after stroke: the EXCITE randomized clinical trial. *JAMA* 2006;296(17):2095-2104.	Constraint-induced movement therapy vs. usual care	The CIMT group showed significantly greater improvements in the Wolf Motor Function Test (Performance time) and the Motor Activity Log.
EXPRESS	Effect of urgent treatment of transient ischemic attack and minor stroke on early Recurrent Stroke Study	Rothwell PM, Giles MF, Chandratheva A, Marquardt L, Geraghty O, Redgrave JNE et al. on behalf of the Early use of Existing Preventive Strategies for Stroke (EXPRESS) study. Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison. Lancet 2007; 370: 1432- 1442	The objective was to determine the effect of rapid treatment following TIA and minor stroke in pts who are not admitted directly to hospital *(Acute management of TIA and minor stroke)*	Early initiation of existing treatments after TIA or minor stroke was associated with an 80% relative reduction in the risk of early recurrent stroke.
EXTEND IA	Extending the Time for Thrombolysis in Emergency Neurological Deficits - Intra-Arterial	Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N et al. Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection. N Engl J Med 2015;372:1009-18.	Intra-arterial mechanical clot retrieval with the Solitaire device following therapy with IV t-PA vs. IV t-PA only (*Endovascular therapy)*	There was a significant shift in mRS scores towards lower scores associated with the intervention group (p=0.006). A significantly greater proportion of patients in the intervention group experienced early neurological improvement (80% vs. 37%, p<0.001).

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
FAST	Factor Seven for Acute Hemorrhagic Stroke	Diringer M, Skolnick B, Mayer S, Steiner T, Davis S, Brun N and Broderick J. Thromboembolic events with recombinant factor VII in spontaneous intracerebral hemorrhage: Results from the factor seven for acute hemorrhagic stroke (FAST) trial. Stroke 2010;41;48-53	The objective was to define the frequency of and risk factors for thromboembolic events (TEs) with recombinant activated factor VII (rFVIIa) (*Subarachnoid and Intracerebral Hemorrhage)*	Higher doses of rFVIIa in a high-risk population are associated with a small increased risk of what are usually minor cardiac events. Demonstration of the ability of rFVIIa to improve outcome in future studies should be driven by its effectiveness in slowing bleeding outweighing the risk of a small increase in arterial TEs
FASTER	Fast Assessment of Stroke and transient ischemic attack to prevent Early Recurrence	Kennedy J, Hill MD, Ryckborst KJ, Eliasziw M, Demchuk AM, Buchan AM for the FASTER Investigators. Fast assessment of stroke and transient ischaemic attack to prevent early recurrence (FASTER): a randomised controlled pilot trial. Lancet Neurol 2007; 6: 961- 969	Clopidogrel vs. placebo or simvastatin vs. placebo *(Acute management of TIA)*	Early aggressive antiplatelet therapy may be associated with a reduction in these events, although at the cost of slightly increased hemorrhagic complications. The trial failed to meet its recruitment rate target and was stopped prematurely.
FIELD	Fenofibrate Intervention and Event Lowering in Diabetes	Keech A, Simes RJ, Barter P, et al. Effects of long-term fenofibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study): randomised controlled trial. Lancet 2005;366:1849-61.	Micronized fenofibrate vs. placebo	There was a significant reduction in the risk of non-fatal MI associated with fibrate use, but not CHD mortality or any stroke.
FLAME	Fluoxetine for motor recovery after acute ischaemic stroke	Chollet F, Tardy J, Albucher JF, Thalamas C, Berard E, Lamy C, et al. Fluoxetine for motor recovery after acute ischaemic stroke (FLAME): a randomised placebo-controlled trial. Lancet Neurol 2011; 10(2):123-30.	Fluoxetine (20 mg/day) vs. placebo for 90 days (plus physiotherapy for both groups)	At 90 days, patients receiving fluoxetine had greater motor recovery (upper and lower limbs) and there were fewer cases of depression.
FOOD	The Food or Ordinary Diet trial (part I- timing and method of feeding)	Dennis, M. S., Lewis, S. C., & Warlow, C. Effect of timing and method of enteral tube feeding for dysphagic stroke patients (FOOD): a multicentre randomised controlled trial. Lancet 2005a;365: 764-772.	i) Enteral feeding using a either a percutaneous endoscopic gastrostomy (PEG) vs. nasogastric (NG) feeding tube within 3 days of enrolment into the study. ii) Early feeding (initiated as possible vs. no feeding for 7 days using either a PEG or	i) There was a non-significant trend in the absolute reduction in the risk of death or poor outcome at 6 months associated with early feeding. ii) PEG feeding was associated with a non-significant increase in the risk of death

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
			NG feeding tube	
FOOD	The Food or Ordinary Diet trial (part 2- oral supplementation)	Dennis, M. S., Lewis, S. C., & Warlow, C. Routine oral nutritional supplementation for stroke patients in hospital (FOOD): a multicentre randomised controlled trial. Lancet 2005b;365: 755-763.	Oral nutritional supplement (540 Kcals) in addition to a hospital diet vs. hospital diet only	Routine supplementation was not associated with reductions in the risk of death or disability at 6 months
GIST	Glucose in Stroke Trial	Gray CS, Hildreth AJ, Sandercock PA, O'Connell JE, Johnston DE, Cartlidge NE, Bamford JM, James OF, Alberti KG; GIST Trialists Collaboration. Glucose-potassium-insulin infusions in the management of post-stroke hyperglycaemia: the UK Glucose Insulin in Stroke Trial (GIST-UK). Lancet Neurol. 2007; 6: 397-406	Intravenous glucose potassium insulin vs. normal saline infusion *(Blood glucose management)*	90-day mortality was not significantly different between groups. The study could be underpowered due to poor recruitment.
HAMLET	Hemicraniectomy After MCA infarction with Life-threatening Edema Trial	Hofmeijer, J., Kappelle, L. J., Algra, A., Amelink, G. J., van, G. J., & van der Worp, H. B. Surgical decompression for space-occupying cerebral infarction (the Hemicraniectomy After Middle Cerebral Artery infarction with Life-threatening Edema Trial [HAMLET]): a multicentre, open, randomised trial. Lancet Neurol 2009; 8: 326-333.	Surgical decompression vs. best medical treatment (*Hemicraniectomy)*	There was no difference between groups in functional outcome between groups at 1 year, while more patients in the surgical group had died. However, at 3 years, a significantly lower percentage of patients in the surgical group had died
HOPE	Health Outcomes Prevention Study	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;355(9200):253-9	Ramipril vs. placebo or Vitamin E or placebo. *(Blood pressure management)*	The study was stopped prematurely with imbalanced outcomes in favor of Ramipril. There was a significant reduction in the composite outcome of myocardial infarction, stroke or cardiovascular death in the ramipril group compared to placebo.
HOT	Hypertension Optimal Treatment	Hansson L, Zanchetti A, Carruthers SG, Dahlof B, Elmfeldt D, Julius S, et al. 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;351(9118):1755-62	Target blood pressure groups: ≤90 mmHg vs. ≤85 mmHg vs. ≤80 mmHg. Protocol included felodipine and an addition of ASA vs. placebo. *(Blood pressure management)*	The composite risk of all major cardiovascular events was not significantly different among groups. Significantly fewer strokes occurred in the lowest blood pressure target group, cv event risk was greatest for those in the highest blood pressure group compared to the lowest blood

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
				pressure group. ASA therapy group had a reduction in CV events and all MIs compared to placebo.
HPS	Heart Protection Study	Collins R, Armitage J, Parish S, Sleight P, Peto R. 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;363(9411):757-67	Simvastatin vs. placebo *(Lipid management)*	There was a significant reduction in rate of first stroke for the simvastatin vs. placebo group – particularly for ischemic stroke reduction; no difference in risk of stroke was seen for hemorrhagic stroke.
HYVET	Hypertension in the Very Elderly trial	Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, et al. Treatment of hypertension in patients 80 years of age or older. The N Engl J Med 2008;358:1887-98.	Indapamide vs. placebo. Supplemented by perindopril vs. placebo. *(Blood pressure management)*	A significant reduction in fatal stroke and number of cardiovascular events was observed for the indapamide group.
ICH-ADAPT	Intracerebral Hemorrhage Acutely Decreasing Arterial Pressure Trial	Butcher KS, Jeerakathil T, Hill M, et al. The intracerebral hemorrhage acutely decreasing arterial pressure trial. Stroke 2013;44:620-26.	Target systolic BP groups < 150 mmHg vs. < 180 mmHg treated within one hour of admission *(Intracerebral hemorrhage)*	There were no significant differences in the probability of a good outcome between the 2 groups at 24 hours or 90 days.
ICSS	International Carotid Stenting Study	Ederle J, Dobson J, Featherstone RL, Bonati LH, van der Worp HB, de Borst GJ, et al. Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an interim analysis of a randomised controlled trial. Lancet. 2010;375(9719):985-97	Stenting vs. endarterectomy *(Carotid intervention)*	Interim results indicate a significantly higher risk of stroke and all-cause death in the stenting group vs. the endarterectomy group.
IDEAL	Incremental Decrease in End Points Through Aggressive Lipid Lowering	Pedersen TR, Faergeman O, Kastelein JJ, Olsson AG, Tikkanen MJ, Holme I, et al. High-dose atorvastatin vs usual-dose simvastatin for secondary prevention after myocardial infarction: the IDEAL study: a randomized controlled trial. JAMA 2005;294(19):2437-45	High dose atorvastatin vs. usual-dose simvastatin *(Lipid management)*	Nonfatal acute MI occurred significantly more often in the simvastatin group vs. the atorvastatin group. Differences in coronary death and cardiac arrest were not significantly different between groups.
IMAGES	Intravenous Magnesium Efficacy in Stroke	Muir KW, Lees KR, Ford I, Davis S. Magnesium for acute stroke (Intravenous Magnesium Efficacy in	Intravenous $MgSO_4$ within the first 24 hours of stroke vs. placebo	

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
		Stroke trial): randomised controlled trial. Lancet 2004; 363(9407):439-445.	*(Acute evaluation and management)*	
IMS III	Interventional Management of Stroke III	Broderick JP, Palesch YY, Demchuk AM, et al. for the IMS III Investigators. Endovascular therapy after intravenous t-PA versus t-PA alone for stroke. N Eng J Med 2013;368:893-903.	Partial dose of i.v. t-PA + remainder of the total dose of delivered via i.v. vs. endovascular therapy *(Endovascular therapy).*	The trial was stopped early (futility). At the point of termination there was no difference between groups in the proportion of patients who had experienced a good outcome at 90 days.
INTERACT 1	The Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial	The INTERACT Investigators. Effects of early intensive blood pressure-lowering treatment on the growth of hematoma and perihematomal edema in acute intracerebral hemorrhage. Stroke 2010;41;307-312	Intensive BP lower with oral agents to obtain a target SBP of <140 mm Hg within 1 hour of randomization vs. standard care when SBP > 180 mm Hg was treated, for 7 days. *(Intracerebral hemorrhage)*	Early intensive BP-lowering treatment attenuated hematoma growth over 72 hours in intracerebral hemorrhage. There was no appreciable effect on perihematomal edema.
INTERACT2	The Second Intensive Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial	Anderson CS, Heeley E, Huang Y, et al. for the INTERACT2 Investigators. Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. N Eng J Med 2013;368:2355-2365.	Intensive BP lower with oral agents to obtain a target SBP of <140 mm Hg within 1 hour of randomization vs. standard care when SBP > 180 mm Hg was treated, for 7 days. *(Intracerebral hemorrhage)*	More patients in the control group experienced substantial hematoma growth, although there were no differences between groups on any of the clinical secondary outcomes at 90 days.
ISAT	International Subarachnoid Aneurysm Trial	International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group. International Subarachnoid Aneurysm Trial (ISAT) of neurological clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. Lancet 2002; 360: 1267- 1274	Endovascular treatment vs. neurosurgical treatment in patients with aneurysmal SAH (*Management of subarachnoid and intracerebral hemorrhage)*	The study was stopped by the study steering committee following a planned interim analysis. Outcomes at one year demonstrated an early survival advantage for those patients treated with endovascular methods.
IST-3	International Stroke Trial-3	The IST-3 collaborative group. Effect of thrombolysis with alteplase within 6 h of acute ischaemic stroke on long-term outcomes (the third International Stroke Trial [IST-3]): 18-month follow-up of a randomized controlled trial. Lancet Neurol 2013;12:768-76.	Intravenous alteplase vs. placebo (*Acute thrombolytic therapy)*	There was no significant difference between groups in the percentage of patients who were treated with t-PA who were alive and independent at 6 months
ISTAPS	Effectiveness of a stepped primary care smoking cessation	Cabezas C, Advani M, Puente D, Rodriguez-Blanco T, Martin C.	Smoking cessation program tailored to the smokers stage	A significantly higher percentage of individuals in the intervention

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
	intervention	Effectiveness of a stepped primary care smoking cessation intervention: cluster randomized clinical trial (ISTAPS study). Addiction 2011;106(9):1696-706	of change (i.e. precontemplation-contemplation, preparation-action, maintenance) vs. usual care *(Smoking cessation)*	group were abstinent for 1 year (continuous) vs. the usual care group.
JUPITER	Justification for the Use of Statins in Prevention	Everett BM, Glynn RJ, MacFadyen JG, Ridker PM. Rosuvastatin in the prevention of stroke among men and women with elevated levels of C-reactive protein: justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER). Circulation. 2010;121(1):143-50	Rosuvastatin vs. placebo *(Lipid Management)*	There was a significant reduction in fatal and non-fatal stroke in the rosuvastatin group compared to the placebo group. This finding was due to a reduction in ischemic strokes, not hemorrhagic.
LEAPS	Locomotor Experience Applied Post Stroke Trial	Duncan PW, Sullivan KJ, Behrman AL et al. Body-weight-supported treadmill rehabilitation after stroke. N Engl J Med 2011;364(21):2026-2036.	Early Locomotor Training Program using body weight supported training program with treadmill vs. late Locomotor Training Program using body weight supported training program with treadmill vs. early Home Exercise Program	At one-year, 52% of all patients had improved functional walking ability. There was no significant difference in the proportion of patients who had improved among the three groups.
LIFE	Losartan Intervention For Endpoint Reduction Study	Devereux R, Palmierei V, Liu J, Wachtell K. Bella J, Boman K, Gerdts E, Nieminen M, Papademetriou V and Dahlof B. Progressive hypertrophy regression with sustained pressure reduction in hypertension: the Losartan Intervention For Endpoint Reduction study. J Hypertens 2002; 20:1445	Losartan vs. atenolol (*Prevention – blood pressure management)*	The data documents cardiac benefit of sustained BP control and suggests that maximum LVH regression with effective antihypertensive treatment requires at least 2 years.
MATCH	Management of ATherothrombosis with Clopidogrel in High-risk patients),	Diener HC, Bogousslavsky J, Brass LM, Cimminiello C, Csiba L, Kaste M, Leys D, Matias-Guiu J, Rupprecht HJ; MATCH investigators. 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.	Clopidogrel plus ASA vs. clopidogrel alone *(Prevention-Antiplatelet therapy)*	The addition of ASA to clopidogrel in high-risk patients is associated with a non-significant reduction in major vascular events; however, is associated with major bleeding after 18 months of follow-up.

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
		Lancet. 2004; 364(9431): 331-337		
MOSES	Morbidity & Mortality after Stroke	Schrader J, Luders S, Kulschewski A, Hammersen F, Plate K, Berger J, et al. Morbidity and Mortality After Stroke, Eprosartan Compared with Nitrendipine for Secondary Prevention: principal results of a prospective randomized controlled study (MOSES). Stroke 2005;36(6):1218-26	Nitrendipine vs. eprosartan *(Blood pressure management)*	No differences in mortality between the groups. There were significantly fewer fatal and nonfatal stroke in the eprosartan group,
MR CLEAN	A Multi center Randomized Clinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands	Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 2015; 372(1):11-20.	Endovascular treatment with t-PA or urokinase, and/or mechanical treatment with retrievable stents (intervention) vs. best medical management only, which could include intravenous t-PA (control) *(Endovascular therapy)*	There was a significant shift towards more favourable mRS scores among patients in the intervention group (adj common OR=1.67, 95% CI 1.21-2.30).
MR RESCUE	Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy	Kidwell CS, Jahan R, Gornbein J, et al. for the MR RESCUE Investigators. A trial of imaging selection and endovascular treatment for ischemic stroke. N Eng J Med 2013;368:914-923.	Mechanical embolectomy with the Merci Retriever or Penumbra System vs. standard care. *(Endovascular therapy)*	There were no differences in the percentage of patients who experienced a good outcome or who died, at 90 days
NINDS	The National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Stroke Study	The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med 1995; 333:1581-7.	Intravenous alteplase vs. placebo (*Acute thrombolytic therapy)*	At 3 months, significantly more patients in the t-PA group had experienced a good outcome
ONTARGET/ TRANSCEND	ONgoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial/Telmisartan Randomized AssessmeNT Study in ACE-INtolerant Subjects with Cardiovascular Disease	ONTARGET Investigators, Yusuf S, Teo KK, Pogue J, Dyal L, Copland I, Schumacher H, Dagenais G, Sleight P, Anderson C. Telmisartan, ramipril, or both in patients at high risk for vascular events. N Engl J Med 2008; 358(15):1547-59	ACE inhibitor ramipril vs. angiotensin-receptor blocker telmisartan as well as the combination of the two drugs in patients with vascular disease or high-risk diabetes *(Blood pressure management)*	Telmisartan was found to be equivalent to ramipril in the treatment of patients with vascular disease or high-risk diabetes with less angioedema. The combination of the two drugs was associated with more adverse events without an increase in benefit.
PAIS	Paracetamol (Acetaminophen) In Stroke (PAIS) trial	den Hertog HM, van der Worp HB, van Gemert HM et al. The Paracetamol (Acetaminophen) In Stroke (PAIS)	Paracetamol, 6x daily for 3 days vs. placebo*. (Acute*	Treatment with paracetamol was not associated with improvement

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
		trial: a multicentre, randomised, placebo-controlled, phase III trial. Lancet Neurol 2009;8:434-440.	*Management)*	beyond expectation or an increased odds of favourable outcome at 3 months.
PC	Clinical Trial Comparing Percutaneous Closure of Patent Foramen Ovale Using the Amplatzer PRO Occluder with Medical Treatment in Patients with Cryptogenic Embolism	Meier B, Kalesan B, Mattle HP, et al., for the PC Trial Investigators. Percutaneous closure of patent foramen ovale in cryptogenic embolism. N Engl J Med 2013;368:1083-1091.	PFO closure vs. medical therapy *(Prevention-PFO*)	Compared to medical therapy, PFO closure was not associated with a significant reduction in the composite outcome of stroke or death.
PHANTOM-S	Prehospital Acute Neurological Treatment and Optimization of Medical care in Stroke Study	Ebinger M, Winter B, Wendt M, Weber JE, Waldschmidt C, Rozanski M et al. Effect of the use of ambulance-based thrombolysis on time to thrombolysis in acute ischemic stroke: a randomized clinical trial. JAMA 2014; 311(16):1622-1631.	Response from a Stroke Emergency Mobile (STEMO) ambulance, equipped with a CT scanner, point-of-care-lab and a specialized pre-hospital stroke team vs. routine care *(Hyperacute-EMS management)*	The proportions of patients treated with t-PA within 90 minutes of stroke were significantly higher when STEMO was deployed (58%), compared with 48% during STEMO weeks (ie. STEMO not deployed) and 37% during control weeks.
PREDIMED	Prevention with Mediterranean Diet	Estruch R, Ros E, Salas-Salvado J, et al. for the PREDIMED Investigators. Primary prevention of cardiovascular disease with a Mediterranean diet. . N Engl J Med 2013;368:1279-1290.	Mediterranean diet supplemented with extra-virgin olive oil (EVOO) vs. Mediterranean diet supplemented with mixed nuts, vs. control diet (advice to reduce dietary fat). (*Prevention-lifestyle)*	The risk of any major cardiovascular event during a median follow-up of 4.8 years was significantly reduced in the 2 Mediterranean diet groups compared with the control group.
PREVAIL	The efficacy and safety of enoxaparin versus unfractionated heparin for the prevention of venous thromboembolism after acute ischaemic stroke	Sherman DG, Albers GW, Bladin C, Fieschi C, Gabbai AA, Kase CS, O'Riordan W, Pineo GF, on behalf of the PREVAIL Investigators.The efficacy and safety of enoxaparin versus unfractionated heparin for the prevention of venous thromboembolism after acute ischaemic stroke (PREVAIL Study): an open-label randomised comparison. Lancet 2007; 369: 1347- 1355	Enoxaparin vs. unfractionated heparin for prevention of venous thromboembolism in patients who were unable to walk unassisted within 48 hrs (*Components of acute care management)*	Enoxaparin reduced the risk of venous thromboembolism compared with unfractionated heparin. The occurrence of any bleeding was similar with enoxaparin or unfractionated heparin.
PROACT II	Prolyse in Acute Cerebral Thromboembolism II	Furlan A, Higashida R, Wechsler L, Gent M, Rowley H, Kase C, et al. Intra-arterial prourokinase for acute ischemic stroke. The PROACT II study: a randomized controlled trial.	Intra-arterial r-proUK over 2 hours +I.V. heparin vs. I.V. heparin only (control) *(Hyperacute- thrombolytic*	Treatment with IA r-proUK within 6 hours of symptom onset was associated with a better chance of a good outcome at 90 days

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
		Prolyse in Acute Cerebral Thromboembolism. JAMA 1999 Dec 1;282(21):2003-11.	*therapy)*	
PROACTIVE	PROspective pioglitAzone Clinical Trial In macroVascular Events	Dormandy JA, Charbonnel B, Eckland DJ, et al. Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomised controlled trial. Lancet 2005;366:1279-89.	Pioglitazone vs. placebo	Treatment with pioglitzone was not associated with a significant reduction in the composite outcome of mortality, non-fatal MI, stroke, acute coronary syndrome, endovascular or surgical intervention (coronary or leg arteries), amputation above the ankle.
PRoFESS	Prevention Regimen For Effectively avoiding Second Stroke	Diener HC, Sacco R, Yusuf S; Steering Committee Rationale, design and baseline data of a randomized, double-blind, controlled trial comparing two antithrombotic regimens (a fixed-dose combination of extended-release dipyridamole plus ASA with clopidogrel) and telmisartan versus placebo in patients with strokes: the Prevention Regimen for Effectively Avoiding Second Strokes Trial (PRoFESS). Cerebrovasc Dis 2008; 25 (1-2): 192	ASA plus extended-release dipyridamole vs. clopidogrel *(Prevention/ Antiplatelet therapy)*	Stroke recurrence rates were similar for both treatment groups and no significant difference of composite outcome of stroke, MI or vascular death. PRoFESS failed to meet its primary endpoint of non-inferiority of ASA extended-release dipyridamole versus clopidogrel.
PROGRESS	The perindopril protection against recurrent stroke study	PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. Lancet. 2001; 358(9287): 1033-41	Active treatment (comprised of a flexible regimen based on the angiotensin-converting-enzyme inhibitor perindopril with the addition of the diuretic indapamide) vs. placebo (*Blood pressure management)*	The blood pressure lowering regimen reduced the risk of stroke among both hypertensive and non-hypertensive individuals with a history of stroke or TIA. Combination therapy with perindopril and indapamide produced larger blood pressure reductions and larger risk reductions than did single therapy alone.
PROSPER	PRospective Study of Pravastatin in the Elderly at Risk	Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. Lancet	40 mg/day pravastatin vs. placebo (*Prevention-lipids)*	The risk of the primary outcome (composite of CHD, non-fatal MI, non-fatal or fatal stroke) was significantly reduced in the pravastatin group (HR=0.85, 95%

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		2002; 360(9346):1623-1630.		CI 0.74-0.97, p=0.014), although no reduction in the risk of stroke (non-fatal or fatal)
PROTECT	PROphylaxis of Thromboembolic Events by Certoparin Trial (non-inferiority study)	Diener HC, Ringelstein EB, von KR et al. Prophylaxis of thrombotic and embolic events in acute ischemic stroke with the low-molecular-weight heparin certoparin: results of the PROTECT Trial. Stroke 2006;37:139-144.	Certoparin (3000 U Anti-Xa o.d.) vs. Unfractionated Heparin (5000 IU t.i.d.)	No difference in the composite outcome of symptomatic or asymptomatic proximal DVT, symptomatic PE, or death related to VTE occurring during treatment period of 12-14 days.
RE-LY	Randomized Evaluation of Long-term Anticoagulation Therapy	Wallentin L, Yusuf S, Ezekowitz MD, Alings M, Flather M, Franzosi MG, et al. Efficacy and safety of dabigatran compared with warfarin at different levels of international normalised ratio control for stroke prevention in atrial fibrillation: an analysis of the RE-LY trial. Lancet 2010;376(9745):975-83	110mg dabigatran 2x/day vs. dose-adjusted warfarin (INR 2.0-3.0) and 150mg dabigatran 2x/day vs. dose-adjusted warfarin (INR 2.0-3.0) (*Antithrombotic therapy in atrial fibrillation)*	110mg dabigatran was not inferior to warfarin in preventing stroke and systemic embolism; while 150mg dabigatran was superior to warfarin in preventing stroke and systemic embolism. Similar results were seen for the rate of hemorrhagic stroke. Outcomes were assessed according to time in therapeutic range (TTR) – rates of total bleeding were higher with higher TTR in all groups.
REGARDS	Reasons for Geographic and Racial Differences in Stroke study	McDonnell MN, Hillier SL, Hooker SP, et al. Physical activity frequency and risk of incident stroke in a national US study of blacks and whites. Stroke 2013;44:2519-24.	Risk of stroke in individuals who do not engage in physical exercise as compared to those who do so 1-3 or ≥4 times per week. (*Prevention-lifestyle)*	Compared with persons exercising ≥4x/week, the risk of stroke was increased in persons who engaged in no physical activity, although results were not significant after adjusting for traditional stroke risk factors.
RESPECT	Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment	Carroll JD, Saver JL, Thaler DE, et al., for the RESPECT Investigators. Closure of patent foramen ovale versus medical therapy after cryptogenic stroke. N Engl J Med 2013;368:1092-1100.	PFO closure vs. medical therapy. *(Prevention-PFO)*	As compared to medical therapy, PFO closure was associated with a non-significant trend in preventing the composite outcome of stroke or death. A significant between group difference in the primary composite outcome was reported for the per protocol analysis.
REVASCAT	Randomized Trial of Revascularization with Solitaire	Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A et al.	Mechanical embolectomy with Solitaire FR device + best	The odds of achieving mRS score of 0-2 at 90 days were increased

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
	FR Device versus Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting within Eight Hours of Symptom Onset	Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke. *N Engl J Med 2015*; 372(24): 2296-2306.	medical management vs. best medical management *(Hyperacute- Endovascular therapy)*	significantly in the intervention group (adj OR=2.1, 95% CI 1.1-4.0).
ROCKET AF	The Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Precention of Stroke and Embolism Trial in Atrial Fibrillation	Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med 2011;365(10):883-91	20mg/day rivaroxaban vs. dose-adjusted warfarin (*Antithrombotic therapy in atrial fibrillation)*	Rivaroxaban was not inferior to warfarin for preventing stroke or systemic embolism. There were no differences in major and non-major bleeding, but there was a significant reduction in intracranial hemorrhage and fatal bleeding in the rivaroxaban group.
SAFE	Screening for Atrial Fibrillation in the Elderly	Hobbs FD, Fitzmaurice DA, Mant J, Murray E, Jowett S, Bryan S, et al. A randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in people aged 65 and over. The SAFE study. Health Technol Assess (Winchester, England) 2005;9(40):iii-iv, ix-x, 1-74	Systematic vs. opportunistic screening for atrial fibrillation *(Screening for atrial fibrillation)*	Opportunistic (identifying cases by taking a patient's pulse) screening was most effective and cost-effective for detecting atrial fibrillation.
SAMMPRIS	Stenting vs. Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis	Chimowitz MI, Lynn MJ, Derdeyn CP, Turan TN, Fiorella D, Lane BF, et al. Stenting versus aggressive medical therapy for intracranial arterial stenosis. The N Engl J Med 2011;365(11):993-1003	Aggressive management of stenosis (70-99%) vs. aggressive management of stenosis (70-99%) with percutaneous transluminal angioplasty and stenting. *(Carotid intervention)*	The trial was stopped prematurely due to significantly greater rates of stroke or death in the aggressive management with stenting group.
SAPPHIRE	Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy	Yadav JS, Wholey MH, Kuntz RE et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med 2004;351:1493-1501.	Stenting (with protection device) plus peri-operative antiplatelet therapy vs. carotid endarterectomy. (*Prevention-carotid disease)*	The combined outcome of stroke, death or MI occurred in more patients in the CEA group. No significant difference was reported in the number of patients who experienced a stroke at 1 year. At 3 years, there was no

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
				difference between groups in the incidence of stroke or mortality.
SCAST	Scandinavian Candesartan Acute Stroke Trial	Sandset EC, Bath PM, Boysen G, Jatuzis D, Korv J, Luders S et al. The angiotensin-receptor blocker candesartan for treatment of acute stroke (SCAST): a randomised, placebo-controlled, double-blind trial. Lancet 2011; 377(9767):741-750.	Treatment with candesartan vs. placebo initiated within 30 hours of stroke and continued for 7 days. *(Acute evaluation and management*)	During 6 months of follow-up, the risk of the composite vascular endpoint did not differ between treatment groups (HR=1.09, 95% CI 0.84–1.41; p=0.52)
SCOPE	The Study on COgnition and Prognosis in the Elderly	Trenkwalder. The Study on Cognition and Prognosis in the Elderly (SCOPE) – recent analyses. J Hypertens 2006, 24(suppl 1):sS107	Candesartan vs. a control group that received various other antihypertensive drugs, mostly diuretics (*Prevention - blood pressure management)*	Cardiovascular outcome benefit of candesartan-based treatment was most evident in patients without add-on treatment and in those with a history of stroke. Results in other subgroups were generally consistent with those in the entire SCOPE study population.
SEARCH	Study of the Effectiveness of Additional Reductions in Cholesterol & Homocycteine (Cholesterol)	Armitage J, Bowman L, Wallendszus K, Bulbulia R, Rahimi K, Haynes R, et al. Intensive lowering of LDL cholesterol with 80 mg versus 20 mg simvastatin daily in 12,064 survivors of myocardial infarction: a double-blind randomised trial. Lancet. 2010;376(9753):1658-69	80mg/day of simvastatin vs. 20mg/day of simvastatin *(Lipid management)*	Numbers of major vascular events were not significantly different between the two groups. Rate of myopathy was higher in the 80mg simvastatin group.
SEARCH	Study of the Effectiveness of Additional Reductions in Cholesterol & Homocycteine	Armitage JM, Bowman L, Clarke RJ, Wallendszus K, Bulbulia R, Rahimi K, et al. Effects of homocysteine-lowering with folic acid plus vitamin B12 vs placebo on mortality and major morbidity in myocardial infarction survivors: a randomized trial. JAMA 2010;303(24):2486-94	2mg of Folic Acid and 1mg Vitamin B12 vs. placebo	There were no significant differences between the groups in major vascular events, fatal or nonfatal stroke or non-coronary revascularization.
SHEP	Systolic Hypertention in the Elderly Program	Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). SHEP Cooperative Research Group. JAMA 1991;265(24):3255-64	Treatment occurred in two steps: 1. 12.5mg/day of chlorthalidone followed by 25mg/day if necessary; 2. 25mg/day atendol, followed by 50mg/day if necessary vs. equivalent placebo. *(Prevention-Blood pressure*	The incidence of ischemic stroke and hemorrhagic stroke was lower for patients in the active treatment group. There were no differences between the groups for stroke recurrence.

Acronym	Trial name	Author, Publication	Comparisons made (topic)	Key Outcomes
			management)	
SIFA	Studio Italiano Fibrillazione Atriale	Morocutti C, Amabile G, Fattapposta F, Nicolosi A, Matteoli S, Trappolini M, et al. Indobufen versus warfarin in the secondary prevention of major vascular events in nonrheumatic atrial fibrillation. SIFA (Studio Italiano Fibrillazione Atriale) Investigators. Stroke 1997;28(5):1015-21	100-200mg 2x/day of Indobufen vs. dose adjusted warfarin (INR 2.0-3.5) (*Prevention-Antithrombotic therapy in atrial fibrillation)*	No significant differences between the two groups.
SPACE	Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy	Ringleb PA, Allenberg J, Bruckmann H, Eckstein HH, Fraedrich G, Hartmann M, et al. 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial. Lancet. 2006;368(9543):1239-47	Carotid-artery stenting vs. carotid endarterectomy *(Prevention-Carotid Intervention)*	There was no evidence to support the non-inferiority of stenting compared to carotid endarterectomy at the 30 day mark.
SPARCL	Stroke Prevention by Aggressive Reduction in Cholesterol Levels trial	The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators. High-dose atorvastatin after stroke or transient ischemic attack. N Engl J Med 2006; 355: 549–59	Atorvastatin vs. placebo *(Prevention-Lipid management)*	The reduction in ischemic stroke was offset by a statistically significant increase in hemorrhagic stroke. The five-year absolute reduction in risk of major cardiovascular events was 3.5%.
SPARCL ICH	Stroke Prevention by Aggressive Reduction in Cholesterol Levels trial	Goldstein LB, Amarenco P, Szarek M, Callahan A 3rd, Hennerici M, Sillesen H, Zivin JA, Welch KM; SPARCL Investigators. Hemorrhagic stroke in the Stroke Prevention by Aggressive Reduction in Cholesterol Levels study. Neurology. 2008; 70(24 Pt 2):2364-70	Atorvastatin vs. placebo *(Prevention-Lipid management)*	Sub- analysis of SPARCL trial to further investigate the relationship between hemorrhage risk and treatment.
SPS3	Secondary Prevention of Small Subcortical Strokes	Benavente OR, Hart RG, McClure LA, Szychowski JM, Coffey CS, Pearce LA. Effects of clopidogrel added to aspirin in patients with recent lacunar stroke. The N Engl J Med 2012;367(9):817-25.	325mg/day of Aspirin and 75mg/day of clopidogrel vs. 325mg/day of aspirin and placebo. *(Prevention-Antiplatelet therapy)*	There was a significant increase in major hemorrhage and all-cause mortality in the aspirin + clopidogrel group compared to the aspirin only group. There were no differences in the risk of recurrent stroke between the two groups.
STASH	Simvastatin in Aneurysmal Subarachnoid Haemorrhage	Kirkpatrick PJ, Turner CL, Smith C, et al. Simvastatin in aneurysmal subarachnoid haemorrhage (STASH): a multicentre randomised phase 3 trial. Lancet Neurol 2014;13:666-75	40 mg simvastatin vs. placebo x 3 weeks *(Hyperacute-Management of Subarachnoid Hemorrhage)*	There were no differences in the proportion of patients who had experienced a good outcome at discharge or 6 months

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STITCH	Simplified Treatment Intervention to Control Hypertension	Feldman R, Zou G, Vandervoort M, Wong C, Nelson S, Feagan B. A simplified approach to the treatment of uncomplicated hypertension: A cluster randomized, controlled trial. Hypertension. 2009;53;646-653	A simplified treatment algorithm vs. guideline-based management *(Hyperacute-Management of Subarachnoid and Intracerebral Hemorrhage).*	A simplified antihypertensive algorithm using initial low-dose fixed-dose combination therapy is superior to guideline-based practice for the management of hypertension.
STICH II	Surgical Trial in Lobar Intracerebral Haemorrhage	Mendelow AD, Gregson BA, Rowan EN, Murray GD, Gholkar A, Mitchell PM, for the STITCH II Investigators. Emergency surgery versus initial conservative treatment in patients with spontaneous supratentorial lobar intracerebral haematomas (STICH II): a randomised trial. Lancet 2013;382:397-408.	Early surgery for the evacuation of the hematoma + best medical care vs. best medical care (*Hyperacute-Management of Intracerebral Hemorrhage).*	At 6 months, there was no difference between groups in the number of patients who had achieved a favourable outcome.
SWIFT	SOLITAIRE™ FR With the Intention For Thrombectomy (SWIFT) Study	Saver JL, Jahan R, Levy EI, Jovin TG, Baxter B, Nogueira RG, et al. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. Lancet 2012;380(9849):1241-9.	Thrombectomy with either the Solitaire Device or Merci Retriever *(Hyperacute-Endovascular therapy)*	A greater percentage in the SOLITAIRE group achieved revascularization success (TICI flow of ≥2 of the occluded territory)
SWIFT-PRIME	Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment	Saver JL, Goyal M, Bonafe A, Diener HC, Levy EI, Pereira VM et al. Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke. *N Engl J Med 2015;*372(24):2285-9.	intravenous t-PA + intra-arterial mechanical clot retrieval with the Solitaire FR device vs. treatment with intravenous t-PA only *(Hyperacute-Endovascular therapy)*	A significantly higher percentage of patients were independent at day 90 (mRS 0-2) (60.2% vs. 35.5%, RR=1.70, 95% CI 1.23-2.33, p=0.001).
SYNTHESIS EXP	Intra-arterial Versus Systemic Thrombolysis for Acute Ischemic Stroke	Ciccone A, Valvassori L, Nichelatti M, et al. for the SYNTHESIS Expansion Investigators. N Engl J Med 2013;368:904-913.	Pharmacological vs. mechanical thrombolysis *(Hyperacute-Endovascular therapy)*	There was no difference between groups in the proportion of patients surviving without disability at 90 days.
TREVO-2	Thrombectomy REvascularization of Large Vessel Occlusions in Acute Ischemic Stroke	Nogueira RG, Lutsep HL, Gupta R, Jovin TG, Albers GW, Walker GA, et al. Trevo versus Merci retrievers for thrombectomy revascularisation of large vessel occlusions in acute ischaemic stroke (TREVO 2): a randomised trial. Lancet 2012;380(9849):1231-40.	Thrombectomy with either the Merci Retriever or the Trevo Stentriever devices *(Hyperacute-Endovascular therapy)*	Successful revascularization was achieved by more patients in the Trevo group

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TNT	Treating to New Targets	LaRosa JC, Grundy SM, Waters DD, Shear C, Barter P, Fruchart JC, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. N Engl J Med 2005;352(14):1425-35	10mg of atorvastatin/day vs. 80mg of atorvastatin/day *(Prevention-Lipid management)*	Significantly fewer first major cardiovascular events in the 80mg group. Occurrence of fatal and non-fatal strokes or TIAs was also lower in the 80mg group. Adverse events more common in the 80mg group.
TRANSCEND	Telmisartan Randomised AssessmeNt Study in ACE iNtolerant subjects with cardiovascular Disease	Yusuf S, Teo K, Anderson C, Pogue J, Dyal L, Copland I et al. Effects of the angiotensin-receptor blocker telmisartan on cardiovascular events in high-risk patients intolerant to angiotensin-converting enzyme inhibitors: a randomised controlled trial. Lancet 2008; 372(9644):1174-1183.	80 mg/day telmisartan vs. placebo *(Prevention-BP control)*	There were no significant differences between groups for either the primary outcome (cardiovascular death, MI, stroke or hospitalization for heart failure) or its components.
UKPDS	United Kingdom Prospective Diabetes Study 38	Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. BMJ 1998;317:703-13.	Tight control vs. less tight control of blood pressure *(Prevention-Diabetes)*	There was a reduced risk of developing any end point related to diabetes associated with tight blood pressure control, including any stroke.
VECTORS	Very Early Constraint-Induced Movement during Stroke Rehabilitation	Dromerick AW, Lang CE, Birkenmeier RL et al. Very Early Constraint-Induced Movement during Stroke Rehabilitation (VECTORS): A single-center RCT. *Neurology* 2009;73(3):195-201.	Standard CIMT vs. high-intensity CIMT vs control condition (ADL training + bilateral upper-extremity training exercises), initiated within the first two weeks of stroke.(*Rehabilitation)*	Patients in the standard CIMT and control treatment groups achieved similar gains in total Action Research Arm Test scores, while subjects in the high-intensity CIMT group gained significantly fewer points (24.2 vs. 25.7 vs. 12.6).