



March 2015, Volume 2, Issue 1

## INSIDE THIS ISSUE

Director's Message.....	1
NICR Talks at ACC .....	1
Highlight: Dr. Bagai .....	2
Member Grants .....	2
Ongoing Clinical Trials .....	3
Publications .....	4

## NICR WEBSITE

Please visit the [NICR webpage](#) for up-to-date information and for a comprehensive list of NICR members' research activities.

If you would like to have your information included in the newsletter or NICR webpage, please email Liz Thuo at [liz.thuo@utoronto.ca](mailto:liz.thuo@utoronto.ca).

## CONTACT INFO

NICR  
c/o Dr. Michael Farkouh  
585 University Street  
Room 4N474  
Toronto, Ontario M5G 2C4

<http://hsrlce.utoronto.ca/research/network-for-innovation-in-clinical-research-nicr/>

# Network for Innovation in Clinical Research (NICR) Newsletter

In this issue of our Winter Report 2015, we are excited to report on the progress of the Network for Innovation in Clinical Research. At this time, we have a varied portfolio of clinical trials ranging from participation in on-going clinical trials, small proof of concept trials, and larger trials led by investigators at the University of Toronto.

Our greatest advantage is our young investigators. In this edition, we feature Dr. Akshay Bagai, a University of Toronto product who trained at the Duke Clinical Research Institute (DCRI) and is now leading an exciting interventional cardiology investigative program in ST-elevation MI research. He is also a noted investigator in the ISCHEMIA Trial.

As well, we highlight our productivity. We are excited to be moving forward with an international collaborative program. Recently, Shaun Goodman, Jay Udell and I met at the American Heart Association along with colleagues from the United States, Australia and Canada. We forged ahead with a plan to conduct strategy-driven trials across the spectrum of cardiovascular research.



I also wanted to express my appreciation to Muhammad Mamdani for his leadership at the Applied Health Research Centre and their support of young investigators to bring their questions forward to a viable grant proposal. This has allowed many young investigators to gain knowledge of methodology and trial design. Because of Muhammad's leadership, our program is highly regarded by programs across North America as a model for developing careers in CV research.

In the weeks to come, we are presenting the NICR concept to our surgical colleagues and colleagues in other disciplines so that we can bring the University of Toronto together in a multi-disciplinary, multi-institutional fashion to answer the most important questions for our patients. We hope to see you at ACC '15 in San Diego.

Let's keep collaborating!

Yours sincerely,  
Mike Farkouh

## Upcoming Talks by NICR Members: ACC Conference

Dr. Michael Farkouh, Dr. John Floras, Dr. Shaun Goodman, and Dr. Jacob Udell will present talks at the American College of Cardiology Scientific Session taking place on March 14-16, 2015 in San Diego, California. Please [click here](#) for their talk details and timing.



*We have a varied portfolio of clinical trials ranging from participation in on-going clinical trials, small proof of concept trials, and larger trials led by investigators at the University of Toronto.*

*Our greatest advantage is our young investigators.*

*We excited to be moving forward with an international collaborative program.*

## NICR Member Highlight: Dr. Akshay Bagai

Dr. Akshay Bagai is a practicing interventional cardiologist and an assistant professor of medicine at the University of Toronto. He received his MD and trained in Internal Medicine and Cardiology at the University of Toronto. He completed his training in Interventional Cardiology at St. Michael's Hospital and graduated from the Clinical Research Training Program obtaining a Masters degree in Health Sciences from Duke University, USA. He returned to Toronto and joined the Division of Cardiology at St. Michael's Hospital in August 2013.



His clinical and research interests are closely aligned and include systems of care for acute coronary syndrome and out-of hospital cardiac arrest, adjunctive therapy in coronary syndromes and percutaneous coronary intervention, and revascularization strategies in acute and stable coronary disease. He is the co-principal investigator of the RevAScularization Strategies for ST Elevation Myocardial Infarction (ASSIST) trial, investigating the optimal management of significant non-culprit stenoses in acute myocardial infarction patients with multivessel disease, and the University of Toronto PCI Outcomes project, with aim to improve clinical outcomes in patients undergoing PCI. You may reach Dr. Bagai via e-mail at [BagaiA@smh.ca](mailto:BagaiA@smh.ca).

## Research Activity: Grants

NICR membership currently has more that \$21 million in active grants. Below is a sampling of awards received by NICR Members in 2014/2015. [Click here](#) for the complete list (click on the 'Grants' and the 'Awards' tab).

1. **Connelly, Kim** – Canadian Institutes of Health Research (CIHR) New Investigator Award. \$300,000 - July 2014
2. **Dorian, Paul** – Co-investigator - Heart & Stroke Foundation of Canada (HSFC) Grant-in-Aid. Atrial Fibrillation in the Emergency Room (The AFTER Study): Prospective validation of a clinical decision instrument. (Principal Investigator – Clare Atzema); Collaborators: Lee DS, Tu JV, Austin PC. \$299,584 - 03/2015 - 04/2018
3. **Ko, Dennis** - Principal Investigator - Ontario Transcatheter Aortic Valve Implantation Report Card. Cardiac Care Network of Ontario (CCN). PI: Humphries, Karin - \$350,000. 2014 – 2015
4. **Lee, Douglas** - Co-Investigator - Canadian Institutes of Health Research (CIHR) Operating Grant (location- Sunnybrook). Statistical Methods for Health Services Research. PI: Peter Austin - \$214,105- 2014 (5 years)
5. **Leong-Poi, Howard** - Principal Investigator - Canadian Institutes of Health Research (CIHR) Operating Grant. Next Generation Ultrasound-Mediated Gene Delivery: Targeting Acute Myocardial Infarction-Reperfusion. \$93,693 - 2014-2015
6. **Wijeyesundera, Harindra** – Co-Investigator - Canadian Institutes of Health Research (CIHR). Operating Grant. Assessing and improving the quality of care of patients with out-of-hospital cardiac arrest. PI: Ko, Dennis. Collaborators: Austin P, Cheskes S, Dorian P, Morrison L, Rac V, Scales D, Stukel T, Tu J, Verbeek P, \$443,022 - 2014 Apr - 2017 Mar
7. **Wright, Graham** – Principal Investigator - Canadian Institutes of Health Research (CIHR) Operating Grant. MRI for Arrhythmia Management in Ischemic Heart Disease. Co-applicants: Eugene Crystal, Sheldon Singh. \$820,920 - 04/2014-03/2019

# Research Activity: Ongoing Clinical Trials with University of Toronto Leadership

Members of NICR are currently involved and recruiting in numerous local, multi-centre and multi-national clinical trials. These include testing novel drugs or strategies of care to reduce cardiovascular (CV) risk in patients across the spectrum of atherosclerosis and other CV disease (CVD). Please visit the [NICR webpage](#) for a summary of these trials or click on each trial's name for comprehensive details and information on how you can enrol your patients to the studies.



## Patients at risk for ischemic heart disease:

1. **ECAD**: low-dose statin vs standard care in patients with low Framingham Risk for IHD
2. **PISCES**: fish oil vs placebo in patients with chronic kidney disease (CKD)
3. **TOSCA-5**: a 2-stage study to evaluate single doses of MZ-004 at different dose levels vs placebo in patients with chronic total occlusions

## Patients with stable ischemic heart disease (SIHD):

1. **ISCHEMIA**: ischemic-guided vs medical therapy in patients with at least moderate ischemia
2. **CAMELLIA-TIMI 61**: lorcaserin vs placebo in patients with T2DM with or at risk for CVD
3. **CIRT**: low-dose methotrexate vs placebo in patients with T2DM or metabolic syndrome and SIHD

## Acute coronary syndrome (ACS):

1. **EMPRES**: assesses the effect of exenatide vs placebo on myocardial injury in patients undergoing emergent PCI STEMI
2. **TAILOR-PCI**: tailored antiplatelet therapy based on genetic carrier status vs standard care in patients with ACS and SIHD for PCI
3. **ASSIST**: same-sitting non-culprit stenosis PCI during index primary PCI for STEMI
4. **CRIC-RCT**: A preliminary study to see if daily RIC can help heart muscle recovery after a heart attack

## Stabilized following ACS:

1. **ODYSSEY Outcomes**: alirocumab (PCSK9 inhibitor) vs placebo in post-ACS patients on maximally tolerated atorvastatin or rosuvastatin

## Heart Failure:

1. **PARAGON-HF**: LCZ696 vs valsartan in patients with heart failure with preserved ejection fraction
2. **EMBRACE-MRI**: Cardiac MRI vs standard care surveillance of women for early cardiotoxicity during treatment for breast cancer
3. **ADVENT-HF**: assessing the effects of adaptive servo ventilation on survival and frequency of hospital admissions in patients with heart failure and sleep apnea
4. **MITNEC B5**: non-isotope based imaging modalities vs 99mTcSPECT to detect myocardial ischemia in patients at high risk for ischemic CV events
5. **IMAGE-HF**: alternative imaging modalities in ischemic heart failure (PET/CT or CMR or CTA)

## Appropriateness:

1. **Echo-WISELY**: A randomized blinded education and feedback intervention to reduce inappropriate echocardiograms

## Electrophysiology (EP):

1. **TOUCH AF**: comparison of two strategies of wide antral PV isolation plus linear ablation for persistent AF: guided by contact force sensing (CFS) vs blinded to CFS
2. **MARE**: ambulatory electrocardiographic monitoring for the detection of high-degree AVB in patients with NOP-LBBB after TAVI

## Cardio-medical:

1. **NEAT**: safety/efficacy of the FLEX System when used to create an arteriovenous fistula percutaneously in patients with CKD who require hemodialysis vascular access
2. **SUCCOUR**: ejection fraction vs myocardial strain to initiate cardiac therapy during cancer therapy
3. **TRICS-III**: study of two commonly used transfusion strategies (restrictive vs liberal) in high risk patients having cardiac surgery using a non-inferiority trial design

## Peripheral Arterial Disease (PAD):

1. **BEST-CLI**: compare effectiveness of best available surgical treatment with best available endovascular treatment in adults with CLI who are eligible for both treatment options
2. **ACP-CLI**: randomized double blind placebo controlled clinical study to assess blood-borne autologous angiogenic cell precursors therapy in patients with CLI

## Research Activity: Publications

The below is just a sampling of recent publications by NICR Members. [Click here](#) for the complete list of publications, abstracts and media appearances (*click on the 'Publications' tab*).

**Bagai A**, Peterson ED, Honeycutt E, Effron MB, Cohen DJ, **Goodman SG**, Anstrom KJ, Gupta A, Messenger JC, Wang TY. "In-hospital switching between adenosine diphosphate receptor inhibitors in patients with acute myocardial infarction treated with percutaneous coronary intervention: Insights into contemporary practice from the TRANSLATE-ACS study." *Eur Heart J Acute Cardiovasc Care*. 2014 Dec 16. pii: [2048872614564082](#) [Epub ahead of print].

**Connelly KA**, Advani A, Advani SL, Zhang Y, Kim YM, Shen V, Thai K, Kelly DJ, Gilbert RE. "Impaired cardiac anti-oxidant activity in diabetes: human and correlative experimental studies." *Acta Diabetol*. [2014 Jun 13](#).

**Dorian P**, Kongnakorn T, Phatak H, Rublee DA, Kuznik A, Lanitis T, Liu LZ, Iloeje U, Hernandez L, Lip GY. "Cost-effectiveness of apixaban vs. current standard of care for stroke prevention in patients with atrial fibrillation." *Eur Heart J* 2014 Jul 21;[35\(28\):1897-906](#). Epub 2014 Feb 16.

**Farkouh ME**. "Primary prevention of atherosclerotic cardiovascular disease: Bringing clinicians and patients to the starting line." *JACC*. 2014 Sept; [64\(10\):969-70](#)

**Floras JS** (2014). "Renal denervation for drug resistant hypertension: suffering its original sin, seeking redemption". *Canadian Journal of Cardiology* [30:476-478](#).

**Goodman SG**, Wojdyla DM, Piccini JP, White HD, Paolini JF, Nessel CC, Berkowitz SD, Mahaffey KW, Patel MR, Sherwood MW, Becker RC, Halperin JL, Hacke W, Singer DE, Hankey GJ, Breithardt G, Fox KAA, Califf RM, for the ROCKET AF Investigators. "Factors Associated with Major Bleeding Events: Insights from the Rivaroxaban Once-daily oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF)". *J Am Coll Cardiol*. 2014; [63\(9\):891-900](#).

**Ko DT**, Austin PC, Tu JV, Lee DS, Yun L, Alter DA. "Relationship between care gaps and projected life expectancy after acute myocardial infarction." *Circ Cardiovasc Qual Outcomes*. 2014 Jul 1;[7\(4\):581-8](#).

**Lee DS**, Ezekowitz JA. "Risk stratification in acute heart failure." *Can J Cardiol* 2014; [30\(3\):312-319](#)

Lee PJ, Rudenko D, Kuliszewski MA, Liao C, Kabir MG, **Connelly KA**, **Leong-Poi H**. "Survivin gene therapy attenuates left ventricular systolic dysfunction in doxorubicin cardiomyopathy by reducing apoptosis and fibrosis." *Cardiovascular Research*. 2014;[101\(3\):423-33](#)

**Udell JA**, Morrow DA, Jorolim P, Sloan S, Hoffman EB, O'Donnell TF, Vora AN, Omland T, Solomon SD, Pfeffer MA, Braunwald E, Sabatine MS. "Fibroblast growth factor-23, cardiovascular prognosis, and benefit of angiotensin-converting enzyme inhibition in stable ischemic heart disease." *JACC*. 2014;[63:2421-8](#).

**Wijesundera HC**, Qiu F, Bennell MC, Natarajan MK, Cantor WJ, Smith S, Kingsbury KJ, **Ko DT**. "Impact of system and physician factors on the detection of obstructive coronary disease with diagnostic angiography in stable ischemic heart disease." *Circ Cardiovasc Qual Outcomes*. 2014 Sep 1;[7\(5\):648-55](#).

G. Liu, **G.A. Wright**. "Cardiac Gating Calibration by the Septal Scout for Coronary Magnetic Resonance Angiography". *Journal of Cardiovascular MR*. 2014 Jan [16:12](#).

**Yan AT**, Gupta P, Deva D, Choi R, Kirpalani A. "An Unusual Case of Metastatic Carcinoid Tumour in the Interventricular Septum (case report)." *Journal of Cardiovascular Medicine* [2014 Jul 10](#) [Epub ahead of print]. In Press.

