Major Ongoing Stroke Trials

The following is a list of major ongoing studies about stroke. Information about other multicenter studies that might be included in this list should be submitted to the Stroke Editorial Office by the Principal Investigator. The list will appear in the February, June, and October issues of Stroke.

Acute Candesartan Cilexetil Evaluation in Stroke Survivors (ACCESS Study)

The ACCESS Study was designed to evaluate the influence of an early, moderate BP reduction in patients with acute cerebral ischemia in comparison to restrictive antihypertensive therapy. Outcome parameters are mortality and morbidity, measured by the neurological status. In total, 400 patients with acute cerebral ischemia and neurological deficit (motor paresis) are treated. Inclusion criteria are initial BP values of >200/110 mm Hg (systolic and/or diastolic) in occasional BP measuring or >180/105 mm Hg as median value of two measurements in 30 minutes. Furthermore, a motor paresis (monoparesis, hemiparesis, Bell’s palsy) has to be present. Patients are randomized and treated double-blind for 7 days with placebo or the AT1 receptor antagonist candesartan cilexetil. This substance was chosen due to its slow onset of action (maximum 6 hours after intake), and the low rate of side effects. Further, animal experiments have shown a neuroprotective effect. The study design is double-blind, randomized, and multicenter. The follow-up phase lasts 1 year. The placebo group is treated with candesartan if they are hypertensive after 7 days. Normotensive patients are followed up but not treated. The verum group is also continued on candesartan. If hypertension remains, a combination therapy with other substance classes is possible. Primary end points are patient morbidity (functional status measured with Rankin Scale and Barthel Index, degree of motor deficit by NIH scale) and mortality rates after 3 months. Follow-up will be continued for 12 months.

Principal Investigators: Prof Dr J. Schrader, Prof Dr P. Dominik
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Location: Germany
Number of Centers: 60 –70
Sponsor: ASTRA GmbH Germany

African American Antiplatelet Stroke Prevention Study (AAASPS)

AAASPS is a randomized, double-blind, multicenter, controlled clinical trial to compare the effect of ticlopidine (500 mg/day) and aspirin (650 mg/day) in the prevention of recurrent stroke, myocardial infarction, and vascular death in African Americans with recent, noncardioembolic ischemic stroke. Eighteen hundred patients (900 in each group) at 50 sites nationally will be randomized at least 7 days but no more than 90 days after the qualifying event. Study patients will be followed up for 2 years. Analysis of key end points will use the intention-to-treat principle, and time-to-event data will be analyzed using Mantel-Haenszel and various regression methods. Safety analyses will focus on the incidence of severe adverse events, such as neutropenia, thrombocytopenia, gastrointestinal bleeding, and hepatic dysfunction.

Principal Investigator: Philip B. Gorelick, MD, MPH
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Location: Clinical Management Center and Data Management Center, Rush Medical Center, Chicago, IL

Number of Centers: 50 (recruitment is estimated to continue through September 2001)
Sponsor: National Institute of Neurological Disorders and Stroke, National Institutes of Health (study medication supplied by Roche Laboratories and the Bayer Company)
Dates of Study: Randomization and follow-up December 15, 1995, through September 2003

Anticoagulants Versus Aspirin and the Combination of Aspirin and Dipyridamole Versus Aspirin Only in Patients With Transient Ischemic Attacks or Nondisabling Ischemic Stroke: ESPRIT (European/Australian Stroke Prevention in Reversible Ischemia Trial)

The Dutch TIA Trial and a literature review indicate that low-dose aspirin in any daily dose of at least 30 mg up to 325 mg is effective in the prevention of threatened stroke, but 87% of subsequent strokes in patients with TIAs or nondisabling ischemic strokes are not prevented. Anticoagulants have been proven highly efficacious in recently completed trials after myocardial infarction and after cerebral ischemia and atrial fibrillation. In patients after cerebral ischemia of presumed atherothrombotic origin, high-intensity anticoagulation (INR 3.0 to 4.5) is not safe. Data from SPIRIT (Stroke Prevention in Reversible Ischemia Trial) indicate that anticoagulant therapy with an intensity of INR 2.0 to 3.0 is both safe and efficacious in stroke prevention. In the 2nd European Stroke Prevention Trial (ESPS-2) a 22% relative risk reduction of the combination of aspirin and dipyridamole above that of aspirin only is reported; the results of this trial, however, are controversial. ESPRIT is designed to randomize 4500 patients between oral anticoagulation (INR 2.0 to 3.0), the combination of dipyridamole (400 mg daily) plus aspirin (in any dose between 30 and 325 mg), and aspirin only (in any dose between 30 and 325 mg). Primary outcome event is the composite event of vascular death, stroke, myocardial infarction, or major bleeding complication; the outcome assessment will be blinded.

ESPRIT is an international, multicenter study in (at least) the following countries: Australia, Austria, Belgium, Germany, France, Israel, Italy, the Netherlands, Portugal, Singapore, Spain, India, Switzerland, the United Kingdom and the United States. Recruitment for this trial started in July 1997; as of November 2001, 1798 patients from 76 hospitals had been included. With over 2900 patient-years of follow-up, a total of 232 outcome events have been reported, including 11 intracranial bleeds. As the investigators are still blinded, these outcome events are not yet separated by treatment group. However, these data suggest that treatment with oral anticoagulants in the current INR range is safe. New centers are still invited to participate.

Steering Committee: Australia, G.J. Hankey, MD; Austria, F. Aichner, MD; Belgium, G. Vanhooreen, MD; France, D. Leys, MD; Germany, E.B. Ringelstein, MD; Israel, N.M. Bornstein, MD; Italy, S. Ricci, MD; the Netherlands, A. Algra, MD, J. van Gijn, MD, J.W. Gorter, MD, P.J. Koudstaal, MD, Y.M. Ruigrok, MD, and E.L.L.M. De Schryver, MD; Portugal, J. Ferro, MD; Singapore, C. Chen, MD; Spain, A. Chamorro, MD; Sweden, A. Terent, MD; Switzerland, J. Bogousslavsky, MD; United Kingdom, G.S. Venables, MD; for the ESPRIT group.
Aspirin Versus Anticoagulants in Symptomatic Intracranial Stenosis of the Middle Cerebral Artery (AVASIS)

In retrospective studies, oral anticoagulants are reported to be superior to aspirin in preventing stroke or other vascular recurrences in patients with intracranial stenosis. AVASIS is a trial aimed at comparing both treatments in symptomatic stenosis of the middle cerebral artery (MCA). The AVASIS study is a randomized, multicenter, open trial designed to compare the efficacy and safety of aspirin (300 mg/d) and coumarin (INR 2–3) in the secondary prevention of ischemic stroke, other vascular events, and major hemorrhagic complications among patients with transient ischemic attack and/or cerebral infarction attributable to MCA stenosis. To rule out other sources of cerebral ischemia, all patients must have normal hematologic studies, no cardioembolic or aortic potential embolic sources (including normal transesophageal echocardiography), no other arterial occlusive diseases (stenosis <50% in proximal arterial segments), and no other potential stroke etiology. The MCA stenosis will be diagnosed by conventional angiography or by at least 2 noninvasive diagnostic tests (transcranial Doppler, MR angiography, or CT angiography). The primary combined end point includes (1) nonfatal cerebral infarction, (2) nonfatal acute myocardial infarction, (3) vascular death (including death after cerebral infarction, acute myocardial infarction, aortic dissection, congestive heart failure, pulmonary thromboembolism, and sudden death), and (4) major hemorrhagic complications. Twenty-six Spanish centers will recruit 300 patients (150 in each therapeutic arm). Follow-up will range from 1 to 3 years. For further details, visit the web www.santpau.es/AVASIS.

Principal Investigator: Dr Joan Martí-Fàbregas
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Location: Spain and Portugal
Number of Centers: 16 currently authorized. Investigators from any country are invited to participate. E-mail jmarti@hsp.santpau.es
Sponsor: Grant from FIS (Fondo de Investigaciones Sanitarias), Ministerio de Sanidad y Consumo, Spain.
Dates of study: Randomization started by the end of 2000. Recruitment is expected to finish by the end of 2003.

Asymptomatic Carotid Emboli Study (ACES)

Better ways are required to identify high-risk patients with asymptomatic carotid stenosis who may be suitable for endarterectomy. Previous small studies have suggested that the presence of asymptomatic embolic signals detected using transcranial Doppler ultrasound may identify a high-risk group. ACES is a large, multicenter, international prospective study that will determine whether asymptomatic emboli detected in the middle cerebral artery are an independent predictor of stroke and TIA risk in patients with asymptomatic carotid stenoses (≥70%). Carotid stenosis is identified by duplex ultrasound. Unilateral middle cerebral artery transcranial Doppler recordings are made for 1 hour on each of 2 occasions at study entry. Recordings are made onto digital audio tape and are analyzed by the coordinating center, blinded to subject identity. Subjects are then followed for 2 years at 6-month intervals. There is also an option to perform cerebrovascular reactivity measurements at study entry. Six hundred subjects will be recruited. Recruitment began in 2000 and is planned to finish in 2002–2003, with follow-up complete in 2004–2005.

Principal Investigator: Hugh Markus, FRCP
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Location: Eire, Germany, Israel, Italy, Netherlands, United Kingdom, United States
Number of Centers: 12 (still recruiting)
Sponsor: British Heart Foundation
Dates of Study: 2000–2005

Asymptomatic Carotid Surgery Trial (ACST)

This is an international, multicenter trial to assess the place of carotid endarterectomy in the management of patients with severe carotid stenosis who are currently asymptomatic. Patients will be randomized to best medical treatment alone or to best medical treatment plus carotid endarterectomy.

Principal Investigators: A.W. Halliday, FRCS; A.O. Mansfield, FRCS; and D.J. Thomas, MD, FRCP
Contact: Angela Rua, PhD, Trial Coordinator. Phone 44(0)20-8725-3746. Fax 44(0)20-8725-3782. E-mail acst@sghms.ac.uk
Location: The ACST Office, Department of Cardiological Sciences, St Georges Hospital Medical School, Cranmer Terrace, London SW17 0RE, UK
Number of Centers: 160+
Sponsor: Stroke Association and Medical Research Council (UK)
Dates of Study: April 1993 (continuing)

Australian Urokinase Stroke Trial (AUST)

This study is designed to test the hypothesis that the administration of intra-arterial urokinase plus anticoagulants in patients with acute posterior circulation ischemic stroke and a lyeable lesion seen angiographically will reduce morbidity and mortality assessed at 6 months compared with the administration of anticoagulants alone. Two hundred eligible patients will be randomized in a blinded fashion to receive either urokinase plus anticoagulants or anticoagulants alone. Patients will be accrued over a 2-year period and the results analyzed on an intention-to-treat basis. An initial pilot study of 15 patients has been undertaken.

Contacts: Prof Geoffrey Donnan, Co-ordination Centre, Dept of Neurology, Austin & Repatriation Medical Centre, Heidelberg Vic 3084, Australia. Phone 61-3-9496-5455. Fax 61-3-9457-4605. Prof Stephen Davis, Dept of Neurology, Royal Melbourne Hospital, Parkville Vic 3050, Australia. Phone 61-3-9342-8848. Fax 61-3-9342-8427.
Location: Co-ordination Centre, Dept of Neurology, Austin & Repatriation Medical Centre, Heidelberg 3084, Australia
Number of Centers: 8
Sponsor: The Serono Company has withdrawn its sponsorship. Centers are in the process of obtaining local indemnity while alternative sponsorship is being sought.

*Indicates centers that are currently recruiting.
Dates of Study: February 1996 to 2004

*Blood Pressure in Acute Stroke Collaboration (BASC)*

Hypertension and hypotension in the acute phase of stroke are associated with a poor outcome; paradoxically, lowering blood pressure may also worsen outcome. BASC is performing a systematic review of blood pressure changes versus outcome in acute stroke trials that involve vasoactive agents. Both group and individual patient data will be analyzed to assess whether therapeutic alteration of blood pressure is safe and effective in improving outcome, and if so, with which agent. Authors of such trials are invited to contact the investigators.

Principal Investigator: P.M.W. Bath, MD, FRCP
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Location: University of Nottingham, Nottingham, UK
Number of Centers: Those centers that have organized a randomized controlled trial in acute stroke involving a vasoactive drug.
Sponsor: Trent Regional Health Authority National Health Service Research and Development Executive. The study is being performed under the auspices of the Cochrane Collaboration Stroke Review Group and is published in the Cochrane Library.
Dates of Study: November 1995 (continuing)

Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS)

CAVATAS is a randomized, multicenter trial to determine the benefits and risks of percutaneous transluminal angioplasty of the carotid and/or vertebral arteries in patients with symptomatic and asymptomatic cerebrovascular disease. The study includes a randomized comparison between carotid angioplasty and carotid endarterectomy.

Principal Investigator: M.M. Brown, MD
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Location: Europe, North America, and Australia
Number of Centers: 24. Total number of patients recruited = 562.
Sponsor: British Heart Foundation, National Health Service Research and Development Programme, and The Stroke Association
Web address: www.ion.ucl.ac.uk/cavatas_icss/

Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST)

CREST is a prospective, randomized, multicenter, clinical trial to assess the relative efficacy of carotid endarterectomy (CEA) versus carotid artery stenting (CAS) using the ACCULINK Carotid Stent System in preventing stroke, myocardial infarction, and death during the 30-day periprocedural period and ipsilateral stroke thereafter. The study includes a lead-in phase for credentialing of interventionists, beyond their initial training and certification requirements. Approximately 2500 patients with TIA, amaurosis fugax, or nondisabling stroke within 180 days of randomization and ipsilateral carotid stenosis >50% (defined as >70% by ultrasound or >50% by angiography) will be followed for up to 4 years. Follow-up includes clinic visits at 1, 6, and 12 months, then every 6 months for study duration, with phone contact every 3 months. All patients will receive best medical management, which includes treatment with aspirin and management of hypertension and medical risk factors. Recruitment of patients began in December 2000, but the start-up date will vary across centers depending on their completion of certification and regulatory requirements.

Principal Investigator: Robert W. Hobson II, MD
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Location: North America
Number of Centers: 50–60
Sponsors: National Institute of Neurological Disorders and Stroke, National Institutes of health; Advanced Cardiovascular Systems, Inc, is the device sponsor.
Dates of Study: 2000–2004

Early GABA-ergic Activation Study In Stroke (EGASIS)

EGASIS is a multicenter, randomized, placebo-controlled, double-blind trial evaluating the use of diazepam in the acute phase of stroke. GABA-ergic activation, which can easily be achieved by diazepam, may be neuroprotective in acute stroke. Experimental data and preliminary clinical data suggest efficacy of diazepam. EGASIS aims to detect an absolute reduction of at least 4% (10% relative reduction) in the chance of dying or surviving with a major handicap at 3 months after stroke. This requires about 5000 patients, half of whom will receive diazepam and the other half a placebo. The following dose schedule was found to be safe and feasible in a safety study: 10 mg diazepam every 12 hours for 3 days (total 6 doses), the first dose to be delivered by means of a rectiole as soon as possible after the stroke but at least within 12 hours. Randomization, which is done by telephone to a 24-hour service in Amsterdam, is stratified for center, whether the patient is fully alert or not and the time between the onset of stroke and randomization telephone call (0–3 hours, 3–6 hours, 6–12 hours). Follow-up is at 2 weeks or on earlier discharge. End-point measurement is at 3 months by means of the modified Rankin handicap scale and the Barthel Index. Case record forms (at randomization, 2 weeks and 3 months) are faxed or mailed to the central trial office in Maastricht, where the data will be stored in a comprehensive data base. A cooperative network of centers has been established (and is still expanding) in the Netherlands, Poland, Austria, Belgium, Denmark, Spain, and Germany. In each country a national coordinator serves as the intermediary between the trial office and individual collaborating centers. Data analysis will be performed centrally. Publication of trial results will be in the name of all the participants. An independent Data Monitoring Committee monitors the overall conduct of the trial.

Principal Investigator: Dr J. Lodder, MD, PhD
Contact: Dr J. Lodder/Ms A.M. Hilton, RN, trial coordinator, EGASIS Trial Office, Dept of Neurology, University Hospital Maastricht, PO Box 5800, 6202 AZ Maastricht, The Netherlands. Phone 31-43-3561541. Fax 31-43-3561999. E-mail aki@sneu.azm.nl
Location: The Netherlands, Poland, Austria, Belgium, Spain, Denmark
Number of Centers: 45, with more centers welcome
Sponsor: Special Clinical Research Fund of the Netherlands Heart Foundation, Dutch Brain Association
Dates of Study: 1999 through the end of 2003

Efficacy of Nitric Oxide in Stroke (ENOS) Trial

Nitric oxide is a multimodal molecule that is a candidate treatment for acute ischemic and hemorrhagic stroke, as based on
preclinical and preliminary clinical data. Potential mechanisms of action include lowering blood pressure, improving cerebral perfusion, and neuroprotection. ENOS is a large, academic, prospective, randomized, open, blinded end point, international, collaborative controlled trial designed to test the safety and efficacy of transdermal glyceryl trinitrate (a nitric oxide donor) in 5000 patients when given within 48 hours of stroke onset. Patients who are taking antihypertensive therapy at the time of their stroke will also be randomized to continue or stop this. The primary end point is combined death or disability (modified Rankin Scale score 3–6) at 3 months, to be assessed centrally. Subgroup analyses will include efficacy in patients with ischemic stroke, hypertension (systolic blood pressure >160 mm Hg), or treatment within 12 hours. Randomization and data registration will be performed over the Internet. Centers are invited to join the collaborative group.

**Principal Investigator:** Philip M. Bath, FRCP

**Contact:** P.M.W. Bath, ENOS Trial Centre, Division of Stroke Medicine, University of Nottingham, Nottingham City Hospital Campus, Nottingham NG5 1PB, UK. Phone 44-115-840-4795. Fax 44-115-840-4795. E-mail enos@nottingham.ac.uk. Internet http://www.nottingham.ac.uk/stroke-medicine

**Location:** Global

**Number of Centers:** Looking for 100+

**Sponsor:** None; MRC application pending

**Dates of Study:** July 2001 (continuing)

**FOOD Trial (Feed Or Ordinary Diet): A Multicenter Trial to Evaluate Various Feeding Policies in Patients Admitted to Hospital With a Recent Stroke**

This “family” of trials aim to answer 3 important questions about feeding of patients after a stroke: (1) Does nutritional supplementation increase the proportion of patients with stroke who survive without disability? (2) Does early initiation of tube feeding (nasogastric [NG] or percutaneous endoscopic gastrostomy [PEG]) in patients who are unable to take an adequate diet orally increase the proportion of patients with stroke who survive without severe disability? (3) Is feeding via a PEG tube instead of the traditional NG tube associated with improved outcomes after stroke? These 3 simple pragmatic trials aim to randomize a total of 9000 patients by 2004.

**Principal Investigator:** Dr Martin Dennis

**Contact:** Dr Martin Dennis, FOOD Trial Clinical Coordinator, FOOD Trial Coordinating Center, Neurosciences Trials Unit, Western General Hospital, Crewe Road, Edinburgh, UK EH4 2UX. Phone 44-131-537-3126. Fax 44-131-332-5150. E-mail FOOD@skull.dcn.ed.ac.uk.

**Location:** Currently, international, collaborating centers in Europe, Australasia, North and South America, and Southeast Asia

**Number of Centers:** 145 at present, but actively seeking centers to increase this number to over 150 worldwide.

**Sponsors:** NHS R&D HTA Program; The Stroke Association, Chief Scientist Office, Scotland; Chest Heart & Stroke Scotland

**Dates of Study:** 1996 through 2004

**Global Carotid Artery Stent Registry**

This registry is an expanding multicenter, retrospective study to determine the benefits and risks of percutaneous transluminal angioplasty with stent placement of the cervical carotid arteries in patients with cerebrovascular disease. The basic intent of the survey is to evaluate the growth of carotid stent placement and obtain an early review of its results, including stent procedures, technical success, and types of stents placed. In addition, complications such as TIAs, minor and major strokes, and deaths for symptomatic and asymptomatic patients will be studied. Long-term follow-up involving restenosis rates and neurological events will be monitored.

**Principal Investigator:** Michael H. Wholey, MD, MBA

**Contact:** Michael H. Wholey, MD, MBA, Department of Radiology, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Dr, San Antonio, TX 78284. Phone 210-567-6433. Fax 210-567-5541. E-mail wholey@uthscsa.edu

**Location:** Global

**Number of Centers:** Currently 30, looking for 100+.

**Sponsor:** None

**Dates of Study:** June 1997 (continuing)

**Home Evaluation of Stroke Induced Aid (HESTIA)**

The HESTIA study is a multicenter, randomized controlled trial designed to evaluate the effect of a nursing care program in recently discharged stroke patients. Six stroke nurses have been appointed (1 full-time equivalent) to include 600 patients and carry out the intervention. Dutch-speaking adult patients are included if they have not been hospitalized before as a result of a stroke and are discharged home. In addition to conventional care, the stroke nurse will contact the patients (and their primary carers) in the intervention group 3 times by telephone (1–3 weeks, 4–6 weeks, and 18–22 weeks after discharge) and once by a home visit (10–12 weeks after discharge). During all contacts, a semistructured protocol is used in which the poststroke care is described, such as information concerning diagnosis, consequences of the stroke, and secondary prevention. Problems perceived by the patient (and primary carer) and the interventions carried out by the nurse are recorded. Patient outcomes will be assessed 6 months after discharge: SF-36 and satisfaction with care (both are primary outcomes); HADS; EuroQol; Barthel; Rankin; compliance (secondary prevention drugs); number/kind of unmet care demands; number of readmission days in hospital/other center; number of contacts with general practitioner/para)medics; knowledge about stroke. Informal caregiver outcomes are caregiver strain index; sense of competence questionnaire, social support, and knowledge about stroke.

**Steering Committee:** K.W.J. Albrecht, MD; A. Algra, MD; J.P. Boter, MSc; J.A. Carpay, MD; J. van Gijn, MD; R. de Haan, PhD; L.J. Kappelle, MD; V.I.H. Kwa, MD; G.J.E. Rinkel, MD; M. Vermeulen, MD

**Contact:** Han Boter, MSc, Trial Office Neurology, Room H 02 128, University Medical Center Utrecht, PO Box 85500, 3508 GA Utrecht, Netherlands. Phone 31-30-2508350. Fax 31-30-2522782. E-mail J.Boter@neo.azu.nl

**Number of Centers:** 11–14

**Sponsor:** The Netherlands Heart Foundation, The Netherlands Organization for Scientific Research, and the University Medical Center Utrecht

**Dates of Study:** September 1998 through August 2002

**International Carotid Stenting Study (ICSS)**

ICSS is a randomized, multicenter trial to compare the risks of treatment and benefits in the prevention of stroke of primary carotid stenting in comparison with conventional carotid endarterectomy.

**Principal Investigator:** M.M. Brown, MD

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**Location:** Europe, North America, Japan, and Australia

**Global Carotid Artery Stent Registry**
International Subarachnoid Aneurysm Trial (ISAT)

ISAT is an open, randomized, controlled clinical trial of patients with acute subarachnoid hemorrhage admitted to participating centers, in whom the responsible doctor is uncertain whether endovascular or neurosurgical treatment policy is best for that patient. ISAT aims to compare the safety and efficacy of an endovascular treatment policy of ruptured intracranial aneurysms with a conventional neurosurgical treatment policy in an eligible population. The primary objective is to determine whether endovascular treatment of acutely ruptured intracranial aneurysms, compared with neurosurgery, reduces the proportion of patients with a moderate or poor outcome (defined by Rankin grade 3–6) by 25% at 1 year. Secondary objectives are to determine whether endovascular treatment is as effective as surgery in preventing rebleeding, results in a better quality of life, is more cost effective than surgery, and improves the neuropsychological outcome at 1 year. Randomization to endovascular or neurosurgical treatment is via a 24-hour telephone service provided by the Clinical Trials Services Unit at the Oxford coordinating center. The study will complete recruitment in late 2002 and produce its initial report on the primary outcome data in 2003. To date, 45 participating clinical centers have randomized over 1948 of the 2500 patients required. This study is the largest randomized trial of the management of SAH and is likely to have a significant impact on the future management of this disease.

Principal Investigators: Mr Richard Kerr (consultant neurosurgeon), Dr Andrew Molyneux (consultant neuroradiologist)

Contact: Julia Shrimpton (Clinical Research Manager), Neurovascular Research Unit, The Radcliffe Infirmary, Woodstock Road, Oxford, UK OX2 6HE. Phone 44-1865-224929. Fax 44-1865-224490. E-mail isat@radiology.ox.ac.uk and julia.shrimpton@radiology.ox.ac.uk

Location: Europe, North America, Canada, Australia

Number of Centers: 45

Sponsors: United Kingdom Medical Research Council, Canadian Medical Research Council, French Health Ministry, and the Stroke Association of United Kingdom


Intraoperative Hypothermia for Aneurysm Surgery Trial, Part 2 (IHAST2)

While hypothermia has been used for many years to “protect the brain” during neurovascular surgery, its value has never been rigorously evaluated. The IHAST2 trial is designed to examine the protective efficacy of mild intraoperative hypothermia (target core temperature 33°C) during open craniotomies performed to clip intracranial aneurysms. Eligibility is restricted to adults with recent (<14 days), documented aneurysmal subarachnoid hemorrhage who are World Federation of Neurosurgeons grade I, II, or III at the time of surgery. Eligible, consenting patients undergo a standardized anesthetic and are randomized to either normothermia (target temperature 36.5°C) or hypothermia. The duration of cooling is limited only to the intraoperative period; rewarming of hypothermic patients begins immediately after application of the aneurysm clip. Short-term follow-up will involve daily evaluations for 14 days or until discharge. After surgery, patients are followed for 3 months. The primary outcome variable is Glasgow Outcome Score (GOS) at 3 months after surgery. Secondary outcomes at 3 months also include NIH Stroke Scale Score, Barthel Activites of Daily Living Index Rankin Disability Score, a 6-test neuropsychology battery, and the Mini-Mental State Examination. The trial will enroll 1000 patients and is powered to permit detection of a 10% absolute difference in the fraction of patients with 3-month postoperative “good outcome” GOS (eg. 65% normothermic vs 75% hypothermic).

Principal Investigator: Michael M. Todd, MD, Dept of Anesthesia, University of Iowa

Contact: Michael M. Todd, MD, Department of Anesthesia, University of Iowa College of Medicine, 200 Hawkins Dr, Iowa City, IA 52242. Phone 319-356-0461. Fax 319-384-8072. E-mail ihast2@iowa.edu. Web site http://ctsdmc.public-health.uiowa.edu/IHAST2/home.htm

Location: Australia, United States, Canada, Great Britain, Austria, Germany

Number of Centers: 25

Sponsor: National Institute of Neurologic Disorders and Stroke, National Institutes of Health


*Intravenous Magnesium Efficacy in Stroke Trial (IMAGES)

Intravenous magnesium salts are neuroprotective in preclinical models of stroke, and preliminary clinical data indicate that magnesium sulfate is safe and well-tolerated in stroke patients. IMAGES is a randomized, double-blind, placebo-controlled, multicenter collaborative trial designed to test the efficacy of magnesium sulfate given within 12 hours of onset of clinically diagnosed acute stroke. Randomization of approximately 2700 patients is planned. The primary end point is combined death and disability (Barthel score of 0/100) at 90 days. Separate analysis of patients treated 1–6 hours after onset is planned. Telephone randomization and simplified data collection permit recruitment by centers with minimum effort and delay. Further centers are invited to join the collaborative group. An MRI substudy (MR IMAGES) is being coordinated by Drs J. Saver and C. Kidwell at UCLA (ckidwell@ucla.edu).

Principal Investigators: Kenneth R. Lees, MD, FRCP, and Keith W. Muir, MD, MRCP

Contacts: K.R. Lees, International Coordinating Center, Acute Stroke Unit, University Department of Medicine and Therapeutics, Western Infirmary, Glasgow G11 6NT, Scotland. Phone 44-141-211-2474. Fax 44-141-211-6312. E-mail k.r.lees@clinmed.gla.ac.uk or images@clinmed.gla.ac.uk. Internet: http://www.medther.gla.ac.uk/studies/images/index.htm

Location: Acute Stroke Unit, University Department of Medicine and Therapeutics, Western Infirmary, 44 Church St, Glasgow, Scotland, UK

Number of Centers: 94 (center recruitment continues; up to 100 centers required)

Sponsor: UK Medical Research Council. MR-IMAGES is sponsored by the NIH.

Dates of Study: Recruitment presently over 1900 patients and expected to continue until mid 2003.

Magnesium and Acetylsalicylic Acid in Subarachnoid Hemorrhage (MASH)

The MASH study is a prospective randomized, placebo-controlled, multicenter trial to determine whether magnesium and/or acetylsalicylic acid reduce the frequency of delayed cerebral ischemia in patients admitted within 4 days after aneurysmal subarachnoid hemorrhage. Magnesium sulfate 64 mmol/d (or placebo) is started intravenously as soon as possible after admission and continued until 14 days after operation or embolization of the aneurysm, or for a maximum of 18 days when aneurysm treatment is
done 4 days after hemorrhage or not at all. Acetylsalicylic acid 100 mg/d sup. (or placebo) is given only if operation or embolization is performed within 4 days after subarachnoid hemorrhage. It is started immediately after aneurysm treatment and continued for 14 days postoperatively. Secondary outcome measurements include the modified Rankin scale after 3 months, rebleed, and postoperative hemorrhage. We plan to include 230 patients in 3.5 years.

Steering Committee: K.W.J. Albrecht, MD; A. Algra, MD; W.M. van den Bergh, MD; J.W. Berkelbach van der Srenkel; C. Dirven, MD; J. van Gijn, MD; G.J.E. Rinkel, MD; M. Vermeulen, MD

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Number of Centers: 3
Sponsor: The Netherlands Heart Foundation (grant 99.107)
Dates of Study: Recruitment started in November 2000.

Morbidity and Mortality After Stroke—Eprosartan vs Nitrendipine for Secondary Prevention (MOSES)

The benefit of antihypertensive treatment for primary prevention of stroke is well documented in several trials. Hypertension after stroke seems to be associated with a poor outcome. There are only a small number of studies on secondary prevention of hypertensive stroke patients, which are also of limited prognostic value. Furthermore, it is still an open question which antihypertensive drug should preferably be used in this group of patients. Thus, no evidence-based treatment for hypertensive patients with cerebrovascular diseases can be recommended. MOSES is a prospective, multicenter, randomized, controlled, PROBE-designed (Prospective, Randomized, Open, Blinded End point) trial in Germany. The study will compare the AT1 receptor antagonist eprosartan with the calcium channel blocker nitrendipine; 2128 hypertensive patients who have had an ischemic or hemorrhagic stroke during the last 24 months prior to study start will be included. The duration of treatment will be 2 years. Primary end point is the combination of total mortality and of hospitalizations due to cardiovascular and cerebrovascular events.

Principal Investigator: Prof Dr J. Schrader
Contact: Prof Dr J. Schrader, St Josefs Hospital, Ritterstr 17, D-49561 Cloppenburg, Germany. Phone: 49-4471-162951. Fax 49-4471-915555. E-mail J.R.Schrader@t-online.de
Location: The MOSES Study Center, Cloppenburg, Germany
Number of Centers: 600
Sponsor: HMR Germany, Solvay Pharma

MRC/BHF Heart Protection Study

This is a randomized 2×2 factorial trial of cholesterol reduction with Simvastatin and/or antioxidant vitamin therapy in 20,000 high-risk subjects, including over 3000 with TIA, and nearly 7000 with minor ischemic stroke or other peripheral vascular disease.

Principal Investigator: Prof R. Collins and Prof R. Peto
Location: United Kingdom
Number of Centers: Approximately 70
Sponsor: UK Medical Research Council, British Heart Foundation, Merck Sharp & Dohme, and Hoffman-LaRoche
Dates of Study: 1994 through 2001

Prevention of Poststroke Depression After Acute Ischemic Stroke Using the Selective Serotonine Reuptake-Inhibitor Sertraline (PreDIS-Study)

The development of persistent depressive symptoms is a severe and frequent complication of ischemic stroke (ie, poststroke depression [PSD]). The reported prevalences of depressive symptoms in stroke patients varied from 20% to 50% and from 12% to 26% for major depressive symptoms in previous studies. Several follow-up studies revealed a higher overall mortality and a less beneficial functional outcome in stroke patients with major depression. Data from interventional studies treating or preventing PSD are rare. In most trials, tricyclic or tetracyclic antidepressive agents were used, which are often accompanied by therapy limiting adverse events, especially in elderly patients with cardiovascular disease. The PreDIS-Study was designed to limit such adverse events by the use of paradoxical embolism. Paradoxical embolism has been suggested as an important mechanism of stroke pathogenesis in light of the high prevalence of intracardiac shunting in patients with cryptogenic stroke. However, there is little information on pelvic deep venous thrombosis (DVT) in stroke patients, cryptogenic or otherwise. The PELVIS study aims to acquire information on the incidence and nature of pelvic DVT in this population. All patients aged 18–60 years with ischemic stroke are scanned within 72 hours of stroke onset. Scanning involves 2 brief MRI venogram pulse sequences. Further clinical data are then collected, and stroke subtype is determined by the time of discharge. The PELVIS study aims to determine the prevalence of pelvic DVT early after an ischemic stroke and hypothesizes that this value will be greater in those with cryptogenic stroke compared to those with stroke of determined origin. Furthermore, it is hypothesized that stroke patients with pelvic DVT will have more risk factors for venous thrombosis compared to patients without pelvic DVT.

Principal Investigators: Will Longstreth, MD, and Steven C. Cra-mer, MD
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Location: United States
Number of Centers: 5–8
Sponsor: American Heart Association
Dates if Study: 1999–2002
of a selective serotonin reuptake inhibitor for which safety, tolerability, and efficacy has been shown in depressive patients with stroke or myocardial infarction. The primary endpoint of the study is to demonstrate a preventive effect of sertraline on the incidence of PSD. Secondary endpoints are improvement of functional outcome and quality of life. The PreDIS-Study is a double-blind, randomized, placebo-controlled trial that will enroll 300 patients from 6 neurological stroke units in Hessen, Germany. Inclusion criteria is a unilateral ischemic cerebral infarction within 3 days prior to hospital admission. Major exclusion criteria are early and complete recovery of neurological symptoms, mechanical ventilation for more than 2 days, severe aphasia, dementia, and preexisting antidepresive medication. Patients will be randomized to 50mg/d sertraline or placebo within the first 6 days after hospital admission. Depressive symptoms will be assessed using the Hospital Anxiety and Depression Scale, the Montgomery-Asberg Depression Scale, and the International Diagnosis Checklist for ICD-10 at baseline, 4 weeks, 12 weeks, and 24 weeks. Functional outcome will be determined by the European Stroke Scale, the Modified Rankin Scale, and the Barthel Index. Cognitive performance will be assessed by the Mini-Mental State Examination and the Digit Span Test. Quality of life will be determined at 12 and 24 weeks using the SF-36. Treatment and follow-up are scheduled to continue for 6 months with follow-up visits after 4 weeks, 3 months, and 6 months.

**Principal Investigators:** Dr W. Huff, PD Dr M. Sitzer, Dr R. Steckel, Prof Dr H. Steinmetz

**Contact:** PD Dr M. Sitzer, Zentrum der Neurologie und Neurochirurgie, J.W. Goethe-Universität Frankfurt/Main, Schleusenweg 2-16, D-60528 Frankfurt/Main, Germany; Phone 49-6301-5942. Fax 49-6301-4498. E-mail sitzer@em.uni-frankfurt.de

**Location:** Germany/Hessen

**Number of Centers:** 6

**Sponsor:** Pfizer Inc.

**Dates of Study:** Randomization and follow-ups August 2001 through January 2003

**PROGRESS (Perindopril Protection Against Recurrent Stroke Study)**

PROGRESS is a randomized controlled trial designed to determine the effects of angiotensin converting enzyme (ACE) inhibitor–based blood pressure lowering on the risks of stroke and other major events. Eligible patients had a history of prior stroke or transient ischemic attack with no indication for, or contraindication to, treatment with an ACE inhibitor. There were no prespecified blood pressure entry criteria. A total of 6105 participants have been recruited from 10 countries and 172 clinical centers around the world, and mean follow-up is now about 3.0 years. Following an open run-in period, patients were randomly assigned to treatment with the ACE inhibitor perindopril (plus the diuretic indapamide for open run-in period, patients were randomly assigned to treatment with an ACE inhibitor. There were no prespecified blood pressure lowering on the risks of stroke and other major cardiovascu- or contraindicated) or to matching placebos. The principal outcome is stroke, and secondary outcomes include other major cardiovascular events, dementia, dependency, and disability. Treatment and follow-up is scheduled to continue for an average of 4 years, by which time there should be at least 90% (*P*<0.05) power to detect 30% differences between randomized groups in the frequency of the primary outcome. Final results are expected in 2001.

**Management Committee:** J. Chalmers (chair), S. MacMahon (vice chair), M.-G. Bousser (alternate member C. Tzourio), J. Cutler, G. Donnan, L. Hansson (alternate member A. Terent), S. Harrap, (alternate member S. Davis), L. Liu, G. Mancia (alternate member R. Sega), T. Omac, J. Reid (alternate member K. Lees), A. Rodgers, C. Warlow.

**Contact:** R. Currie (project manager), Clinical Trials Research Unit, University of Auckland, Private Bag 92019, Auckland, New Zealand

**Number of Centers:** 172

**Location:** Australia, Belgium, France, Italy, Japan, New Zealand, People’s Republic of China, Republic of Ireland, Sweden, United Kingdom

**Sponsors:** Health Research Council of New Zealand, National Health and Medical Research Council of Australia, Institut de Recherches Internationales Servier

**Dates of Study:** 1995–2001

**Rapid Anticoagulation Preventing Ischemic Damage (RAPID)**

RAPID is an academic, randomized, multicenter trial to test the safety and efficacy for acute, nonlacunar, ischemic stroke of unfracioned heparin given intravenously to patients with <12 hours of symptoms onset. Patients will receive weight-adjusted intravenous heparin or aspirin. Control of heparin will be made using frequent aPTT ratios, with participating centers requested to calibrate aPTT local ratios to determine the therapeutic range in ratios equivalent to heparin levels of 0.3 to 0.5 U/mL.

**Steering Committee:** J. Bogousslavsky, Lausanne, Switzerland (national coordinator); S. Bleccic, Brussels, Belgium (national coordinator); O. Busse, Minden, Germany (national coordinator); J. Castillo, Santiago, Spain; A. Chamorro, Barcelona, Spain (chairman); A. Dávalos, Girona, Spain; J. Ferro, Lisbon, Portugal (national coordinator); A. Grau, Heidelberg, Germany; R. Haberl, Munich, Germany; D. Toni, Rome Italy (national coordinator); N. Wahlgren, Stockholm, Sweden

**Data and Safety Committee:** J. Aponte (statistician), Barcelona, Spain; X. Carné, Barcelona, Spain; W. Hacke, Heidelberg, Germany; P. Sandercock, Edinburgh, UK

**Principal Investigator:** Angel Charmorro, MD

**Contact:** Angel Charmorro, MD, Neurology Service, Hospital Clinic i Provincial, c/ Villarroel 170, Barcelona, 08036 Spain. Phone 34 93 2275400 ext 2212. E-mail chamorro@medicina.ub.es. Study e-mail RAPID@clinic.ub.es

**Number of Centers:** An anticipated enrollment of 1400 patients is expected from at least 35 different European centers, with the participation of countries such as Germany, Italy, Portugal, and Spain, among others. New centers are urgently needed to join the study.

**Dates of Study:** The trial started in July 2001, and the first patients have already been randomized in Spain.

**Siblings With Ischemic Stroke Study (SWISS)**

Cohort and twins studies suggest that there is an important genetic component to the overall risk of acquiring ischemic stroke. SWISS is a prospective, multicentered clinical investigation to search for chromosomal regions of interest that may harbor stroke susceptibility genes. The study will conduct a microsatellite genome-wide screen using DNA obtained from siblings pairs concordant and discordant for ischemic stroke. Three hundred concordant sibling pairs and 200 discordant siblings (800 total study subjects) will be enrolled. A genotype-blinded central committee adjudicates concordance and discordance for ischemic stroke in siblings. Probands are enrolled at participating clinical centers. Probands are potentially eligible for SWISS if they are diagnosed by a study neurologist as having a CT- or MR-confirmed ischemic stroke, at least 1 living sibling with a history of stroke, and are at least 18 years old. Excluded are probands whose index stroke occurred within 48 hours after an invasive cerebrovascular or cardiovascular procedure or within 60 days after a nontraumatic subarachnoid hemorrhage. Also excluded are sub-
Stent-Protected Percutaneous Angioplasty of the Carotid Versus Endarterectomy (SPACE)

SPACE is a multicenter, prospective, randomized trial to determine whether carotid endarterectomy (CEA) and percutaneous angioplasty (PTA) are equivalent with respect to ipsilateral stroke, a restenosis degree of ≥70% ECST criteria, or ≥50% NASCET criteria, respectively, and technical success in patients with transient cerebral ischemia (TIA) or nondisabling stroke because of severe carotid stenosis. This study will include 950 patients per group. Interim analysis is planned after 450 patients per group have been treated or 2 years. Inclusion criterion is symptomatic, high-grade carotid stenosis within 180 days before randomization (TIA or nondisabling stroke). Primary end point is ipsilateral stroke or death within 30 days after intervention. Secondary end points are ipsilateral stroke or death within 24 months after randomization; restenosis ≥70% of treated carotid artery within 6, 12, and 24 months after randomization; technical complications (ME, vascular occlusion, residual stenosis ≥70%) within 6 and 30 days after intervention; stroke of any localization within 30 days and 24 months after intervention. Each study center consists of 3 departments (neurology, vascular surgery, and interventional radiology). Certification for each of the 3 specialties has to be given by a quality standards committee, with documentation of 25 CEAs per vascular surgeon, 25 PTAs per interventional radiologist, and ultrasound expertise for neurologists. An external data monitoring strategy is in place.

Steering Committee: Neurology: Werner Hacke, Heidelberg, Germany (chair); Michael Hennerici, Mannheim, Germany. Vascular Surgery: Jens R. Allenberg, Heidelberg, Germany; Peter C. Maurer, Munich, Germany. Interventional Radiology: Hermann Zeumer, Hamburg, Germany; Olav Jansen, Kiel, Germany.

Contact: Alexandra I.S. Kunze, MD, Department of Neurology, University of Heidelberg, Im Neuenheimer Feld 400, D-69 120 Heidelberg, Phone 49-6221-567524, Fax 49-6221-565348. E-mail alexandra_kunze@med.uni-heidelberg.de Website www.space.stroke-trial.com

Location: Europe
Number of Centers: 30
Sponsors: BMBF (German Ministry of Science), DFG (German Research Council), Guidant, Boston Scientific
Dates of Study: 2000–2004

Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL)

A number of large randomized trials have shown that statin treatment of patients with coronary heart disease (CHD) not only reduces the incidence of myocardial infarction (MI) and death but also the occurrence of stroke. However, data on the effect of statins in the secondary prevention of stroke in patients with previous stroke or transient ischemic attack (TIA) are lacking. The SPARCL trial will evaluate the benefits of aggressive lipid lowering in this patient population by comparing the effects of atorvastatin versus placebo on specified cerebrovascular end points. The SPARCL study is a double-blind, randomized, placebo-controlled trial that will enroll 4200 patients from >160 centers worldwide. Inclusion criteria are previous stroke or TIA and low-density lipoprotein cholesterol >100 mg/dL (2.6 mmol/L) and <190 mg/dL (4.9 mmol/L). Patients with evidence of CHD will be excluded. Patients will be randomized to 80 mg/d atorvastatin or placebo. The primary efficacy parameter is the time from randomization to the first occurrence of a primary end point, defined as a fatal or nonfatal stroke. Secondary efficacy parameters will include the occurrence of at least 1 primary end point, the time from randomization to the first occurrence of a secondary end point (cardiac death, nonfatal MI, resuscitated cardiac arrest, unstable angina), and the occurrence of at least 1 secondary end point. Treatment and follow-up is planned to be an average of 5 years. As of July 2000, approximately 2900 patients have been randomized and inclusion is expected to reach the goal by the end of year 2000.

Steering Committee: K.M.A. Welch, United States (chairman); P. Amarenco, France; J. Bogousslavsky, Switzerland; A. Callahan,
United States; L. Goldstein, United States; M. Hennerici, Germany; H. Sillesen, Denmark; J. Zivin, United States.

**Contact:** K.M.A. Welch, University of Kansas Medical Center, 3901 Rainbow Blvd, Room 3015 Murphy, Kansas City, KS 66160-7300. Fax 913-588-5259. E-mail kwelch2@kumc.edu

**Sponsor:** Pfizer Inc

**Dates of Study:** Recruitment started 1/1/99. Full enrollment (4200 patients) expected by the end of 2000. Follow-up for 5 years.

*Surgical Trial in Intracerebral Haemorrhage (STICH)*

This is an international multicenter trial to determine whether a policy of “early surgical evacuation” of the hematoma in patients with spontaneous supratentorial intracerebral hemorrhage will improve outcome compared with a policy of “initial conservative treatment.” Primary outcome is mortality and morbidity at 6 months as measured by the Glasgow Outcome Scale. Secondary outcome instruments include the modified Rankin Scale and the Barthel Index. The trial will also help to better define the indications for surgery. In total 1000 patients, for whom the surgeon is uncertain about the need for surgical evacuation, will be randomized to receive “early surgery” (within 24 hours of randomization), using the method preferred by the treating neurosurgeon, or “initial conservative treatment.” Patient status is recorded 2 weeks after randomization and then outcome is assessed at 6 months using a structured postal questionnaire to the subject or subject’s relative to ensure assessor blindness. Funding for this trial was activated in March 1998, and as of November 2001, 766 patients and 105 centers had been recruited.

**Principal Investigators:** Prof A.D. Mendelow, Prof D.H. Barer, Prof G.M. Teasdale, Miss H.M. Fernandes, and Prof G.D. Murray

**Contact:** Dr Barbara Gregson, Trial Director. Phone 44-191-219-5000. Fax 44-191-256-3268. E-mail stich@ncl.ac.uk

**Location:** STICH Office, Ward 31, North Wing, Newcastle General Hospital, Westgate Road, Newcastle upon Tyne, NE4 6BE, UK.

**Number of Centers:** 105

**Sponsor:** Medical Research Council (UK) and Stroke Association

**Dates of Study:** 1998–2004

The United Kingdom Glucose Insulin in Stroke Trial (GIST-UK)

There is an increasing evidence from both animal and clinical studies that diabetes and/or hyperglycemia following stroke is associated with an adverse prognosis, although this association has never been confirmed in any clinical trial. In addition, although treatment of hyperglycemia with insulin is increasingly undertaken as part of acute stroke care, the risks/benefits have never been formally explored in a randomized controlled trial. The safety and practicability of glucose/potassium/insulin (GKI) infusions to maintain euglycemia after stroke has previously been demonstrated in the GIST study. GIST-UK seeks to determine by means of a multicenter randomized trial whether outcome from acute stroke can be favourable influenced by GKI-induced and -maintained euglycemia. Patients presenting with CT-proven acute stroke within 24 hours of onset and admission plasma glucose of >6.0 mmol/L and <17 mmol/L are eligible. The primary end points are all-cause mortality and the proportion of patients with a poor outcome (modified Rankin score 4–6) at 90 days.

**Principal Investigator:** Prof C.S. Gray, Newcastle University, Department of Geriatrics, Sunderland Royal Hospital, Kayll Road, Sunderland, UK SR4 7T9. Phone 44-191-565-6256 ext 41245. Fax 44-191-569-9767.

**Location:** United Kingdom

**Number of Centers:** Currently 6, but new centers invited to participate

**Sponsors:** NHS R&D (Northern & Yorkshire)

**Dates of Study:** January 2000 through October 2003

Vitamin Intervention for Stroke Prevention (VISP)

VISP is a double-blind, randomized, multicenter, controlled clinical trial designed to determine whether the addition of a multivitamin with high-dose folic acid, pyridoxine (vitamin B6), and cyanocobalamin (vitamin B12) to best medical/surgical management and risk factor modification reduces recurrent cerebral infarction or coronary heart disease in patients with nondisabling cerebral infarction (NDCI). The study is designed to recruit 3600 patients (1800 in each of two groups), and patients will be followed for 2 years. The primary end point is recurrent cerebral infarction, and secondary end points are myocardial infarction or fatal coronary heart disease. Patients meeting fundamental eligibility criteria include those >35 years old, with an NDCI within 120 days prior to randomization and homocyst(e)ine >9.5 μmol/L for men and >8.5 μmol/L for women at screening visit. Blood specimens will be shipped to a central lab for analysis. Baseline examinations of patients who pass fundamental eligibility criteria will include medical history, physical and neurological examination, cranial CT or MRI, ECG, dietary assessment, stroke severity determination, and blood collection for central laboratory determination of homocyst(e)ine and folic acid and for local laboratory determination of vitamin B12, creatinine, and lipid profile. Eligible patients will be randomly assigned to receive a daily multivitamin containing, in addition to standard multivitamins, a high or low dose of folic acid, pyridoxine, and cyanocobalamin. Follow-up includes 6-month clinic visits for comprehensive evaluation, including a neurological examination, blood tests, and questionnaires for event detection and compliance. Clinic visits will be alternated with telephone interviews at 3-month intervals. Patients will receive best management for risk-factor reduction, which includes counseling and interventions for hypertension, high LDL, low HDL, tobacco use, diabetes, and other recognized factors that add excess risk for stroke and myocardial infarction.

**Principal Investigator:** J.F. Toole, MD

**Contact:** Elizabeth G. Sides, MEd, VISP Project Manager, Wake Forest University School of Medicine, Department of Neurology, Medical Center Blvd, Winston-Salem, NC 27157. Phone 336-716-1074. Fax 336-716-5477. E-mail esides@wfubmc.edu

**Location:** Operations Center: Stroke Center, Dept of Neurology, Wake Forest University School of Medicine, Winston-Salem, NC. Statistical Coordinating Center: Dept of Biostatistics, University of North Carolina at Chapel Hill, Chapel Hill, NC. Central Laboratory: Laboratory of Cardiovascular Disease, Oregon Regional Primate Research Center, Beaverton, Ore. Vitamin Distribution Center: HAS Supply Service Center, Perry Point, Md. Vitamin Supplier: Roche Vitamins Inc, Paramus, NJ. Vitamin Manufacturer: Magno-Humphries Inc, Tigard, Ore.

**Number of Centers:** 53

**Sponsor:** National Institute of Neurological Disorders and Stroke, National Institutes of Health, NS34447

**Dates of Study:** September 1996 through August 2005 (randomization began August 1997 and concluded December 2001)

VITAMINS TO PREVENT STROKE (VITATOPS)

The VITATOPS study is a multicenter, randomized, double-blind, placebo-controlled secondary stroke prevention trial to determine whether the addition of vitamin supplements (B6, 500 μg, B12 25 mg, and folate 2 mg) to best medical/surgical...
management (including modification of risk factors) will reduce the combined incidence of recurrent vascular events (stroke, myocardial infarction) and vascular death in patients with recent stroke or transient ischemic attack (TIA). All patients presenting to one of the participating neurologists or general physicians within 7 months of stroke (ischemic or hemorrhagic) or TIA (eye or brain) are eligible for this trial. Eligible patients will be randomized in a double-blind fashion to receive multivitamins or placebo, 1 tablet daily. The primary outcome event is the composite event “stroke, myocardial infarction, or death from any vascular cause,” whichever occurs first. Our target is to recruit a total of 8000 patients over the next 5 years, with a median follow-up of 2.5 years. Recruitment of the trial began in November 1998 and will continue until December 2003.

Steering Committee: (alphabetically) Dr Ross Baker, Dr John Eikelboom, Ms Anna Gelavis, Clin A/Prof Graeme Hankey (chairman), Mrs Siobhan Hickling, A/Prof Konrad Jamrozik, A/Prof Francesco van Bockxmeer, Dr Samuel Vasikaran

Contact: VITATOPS Trial Office, Stroke Unit, Royal Perth Hospital, Wellington St, Perth 6001, Australia. Phone 61-8-9224-7004. Fax 61-8-9224-3323. E-mail VITATOPS@health.wa.gov.au

Number of Centers: Australia (13), New Zealand (4), United Kingdom (6), Italy (2), Singapore (1), United States (4), Republic of Georgia (1), Philippines (5), Austria (1), Sri Lanka (1), and actively seeking more centers worldwide.

Dates of Study: June 1998–June 2004

Warfarin vs Aspirin for Symptomatic Intracranial Disease (WASID)

There have been no prospective trials comparing antithrombotic therapies for patients with atherosclerotic stenosis of one of the major intracranial arteries (intracranial carotid, middle cerebral, vertebral, or basilar artery). The main objective of this prospective, randomized, double-blind, multicenter trial is to compare warfarin (INR 2-3) with aspirin (1300 mg/d) for preventing stroke (ischemic and hemorrhagic) and vascular death in patients with symptomatic stenosis of a major intracranial artery. Eight hundred six patients with transient ischemic attack or stroke caused by angiographically proved stenosis (≥50%) of a major intracranial artery will be randomized to warfarin or aspirin. Patients will be followed for a mean of 3 years. The primary analysis will compare the rates of stroke (ischemic and hemorrhagic) and vascular death in the 2 treatment groups. Secondary analyses will compare the 2 treatment groups with respect to rates of (1) vascular death and disabling stroke (ischemic and hemorrhagic); (2) stroke (ischemic and hemorrhagic); (3) fatal and nonfatal ischemic stroke; (4) ischemic stroke, myocardial infarction, and vascular death; (5) major systemic and any intracranial hemorrhage; and (6) ischemic stroke in the territory of the stenotic intracranial artery.

Principal Investigator: Marc I. Chimowitz, MBChB

Contact: Marc I. Chimowitz, MBChB, Emory University, 4th Floor Clinic A, 1365 Clifton Rd, Atlanta, GA 30322. Phone 404-778-3153. Fax 404-778-4184. E-mail mchimow@emory.edu or Harriet Howlett-Smith, RN, Emory University, 4th Floor Clinic A, 1365 Clifton Rd, Atlanta, GA 30322. Phone 404-778-3271. Fax 404-778-4184. E-mail lhowlet@emory.edu

Location: Clinical and Statistical Coordinating Centers, Emory University, Atlanta, Ga

Number of Centers: 50–60

Sponsor: National Institutes of Neurological Disorders and Stroke, National Institutes of Health

Dates of Study: Randomization began February 1999 and will close June 2003.
Major Ongoing Stroke Trials

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