SCTNI
Health Research Board
Stroke Clinical Trial Network Ireland

NEWSLETTER

Welcome

Welcome to the third issue of the SCTNI Newsletter, which aims to update you on SCTNI and member activities, upcoming events, resources, and opportunities of interest. Among the items are details of CONVINCE milestones reached over the summer, as well as a link to the recently published HRB review of clinical research infrastructure in Ireland, a review that some SCTNI members contributed to. Also, we are pleased to announce the opening of registration for the SCTNI Conference 2019, details below.

We are keen to hear about your work, announcements, events, or anything that you think can be shared 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 Annual Conference: New Advances in Stroke Treatment

The SCTNI Annual Conference will take place on 22 November 2019 at the Richard Carmichael Lecture Theatre, Beaumont Hospital, Dublin. The SCTNI Conference schedule has an excellent mix of domestic and international speakers, and will also include case presentations. The Conference has become a highlight in the year for training and research in clinical neurovascular medicine. Confirmed speakers to date include Prof Pierre Amarenco (Paris-Diderot Sorbonne University & Bichat Hospital), Prof Sarah Pendlebury (Oxford University & Consultant Physician at Oxford University Hospitals NHS Foundation Trust), Prof Nikola Sprigg (Nottingham University & Honorary Consultant Physician for Nottingham University Hospitals NHS Trust), and Prof Phil

White (Newcastle University & Consultant Neuroradiologist). Further details on speakers, the agenda and registration are available on the SCTNI website.

CONVINCE

The CONVINCE trial has made signifiant progress over the summer months and since the last SCTNI newsletter, and has reached a number of milestones:

- 1000th patient randomised in July - as of last week, 1094 patients randomised;
- 500th patient randomised from the UK in July - UK have now randomised 533 patients;
- 100th patient randomised from Belgium in August - now at 101 patients in Belgium participating in CONVINCE;
- 3 sites recruit their first patients: Altnagelvin Area Hospital (UK), Vancouver General Hospital (Canada), and Bispebjerg Hospital (Denmark);
- 107 sites open - new UK centres have joined, as well as sites from Poland, Denmark and Canada;
- Site initiation visits for our first Estonian and Lithuanian sites due to take place in Sept.

To maintain this momentum, CONVINCE aims to recruit at least one patient per month from each site to meet the goal of finishing recruitment in early 2020. You can view the two most recent CONVINCE Newsletters here (August issue) and here (September issue).

Member Updates

Congratulations to **Dr Niamh Merriman**, who has been awarded the Rising Star prize at the upcoming Organisation for Psychological Research into Stroke (OPSYRIS) conference in taking place in Oxford University in October. Dr Merriman is a Postdoctoral Researcher in the Dept of Psychology, RCSI, and is working on the HRB-ICE funded StrokeCog Study, where she is developing and pilot-testing a post-stroke cognitive intervention.

Upcoming Training Opportunities & Events

Wellcome-HRB Irish Clinical Academic Training (ICAT) PhD Fellowships: CLOSING SOON

The Wellcome-HRB Irish Clinical Academic Training (ICAT) Programme is seeking to appoint its next cohort of well-qualified and ambitious individuals who aspire to become the next generation of clinical academic leaders. ICAT is an all-Ireland clinician PhD programme funded by Wellcome and the Health Research Board, HSE-NDTP, HSC R&D Division, and six academic institutions (Trinity College Dublin, University College Dublin, NUI Galway, Queen's University Belfast, Royal

College of Surgeons in Ireland and University College Cork). The programme is coordinated by Clinical Research Development Ireland.

Integrated with postgraduate medical training, ICAT will support four years of academic training positioned at the beginning of higher specialist training (HST) or equivalent, with clinical and academic mentoring until completion of PhD and CSCST/CCT. The first year is predominantly clinical and incorporates selection of PhD supervisors and development of PhD project proposals. This is followed by a three-year fellowship leading to a PhD in one of the partner academic institutions. Applications for fellowships should be submitted by 5pm on 24th September 2019. Fellowship interviews will take place in Dublin on 4th and 5th December 2019. Successful candidates will take up their fellowships in July 2020. More detail available here.

Evidence Synthesis Ireland Fellowship Scheme: CLOSING SOON

The Evidence Synthesis Ireland (ESI) Fellowship Scheme aims to give Fellows the opportunity to learn about evidence synthesis in general, as well as to develop the practical skills of how to plan, design, conduct and report an evidence synthesis. Fellows may be in full or part time employment, be clinicians or clinician-academic trainees, researchers and/or postgraduate students resident in the island of Ireland and working in health and/or social care areas. The ESI Fellowship scheme involves placing Fellows (in a virtual environment) with experienced evidence synthesis centres and review teams in Ireland and internationally. Up to 16 Evidence Synthesis Ireland Fellowships are available per year. Award duration is until review completion or for up to 24 months maximum. There is a bursary for receipted travel and/or dissemination expenses up to a value of €1,000 available to each Fellow (for example to support travelling to the host centre or seminar/conference attendance). Fellows will be eligible to attend all ESI training workshops for free during their Fellowship. Applications for fellowships should be submitted by 5pm on 19th September 2019. More details available here.

In advance of future fellowships, 2018 Fellow Dr Aoife Egan will present a webinar that reviews her experience of the Evidence Synthesis Ireland Fellowship Scheme. Points of discussion will include the evidence synthesis experience, research output, use of the bursary, mentorship and networking opportunities. The webinar will take place on 21 Nov 2019, 12.00-13.00. More details, and to register, available here.

Evidence Synthesis Ireland Workshops

Evidence Synthesis Ireland and Cochrane Ireland promote evidence based healthcare policy and practice by supporting high quality, relevant systematic reviews and other synthesised research evidence. To this end, a series of workshops are scheduled over the coming months that might

be of interest to SCTNI members interested in, or already conducting, systematic reviews and evidence synthesis. These include:

•A two day workshop in Belfast (23-24 Sep 2019) on writing a Cochrane Systematic Review (details here)

•A one day workshop in Galway (27 Sep 2019) on qualitative evidence synthesis (details here)

•A one day workshop in Dublin (15 Nov 2019) providing Cochrane systematic review advanced author training (details here)

Introduction to Health and Social Research with Stata

Organised by Timberlake, and delivered by Dr. Vincent O'Sullivan (Lancaster University, UK), this 3-day course (30 Sep-2 Oct 2019) is for professionals and researchers from all academic disciplines who are new to Stata. Taking place in Dublin, the course assumes only limited statistical knowledge and experience of using statistical software. The participants will be introduced to Stata's interface. They will be shown how to manage and prepare datasets for analysis. The fundamentals of data analysis and visualisation will also be taught. Then, the participants will be introduced to two of the main data analysis tools: linear regression and logistic regression. Participants will be taught the statistical theory behind these methods, and they will apply these methods to specially chosen datasets using examples from economic, social, and medical research. For example, the Growing Up in Ireland dataset will be analysed during the sessions. Further information available here.

14th UK Stroke Forum Conference: Registration open

Registration is now open for the 14th UK Stroke Forum Conference, to be held on the 3-5 December 2019 at The International Centre in Telford, UK. The 2019 programme has been confirmed - you can view the 'At a glance' programme and full preliminary programme now. For further details, and to register, please follow this link.

Stroke Winter School: Registration Open

Registration is now open for the 7th ESO-ESMINT-ESNR Stroke Winter School, which will take place from 28 – 31 January 2020 in the University Hospital Bern, Switzerland. A series of concentrated high quality teaching sessions and courses on acute stroke management will be offered. The winter school is unique in its kind. Combining plenary sessions, discussions and technical training, it will foster improvement in treatment of cerebrovascular disease and advance research in this complex field, leading to technical developments. The target audience for the winter school are young stroke physicians and neuroradiologists with a major interest in cerebrovascular diseases. Applicants should currently be in training in a European teaching hospital that treats acute stroke patients. For further details about the winter school, the programme, the people involved, and for applications, see here.

Webinar: PPI in health and social research

The newly formed International PPI Network, in collaboration with Cochrane Training, will deliver a regular programme of webinars that cover a wide range of issues related to patient and public involvement and engagement in health and social research in a global context. While the webinar series started on the 24th August 2019, you can sign up for future webinars here. You will need a Cochrane Account to sign up for this webinar. If you don't have a Cochrane Account you will be able to register for free by following the link above.

SCTNI Training Opportunities & Events Webpages

In between our newsletters, you can keep up to date by visiting the SCTNI Training Opportunities & Events section of the website. We regularly add items to this section of the website. Please send us any events or opportunities you are organising or consider of interest to the network (see contact details at the end of this newsletter).

Publications & Resources

Review of clinical research infrastructure in Ireland

A recently published report presents the outcomes of a review of HRB's investment in clinical research infrastructures in Ireland. The aim of the review was to generate appropriate evidence on current strengths, synergies, gaps, duplications and needs in Ireland's clinical research infrastructures, either those funded directly or peripherally by the HRB, in order to inform the HRB's strategic priorities for future investment in this area. The report can be downloaded from the HRB website here.

Findings from the TICH-2 RCT

Tranexamic acid reduces death due to bleeding after trauma and postpartum haemorrhage. Lead by Prof Nikola Sprigg, and including **Prof Rónán Collins** (Tallaght University Hospital), a recently published paper details findings from the TICH-2 RCT, an international randomised, placebo-controlled, phase 3 superiority trial examining tranexamic acid for hyperacute primary IntraCerebral Haemorrhage (ICH). The primary outcome was functional status (death or dependency) at day 90, which was measured by the shift in the mRS score, using ordinal logistic regression, with adjustment for stratification and minimisation criteria. Among the findings, tranexamic acid did not affect a patient's functional status at 90 days after ICH, despite there being significant modest reductions in early death (by 7 days), haematoma expansion and SAEs, which is consistent with an antifibrinolytic effect. Tranexamic acid was safe, with no increase in thromboembolic events.

Commenting via Twitter, Prof Collins added that tranexamic acid "*did improve early mortality [and] in prespecified subanalysis with good blood pressure control it did reach significance for*

the primary outcome". As Prof Collins noted, "*the story of tranexamic acid as a potential acute treatment for intracerebral haemorrhage [is] not over ....bring on TICH-3*". The paper can be accessed here.

The Impact of Cognitive Impairment on Poststroke Outcomes

A recently published paper in the Journal of Geriatric Psychiatry and Neurology details findings from a five-year follow-up of the Action on Secondary Prevention Interventions and Rehabilitation in Stroke (ASPIRE-S) prospective cohort. Led by **Dr Daniella Rohde** (RCSI), findings highlight how cognitive impairment at 6 months was independently associated with worse quality of life; lower levels of independence; increased likelihood of receiving informal care; and increased likelihood of depressive symptoms. Noting that cognitive impairment post-stroke is associated with a range of worse outcomes, the authors highlight the need for more effective interventions to improve outcomes for this vulnerable group of patients. The paper is available here.

Fluoxetine and Fractures After Stroke

The FOCUS trial (Fluoxetine or Control Under Supervision) showed that fluoxetine did not improve modified Rankin Scale scores (mRS) but increased the risk of fractures. Published in the journal Stroke, an exploratory analyses from the FOCUS Trial involving among others **Prof John Forbes** (University of Limerick) aimed to describe the fractures, their impact on mRS and factors associated with fracture risk. Findings confirmed that most fractures resulted from falls. Although many fractures were serious, and likely to impair patients' function, the increased fracture risk did not explain the lack of observed effect of fluoxetine on mRS. Only increasing age, female sex, and fluoxetine were independent predictors of fractures. Further details available here.

Outcome-Driven Thresholds for Ambulatory Blood Pressure

The new American College of Cardiology/American Heart Association guideline reclassified office blood pressure and proposed thresholds for ambulatory blood pressure (ABP). A study published in the journal Hypertension derives outcome-driven ABP thresholds corresponding with the new office blood pressure categories. Writing on behalf of the International Database on Ambulatory blood pressure in relation to Cardiovascular Outcomes (IDACO) Investigators, the authors (including **Dr Eamon Dolan**, Connolly Hospital), performed 24-hour ABP monitoring in 11,152 participants representative of 13 populations. Findings from the study demonstrate that outcome-driven ABP thresholds corresponding to elevated blood pressure and stages 1 and 2 of hypertension are similar to those proposed by the current American College of Cardiology/ American Heart Association guideline. The paper can be accessed here.

ESOTA - Building a European 'network of networks' for stroke clinical research

To increase international collaboration on randomised trials for stroke in Europe, the ESO Trials Network Committee is leading the development of an alliance of national networks, the ESO Trials Alliance (ESOTA). Following initial consultation work in 2017, a recently published paper in the *European Stroke Journal* led by **Prof Peter Kelly** (Mater/UCD) describes an overview of

progress to date in the first year of ESOTA activity. Beginning with five founding networks in England, Ireland, Netherlands, Spain, and Switzerland, ESOTA aims to gradually grow, to ultimately include several hundred stroke centres and affiliated investigators working collectively on randomised trials of new stroke treatments. The paper can be accessed here.

Effects of cardiac rehabilitation interventions on cognitive impairment following stroke

The cardiac rehabilitation model has potential as an approach to providing rehabilitation following stroke. Led by **Isabelle Jeffares** (RCSI), a recently published review set out to identify evidence for the participation of stroke patients in cardiac/cardiovascular rehabilitation programs internationally, whether or not such programs offer a cognitive intervention as part of treatment, and the impact of rehabilitation on post-stroke cognitive function. Among the findings, cardiac rehabilitation had no statistically significant effect on cognitive function in five randomized controlled trials, or in three one group pre-post studies. This review highlights that there are very few studies of delivery of cardiac rehabilitation to stroke patients and that the inclusion of cognitive interventions is even less common, despite the high prevalence of post-stroke cognitive impairment. The paper is available here.

The rise and fall of aspirin in the primary prevention of cardiovascular disease

Aspirin is one of the most frequently used drugs worldwide and is generally considered effective for the secondary prevention of cardiovascular disease. By contrast, the role of aspirin in primary prevention of cardiovascular disease is controversial. Early trials evaluating aspirin for primary prevention, done before the turn of the millennium, suggested reductions in myocardial infarction and stroke (although not mortality), and an increased risk of bleeding. In an effort to balance the risks and benefits of aspirin, international guidelines on primary prevention of cardiovascular disease have typically recommended aspirin only when a substantial 10-year risk of cardiovascular events exists. However, in 2018, three large randomised clinical trials of aspirin for the primary prevention of cardiovascular disease showed little or no benefit and have even suggested net harm. A narrative review published in the Lancet, with Prof Bill McEvoy (NUI Galway) among the co-authors, reappraises the role of aspirin in primary prevention of cardiovascular disease, contextualising data from historical and contemporary trials. The article can be accessed here.

Impact of patient and public involvement on enrolment and retention in clinical trials

Researchers in the UK and Spain conducted a systematic review and meta-analysis to investigate the impact of patient and public involvement (PPI) on rates of enrolment and retention in clinical trials and explore how this varies with the context and nature of PPI. On average, PPI interventions modestly but significantly increased the odds of participant enrolment in the main analysis, with non-PPI components of interventions potentially contributing to this effect. In exploratory subgroup analyses, the involvement of people with lived experience of the condition under study was significantly associated with improved enrolment. The findings for retention were inconclusive owing to the paucity of eligible studies for main analysis. The authors conclude that findings add weight to the case for PPI in clinical trials by indicating that it

is likely to improve enrolment of participants, especially if it includes people with lived experience of the health condition under study. The paper is available here.

In other news…

The People's Trial

The HRB-TMRN have launched *The People's Trial*, a project aimed at challenging people to get involved in running their own (fun) clinical trial. The People's Trial is one of the first of its kind to establish an online clinical trial platform and to fully engage with the general public at every step of the trial process, from question selection, to recruitment, to data analysis and beyond. It is designed to offer an accessible, fun environment that provides the public with the tools to help recognise a reliable health claim and thereby help participants consider some of the key concepts needed to make informed decisions about their own health. You can find out more and get involved by visiting The People's Trial website.

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