**2017 Awards: Canadian Stroke Trials for Optimized Results (CaSTOR).**

**A joint initiative of the Canadian Stroke Consortium and the Heart and Stroke Foundation Canadian Partnership for Stroke Recovery**

CaSTOR is excited to announce that six teams of stroke clinical trial investigators have been awarded CaSTOR Collaborative Networking Grants. These top-ranked grants were selected from an excellent pool of research proposals submitted for CaSTOR funding. Each proposal was reviewed by two experts in the field and by a member of the CaSTOR Stroke Patient Advisory Group. Following individual reviews, a review committee convened to discuss all applications.

The review committee was composed of members from the CaSTOR Steering Committee and the CaSTOR Patient Advisory Group, who were not in direct conflict with any of the applications. The review committee discussion was chaired by international stroke and clinical trials expert, **Dr. Joseph Broderick**, PI for the National Coordinating Centre for NIH StrokeNet.

The review committee discussed the reviewer comments and evaluated each proposal against CaSTOR’s overarching goal of increasing stroke clinical trial capacity in Canada. To be eligible for funding, applications needed to have an average review score of 3.5 or higher (out of 5). Final decisions for funding approval were based on score rankings, until the funding envelope was depleted. Six grants totaling just over $180,000 (~$30,000/grant) were funded. They are:

**CANADIAN PLATFORM FOR TRIALS IN NON-INVASIVE BRAIN STIMULATION (CANSTIM)**
**\*\*\*Top Ranked Grant in competition\*\*\***
Principal Investigators: **DR. ALEXANDER THIEL, *McGill University,*Dr. JODI EDWARDS**, ***Sunnybrook Research Institute***
More Canadians are surviving stroke today than in previous years, but improved survival also means that more Canadians are living with stroke-related disabilities. Over 400,000 Canadians are living with a disability due to stroke, with the majority of stroke survivors experiencing difficulties conducting daily activities. Rehabilitation is critical for reducing the impact of these disabilities on survivors and it is now known that changes in the brain’s structure and function that help survivors recover are possible for years after stroke. However, standard rehabilitation sessions do not provide frequent enough therapy to produce these long lasting changes. New approaches to stroke rehabilitation that maximize improvements in function are needed to help reduce disability in stroke survivors. Transcranial magnetic stimulation (TMS) is a way to noninvasively stimulate the brain to enhance its ability to relearn movement and language abilities after stroke. TMS is safe and painless and reduces the amount of therapy needed to see improvements in function after stroke. However, to date, the use of TMS in stroke rehabilitation trials in Canada has been limited by: 1) a lack of agreement about the best TMS parameters to use in stroke survivors; 2) the need for standardized protocols for the use of TMS after stroke; and 3) the absence of a national platform for the use of these protocols in stroke rehabilitation clinical trials. The purpose of this proposal is to address these limitations and **establish a national platform for the use of non-invasive brain stimulation techniques, including TMS, in stroke rehabilitation clinical trials in Canada.**

**SECRET – STUDY OF EARLY RIVAROXABAN FOR CEREBRAL VENOUS THROMBOSIS**
Principal Investigators: **DR. THALIA FIELD, *University of British Columbia,*DR. MICHAEL HILL** (***University of Calgary***)
Co-Investigators: **Dr. Oscar Benavente** (*University of British Columbia*), **Dr. Dylan Blacquiere** (*Dalhousie University*), **Dr. Mark Boulos** (*University of Toronto*), **Dr. Brian Buck** (*University of Alberta*), **Dr. Shelagh Coutts** (*University of Calgary*), **Dr. Andrew Demchuk** (*University of Calgary*), **Dr. Dar Dowlatshahi** (*University of Ottawa*), **Dr. Laura Gioia** (*University of Montreal*), **Dr. Asaf Honig** (*University of British Columbia*), **Dr. Agnes Lee** (*University of British Columbia*), **Dr. Jennifer Mandzia** (*University of Western Ontario*), **Dr. Janel Nadeau** (*Calgary*), **Dr. Jacqueline Pettersen** (*University of British Columbia*), **Dr. Aleksandra Pikula** (*University of Toronto*), **Dr. Ashkan Shoamanesh** (*McMaster University*), **Dr. Jeff Weitz** (*McMaster University*), **Dr. Hubert Wong** (*University of British Columbia*)
Collaborators: **Dr. Gord Gubitz** (*Dalhousie University*), **Dr. Meera Gupta** (*University of British Columbia*), **Dr. Albert Jin** (*Queen’s University*), **Dr. Matthew Kula** (*University of British Columbia*), **Dr. Sylvain Lanthier** (*University of Montreal*), **Dr. Robert Hart** (*McMaster University*), **Dr. George Medvedev** (*Royal Columbian Hospital*), **Dr. Manu Mehdiratta**(*Trillium Brain & Spine Institute*), **Dr. Luciano Sposato** (*London Health Sciences*), **Dr.** **Deepa Suryanarayan** (*University of Calgary*), **Karina Villaluna** (*Vancouver Stroke Program*), **Katie White** (*Stroke Services BC*), **Dr. Daryl Wile** (*University of British Columbia*), **Dr. Samuel Yip** (*University of British Columbia*)

Cerebral venous thrombosis (CVT) refers to clotting of the draining veins of the brain – a deep venous thrombosis within the head. It is an uncommon cause of stroke that tends to affect younger women, with 80% of patients under the age of 50 and a 3:1 female:male ratio. Symptoms include headache, vision loss, weakness, seizures and coma. 15% of patients die or are left disabled, 25% cannot return to work, and over half are left with long-term issues with thinking, fatigue or mood.
Because CVT is a rare condition it is difficult to test the best treatments in clinical trials. We are using novel ways to find patients with CVT, including partnerships with rural hospitals via telemedicine, and will speak to patients with CVT to learn more about their condition so that we can improve care.
We will compare the safety of a newer blood thinner, rivaroxaban, to current standard blood-thinning treatment with warfarin to see if rivaroxaban is a safer option with less bleeding. We will also see if it is more cost-effective to use rivaroxaban. We will collect higher quality data on symptoms after CVT that can affect patients' quality of life, and will evaluate how improvements in vein blood flow over time may affect recovery and duration of treatment with blood thinners.
We hope to **learn more about this rare disease and to create a model for studying other rare diseases using clinical trials to determine the best evidence for care**.

**HIGH INTENSITY INTERVAL TRAINING: AN OPPORTUNITY TO PROMOTE NEURORECOVERY AND CARDIOVASCULAR HEALTH IN STROKE REHABILITATION**
Principal Investigator: **DR. MARC ROIG, *McGill University***
Co-Investigators: **Dr. Ada Tang** (*McMaster University*), **Jennifer Crozier** (*McMaster University*), **Dr. Marilyn MacKay-Lyons** (*Dalhousie University*), **Dr. Joyce Fung** (*McGill University*), **Dr. Janice Eng** (*University of British Columbia*), **Dr. Damian Bailey** (*University of South Wales*), **Dr. Shane Sweet** (*McGill University*), **Dr. Nico Giacomantonio** (*Dalhousie University*)
Collaborators: **Dr. Alexander Thiel** (*McGill University*), **Dr. Anita Menon** (*McGill University*), **Claire Fritz Perez** (*Jewish Rehabilitation Hospital*), **Franceen Kaizer** (*Jewish Rehabilitation Hospital*), **Michael Trivino** (*Jewish Rehabilitation Hospital*)

High exercise intensities are critical to maximize the effects of cardiovascular training on
cardiorespiratory fitness and motor function after stroke. However, vigorous intensities for long
periods of time are difficult to sustain for most patients due to their poor cardiorespiratory fitness
and motor limitations. High-intensity interval training (HIIT) offers a potentially feasible
alternative as it allows higher intensities over short bursts of exercise interspersed with periods
of active recovery or rest. In individuals without disability, HIIT has shown to be a time-efficient
alternative to moderate-intensity continuous training (MICT) providing similar or even superior
physiological gains despite substantially lower exercise volumes. HIIT has also been
implemented successfully in the rehabilitation of individuals with chronic conditions such as
coronary heart disease, diabetes and obstructive pulmonary disease. Preliminary evidence from
six small studies suggests that HIIT could be incorporated into stroke rehabilitation to improve
cardiorespiratory fitness and some aspects of mobility. The objectives of this project are to appraise the scientific evidence underlying the potential use of HIIT in stroke rehabilitation and to design a study to determine if HIIT offers any advantage over MICT. The deliverables include the publication of a position paper providing a detailed critical appraisal of the potential use of HIIT post-stroke and the submission of an operating grant for a multisite randomized clinical trial (RCT) comparing the efficacy of HIIT versus traditional MICT on different recovery and health rehabilitation outcomes. Although this project focuses mainly on stroke rehabilitation, it also addresses important gaps in different areas of the stroke care continuum. Appropriately prescribed, HIIT could be implemented to improve risk factors (prevention), minimize the short-term consequences (acute care) of stroke as well as to promote long-term recovery (rehabilitation). The project gathers together a group of experts in the prescription of exercise in stroke rehabilitation, neuroplasticity and cardiovascular health to form a new research network. Furthermore, individuals with stroke, neurologists, cardiologists, physical therapists, clinical coordinators, advanced practice leaders and knowledge transfer experts are also actively involved in the activities of the project. Although this initial project investigates specifically the potential use of HIIT in stroke rehabilitation, the long-term goal of our newly established network is **to create a permanent platform exploring novel interventions to improve recovery after stroke, fostering knowledge co-creation and translation as well as the training of highly qualified personnel**.

**CANADIAN HEMORRHAGIC STROKE TRIALS INITIATIVE (CoHESIVE)**
Principal Investigators: **DR. ASHKAN SHOAMANESH, *McMaster University (Hamilton, ON),*** **Dr. ROBERT HART (*McMaster University*, *Hamilton Health Sciences Centre*)**, **DR. KENNETH BUTCHER** **(*University Of Alberta*)**
Co-Investigators: **Dr. Mukul Sharma** (*McMaster University*), **Dr. Oscar Benavente** (*University of British Columbia*), **Dr. Dariush Dowlatshahi** (*University of Ottawa, Ottawa Hospital*), **Dr. Laura Gioia** (*University of Montreal*), **Dr. Eric Smith** (*University of Calgary*), **Dr. Christian Stapf** (U*niversity of Montreal*), **Dr. Wieslaw Oczkowski** (*McMaster University*), **Dr. Shelagh Coutts** (*University of Calgary*), **Dr. Manu Mehdiratta** (*University of Toronto*), **Dr. Aleksandra Pikula** (*University of Toronto*), **Dr. Thalia Field** (*University of British* *Columbia*), **Dr. Alexander Khaw** (*Western University*), **Dr. Carlos Kase** (*Emory University*), **Dr. Steven Greenberg** (*Harvard Medical School, Massachusetts General Hospital*), **Dr. Rustam Al-Shahi Salman** (*University of Edinburgh*), **Dr. Magdy Selim** (*Harvard Medical School*), **Dr. Stuart Connolly** (*McMaster University*), **Dr. Jeff Healy** (*McMaster University*), **Dr. John Eikelboom** (*McMaster University*), **Dr. Guillaume Paré** (*McMaster University*), **Dr. Jackie Bosch** (*McMaster University*)
Collaborators: **Dr. David Gladstone** (*Sunnybrook Health Sciences Centre*), **Dr. Richard Swartz** (*University of Toronto*)

Hemorrhagic strokes (HS) caused by uncontrolled bleeding into the brain tissue from the rupture of diseased blood vessels account for 15-20% of all strokes. HS have the greatest level of mortality amongst all stroke subtypes, averaging 55% at 1 year, and only one quarter of HS victims resume independent life. In contrast to the significant reductions in the incidence of ischemic stroke achieved across high-income countries over the past four decades, the incidence of hemorrhagic strokes has remained the same during this time. Moreover, we have yet to develop proven treatments or prevention strategies for HS patients.The Canadian HEmorrhagic Stroke trIals initiatiVE (CoHESIVE) aims to establish a Canada-wide multidisciplinary network of collaborators devoted to the development, and successful and efficient execution of hemorrhagic stroke (HS) trials. With this aim we propose a full-day CoHESIVE symposium to be held during the Spring of 2017. This platform will be used to establish a consortium of investigators dedicated to the successful completion of HS-related clinical trials in Canada, refine the protocol of NASPAF-ICH for future large public funding applications, define key ‘gap’ areas in our understanding and treatment of HS where we could concentrate initial CoHESIVE’s efforts, propose and organize a distinct Heart and Stroke Foundation of Canada Best Practice Recommendations Writing Group for the management of spontaneous HS (still embedded in fragmented fashion across other sections), develop a survey to be disseminated to surviving HS patients across Canada, in order to establish **patient-centered outcomes for the design of CoHESIVE trials, amongst others.**

**ENDOVASULAR ACUTE STROKE INTERVENTION – TANDOM OCCLUSION TRIAL (EASI-TOC): A PILOT TRIAL OF ACUTE CERVICAL INTERNAL CAROTID ARTERY ANGIOPLASTY AND STENTING DURING ENDOVASCULAR THROMBECTOMY FOR ANTERIOR CIRCULATION STROKE**
Principal Investigator: **DR. ALEXANDRE POPPE, *University of Montreal***
Co-Investigators: **Dr. Christian Stapf** (*University of Montreal*), **Dr. Nicole Daneault** (*University of Montreal*), **Dr. Yan Deschaintre** (*University of Montreal*), **Dr. Laura Gioia** (*University of Montreal*), **Dr. Grégory Jacquin** (*University of Montreal*), **Dr. Sylvain Lanthier** (*University of Montreal*), **Dr. Céline Odier** (*University of Montreal*), **Dr. Dar Dowlatshahi** (O*ttawa Hospital, University of Ottawa*), **Dr. Jean Raymond** (*University of Montreal*), **Dr. Daniel Roy** (*University of Montreal*), **Dr. Alain Weill** (*University of Montreal*), **Marlène Lapierre** (*University of Montreal*)

Six major randomized clinical trials, five published in 2015 and one in 2016, have demonstrated the superiority of endovascular therapy (clot-retrieval or EVT) in addition to standard care (including intravenous thrombolysis if indicated) over standard care alone in patients with acute anterior circulation stroke. The goal of this study is to determine if, in patients undergoing acute intracranial thrombectomy for anterior circulation stroke with concurrent ipsilateral symptomatic high-grade (>70%) atherosclerotic stenosis or occlusion of the extracranial ICA, endovascular ICA revascularization using angioplasty and stenting is superior to intracranial thrombectomy alone with possible deferred cervical carotid intervention with regards to any symptomatic recurrent stroke (ischemic or hemorrhagic) or death at 30 days. One pressing question facing stroke physicians and neuro-interventionalists when treating stroke patients using EVT is how to manage those who have concurrent severe (>70%) narrowing or occlusion of the internal carotid artery (ICA) in the neck on the same side as the patient’s stroke (so-called “tandem lesion”). In these cases, embolization of clot from an unstable atherosclerotic plaque in the ICA to the middle cerebral artery (MCA) is usually the cause of the patient’s stroke.

The team will build upon an existing network of high-volume Canadian stroke centres offering EVT as developed during the ESCAPE trial, including both stroke physicians and neurointerventionalists. A first step will be to ascertain current practice across Canada when treating patients with tandem occlusions using a web-based survey sent to physicians involved in EVT as well as through teleconferences with stroke experts from representative and interested EVT centres across the country. A proposed trial protocol will be presented and discussed in order to produce a final protocol, publish a position statement, begin the trial locally and submit for peer-reviewed funding agency funding in order to expand the trial to other sites.

**RECOVERNOW: BRINGING REHABILITATION TO THE ACUTE CARE SETTING USING MOBILE PLATFORM TECHNOLOGY**
Principal Investigators: **DR. DAR DOWLATSHAHI, *Ottawa Hospital Research Institute and University of Ottawa,*DR. DALE CORBETT** **(*University of Ottawa*)**
Co-Investigators: **Dr. Tim Ramsay** (*University of Ottawa, Ottawa Hospital Research Institute)*, **Dr. Sean Dukelow** (*University of Calgary, Calgary Stroke Program*), **Dr. Robert Teasell** (*Western University*), **Dr. Janice Eng** (*University of British Columbia, GF Strong Rehab Centre*), **Dr. Elizabeth Rochon** (*University of Toronto, Toronto Rehabilitation Institute, University Health Network*), **Karen Mallet** (*Ottawa Hospital Research Institute*), **Dr. Simon Hatcher** (*University of Ottawa*), **Dr. Luciana Catanese** (*McMaster University*), **Dr. Richard Swartz** (*University of Toronto*), **Dr. Thalia Field** (*University of British Columbia, Vancouver Stroke Program*), **Dr. Dylan Blacquiere** (*Dalhousie University, University of Newfoundland, Horizon Health Network*), **Michael Pugliese** (*University of Ottawa*), **Rany Shamloul** (*Ottawa Hospital Research Institute*), **Dr. Kumanan Wilson** (*University of Ottawa*), **Dr. Katherine Atkinson** (*Ottawa Hospital*), **Julien Guerinet** (*Ottawa Hospital*)

Stroke is the leading cause of disability in Canada; fortunately, recovery is possible. When combined with acute stroke therapy, stroke rehabilitation reduces odds of death, dependency, and institutionalization. Following acute treatments, the current paradigm for stroke rehabilitation requires transportation of patients to specialized facilities, with frequent delays due to limited space. In Canada, the proportion of patients transferred to inpatient rehabilitation is around 16%, even though 40% of patients would benefit from it. Among those transferred, only 50% begin rehabilitation within two weeks. Rather than waiting for patients to be “cleared for rehab” and transported to a specialized facility, we propose to “bring rehab” to the inpatient setting. We believe we can leverage existing mobile technology platforms to administer rehabilitation therapy during patient down time. The primary objective for this proposal is to form a steering committee, consisting of both acute stroke and stroke recovery experts, to design and launch a multi-centre randomized controlled trial comparing routine stroke care with routine stroke care + RecoverNow mobile tablet therapy in the acute care setting. Our secondary objective is to leverage this RecoverNow paradigm to form a Canada-wide collaboration and infrastructure poised to perform multiple recovery trials in the acute care setting. Our long-term goal is t**o determine whether earlier, focused rehabilitation therapies delivered in acute care hospitals through the RecoverNow platform will result in improved outcomes, shorter length of stay, and decreased healthcare utilization.** Our collaboration will seek funding from external granting agencies and technology industry partners to achieve this goal.