Web-appendix:

Summary of symposium workshop proceedings:

Workshop 1: How to start a stroke research network:

There was general consensus among workshop attendees that new stroke research networks should begin with a group of centres which are already closely collaborating. In some countries stroke registries have been operating for many years, thus forming a suitable foundation for further progression to a trials network. Participation in new trials networks should be open to any specialists (including non-physicians) interested in stroke research, and not restricted to academic vascular neurologists and stroke specialists. Governance requirements are network leader(s) and a representative committee (consisting of clinician-scientists with a focus on randomised trials but not excluding other groups [eg. nurses, therapists, patient representatives]). Structures should be put in place for regular opportunities for investigators to provide input to the network as it develops (ie. a 'bottom-up' approach). Regular meetings (in person or by telephone) are recommended to sustain the network and to establish its operations. Early in the development of the network, it may be useful to agree a brief strategy document, outlining research priorities, types of studies which will be done (eg. randomised trials only, or trials and other study types, mix of simple versus complex studies), approach to trial identification and selection, key stakeholder partnerships to be developed, and funding sources to be targeted.

Once operating, trial experiences can be shared between centres and perhaps collected in an operations manual for future studies. Other examples of efficient

collaborative working were suggested. For example, stroke research networks may also adopt industry trials, where the network may negotiate study payments collectively. In some countries, it may be possible for a single contract to be used for all centres in the network. New networks might consider ways to involve and train research nurses, research coordinators, and young physician-investigators and PhD researchers. Training visits to sites for research coordinators and organised courses might be arranged, which may support under-recruiting sites. Small working groups may be developed for mentorship of PhD students who may provide valuable support to conduct academic trials. Academic recognition for such students may come from authorship on papers describing the main results of trials, and from research on other projects related to these trials (eg. systematic reviews, pilot studies, secondary analyses).

Workshop 2: Practical issues for stroke and lessons from InFACT:

Participants at this workshop agreed that a short-term priority should be to increase collaboration on one or more simple randomised trials within the ESOTA network. Key steps towards this goal will be developing processes to identify ongoing trials and to develop new trials among ESOTA researchers. Other short-term goals will be to prioritise 'researcher connecting', by nomination of key figures in each country that can lead ESOTA researchers to others in a specific area of expertise, and enhancing mentorship, both for colleagues who wish to set up a new stroke research network and for young researchers in the practical steps to set up a large international randomised trial.

In the medium- and long-term, priorities should be to increase the profile of stroke as a disease of high importance among research funders, and to support measures to improve the competitiveness of stroke researchers for EU and national funding. Formal endorsement by ESO and international participation across ESOTA countries may improve funding success. ESOTA might discuss withnational funding agencies to pool resources to fund an ESOTA-led randomised trial. Another suggested medium-term priority was to enhance co-enrolment in different trials and to begin platform trials addressing research questions in stroke.

Workshop 3: Further development of ESOTA:

Several ideas to further develop ESOTA were suggested and discussed by participants at this workshop. Examples are:

In several European countries without stroke research networks there are well-established networks based on stroke registries. These registry networks could be invited to join ESOTA despite not fulfilling the criteria of having developed at least one clinical trial, providing that they have a clear organisational structure, are committed to establishing a stroke trials network and are approved and/or supported by the relevant national Stroke Society.

To disseminate the knowledge of ESOTA, the workshop participants suggested developing a specific session at the ESO conferences to present the trials that are being conducted under the ESOTA collaboration as well as new proposals. The attendance of the

coordinators of each national stroke trials network at the annual ESO conference could be encouraged. National stroke trials coordinator could then present proposals for new trials to national investigators in each country to seek expressions of interest in participation.

An ESOTA mentoring program could be developed to link mentors with young physician researchers and build closer collaboration between national networks. This program could include ESOTA visiting grants to trials centres (one or two weeks duration), similar to the ESO Department visiting program already established. In addition, the ESO Summer/Winter Schools could represent an opportunity to develop specific workshops focused on trials networking. A similar initiative organised by the Global Alliance of Independent Networks for Stroke Trials (GAINS) was recently successful at the World Stroke Organisation conference.

Information could be provided on the ESOTA web-site about existing European stroke research networks to understand their structure, remit and funding arrangements. Other suggestions for material on the web-site included a list of ongoing trials, a repository of trialists in each national network, and information on trial regulations for each country.

An advisory group on core outcomes for stroke trials and other working groups to support ESOTA clinical trials could be developed.

ESO Trials Alliance Steering Group:

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Thompson Robinson (UK Stroke Research Network representative)

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Trial title	**Research question**

MR ASAP	Pre-hospital augmentation of collateral blood flow and blood pressure reduction
MR CLEAN MED	Anti-thrombotic agents to prevent microvascular occlusion after IAT
MR CLEAN NO IV	Immediate IAT without preceding thrombolysis
MR CLEAN LATE	IAT in the 6 to 24 hour time window
DUTCH ICH pilot	Microsurgical hematoma evacuation in patients with ICH

Web-table 1: Current trials in the CONTRAST network, Netherlands.

Web-table 2: Stroke trials ongoing or planned in the Swiss Stroke Trialist's Collaboration:

Trial title	Research question
ELAN	Early versus Late initiation of direct oral anticoagulants in post-ischaemic stroke patients with atrial fibrillatioN
TREAT-CAD	Anticoagulation versus antiplatelet therapy in acute cervical artery dissection
TICH-NOAC	Tranexamic acid in intracerebral haemorrhage due to direct oral anticoagulants
SWITCH	Swiss trial of decompressive craniectomy versus best medical treatment of spontaneous supratentorial intracerebral haemorrhage
CISS	Cortical Ischemic Stroke and Serotonin
SWIFT-DIRECT	Solitaire™ With the Intention For Thrombectomy Plus Intravenous t-PA Versus DIRECT Solitaire™ Stent-retriever Thrombectomy in Acute Anterior Circulation Stroke
PRECISE-MRI	Ticagrelor versus clopidogrel in carotid artery stenting
eSATIS	Early Sleep Apnea Treatment in Stroke: A Randomized, Rater-Blinded, Clinical Trial of Adaptive Servo-Ventilation
TRIDENT	Triple therapy prevention of recurrent intracerebral disease events trial
CONVINCE	Colchicine for Prevention of Vascular Inflammation in Non-cardio Embolic Stroke
TWIST	Tenecteplase in Wake-up Ischaemic Stroke trial

ECST2	revascularisation versus optimised medical care alone for symptomatic or asymptomatic carotid stenosis
PROOF	Penumbral Rescue by normobaric oxygen administration in patients with acute ischaemic stroke and target mismatch profile
EX-COA	EXtending oral antiCOAgulation treatment after acute Cerebral Vein Thrombosis
ESTREL	Enhancement of stroke rehabilitation with levodopa
ISEAR	Encouragement-induced movement therapy in daily life
ArmeoSenso-Reward	Rewarding vs. non-rewarding therapy of patients with arm impairments based on wearable movement sensors