TrialScribe
Clinical Research News
at University Health Network

Welcome to the September 2014 edition of *TrialScribe*, a bi-monthly e-newsletter designed to inform researchers and trainees about clinical research news and information at UHN. Included in this issue:

- Charles Chan, FACP, FRCPC, MD, Vice President, Medical Affairs and Quality, and Christopher J. Paige, PhD, FCAHS, Vice President, Research; September 2014

Research Spotlights

Heart Transplant: Delayed Cardiac Rehab Increases Health Risks

After a heart transplant (HT), recipients are at a greater risk of developing other health complications including stroke, heart disease, osteoporosis and diabetes. To address this, Canadian guidelines recommend that HT patients should start a cardiac rehabilitation program within two months of their surgery.

A team of TRI researchers has found that HT recipients are referred for cardiac rehabilitation much later than what is recommended and that this delay is linked to a greater decline in the recipient's body composition.

This retrospective study, led by Drs. Susan Marzolini (TRI Research Fellow) and Paul Oh (TRI Scientist), examined a group of 43 men and women who received a HT between 1996 and 2013. The researchers found that HT recipients were referred for rehabilitation 24.9 months after their surgery, which was 12 times longer than the time-to-referral observed in a comparable group of patients who had received another type of heart surgery. Moreover, the longer the delay to start the rehabilitation program, the greater a patient's waist circumference, body mass index, hip circumference and body fat percentage upon starting their rehabilitation program, putting them at greater cardiovascular risk. However, once in the program, HT recipients experienced significant gains in their cardiovascular fitness.

"Additional research is required to determine the appropriateness of waiting so long to refer HT patients to a cardiac rehabilitation program and to elucidate the optimal exercise prescription strategies for these patients", says Dr. Marzolini.

This work was supported by the Toronto Rehab Foundation and the Ontario Ministry of Health and Long-Term Care.

Time-to-referral, use, and efficacy of cardiac rehabilitation after heart transplantation. Marzolini S, Grace SL, Brooks D, Corbett D, Mathur S, Bertelink R, Skeffington V, Alter D, Oh P. Transplantation. *2014 Aug 12.* [Pubmed abstract]

Obesity and Depression: Two Sides of the Same Coin?

Major depressive disorder is often associated with obesity, suggesting that they may be linked. A handful of previous studies have tried to examine whether a person's body weight or body mass index (BMI)—a measure of body weight relative to body length—is able to predict response to antidepressant therapies, but have failed to provide conclusive results. A limitation of these previous studies is that BMI data were grouped into broad categories (eg, normal, overweight or obese), thus potentially concealing subtle differences.

The research team led by Dr. Roger McIntyre, Clinical Researcher at TWRI, used a more direct approach. Rather than grouping patients into categories, they simply recorded the body weight and BMI of people with depression, and then initiated treatment with the antidepressant fluoxetine. Patients' response to treatment was assessed using two different depression questionnaires and rating scales. This approach revealed that higher body weight and BMI before treatment were associated with having a worse response to the drug.

Currently, different BMI cutoff points are used to define overweight and obese categories depending on ethnicity. This study highlights that different BMI category definitions may result in loss of information and explain the inconsistent results seen in the past.

This work was supported by the Kai-Syuan Psychiatric Hospital and the National Science Council of Taiwan.

Both body weight and BMI predicts improvements in symptom and functioning for patients with major depressive disorder. Lin CH, Chen CC, Wong J, McIntyre RS. Journal of Affective Disorders. *2014 June.* [Pubmed abstract].

News and Events

New Research Intranet Launched

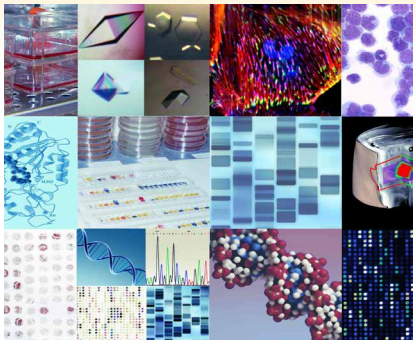
UHN has launched a new version of the Research Intranet featuring service pages to help UHN staff find the answers to their questions more easily. Service categories of interest to clinical researchers include:

- Clinical Research
- CAPCR - Coordinated Approval Process for Clinical Research
- Clinical Research Record
- Research Ethics Board Review

To explore the new Intranet and start familiarizing yourself with its content, please click here. For more information contact intranet.devteam@uhnresearch.ca.

Research Intranet

Facilities and Equipment Available to Researchers at UHN



Find out what research-related resources are available by looking through the UHN Facility Information Sheets, which list the equipment and expertise available at and the contact information for each of UHN's 19 core facilities. The following facilities offer services applicable to clinical research:

- Philip S. Orsino Cell Therapy Facility
- Drug Development Program (DDP) Biomarker Laboratory (formerly AMPL)
- UHN BioSpecimen Sciences Program (BSP)
- UHN Pathology Research Program (PRP) Laboratory
- Guided Therapeutics Program (GTx)
- STTARR (Spatio-Temporal Targeting and Amplification of Radiation Response Innovation Centre)

To update or add your Facility Information Sheet to the list, please contact www@uhnresearch.ca.

Vital Signs Certification Program

All clinical research personnel who are non-regulated health care professionals (e.g. CRSA, CRC I or CRC II) performing vital signs measurement as part of a clinical research study are required to have successfully completed the designated training and certification program in vital signs measurement in accordance with the requirements of UHN Policy #40.20.012 Requirements for Performing Vital Signs Measurement in Clinical Research Studies.

Vital signs training consists of the following three components:

1. An Online Training Module that must be completed prior to the in-class demonstration and training session
2. An in-class demonstration and training session
3. A competency assessment within the research unit that must be completed following the in-class demonstration and training session

If all of the following statements describe your current position, then you should complete the Vital Signs Certification Program:

- You are a clinical research employee whose job description includes interaction with research participants (e.g. CRSA, CRC I or CRC II)
- You are a non-regulated health care professional
- Vital signs measurement is a study-related task that you are being delegated to perform by a clinical investigator

For more details, please visit the Research Quality Integration webpage. If you have additional questions, contact the Research Quality Integration department at rqi@uhnresearch.ca.

Research Policy Corner

Several projects have been initiated by the Clinical Research Support Services Planning and Implementation (CRSSPI) team, chaired by Lisa Alcia, Executive Director of Research Operations. In this section you will find the new research policies available on the Corporate Intranet.

Institutional Authorization for Research Involving Human Participants Policy

GOT IA?
Institutional Authorization

Institutional Authorization (IA) was implemented at UHN in June 2011 to ensure that researchers obtain all requisite approvals prior to starting a study involving human participants. IA is granted on a per-protocol basis by Dr. Christopher Paige, Vice President, Research at UHN or his designate. The approvals and documentation needed for IA include but are not limited to REB approval; contracts/agreements with affected service departments or external parties; and safety and training certifications. If any approvals or documentation are withdrawn or expire, IA may be suspended or revoked. To read the policy, click here or visit the UHN Policies webpage.

The Research Quality Integration (RQI) program focuses on areas critical to maintaining subject safety, data integrity and regulatory compliance. Through internal quality auditing and site support, the QI team assists researchers in recognizing opportunities for enhancing effective processes and operations, and identifies best practices that can be shared throughout the organization. The following is a continuation of a series of case studies highlighting examples of how to manage gaps in procedure and improve research best practices.

How is IA obtained for a research study?

It is the responsibility of a study's Principal Investigator (PI) to apply for IA through the UHN Coordinated Approval Process for Clinical Research (CAPCR) system. While IA is the framework for bridging all of the different approvals that researchers must obtain prior to beginning their studies, CAPCR is the mechanism that identifies, coordinates and tracks all approvals required for IA. Once all of the requisite approvals have been obtained, the study PI will receive notification of IA through email, at which point they may begin conducting the proposed research.

Institutional Authorization - Case Study

Note: the following is a fictional case concerning the responsible conduct of research

Dr. X submitted an application through the CAPCR system seeking approval to conduct a new investigator-initiated trial involving human participants. The aim of the study was to elucidate the pro-cognitive effects of an experimental drug in people afflicted with Alzheimer's disease. Once Dr. X received the REB approval letter, the study team commenced the study without having received IA. The team recruited 22 participants who underwent a memory performance evaluation and provided blood samples as part of the research protocol. The study protocol also required that a combined positron emission tomography and computed tomography (PET/CT) scan be performed prior to the participants receiving the drug intervention.

Dr. X booked appointments for his first set of participants at the Medical Imaging Department (MID) at UHN. However, a cost recovery service agreement had not yet been approved because, during the review process, Dr. X forgot to provide MID with the information they requested. Furthermore, Dr. X had not informed the MID research division that these appointments were for research participants. Accordingly, the PET/CT staff at MID assumed that the participants were being scanned for clinical purposes, so the imaging was performed using the standard clinical imaging protocol as opposed to the specific imaging requirements of Dr. X's research protocol. As a result, the correct data series was not obtained and the participants could not be started on the experimental drug until the correct scan was completed.

When Dr. X informed the study participants that the administration of the experimental drug intervention would be delayed and that they would need to undergo another PET/CT scan (and further irradiation), nine of the participants withdrew from the study. When MID submitted billing information to the Ontario Health Insurance Plan (OHIP) to recover the cost of each scan, OHIP refused payment because the PET/CT scans were considered above the standard of care.

Beginning a Study Involving Human Participants Without Institutional Authorization - What are the Risks?

As a result of Dr. X beginning the study without IA, the study proceeded without having the proper service agreement in place with JDMI and the cost of imaging could not be recovered by the institution. The samples collected from participants who withdrew from the study had to be destroyed. In addition to these financial losses, the study lost nine eligible participants, who were unnecessarily exposed to radiation. The participants who remained in the study had to undergo another dose of radiation, exposing them to unnecessary risk, so that the correct imaging protocol could be completed.

Commencing a research study without IA puts all parties involved in a research study (PI, research study team and participants, UHN and its departments) at risk.

Why is it Important to Have Institutional Authorization?

The primary goal of IA is to protect research participants, researchers and their research teams, as well as UHN and its departments. IA accomplishes this by:

- Providing assurance that the departments impacted by the activities of the study have agreed on a structure for allocating resources to the study team and that the costs incurred by the research do not negatively impact departmental resources
- Confirming that appropriate contracts and agreements with external parties have been established
- Confirming that the PI listed on the study protocol has completed the required training programs and is fully qualified to perform their role in the study

TrialScribe is brought to you by UHN Research Communications. We hope you have enjoyed reading this newsletter.
Please note: this newsletter is designed for UHN internal purposes and, as such, contains links to some documents that can only be accessed through UHN's Research or Corporate Intranet.
The next issue of *TrialScribe* will be released in November 2014.
Some images adapted from the image archives of stock.xchng.ca.
If you would like to provide feedback, please email www@uhnresearch.ca.