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# NEWSLETTER

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## Welcome

Welcome to the fourth issue of the SCTNI Newsletter, in which we update you on SCTNI and member activities, upcoming events, resources, training and other opportunities of interest. In particular, we wish to flag the inclusion of a new section, the “Spotlight On...”. This will feature a profile of the research, achievements and pressing issues of SCTNI member teams. We open this new feature with a profile of the work being conducted by Prof Dominick McCabe and his team at AMNCH-Tallaght University Hospital (TUH)/Trinity College Dublin (TCD).

This issue of the Newsletter also comes in advance of the SCTNI 2019 Conference, which will take place in Beaumont Hospital on the 22nd November. Details of the conference, including the agenda, are [available on the SCTNI website](#).

We are keen to hear about your work, announcements, events, or anything you wish to share with SCTNI members. Please forward information to us [by email](#) and we will ensure it is included in a future issue.

Best wishes,

SCTNI Team

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## SCTNI News

### SCTNI Strategy

Following its 2018 mid-award review, the SCTNI established a Network Management Group, one task of which was to consult with a wide range of relevant stakeholders in Ireland for the development of strategic overview to guide the SCTNI for the period 2016-2021. The newly adopted SCTNI Strategy sets out the mission and strategic goals of the Network across core functions and activities: i) Governance; ii) Research; iii) Supporting women in the SCTNI; iv)

Training and education; v) Membership; vi) Communications and outreach; vii) Patient and public involvement; viii) Strategic collaboration with international partners; ix) Sustainability. The SCTNI Strategy is [available here on the SCTNI website](#). A strategic review and update will be undertaken at the end of this period.

## CONVINCE



September and October were a momentous two months for the CONVINCE Study. Current recruitment stands at 1192 patients, with 56 patients randomised in September and 53 patients randomised in October. Also during this time, the study team welcomed their first Lithuanian and Swiss sites, and received news of two new grants to extend the study in both Belgium (6 new sites) and Germany (approx 26 additional sites). In October, the team from H Parc Tauli, Sabadell in Spain randomised the 100th patient, while the 300th Irish patient was randomised by the team from Beaumont Hospital, Dublin. A key date for the CONVINCE diary is Wednesday 4th December, when the CONVINCE Investigator Meeting will be held at the Stroke Forum in the UK. For more details about CONVINCE, including a profile of the team at St Anne's, Brno, Czech Republic, you can access the most recent [CONVINCE Newsletter here](#).

## New Trials Join the SCTNI

Towards its goal of supporting investigator-led and industry-led clinical trials and related studies in the field of stroke acute (treatment, prevention, and recovery), the SCTNI welcomes applications for the inclusion of trials within the SCTNI that fit the capacity and resources of participating hospitals (see the SCTNI Strategy above for application details). The SCTNI are delighted to announce the inclusion of three new trials within the SCTNI:

- *BIOVASC (Biomarker and Imaging Of Vulnerable Atherosclerosis in Symptomatic Carotid artery disease): extended follow-up study.*

BIOVASC is a prospective multi-centred observational cohort study, an extended follow-up study of an existing cohort, and led by PI **Prof Peter Kelly** (Mater/UCD). The primary outcome of BIOVASC is recurrent ipsilateral ischaemic stroke, with six secondary outcomes: i) Recurrent ischaemic stroke; ii) Any recurrent stroke or TIA; iii) Composite outcome of recurrent vascular events (recurrent stroke/TIA, myocardial infarction, unstable angina requiring hospital admission, percutaneous coronary intervention, coronary artery bypass grafting, non-fatal cardiac arrest, limb amputation, angioplasty or stenting for peripheral vascular disease, or vascular death; iv) Dementia; v) Mild cognitive impairment without dementia; vi) Functional outcome.



- *The StrokeCog study: assessing the feasibility of an intervention to improve post-stroke cognitive impairment*

Led by PI **Prof Anne Hickey** (RCSI), StrokeCog involves economic and epidemiological modelling and modifying the consequences of stroke-related cognitive impairment through a



post-stroke cognitive intervention in a pilot RCT. The feasibility study design focuses on a 5 week group-based cognitive rehabilitation intervention. The primary objectives of this study include: i) feasibility test the delivery of a cognitive rehabilitation intervention aimed at improving cognitive function in patients with acute stroke; ii) feasibility test the recruitment of stroke patients from a rehabilitation/outpatient setting as well as an acute setting; iii) assess the acceptability of delivering a cognitive rehabilitation intervention to stroke patients in the acute and post-acute stroke phases; iv) investigate the level of demand of the intervention on patients and staff resources, its acceptability to patients, its suitability to patients at different levels of cognitive impairment, dropout rates and reasons for drop out, consultation times and associated cost of resources and threats to implementing it in a larger pilot RCT study. Further details on StrokeCog can be [accessed here](#).

- *Early versus Late initiation of direct oral Anticoagulants in post-ischaemic stroke patients with atrial fibrillation (ELAN): an international, multicentre, randomised-controlled, two-arm, assessor-blinded trial*

The main objective of the ELAN study is to estimate the net benefit of early versus late initiation of DOACs in patients with acute ischaemic stroke related to atrial fibrillation (AF). Led by Prof. Dr. med. Urs Fischer (University Hospital Inselspital, Bern), the secondary objectives of this Phase 4 study are to assess all vascular events and all-cause mortality after early initiation of DOACs in patients with acute ischaemic stroke related to AF compared to late initiation.



## Spotlight on...

### **Translational platelet science and haemostasis research in cerebrovascular disease by Prof Dominick McCabe's Vascular Neurology research group at TCD**

#### Summary of research activity



**Prof Dominick McCabe's** Vascular Neurology Research group at AMNCH-Tallaght University Hospital (TUH)/Trinity College Dublin (TCD), has an international reputation for conducting innovative, clinically-relevant, collaborative research studies on translational platelet science, haemostasis and thrombosis in patients with ischaemic cerebrovascular disease (CVD) and in assessing the response to commonly-prescribed antiplatelet regimens *ex vivo*. They also have particular expertise in performing transcranial Doppler ultrasound imaging to detect micro-embolic signals (MES) in the cerebral circulation *in vivo*, and in combining these data with other neurovascular imaging, blood and endothelial biomarkers to understand the pathogenesis of

TIA/stroke and potentially improve risk-stratification of patients with moderate-severe asymptomatic and symptomatic extracranial carotid stenosis.

### Some recent achievements

The service at AMNCH-TUH/TCD has facilitated clinical and academic training & education in Vascular Neurology, Stroke Medicine, Translational Medicine and enhanced clinical care of TIA and stroke patients, with several clinical PhD candidates having successfully defended their theses to date. Prof McCabe is currently supervising 2 further PhD students and 3 MSc students in Clinical Neurosciences/Clinical Medicine (see below), is the Principal Investigator (PI)/Co-PI in 9 local or multi-centre studies, and is collaborating in 7 national or international multi-centre research studies or trials. Prof McCabe (SCTNI Network Lead Investigator and Chair of the Research and Education Committee, NSP's CAG for the RCPI/HSE) and his team actively collaborate to support the important work of the SCTNI locally and on the international stage.

They have conducted several original pilot studies in this subspecialty area over the past 13 years (e.g. the PACS, HEIST, TRAP & OATS studies). These studies have shown that platelets may be excessively activated/hyper-reactive following a non-cardioembolic TIA or ischaemic stroke and that an important proportion of CVD patients are 'poorly-responsive' to antiplatelet agents with 'high on-treatment platelet reactivity (HTPR)' in the laboratory.

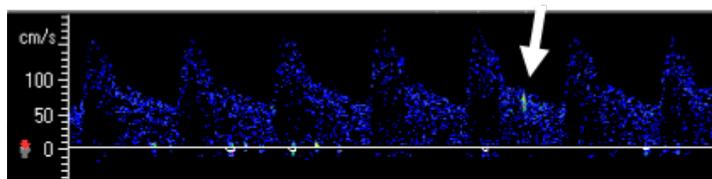
They have also found an ongoing stimulus to increased platelet production and secretion, and enhanced platelet and endothelial

activation and coagulation system potential after TIA/ischaemic stroke in patients with symptomatic compared with asymptomatic moderate-severe carotid stenosis, including in those who do not have micro-emboli on transcranial Doppler ultrasound. These data improve our understanding of the underlying biological mechanisms which may contribute to the disparity in the risk of TIA/stroke in subgroups of patients with recently symptomatic vs. asymptomatic carotid stenosis, and in subgroups of symptomatic patients with different plaque types and MES status.

We have presented data at 13 National or International Meetings and published 30 collaborative peer-reviewed manuscripts over the past 2 years. Prof McCabe has also collaborated with international experts in Vascular Surgery, Interventional Neuroradiology and Vascular Neurology to finalise the 2017 ESVS international guidelines for the management of patients with atherosclerotic carotid and vertebral artery stenosis.

### Two pressing issues which need be resolved within this subspecialty field

- We need to determine whether monitoring 'antiplatelet-HTPR status' with platelet function/reactivity assays, in combination with pharmacogenetic testing, definitively predicts the risk of



Transcranial Doppler ultrasound recording of a spectral waveform display of the middle cerebral artery: Micro-embolus in the left middle cerebral artery *in vivo* in a patient with > 50% extracranial left internal carotid artery stenosis (bold white arrow)

recurrent vascular events in CVD patients on antiplatelet therapy. Such information would facilitate 'personalised antiplatelet therapy' to optimise secondary prevention following TIA/ ischaemic stroke. To address this issue, we have designed the adequately-sized **Optimal Antiplatelet Therapy in TIA and Ischaemic Stroke-International (OATS-I)** multicentre study.

- We need to collate established and novel blood, endothelial and neurovascular imaging biomarker data to aid risk-stratification of patients with symptomatic and asymptomatic carotid stenosis to identify patients who may benefit most from early surgical or endovascular intervention or optimised medical therapy alone.

### Current Research Team

**Professor Dominick J. H. McCabe** PhD, FRCPI, FESO, FAHA: Consultant Neurologist / Clinical Associate Professor in Neurology, and Chairperson of the Vascular Neurology Research Foundation, Department of Neurology/Stroke Service, AMNCH- TUH/ TCD, Ireland;

**Dr Chika Offiah**, BSc. Biochemistry, MUDr: Research Registrar in Vascular Neurology (PhD Student);

**Dr Deirdre R. Smith** MB, BCh, BAO, MICGP, DCh: Research Registrar in Vascular Neurology (MSc Student);

**Dr Arun Subramanian**, MD, MPH, MRCPI: Research Registrar in Vascular Neurology (MSc Student);

**Dr Stephen Murphy** MB, BCh (Sch), MRCPI, MRCP (UK), Dip Stat, PhD: Research SpR in Vascular Neurology ('Post-Doc' MSc Student);

**Dr Soon Tjin Lim**, MRCPI, MRCP (UK): Research SpR in Vascular Neurology (PhD Student).



## Upcoming Events, Training and Opportunities

### The European Clinical Research Infrastructure Network (ECRIN)



Dr Fionnuala Keane (COO. HRB CRCI) and Prof Jacques Demotes (Director General, ECRIN)

On November 20<sup>th</sup> 2018, Ireland became full members of the ECRIN, a not-for-profit intergovernmental organisation that supports the conduct of multi-national clinical research in Europe. Ireland's membership of ECRIN will bring the number of full members to nine - France, Germany, Czech Republic, Hungary, Italy, Norway, Spain, Portugal and Ireland. Switzerland, Poland and Slovakia have observer status.

Established as a European Research Infrastructure Consortium (ERIC), ECRIN is a distributed organisation, with a core office in Paris and a network of Clinical Trials Units (CTUs) across the partner countries. Each member country has a scientific partner which houses the ECRIN European

Correspondents. The scientific partner for ECRIN in Ireland is the HRB Clinical Research Coordination Ireland (HRB-CRCI) and the European Correspondents for Ireland are Dr Suzanne Bracken and Fiona Cregg. **HRB-CRCI** is an independent integrated national clinical research network, providing centralised support in the conduct of multicentre clinical research (both commercial and academic) across Ireland. This network consists of the HRB-CRCI central office, based in Clinical Research Development Ireland (CRDI) and the partner University Clinical Research Facilities/Centres across Ireland.



Dr Suzanne Bracken (Irish EuCo), Prof Jacques Demotes (Director General, ECRIN), Fiona Cregg, (Irish EuCo) and Dr Fionnuala Keane (COO, HRB CRCI)

As a member of ECRIN, Irish researchers can benefit from a full range of ECRIN services for multinational clinical research study preparation, protocol evaluation and study management. A summary of the supports available can be [accessed here](#), and Irish researchers working in academic-led clinical research are encouraged to get in touch with the Irish European Correspondents to see what further services/supports could be available via ECRIN.

ECRIN is currently supporting 35 multi-national clinical trials, two of which are being coordinated by Irish Principal Investigators, CONVINCENCE and POPART.

- CONVINCENCE (Colchicine for prevention of Vascular Inflammation in Non-CardioEmbolic stroke) is an interventional clinical trial testing low dose colchicine versus standard of care. Colchicine is a drug used for many years to treat gout and other joint disorders. As regular readers of this newsletter will be aware, CONVINCENCE is led by **Prof Peter Kelly**, Consultant Stroke Neurologist, Mater University Hospital and University College Dublin.
- POPART (Prophylactic oropharyngeal surfactant for preterm infants: a randomised trial) is an interventional study aimed at finding a better way to help premature babies who have breathing difficulties. Led by Prof. Colm O'Donnell, Neonatologist at the National Maternity Hospital and University College Dublin (UCD), POPART is half-way through enrolling 250 babies across 6 European countries (Ireland, Sweden, Norway, Belgium, Czech Republic & Portugal).

Readers of this newsletter interested in learning more about ECRIN, or availing of the opportunities available to Irish researchers, should contact the ECRIN European Correspondents for Ireland: [fiona.cregg@hrb-crci.ie](mailto:fiona.cregg@hrb-crci.ie) or [suzanne.bracken@hrb-crci.ie](mailto:suzanne.bracken@hrb-crci.ie).

### Registration - 5th Trial Methodology Symposium

Registration remains open for the upcoming 5th Trial Methodology Symposium, which will take place on 6 December 2019 in Dublin, at the Grand Hotel in Malahide. This flagship network event is hosted by Trinity College



Dublin on behalf of the HRB-TMRN. The Symposium welcomes some of the worlds leading experts in Trial Methodology, and the theme for this years event is “Clinical trial design - partnering pragmatism with complexity to achieve excellence”. The schedule for the day is available [here](#), and you can [register at this site](#).

### Evidence and Gap Maps Webinar



Evidence Synthesis Ireland will host a webinar with Dr Ashrita Saran on Evidence and Gap Maps. The webinar will take place on 2nd Dec, from 12pm. Dr. Ashrita has been working as an Evidence Synthesis Specialist with Campbell Collaboration since December 2016 and is also the editor of Campbell International Development Coordinating Group. She is an epidemiologist by background and is trained in systematic reviews and information science. At Campbell she has led the development of Campbell discussion paper on Evidence and Gap Map. She manages systematic reviews grants and conducts in-house evidence and gap maps and systematic review research. In this webinar, discussion will be based on what are EGMs, how are they used and initiatives by Campbell Collaboration in this area. The event is free, and you can [register for the webinar by clicking here](#).

### Call for Abstracts, Travel Grants & Young Investigator Awards: ESO-WSO Conference 2020

The European Stroke Organisation and the World Stroke Organization are jointly organising their conference for 12-15 May 2020, and this will take place in Vienna, Austria. This new level of collaboration will provide access



to major clinical trials, state-of-the-art presentations by renowned clinicians and researchers, and updates on the latest guidelines. Abstracts are now being accepted for all topics and ongoing trials. The Abstract submission deadline for all topics (except ongoing trials) is on Wednesday 15 Jan 2020 midnight CET. The abstract submission deadline for ongoing trials is Wednesday 25 March 2020, midnight CET. Travel Grants & Young Investigator Awards are available for selected presenters. For more details, [please visit the ESO-WSO website](#).

### RCSI StAR MD Programme 2020



**RCSI**

The RCSI School of Postgraduate Studies is accepting applications from interested registrars/specialist registrars for the StAR MD Programme, to commence in July 2020. This programme encompasses funded MD fees for two years sponsored by a private hospital, a RCSI research consumable budget (€10,000 p.a. for two years) and a paid clinical commitment to Highfield Healthcare, Hermitage Medical Clinic or Blackrock Clinic. Interested applicants should have:

- Obtained general or trainee specialist registration with the Irish Medical Council
- Previously undertaken research or audit projects at undergraduate and/or postgraduate level
- Presentations and publications confirming the quality of their research activity

The closing date for applications is 6 Jan 2020, with interviews of shortlisted candidates expected to take place late January/early February. For more details on the Programme, and to apply, [please visit the website here](#).

### SPHeRE Network 6th Annual Conference

The SPHeRE Network 6th Annual Conference will take place in RCSI, 25 Feb 2020 (09.30-17.00). The theme for this conference is “Data to Policy”, and the specific role of population health research and health services research in evaluating the impact of data on policy and practice. The confirmed keynote speakers this year are:



- Professor Mary Dixon-Woods, Director of THIS Institute/The Health Foundation Professor of Healthcare Improvement Studies, University of Cambridge
- Dr Lorelei Jones, School of Health Sciences, Bangor University
- Professor Cathal Walsh, HRB Research Leader, Department of Mathematics and Statistics, University of Limerick

This conference will be of interest to anyone involved in Population and Health Services Research, Policy or Practice in Ireland and Northern Ireland including healthcare professionals, health and social care managers, patient and citizen groups, universities and research institutes, government and voluntary sector agencies. Please see the [SPHeRE website here for more details](#), including registration

## Publications & Resources

### Estimated stroke risk, yield, and number needed to screen for atrial fibrillation

The precise age distribution and calculated stroke risk of screen-detected atrial fibrillation (AF) is not known. Therefore, it is not possible to determine the number needed to screen (NNS) to identify one treatable new AF case (NNS-Rx) in each age stratum. If the NNS-Rx is known for each age stratum, precise cost-effectiveness and sensitivity simulations can be performed based on the age distribution of the population/region to be screened. Authors of a recently published paper in PLOS Medicine, which includes **Prof Joe Harbison** (TCD), conducted a review of twenty-four eligible studies to determine the exact yield and calculated stroke-risk profile of screen-detected AF and NNS-Rx in 5-year age strata. Findings show that people with screen-detected AF are at elevated calculated stroke risk: above age 65, the majority have a Class-1 oral anticoagulation recommendation for stroke prevention, and >70% have  $\geq 1$  additional stroke risk factor other than age/sex. The data also shows the precise relationship between yield and estimated stroke risk profile with age, and strong dependence for NNS-RX on the age



distribution of the population to be screened: essential information for precise cost-effectiveness calculations. The article is [available here](#).

### Prospective Urban Rural Epidemiology (PURE) study

Global estimates of the effect of common modifiable risk factors on cardiovascular disease and mortality are largely based on data from separate studies, using different methodologies. The Prospective Urban Rural Epidemiology (PURE) study overcomes these limitations by using similar methods to prospectively measure the effect of modifiable risk factors on cardiovascular disease and mortality across 21 countries (spanning five continents) grouped by different economic levels. A recently published Lancet article, which **Prof Martin O'Donnell** (NUI Galway) co-authored, examines associations for 14 potentially modifiable risk factors with mortality and cardiovascular disease in 155,722 participants without a prior history of cardiovascular disease from 21 high-income, middle-income, or low-income countries (HICs, MICs, or LICs). Findings highlight how most cardiovascular disease cases and deaths can be attributed to a small number of common, modifiable risk factors. While some factors have extensive global effects (eg, hypertension and education), others (eg, household air pollution and poor diet) vary by a country's economic level. The article can be [accessed here](#).



### Stent Design, Restenosis and Recurrent Stroke After Carotid Artery Stenting

Open-cell carotid artery stents are associated with a higher peri-procedural stroke risk than closed-cell stents. However, the effect of stent design on long-term durability of carotid artery stenting (CAS) is unknown. Investigators on the International Carotid Stenting Study, which includes **Prof Dominick McCabe** (AMNCH-TUH/TCD), compared the medium- to long-term risk of restenosis and ipsilateral stroke between patients treated with open-cell stents versus closed-cell stents in the Study. Published in the journal **Stroke**, the Investigators analysed data from patients with completed CAS procedures, known stent design, and available ultrasound follow-up. Findings show: 1. moderate or higher restenosis occurred significantly less frequently in patients treated with open-cell than closed-cell stents; 2. there was no significant difference in the risk of severe restenosis after open-cell stenting versus closed-cell stenting; and that the risk of ipsilateral stroke beyond 30 days after treatment was similar with open-cell and closed-cell stents. The authors conclude that both stent designs were equally effective at preventing recurrent stroke during follow-up. The article is [available here](#).

## Stroke

### It is not just about thrombectomy

A recently published paper in Clinical Radiology examines the experience of a regional stroke referral centre of external referrals for endovascular thrombectomy (EVT) in patients with symptoms of acute ischaemic stroke (AIS) and large vessel occlusion (LVO). Based in Beaumont and Tallaght Hospitals, as well as NUI Galway and RCSI, the authors (including Dr Niamh Adams, Dr Emma Griffen and **Prof John Thornton**) collected data prospectively over two 4-

month periods (2017–2018) on consecutive external referrals for EVT. Two hundred and sixty-two patients were referred. Sixty-one percent ( $n=159$ ) were accepted and transferred for treatment. Of those transferred, 86% had EVT. Fourteen percent ( $n=23$ ) were unsuitable for EVT on arrival due to no vessel occlusion, poor Alberta Stroke Program Early CT Score/established infarct haemorrhage, and clinical recovery. 39% were ineligible for EVT following phone discussion due to absence of intracranial occlusion, low ASPECTS, distal occlusion, low/improving National Institutes of Health Stroke Scale, and poor modified Rankin Scale (mRS) at baseline. Patients with LVO but not transferred had longer onset to hospital arrival time compared with those transferred 151.5 versus 91 minutes, with a trend also toward a longer door to CT/CTA 40 minutes versus 30 minutes. As the authors conclude, these data provide valuable insights into the service provision of a comprehensive stroke network. The present rates of EVT and futile transfers are modest compared to published data. The article is [available here](#).



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