Our vision is to generate, translate and disseminate knowledge on novel diagnostic and therapeutic strategies in cardiovascular medicine acquired through collaborative research to enhance the health of the citizens of Alberta, Canada, and the world.
As the cover of this year’s annual report suggests, we at the Canadian VIGOUR Centre are a learning organization, engaged in the business of knowledge. As an academic research organization (ARO), we are uniquely positioned to work with a variety of key partners within the university, health care system, industry and granting agencies. This year’s annual report articulates our distinct value proposition as an ARO and reflects our deep commitment to improving patient care and outcomes. We are forging new relationships with national and international collaborators in the pursuit of novel research directions, as well as translating and disseminating the resulting knowledge.

Our culture embraces the cycle of quality, described in the next few pages. This cycle begins with health science discovery, followed by its application to human disease using careful quantitative and qualitative measures. For any discovery to have impact, its efficacy must first be examined in controlled populations, i.e. the randomised clinical trial. Yet that is not enough since the effectiveness of any new therapy should be evaluated through performance measures in carefully crafted patient registries acquired in selected disease states. Still further along the cyclical process - if we are to achieve meaningful differences in health outcomes at the population level - there must be successful dissemination of new knowledge into clinical practice. Inevitably, a new appreciation for the unmet needs of the population at risk emerges from this phase galvanizing re-entry into the cycle, as the unending quest for improvement in clinical or health system outcomes continues.

With this context, I am pleased to share that 2013 has been a most eventful year for our organization and within the pages of this report we have selected a few highlights of how new knowledge can impact directly and meaningfully on the care of patients. Up close and personal in our own backyard (i.e. some of the smaller and more rural communities in Alberta), we have seen genuine improvements in the outcomes of patients with heart failure after exporting the lessons of a multidisciplinary clinic. As one explores heart failure care across the globe from a large clinical trial, we find large disparities in the quality of care, with high variability between geographic regions, reminding us that we can and should do better in managing this life-threatening disease. Recognizing we must find innovative and more cost effective ways to do clinical trials, we are committed to finding better mousetraps to harness risk assessment in a more dynamic context. It is also clear that we should be taking into consideration the variation and clinical relevance and importance of individual end points and the composite outcomes of our clinical trials since a new appreciation of these can add value and meaningful interpretation to the results.

Knowledge is most worthwhile when it is used. Hence some of the outstanding academic visitors to our institution are chronicled in this year’s report, and so too are some selected travels of our faculty to participate in national and international forums. We are also excited and enthusiastic about the prospects of a re-invigorated partnering with our friends and colleagues at the Duke Clinical Research Institute and extending that collaboration to Robert Harrington and Ken Mahaffey at Stanford University.

It is gratifying to recognize the outstanding contributions of Drs. Justin Ezekowitz and Shaun Goodman and the assumption of their roles as Co-Directors of the Canada VIGOUR Centre. Dr. Ezekowitz’s expertise in acute coronary syndromes and clinical registries is internationally recognized and his positioning at St. Michael’s Hospital and University of Toronto provides a dynamic east/west axis. His leadership in a number of our clinical studies that are noted within the report and his appointment last year as an Adjunct Professor of Medicine at the University of Alberta signals the redeeming value of creative partnerships and collaboration. They are most welcome additions to our leadership team.

For an organization like ours to be successful, it must produce a dynamic synergy that is greater than the sum of its parts. I am proud of our multidisciplinary team who populate the pages herein and the key role they play in advancing the cause of cardiovascular medicine and research.

Message from the Director
Research
Priorities
Vision, Mission and Core Values

**Vision**
Generate, translate and disseminate knowledge on novel diagnostic and therapeutic strategies in cardiovascular medicine acquired through collaborative research to enhance the health of the citizens of Alberta, Canada, and the world.

**Mission**
Aligned with the University of Alberta and the Mazankowski Alberta Heart Institute (MAHI), our mission is to:
- Design, conduct, analyze and disseminate findings arising from novel clinical research
- Interrogate clinical trial, registry and population health data to evaluate outcomes, identify unmet needs and inform future basic and clinical research directions
- Identify, inspire and nurture the next generation of health researchers and professionals.

**Core Values**
- **Quality**
  - Aspire to the highest standard of work while respecting a balanced life perspective.
  - Attract, mentor and retain high quality colleagues and collaborators with similar core values.
- **Collaboration**
  - Promote and support an outstanding team that integrates a diversity of knowledge, experience, ideas, and skills supportive of our mission/vision.
- **Integrity**
  - Perform our roles in an ethical framework which enhances our reputation as honest, trustworthy and responsible.
- **Respect**
  - Create an innovative, engaging and inclusive work environment, appreciative of individual differences and contributions. Our workplace will be conductive to personal growth and development that is aligned with our overall mission.

**Promise**
- Trusted partner
- Effective communicator
- Clinical relevance
- Scientifically robust
- Credible outcomes
- Novel technologies
- System performance measurement
- Fulfill social contract

**Operational priorities**
- Collaborator and site retention through engagement
- Efficient project management
- Early on the ground
- Maximizing return on investment
- Linking trials/registries/populations

---

Vision
Generate, translate and disseminate knowledge on novel diagnostic and therapeutic strategies in cardiovascular medicine acquired through collaborative research.

Operational priorities
- Collaborator and site retention through engagement
- Efficient project management
- Early on the ground
- Maximizing return on investment
- Linking trials/registries/populations

Purpose
To enhance cardiovascular health for current and future generations.

Core values
- Quality
- Collaboration
- Integrity
- Respect

Career development
Clinical impact
Lives, hearts and minds
Continuous innovation

---

Compass
The Value Proposition of an ARO

An academic research organization (ARO) possesses scholarly values of inquiry and truth and shares knowledge in an ethical framework. Dedicated to enhancing public health, it values discovery, novel approaches and methodologies over profit. Intent upon maximizing the return on research investment, an ARO strives to exceed the operational efficiencies of a clinical research organization (CRO), and intentionally seeks funding from diverse sources beyond industry. An ARO is almost always embedded in a University and therefore reserves their right to publish their insights with objectivity. An ARO functions on a not for profit basis, and reinvests all sources of capital, both financial and intellectual, into the education of the next generation of health professionals, and thereby also aims to fulfill its social contract to promote the public good.

Cycle of Quality

As a learning organization committed to enhancing the health of current and future generations through research, CVC relentlessly pursues the generation, translation and dissemination of new knowledge addressing unmet clinical needs. This culture of learning embraces the cycle of quality that begins with health science discovery followed by its application to human disease using careful quantitative and qualitative measures. For discovery to have an impact, its efficacy must be first examined in controlled populations. Subsequently, the effectiveness needs to be evaluated through performance measures in carefully crafted patient registries acquired in selected disease states. To complete this cyclical process there must be successful dissemination of new knowledge into clinical practice resulting in meaningful differences in health outcomes at the population level. Health economic evaluation, demonstrable return on investment, and responsive health policy enrich the success and timeliness of this journey. Professional and public education are seminal components of the process occurring in parallel. The inevitable destination of this construct is a new appreciation for the unmet needs of the population and re-entry into the cycle to continue the quest for improvement in clinical and/ or health system outcomes.
## Metrics

<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>54</td>
<td>Number of publications that CVC’s body of research produced.</td>
</tr>
<tr>
<td>146</td>
<td>Number of Principal Investigators participating in CVC managed trials.</td>
</tr>
<tr>
<td>223</td>
<td>Number of on-site monitoring visits that occurred in Canada.</td>
</tr>
<tr>
<td>139</td>
<td>Number of global users accessing CVC’s online collaborative platform.</td>
</tr>
<tr>
<td>9</td>
<td>Number of industry and grant funded projects currently underway.</td>
</tr>
<tr>
<td>5,770</td>
<td>Number of ECGs analyzed by CVC.</td>
</tr>
<tr>
<td>500,000+</td>
<td>Size of data repository reflecting health of Albertans with cardiovascular disease.</td>
</tr>
</tbody>
</table>
Revenue from industry-sponsored clinical trials and expense recovery January 1, 2013—December 31, 2014

- 38% IMPROVE-IT Trial
- 27% THOSE Trial
- 6% EXCEL Trial
- 19% ODYSSEY Trial
- 3% STABILITY Trial
- 2% STREAM Trial
- 0.2% TRACER Manuscript
- 4% Recovery (Faculty and overhead)

Grants

<table>
<thead>
<tr>
<th>Project</th>
<th>Sponsor(s)</th>
<th>Grant Holders</th>
<th>Term</th>
<th>Total Granted (CAD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Providing Rapid Out of Hospital Acute Cardiovascular Treatment (PROACT)</td>
<td>Mazankowski Alberta Heart Institute and University Hospital Foundation</td>
<td>Paul Armstrong (PI) Justin Ezekowitz Padma Kaul Finlay McAlister Robert Welsh</td>
<td>2010-2013</td>
<td>$325,000</td>
</tr>
<tr>
<td>SODIUM HF</td>
<td>Alberta Health Innovation Solutions University Hospital Foundation</td>
<td>Justin Ezekowitz</td>
<td>2012-2015</td>
<td>$50,000</td>
</tr>
<tr>
<td>Team Grant: Diastolic Heart Failure</td>
<td>Alberta Innovates-Health Solutions</td>
<td>Jason Dyck (PI) Todd Anderson Justin Ezekowitz</td>
<td>2009-2014</td>
<td>$5,000,000</td>
</tr>
<tr>
<td>Evaluating the impact of a Province Wide Disease Management Program on Heart Failure Outcomes in Alberta</td>
<td>Canadian Institutes of Health Research</td>
<td>Finlay A. McAlister (PI) Padma Kaul Justin A Ezekowitz H Quan</td>
<td>2010-2013</td>
<td>$135,765</td>
</tr>
<tr>
<td>Long-term health outcomes of mothers with gestational diabetes mellitus and their children in Alberta</td>
<td>Canadian Institutes of Health Research</td>
<td>Padma Kaul (PI)</td>
<td>2009-2013</td>
<td>$100,000</td>
</tr>
<tr>
<td>Gestational Diabetes Mellitus (GDM) in Alberta</td>
<td>Canadian Institutes of Health Research</td>
<td>Padma Kaul (PI)</td>
<td>2013 (announced) 2014-2017</td>
<td>$278,139</td>
</tr>
<tr>
<td>The VO2 Increase with Testosterone Addition - Heart Failure (VITA-HF)</td>
<td>University of Alberta Bridge Funding</td>
<td>Justin Ezekowitz (PI)</td>
<td>2012-2013</td>
<td>$40,000.00</td>
</tr>
</tbody>
</table>
Introducing CVC Co-Director Shaun Goodman

- Associate Head, Division of Cardiology, Department of Medicine, St Michael’s Hospital
- Heart & Stroke Foundation of Ontario (Polo) Chair and Professor, Department of Medicine, University of Toronto
- Adjunct Professor, Department of Medicine, University of Alberta

Dr. Goodman’s research interests include:
- Facilitating clinical trial, observational, and knowledge translation research in cardiovascular disease in Canada with a focus on:
  - Diagnosis, management, and prognosis of acute coronary syndromes;
  - Optimal stroke prevention risk stratification and management in atrial fibrillation; and,
  - Primary and secondary prevention of cardiovascular disease.

Introducing CVC Co-Director Justin Ezekowitz

- Associate Professor, Division of Cardiology, University of Alberta
- Director, Heart Function Clinic, Mazankowski Alberta Heart Institute
- Alberta Innovates - Health Solutions Population Health Investigator

Dr. Ezekowitz's research interests include:
- Testing the impact of drugs and processes of care for acute heart failure patients;
- Novel interventions for patients with chronic systolic and diastolic heart failure;
- The impact of comorbidities such as atrial fibrillation, anemia and hip fractures;
- Knowledge gaps for drugs and devices in heart failure.

Shaun Goodman
MD, MSc

Justin Ezekowitz
MBCh, MSc
Kevin Bainey, MD

The Canadian VIGOUR Centre is proud to introduce to its faculty Kevin Bainey, MD. Currently an Assistant Professor and Academic Interventional Cardiologist at the Mazankowski Alberta Heart Institute, University of Alberta, he is completing his Masters in Health Research Methodology from McMaster University. Dr. Bainey’s research interests align well with CVC’s extensive research in reperfusion in STEMI. His work on spontaneous reperfusion has led to a definitive understanding of enhanced clinical outcomes seen in these patients. As well, Dr. Bainey is a key faculty member involved in our COAPT study (Alberta Contemporary Acute Coronary Syndrome Patients Invasive Treatment Strategies: Impact on Clinical Outcomes and Health Care Resources). The CVC is pleased to mentor and collaborate with Dr. Bainey at this early stage in his career on several clinical trials and research projects and to foster his special interest in ethnic-based clinical research focusing primarily on South Asians with established coronary artery disease.

As a new faculty member with CVC, I now have the support to pursue meaningful projects in an academic peer-reviewed environment which will enhance the quality of my research.

About the Researcher

- Undergraduate degree in Microbiology at the University of Alberta
- Doctor of Medicine from University of Alberta
- Internal Medicine and Cardiology training at the University of Alberta and Fellowship of the Royal College of Physicians and Surgeons of Canada
- Interventional Cardiology Fellowship at Harvard University’s Brigham and Women’s Hospital
- Clinical Scholar in Interventional Cardiology at McMaster University

Current Research Projects

- A Multi-center Randomized Trial of Remote Ischemic Conditioning in Patients with an ST-elevation Myocardial Infarction (RemCon-STEMI)
- A Multi-center Randomized Trial of Remote Ischemic Conditioning in Patients with an ST-elevation Myocardial Infarction: Cardiac Magnetic Resonance Imaging Sub-study (RemCon-CMR)
- Alberta Contemporary Acute Coronary Syndrome Patients Invasive Treatment Strategies: impact on Clinical Outcomes and Health Care Resources: Alberta COAPT study
- Cardiac Magnetic Resonance Imaging as a Surrogate Endpoint in Clinical Trials of ST-elevation Myocardial Infarction
- Use of Renin-Angiotensin System Blockers in Acute Coronary Syndromes: Findings from Get With The Guidelines-Coronary Artery Disease Program
- Clinical Perspectives on Reperfusion Injury in Acute Myocardial Infarction
- Infarct Location in ST-elevation Myocardial Infarction: Implications When Selecting a Reperfusion Strategy

Sean van Diepen, MD

The Canadian VIGOUR Centre is proud to introduce to its faculty Sean van Diepen, MD. Dr. van Diepen is an academic cardiologist-intensivist. He is currently an Assistant Professor of Critical Care Medicine in the Divisions of Critical Care and Cardiology at the University of Alberta.

Dr. van Diepen completed medical school at the University of Toronto. After moving west, he undertook his Internal Medicine, Cardiology, and Critical Care Training at the University of Alberta. He completed a clinical research fellowship at the Duke Clinical Research Institute in Durham, North Carolina and received his Masters of Science in Experimental Medicine from the University of Alberta.

He has published multiple manuscripts in leading peer reviewed journals and has received multiple research awards including the Canadian Institute for Health Research Resident Research Prize. He is currently on the editorial board of the American Heart Journal.

About the Researcher

- Medical school at the University of Toronto
- Internal Medicine, Cardiology and Critical Care Training at the University of Alberta
- Clinical Research Fellowship at Duke Clinical Research Institute
- Masters of Science, Experimental Medicine at the University of Alberta

Current Projects

- COMPlot (Angiotensin Converting enzyme inhibitor management?) strategies prior to coronary artery bypass surgery (the COMPACT trial): a pilot randomized controlled registry study
- NT-proBNP, hsCRP, and Inflammatory Markers of Reperfusion in Patients with ST-segment Elevation Myocardial Infarction Global Differences in Heart Failure Therapy and Resource Utilization among Patients Admitted to Intensive and Coronary Care Units: Insights from Assent HF
- Risk prediction of atrial fibrillation patients undergoing non-cardiac surgery
- Variation in critical care unit admissions for patients with acute coronary syndromes and heart failure among high and low volume cardiac hospitals
- Peri-operative Cardiac Outcomes and Bleeding Risk in Patients with Acute Coronary Syndromes and Ischemic Cardiomyopathy: TRACER Insights
**Featured Publications**

This high profile randomized trial was featured in last year’s report. Since then it has been the subject of numerous national and international presentations and symposia, some of which are noted elsewhere in this annual report. Importantly, it’s impact on the care of patients has been practice changing both in our local community and internationally and the publication was even translated into Russian! We are continuing to learn from the rich data set STREAM provides and applying it to contemporary care of patients, as well as reflecting on the ever-present new questions arising from its lessons.

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**Clinical Trials**

**ClinicalTrials.gov number, NCT00623623.**

Perfusion in patients with early STEMI who could not undergo primary PCI within 90 minutes of symptom onset (FIBIN, The Florida Interventional Investigators). One-hundred patients (45 in the fibrinolysis group, 55 in the primary PCI group) were randomized to undergo either primary PCI or fibrinolytic therapy with bolus alteplase (25 mg) and 50 mg/hour infusion for 12 hours (primary PCI group). Thereafter, patients were assigned randomly to undergo either primary PCI or fibrinolytic therapy with bolus alteplase (25 mg) and 50 mg/hour infusion for 12 hours (fibrinolysis group). The primary end point was 30-day death, shock, congestive heart failure, or reinfarction. The primary end point was reached in 26 patients (11%) in the primary PCI group and 29 patients (17%; P = 0.45) in the fibrinolytic group. The rates of nonintracranial bleeding were similar in the two groups. The primary end point was reached at a median of 17 hours after randomization. The primary end point was reached in 26 patients (11%) in the primary PCI group and 29 patients (17%; P = 0.45) in the fibrinolytic group. The rates of nonintracranial bleeding were similar in the two groups.

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**Conclusions**

It is not known whether prehospital fibrinolysis, coupled with timely coronary angiography, provides a clinical outcome similar to that with primary percutaneous coronary intervention (PCI) when alteplase is administered to patients with acute STEMI within 90 minutes of symptom onset. Further research is needed to determine whether fibrinolysis can be safely administered to patients with STEMI in settings where PCI is not available.

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**Featured Publications**

There are many satisfactions associated with participating in a leadership role within a large international clinical trial. In this publication, we teamed up with our friend and colleague at the University of Calgary, Jonathan Howlett. He and Justin Ezekowitz collaborated in exploring how the quality of acute heart failure care impacts on outcomes across five regions in the world. Because of our access to the largest ever acute heart failure study of over 7000 patients from 5 continents and 398 centers, they were able to examine how well individual centers and regions conformed to the best established medical therapy for this serious and life threatening disorder. These measures included what drugs were used and whether or not electrical devices, such as implantable defibrillators and resynchronization with specialized pacemakers, were applied.

The analysis unmasks large gaps in quality of care with high variability between geographic regions. Despite participating in a clinical trial whose more careful monitoring of treatment and outcomes is generally applied, there was only modest improvement in quality of care over time. This study then serves as a wake-up call that we can and should do better in managing this life-threatening disease.

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**Original Article**

**Global Variation in Quality of Care Among Patients Hospitalized With Acute Heart Failure in an International Trial**

Findings From the Acute Study Clinical Effectiveness of Nesiritide in Decompensated Heart Failure Trial (ASCEND-HF)

Johanna G. Gerkink, MD; Isabella A. Eusebi, MD, MSc; Mihaela Pojlus, PhD; Adrian F. Hernandez, MD; MPS; Reid Daly, MD; Kenneth D. Rutten, MD; Mark E. Dunlap, MD; Ranjith F. Gomes, MD; Katerina Kostopoulou, MD; Mark C. Massie, MD; Robert Wilcox, MD; Greg C. Flores, MD, on behalf of the ASCEND-HF Investigators

B-3000 Leuven, Belgium, or at frans@med.kuleuven.ac.be. Dr. Van de Werf at the Department of Cardiac Electrophysiology, University of Calgary, Jonathan Howlett. The authors’ affiliations are listed in the online-only Data Supplement, available at NEJM.org.

**Abstract**

of hospitalizations globally each year. Late mortality has been reported at 30% to 50%, and early rehospitalization is generally applied, there was only modest improvement in quality of care over time. This study then serves as a wake-up call that we can and should do better in managing this life-threatening disease.

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**Circulation: Cardiovascular Quality and Outcomes**

**Original Article**

**Regional Variability in Quality of Hospital Care for Patients Hospitalized With Acute Heart Failure**

Decompensated Heart Failure (ASCEND-HF) trial. There was significant variation in conformity among different quality indicators, ranging from 0% to 89%. Of all regional variations in quality indicators as well as the temporal variation of those indicators during the course of the trial. There was significant variation among different quality indicators, ranging from 0% to 89%. Of all regional variations in quality indicators as well as the temporal variation of those indicators during the course of the trial. There was significant variation among different quality indicators, ranging from 0% to 89%. Of all regional variations in quality indicators as well as the temporal variation of those indicators during the course of the trial.

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**Circ Cardiovasc Qual Outcomes**

**Regional Variability in Quality of Hospital Care for Patients Hospitalized With Acute Heart Failure**

Decompensated Heart Failure (ASCEND-HF) trial. There was significant variation in conformity among different quality indicators, ranging from 0% to 89%. Of all regional variations in quality indicators as well as the temporal variation of those indicators during the course of the trial. There was significant variation among different quality indicators, ranging from 0% to 89%. Of all regional variations in quality indicators as well as the temporal variation of those indicators during the course of the trial.
Heart failure constitutes a huge social and economic burden both globally and in Alberta. In this insightful study that brings innovative patient care models and creative research approaches to patient outcome data in Alberta, McLairst and colleagues studied over 25,000 patients hospitalized with heart failure between 1999 and 2009. A key feature of this work was the evaluation of new heart function clinics (such as those that exist at the Mazankowski Heart Institute/University of Alberta) and recently established elsewhere in the province. The study found that access to heart failure management programs improves substantially with the implementation of these programs, and importantly, was associated with a significant improvement in mortality and heart failure re-admission thirty days after hospitalization. Whereas in years prior to the implementation of these programs, the outcomes of heart failure had deteriorated, they improved after the initiation of these programs without a negative impact on healthcare resources. This stands as an excellent example of research in action directly impacting outcomes in an important and common clinical problem.
Association between bleeding and mortality among women and men with high-risk acute coronary syndromes: Insights from the Early versus Delayed, Provisional Eptifibatide in Acute Coronary Syndromes (EARLY ACS) trial

Background

Evidence concerning the relationship between sex and outcomes in acute coronary syndromes (ACS) remains equivocal. Several studies have suggested a sex-related difference in bleeding and 30-day mortality associated with early, routine administration of eptifibatide, a glycoprotein IIb/IIIa receptor antagonist, compared with delayed, provisional administration during percutaneous coronary intervention (PCI) in reducing ischemic complications among high-risk patients with NSTE ACS. However, female sex is an established risk factor for bleeding, which is an important safety end point in patients presenting with non-ST-segment elevation acute coronary syndromes (NSTE ACS). Hence, it is unclear whether the association between bleeding and mortality is modulated by sex in this patient population.

Methods

We examined the interaction between sex and bleeding and 30-day mortality outcomes among 9,406 patients with high-risk NSTE ACS enrolled in the EARLY ACS trial. The Global Utilization of Strategies to Open Occluded Arteries (GUSTO) criteria were used to identify moderate or severe bleeds.

Results

Women (8.2%) had higher bleeding rates than men (5.5%; P < 0.01). However, the association of bleeding and 30-day mortality was stronger among women (P < 0.01; P = 0.01). Sex differences in the association of bleeding and mortality persisted in a landmark analysis of 120-hour survivors.

Conclusions

A contemporary high-risk NSTE ACS cohort, examined 30-day bleeding outcomes among patients with NSTE ACS. Women had higher bleeding rates than men; however, the association between bleeding and mortality is modulated by sex among patients with NSTE ACS.

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http://dx.doi.org/10.1016/j.ahj.2013.07.014

Peer Reviewed Publications

In this insightful analysis of bleeding occurring as a complication of treatment for patients with acute coronary syndromes, Padma Kaul explores whether men and women differ in their propensity for bleeding and how that bleeding ultimately affects their long-term outcome. Taking data from nearly 6000 women and over 6000 men, she confirms that bleeding occurs more frequently in women than in men, but then surprisingly shows that it was the men versus the women that did worse when thirty day mortality was examined. Although the reasons for this are not entirely clear, Kaul and colleagues speculate that there may have been greater surveillance and sensitivity to bleeding in women versus men given their higher incidence of this problem. They also noted that the site of cardiac catheterization was more likely the source of bleeding in women and hence, potentially more readily recognizable and treatable.
## Peer Reviewed Publications

<table>
<thead>
<tr>
<th>Title</th>
<th>Authors</th>
<th>Journal</th>
</tr>
</thead>
</table>
Patients? Add Insight into the Outcomes of STEMI


Heart Failure Association consensus trials: a European Society of Cardiology Clinical outcome endpoints in heart failure Syndromes Managed Without Revascularization: Insights into the Safety of Long-Term Dual Antiplatlet Therapy with Reduced-Dose Prasugrel versus Standard-Dose Clopidogrel.

Do Countries or Hospitals With Longer Hospital Stays for Acute Heart Failure Have Lower Readmission Rates? Findings From ASCEND-HF.

The Systemic Inflammatory Response Syndrome in Patients With ST-Segment Elevation Myocardial Infarction.


The Canadian VIGOUR Centre | 2013 Annual Report
Changes in heart failure outcomes after a province-wide change in health service provision: a natural experiment in Alberta, Canada.

McAllister FA, Bakal JA, Kaul P, Qian H, Blackadar R, Johnstone D, Easkowitz J.
Circ Heart Fail. 2013;6(3):96-82.

Health-Related Quality of Life of Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes: Results from the PLATO Trial.


Use and timing of coronary angiography and associated in-hospital outcomes in Canadian non-ST-segment elevation myocardial infarction patients: Insights from the Canadian Global Registry of Acute Coronary Events.

Gyenes GT, Yan AT, Tan M, Walsh RC, Fox KA, Grondin FR, DeYoung JP, Gallo R, Kormer JM, Wong GC, Goodman SG.

Bridging the gap for nonmetropolitan STEMI patients through implementation of a pharmacoinvasive reperfusion strategy.

Shavadia J, Ibrahim Q, Soorkem S, Brass N, Knapp D, Walsh K.

Impact of physician continuity on death or urgent readmission after discharge among patients with heart failure.

CMAJ. 2013;185(3):E86-E89.

Effects of nesiritide and predictors of urine output in acute decompensated heart failure: Results from ASCEND-HF (Acute Study of Clinical Effectiveness of nesiritide and decompensated heart failure).


Similarities and differences in patient characteristics between heart failure registries versus clinical trials.

Sharma A, Easkowitz J.

Outcomes of apixaban vs. warfarin in by type and duration of atrial fibrillation: Results from the ARISTOTLE trial.


Prognostic implications of left ventricular end diastolic pressure during primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: Findings from the APEX-AMI study.

Bagai A, Armstrong PW, Stelbins A, Mahaffey KW, Hochman JS, Weaver WD, Patel MR, Granger CB, Lopez RD.

Association between bleeding and mortality among women and men with high-risk acute coronary syndromes: Insights from the Early versus Delayed, Provisional Eptifibatide in Acute Coronary Syndromes (EARLY ACS) trial.


Prasugrel versus clopidogrel for patients with unstable angina or non-ST-segment elevation myocardial infarction with or without angiography: a secondary, prespecified analysis of the TRILOGY ACS trial.


Data and Safety Monitoring Boards: Academic Credit Where Credit Is Due?

McAllister FA, Bakal JA, Kaul P, Qian H, Blackadar R, Johnstone D, Easkowitz J.
Circ Heart Fail. 2013;6(3):96-82.

Use and timing of coronary angiography and associated in-hospital outcomes in Canadian non-ST-segment elevation myocardial infarction patients: Insights from the Canadian Global Registry of Acute Coronary Events.

Gyenes GT, Yan AT, Tan M, Walsh RC, Fox KA, Grondin FR, DeYoung JP, Gallo R, Kormer JM, Wong GC, Goodman SG.

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Similarities and differences in patient characteristics between heart failure registries versus clinical trials.

Sharma A, Easkowitz J.

Outcomes of apixaban vs. warfarin in by type and duration of atrial fibrillation: Results from the ARISTOTLE trial.

ARISTOTLE Committees and Investigators. Left ventricular systolic dysfunction, heart failure, and the risk of stroke and systemic embolism in patients with atrial fibrillation: Insights from the ARISTOTLE trial.


Circ Heart Fail. 2013 May;6(3):451-460.

N-terminal Pro-B-type natriuretic peptide for risk assessment in patients with atrial fibrillation: Insights from the ARISTOTLE trial (Apixaban for the prevention of stroke in subjects with atrial fibrillation).


Novel pharmacologic therapies in development for acute decompensated heart failure.


The 2012 Canadian Cardiovascular Society Heart Failure Management guidelines update: Focus on acute and chronic heart failure.


Predictors of early dyspnoea relief in acute heart failure and the association with 30-day outcomes: findings from ASCEND-HF.


Efficacy and safety of apixaban compared with warfarin according to patient risk of stroke and of bleeding in atrial fibrillation: a secondary analysis of a randomised controlled trial.


Mentoring

The CVC continues its enthusiastic commitment to foster a research environment conducive to disciplined academic inquiry and novel approaches to clinical questions and methodologies. We are pleased to offer research opportunities across a full spectrum of experience, education, and backgrounds. Below are testimonials from several of our young researchers, describing their experiences in collaborating with our faculty, and our biostatistical and research assistants. CVC has provided research opportunities for undergraduates, postdoctoral fellows, and medical students, from across Canada and from around the world. The hallmark of an academic research organization, CVC’s mission remains steadfast in its dedicated efforts to inspire and nurture the next generation of health researchers.

Reflections from our Trainees

“Undoubtedly, CVC is a place to learn from internationally recognized leaders in clinical research. My postdoctoral training has been strongly influenced by this academic experience with Drs. Ezekowitz, McAlister and Armstrong, and the CVC. The faculty’s ability to share their knowledge and provide significant and positive feedback encourages learning and academic growth. Without any hesitation, this has been a life changing experience. I feel so fortunate to have been given the opportunity to be a part of this team.”

— Eloisa Colin Ramirez, Postdoctoral Fellow

“Dr. Paul W. Armstrong has moulded me and changed the way I look at things. The experience I gained at CVC is only the start of a longer learning process for me.”

— Jay Shavadia, Co-Chief Resident in Cardiology

“The CVC helped develop the way I think, look and perceive research. Through this experience, I have felt more mature in my thinking and developed a greater appreciation for clinical trials. Looking beyond the original objectives of a manuscript and gaining insights from the paper itself is a skill I learned here at VIGOUR. I am very thankful for all the great help and support I continue to receive.”

— Naji Kholaif, Second Year Cardiology Resident

Senior Mentors

- Dr. Paul W. Armstrong
- Dr. Justin Ezekowitz
- Dr. Shaun Goodman
- Dr. Finlay McAlister
- Dr. Robert Welsh
In October 2013, CVC hosted our 19th annual ground breaking symposium New Concepts in Acute Coronary Syndromes: Beyond 2000, held in Montreal in conjunction with the Canadian Cardiovascular Society and Congress and supported by an unrestricted educational grant from AstraZeneca. As has been our tradition with this symposium, we were pleased to have partnered with the Mazankowski Alberta Heart Institute and the University of Alberta in undertaking this venture which probes new avenues in acute coronary syndromes and also address the role of novel technologies amid the brave new information age in which we work.

This year’s program addressed the exciting evolution of STEMI care, how to navigate our way through the antithrombotic sea amidst a stunning array of choices and how best to incorporate the emerging associated challenges of heart failure and diabetes. Because the future of clinical trials is now positioned at a critical juncture, a look up the ACS pipeline coupled with an examination of new approaches to our unanswered questions was undertaken. This year, topics and interactive case presentations probed new avenues we all travel within acute coronary syndromes, and better positioned us to care for this large and evolving population.

To ensure the high quality presentations and video dialogues with key speakers is preserved from this legacy event, we have established a website: www.Beyond2000.org that is now available for your viewing under the “Continuing Conversation” banner.

Beyond 2000

Making connections
In 2013, the faculty of CVC were privileged to host a quartet of outstanding, internationally renowned academics through the continuation of a program generously sponsored by an unrestricted educational grant from AstraZeneca.

These visits are a highlight of our CVC academic year and allow for one-on-one faculty time and teaching of our cardiology and research trainees. They provide a welcome window on the global state of cardiovascular medicine as it relates to career choices for trainees and potential future directions for meaningful research. They constitute a seminal part of our educational/research mission.

In March, 2013, Professor Hans Boeckler from the Department of Cardiology, Aarhus University Hospital in Denmark, addressed the subject of Remote Conditioning and its impact on myocardial infarction and stroke. This subject is dear to the hearts of Drs. Robert Welch and Kevin Bainey who are currently conducting a pre-hospital trial addressing this potential opportunity to help patients with myocardial infarction. Professor Boeckler then went on to provide a keynote address at the ACC Rockies meeting chaired by Dr. Welch.

In October, Professor William Boden, Chief of Medicine at the Albany Stratton VA Medical Center and head of the COURAGE trial, addressed the subject of how clinical trials create scientific evidence which goes on to shape local clinical practice. He also provided new insight into the AIM-HIGH trial on HDL-raising therapy and reasons for the complexity of that result.

Our quartet of visitors was rounded out in December by Professor John Spertus, Clinical Director of Cardiovascular Education and Outcomes Research at the Mid America Heart Institute in Kansas City. We learned about the opportunities and challenges of implementing personalized medicine, how to create a risk prediction model for clinical use and emerging from that will be new insights for collaborative opportunities.
Reflecting CVIC’s international reach and network of collaborators, this map highlights some of the key travels undertaken in 2013 by our faculty and staff in the pursuit of knowledge translation and dissemination. CVIC’s insights and impact are derived in part from these pursuits, which include professional development and education initiatives, clinical trial investigator and sponsor meetings, cardiology conferences and keynote presentations by our faculty.
Duke University / Duke Clinical Research Institute Visit

In August, members of the CVC leadership team (Paul Armstrong, Dianne Payeur, Cindy Westerhout and Tracy Temple) travelled to the Duke Clinical Research Institute for an in-person collaboration session hosted by its Director Dr. Eric Peterson. This key meeting of the minds was held to reinvigorate and renew our mutual objectives and long standing relationship. Agenda items included an environmental scan of innovations and key players in the international clinical trial arena, opportunities for increased efficiencies in our approach to clinical trials, and a recommitment to our Canadian and U.S investigative sites to offer more value in their collaborations on jointly managed CVC and DCRI clinical trials. Break out discussions across thought leadership, clinical operations and finance/contracts enriched a final plenary planning session.

Worldwide Collaborators

- Stanford University Visit

In conjunction with this academic visit Dr. Armstrong met with key faculty members, including Dr. Ken Mahaffey (Vice Chair of Clinical Research) who was recently recruited by Dr. Robert Harrington (Chair of the Department of Medicine) to plan future collaborative ARO opportunities.

Featured Presentations

- Palo Alto
  - Paul Armstrong
    - 39th Louise and Dorothy Kovitz Visiting Professor at Stanford University December 2013:
      - Acute Myocardial Infarction 2014: Reflections of a Clinical Investigator"
      - Cardiovascular Clinical Trials at the Cross Roads: A Potential Way Forward

- Dallas
  - Justin Ezekowitz
    - November 2013 Invited speaker at the American Heart Association meeting in Dallas Texas: Heart rate as a Risk Factor
  - Paul Armstrong
    - Invited Speaker American Heart Association Meeting: Montreal PQ: Providing Rapid Out of Hospital Acute Cardiovascular Treatment: PROACT-3

- Toronto
  - Finlay McAllister
    - Canadian Society of Internal Medicine Annual October 2013 Scientific Meeting, Toronto, Canada: The PREVENTION Trial primary results.
    - Canadian Society of Internal Medicine Annual October 2013 Scientific Meeting, Toronto, Canada: Presentation as Recipient of Sackett Senior Investigator Award

- Montreal
  - Justin Ezekowitz
    - October 2013 Invited Late Breaking Trial presentation: Canadian Cardiovascular Meeting: Montreal PQ: Providing Rapid Out of Hospital Acute Cardiovascular Treatment: PROACT-3

- Amsterdam
  - Robert Walsh
    - Invited Speaker European Society Cardiology Amsterdam September 2013: Meet the Expert Session: Acute Coronary Syndrome

- Leuven
  - Paul Armstrong
    - Invited Speaker University of Leuven, Belgium Symposium honoring Professor Frans Van de Werf: Major lessons from randomized controlled trials: challenges for the next decade

- Stanford University Medical Center

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- Worldwide Collaborators

<table>
<thead>
<tr>
<th>Collaborator</th>
<th>Location</th>
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<tbody>
<tr>
<td>Professeur Philippe Gabriel Steg, Département de Cardiologie</td>
<td>Bordeaux, France</td>
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<tr>
<td>Hôpital Bichat, Assistance Publique - Hôpitaux de Paris</td>
<td>Paris, France</td>
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<tr>
<td>Brazilian Clinical Research Institute</td>
<td>São Paulo, Brazil</td>
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<td>São Paulo, Brazil</td>
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<tr>
<td>Duke Clinical Research Institute</td>
<td>Durham, USA</td>
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<td>Estudios Clinicos Latinoamericanos</td>
<td>Rosario, Argentina</td>
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<td>University of Auckland, New Zealand</td>
<td>Auckland, New Zealand</td>
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<td>Flinders Medical Centre</td>
<td>Adelaide, Australia</td>
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<td>Leuven Coordinating Centre</td>
<td>Leuven, Belgium</td>
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<td>National Health and Medical Research Council</td>
<td>Sydney, Australia</td>
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<tr>
<td>Duke Clinical Research Institute</td>
<td>Adelaide, Australia</td>
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<tr>
<td>Uppsala Clinical Research Centre</td>
<td>Uppsala, Sweden</td>
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Thought Leadership
- Provide expert advice and promotion of cardiovascular research characterized by quality, scholarship and integrity
- Define unmet needs for patients with and those at risk of cardiovascular disease
- Align new cardiovascular research with these unmet needs
- Seek cost effective solutions and enhance return on investment in research
- Trial architecture, development, data acquisition, integration, analysis, presentation and peer-review publication
- Creation of novel substudies aimed at mechanistically informing primary clinical trial results
- Mentoring junior faculty, medical trainees, students and allied health professionals

Clinical Trials
- Investigator selection, qualification and recruitment
- Investigative site start-up and training
- Ensuring site regulatory compliance
- Project, Site and Data management
- In-house and onsite clinical monitoring (including bilingual services)

Population and Economic Health Outcomes Research
- Collection of resource utilization and cost data
- Development of economic models
- Cost-effectiveness analyses
- Clinical Registry development

Clinical Registries
- Vital Heart Response (VHR): R Welsh
  - CQI
  - Regional Collaboration
  - Trials within registries e.g. PROACT
  - Model for others
- Acute Heart Failure (AHF): J Ezekowitz
  - CIHR: inquiry regarding outcomes/biomarkers
  - Novel Interventions/trials

Biostatistical Analysis
- Design of research protocols and studies
- Development of statistical analysis plans and database specifications
- Data management
- Programming expertise in SAS and R
- Generation of statistical tables, figures and listings and interpretation of findings
- Consultation and execution of advanced statistical methods
- Development and application of novel statistical methods

Population and Economic Health Outcomes Research
- Collection of resource utilization and cost data
- Development of economic models
- Cost-effectiveness analyses
- Clinical Registry development

ECG Core Lab
- Informing trial design
- Monitoring protocol adherence
- Guiding mechanistic insights
- Prognosis and outcomes assessment

CVC Services and Activities
The Canadian VIGOUR Centre is recognized as a thought leader and valuable partner in cardiovascular research across all regions of Canada and amongst key centres around the world. Its track record of conducting, delivering and publishing insightful and unbiased research and health outcomes is strongly influenced by clinical practice and health care.
The clinical trials services of CVC generate valuable data to help support and influence change within clinical practice and the care of patients. In 2013 the CVC was involved in eight Phase III studies, two grant funded studies, and in the initial planning and negotiations for one Phase II study. With a network of over 230 sites across Canada, we had more than two thirds of those sites involved in at least one of our clinical trials enrolling a total of 569 patients in Canada from four recruiting trials in calendar 2013. Since CVC’s inception, the sites collaborating with CVC across Canada have enrolled a total of 19,587 Canadian patients, contributing to the 290,535 patients recruited globally from the 51 Phase II and III trials we have been involved in.

The clinical trials team led by Assistant Director of Clinical Trials, Tracy Temple, is comprised of five Clinical Trial Project Leads and four regulatory and site coordination support staff. Based regionally across the country, the monitoring team, led by Halina Nawrocki, includes a team of six monitors and one report reviewer. In addition to all of our monitors being ICH/GCP trained, many also hold the CCRP designation with SoCRA or the CCRA designation with ACRP. Responsible for ensuring all operational aspects of the clinical trials run smoothly, our Clinical Trial team works closely with our sites to strive for efficient start up, for meeting recruitment and retention targets, for data entry that is accurate, and for meeting trial milestones and timelines from study start-up to study completion. As the primary contact for the Canadian sites, the Clinical Trial Project Leads have a good understanding of all aspects of the study, enabling them to closely monitor trends and issues across Canada. Our Clinical Trial Project Leads maintain a close working relationship with the Canadian National Coordinator(s) and/or Operational Lead ensuring they are kept up to date on the operational aspects of the study in Canada and utilize their expertise and support throughout the study.

In addition to conducting source document verification, drug accountability and other required monitoring related tasks, the CVC monitors use their visits as a teaching opportunity to share lessons learned and ideas from other sites as well as ensuring they are audit and inspection ready. With the ongoing support and expertise of our project and monitoring team and well prepared sites, all CVC monitored sites who underwent inspections in 2013 received compliant ratings.

Seeking out more efficient ways to run clinical trials in Canada, in late 2013 we commenced planning for a CVC Clinical Trials Research Colloquium to be held in Banff, AB, in March 2014 in conjunction with the ACC Rockies Meeting. The intent of this meeting will be to bring together 10 – 12 key Canadian sites, have them complete a detailed survey on all aspects of clinical trials at their site and then meet in person to discuss the survey findings, in an effort to enhance start up and overall efficiencies of clinical trials in Canada. Overall our Clinical Trials team strives to build relationships with sites, sponsors and partners across Canada and globally, enhance efficiency in our processes, achieve the highest level of quality, and deliver a strong Canadian contribution in each clinical trial.
Clinical Trials

TECOS

Trial Evaluating Cardiovascular Outcomes with Sitagliptin

Protocol #: 082-04
Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.
Drug: Sitagliptin
Anticipated timeline: August 2008 - March 2015
Study definition: Randomized, placebo controlled clinical trial to evaluate cardiovascular outcomes after treatment with sitagliptin in patients with Type 2 diabetes mellitus and inadequate glycemic control
Trial status: Target enrollment reached; now in patient retention and event accrual stage

481 / 14,000
Patient Enrollment Target (Canada / Global)

549 / 14,745 COMPLETED
Patient Enrollment Achieved to date (Canada / Global)

26 / 681
Number of Sites participating (Canada / Global)
Clinical Trials

**EXSCEL**

**Exenatide Study of Cardiovascular Event Lowering**

- **Protocol #**: BCB109
- **Sponsor**: Amylin Pharmaceuticals, LLC, a subsidiary of Bristol-Myers Squibb
- **Drug**: Exenatide
- **Anticipated timeline**: May 2009 - December 2017
- **Study definition**: A randomized, placebo-controlled clinical trial to evaluate cardiovascular outcomes after treatment with exenatide once weekly in patients with type 2 diabetes mellitus
- **Trial status**: Actively enrolling

**Patient Enrollment Target** (Canada / Global) 425 / 9,500

**Patient Enrollment Achieved to date** (Canada / Global) 363 / 8,558

**Number of Sites participating** (Canada / Global) 24 / 461

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**ODYSSEY Outcomes**

**Protocol #:** EFC11570

**Sponsor**: Sanofi-aventis Recherche & Développement

**Drug**: Alirocumab (SAR236553/REGN727)

**Anticipated timeline**: June 2012 - March 2018

**Study definition**: A randomized, double blind, placebo controlled, parallel-group study to evaluate the effect of Alirocumab on the occurrence of cardiovascular events in patients who have already recently experienced an acute coronary syndrome

**Trial status**: Actively enrolling

**Patient Enrollment Target** (Canada / Global) 357 / 18,000

**Patient Enrollment Achieved to date** (Canada / Global) 29 / 2,124

**Number of Sites participating** (Canada / Global) 29 / 960
Clinical Trials

**IMPROVE IT**

IMProved Reduction of Outcomes: Vytorin Efficacy International Trial

Protocol #: P04103  
Sponsor: Merck & Co. Inc.  
Drug: Vytorin  
Anticipated timeline: March 2005 - December 2014  
Study definition: A multicenter, double-blind, randomized study to establish the clinical benefit and safety of Vytorin (ezetimibe/simvastatin Tablet) vs. simvastatin monotherapy in high-risk patients presenting with acute coronary syndromes  
Trial status: Target enrollment reached; now in patient retention and event accrual stage

**Patient Enrollment Target**  
Canada / Global: 500 / 18,000  
Status: COMPLETED

**Patient Enrollment Achieved**  
Canada / Global: 682 / 18,142  
Status: COMPLETED

**Number of Sites Participating**  
Canada / Global: 36 / 1,159

*The 500 for Canada is based on original projections and sample size and does not reflect modified sample size.*

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**STREAM**

STrategic Reperfusion Early After Myocardial Infarction

Protocol #: 1123.28  
Sponsor: Boehringer Ingelheim  
Drug: Tenecteplase  
Anticipated timeline: August 2007 - September 2013  
Study definition: Open label, prospective, randomized, parallel and comparative international multi-centre trial comparing the efficacy and safety of a strategy of early fibrinolytic treatment with tenecteplase and additional antiplatelet and antithrombin therapy followed by catheterisation within 6-24 hours or rescue coronary intervention versus a strategy of standard primary PCI in patients with acute myocardial infarction within 3 hours of onset of symptoms  
Trial status: Database Locked, 1 year follow up and closing out sites

**Patient Enrollment Target**  
Canada / Global: UP TO 300 / 2,000

**Patient Enrollment Achieved**  
Canada / Global: 92 / 1,915  
Status: COMPLETED

**Number of Sites Participating**  
Canada / Global: 4 / 134
**Clinical Trials**

**STABILITTY**

The STabilisation of Atherosclerotic plaque By Initiaion of darapLadIb TherapY

- **Protocol #:** LPL100601
- **Sponsor:** GlaxoSmithKline Pharmaceuticals
- **Drug:** Darapladib
- **Anticipated timeline:** September 2008 - December 2013
- **Study definition:** Randomized, placebo-controlled, doubleblind, parallel group, multi-center, event driven trial. A Clinical outcomes study of darapladib vs placebo in subjects with chronic coronary heart disease to compare the incidence of major adverse cardiovascular events.
- **Trial status:** Database locked and closing out sites

- **775 / 15,500**
  - **Patient Enrollment Target** (Canada / Global)
  - **CAPPED FOR EACH COUNTRY**

- **779 / 15,839**
  - **Patient Enrollment Achieved to date** (Canada / Global)
  - **COMPLETED**

- **36 / 1,159**
  - **Number of Sites participating** (Canada / Global)

**REGULATE PCI**

- **Protocol #:** REG1-CLIN310
- **Sponsor:** Regado Biosciences Inc.
- **Drug:** REG1 Anticoagulation System (pegirudacogin & anivamersen)
- **Anticipated timeline:** July 2013 - September 2016
- **Study definition:** Randomized, open-label, multi-center, active-controlled, parallel group study to determine the efficacy and safety of the REG1 Anticoagulation System Compared to Bivalirudin in Patients Undergoing Percutaneous Coronary Intervention.
- **Trial status:** Actively Enrolling

- **405 / 13,200**
  - **Patient Enrollment Target** (Canada / Global)

- **47 / 196**
  - **Patient Enrollment Achieved to date** (Canada / Global)

- **3 / 58**
  - **Number of Sites participating** (Canada / Global)
CVC has an extensive site network across Canada of principal investigators (PIs) who actively participate in CVC managed clinical drug trials, to meet patient enrollment targets. This map represents the locations of the 146 principal investigators who were participating in the nine (9) active clinical trials either coordinated by the CVC, or monitored by the CVC, in 2013. Nearly 50% of these sites have participated in more than one CVC managed clinical trial. In 2013, 223 visits were carried out at these sites by the CVC monitoring team, to ensure adherence to trial protocols and patient safety.
The aim of our ECG Core Laboratory is to translate research results into information useful for clinical applications. Using the ECG parameters to generate an improved understanding of the pathophysiologic processes involved in acute coronary syndromes (ACS) enables improvements in managing cardiac patients, prediction of outcomes, and further stimulates cardiovascular scientific research.

The main projects for the ECG Core Lab in 2013 were PROACT, the J-Point project, and the Vital Heart Response project. In addition, the STREAM study came to its conclusion with the presentation of the primary study results and publication in the New England Journal of Medicine in April 2013. The examination of the STREAM ECGs included the determination of ST deviation (area at risk), ST resolution (as marker of myocardial reperfusion) and QRS Scoring (for infarct size) in patients experiencing Acute Myocardial Infarction (AMI). These data are now being incorporated into novel presentations and publications to enhance our understanding of the STREAM results. The Core Lab also provided central adjudication for patients with rescue percutaneous coronary intervention (PCI) to determine whether they met the clinical indication for this procedure.

In 2013, the ECG Core Lab was involved in PROACT-3, the third stage of the PROACT project. A key component of this project is the timely recognition of patients’ needs, and how best to direct health resources for better and more efficient patient care. Our ECG Core Lab has continued their important role in analyzing the ECGs derived from this project, which will contribute to a database rich in information about outcomes of local Edmonton patients under current practices, and how we can change practice and redirect health care resources to improve patient outcomes for those suffering from acute coronary syndromes and heart failure.

The J-Point Project, begun in 2011, was designed by the CVCECG Core Lab to establish optimal measurement points on ECGs with respect to feasibility, applicability and interobserver agreement. This project involved the collaboration with two other experienced, well-respected ECG Core Labs at the Duke Clinical Research Institute and the St. Louis University. The results of the first phase of the J-Point Project seeded the second phase, completed in 2013, which tested the inter-reader reliability on the application of the universal definition of myocardial infarction in a broad spectrum of ACS patients. The publication of this project was accepted by the Journal of Electrocardiography and was published online in October 2013. The study demonstrated excellent agreement on ST-segment measurements between the two core labs’ experienced readers and will be a real asset and confidence builder for future investigators.

Begun in 2005, the Vital Heart Response (VHR) project is a regional initiative that aims to implement timely, evidence-based reperfusion strategies to maximize the outcomes of patients with ST-segment myocardial infarction (STEMI). In 2013, the ECG Core Lab became involved in analyzing the ECGs collected from VHR patients in order to compare primary PCI to pharmacoinvasive strategies. Numerous ECG measurements are collected in order to assess outcomes of patients with STEMI. In 2013, the ECG Core Lab at the CVC continued its mandate of conducting quality analyses using clinical research data. The Core Lab has accumulated a wealth of experience in its readers and continues to mentor and serve as a valuable training ground for the next generation of talented researchers. To date, ECGs from over 70,928 patients, enrolled in studies around the world, have been analyzed. This provides an excellent database for additional sub-studies, analyses and research.
The CVC houses databases from over 25 clinical trials, which provide a rich cache of patient characteristics, ECGs, treatment and outcomes. The CVC also has access to population based data for over 500,000 Albertan patients seeking cardiovascular medical care between the fiscal years 1999/2000 and 2009/2010, as well as those participating in the following registries or studies:

- Vital Heart Response Registry
- ASCEND-HF Registry
- PROACT Retrospective Cohorts
- AHF-EM Retrospective Cohorts

The CVC Biostatistics Group works with clinician investigators to conduct innovative clinical research in cardiovascular medicine in collaboration with local, national, and international researchers. This research focuses on the assessment of patient, environmental and process-of-care factors and their association with outcomes in patients with acute coronary syndromes, acute and chronic heart failure, cardiac arrest, arrhythmias, and diabetes. Areas of interest include: international and regional differences, time to treatment, use of pharmacologic and mechanical interventions, resource allocation and utilization, and gender/sex and age differences in relation to clinical outcomes. Services provided by CVC’s biostatistical team include data management, development of statistical analysis plans and database specifications, programming expertise in SAS and R, generation of statistical tables, figures and listings and interpretation of findings, and consultation and execution of advanced statistical methods. There are two main data sources on which academic research projects are based: (i) clinical trials and (ii) population-based databases and registries.

In 2013, the Biostatistics Group participated in numerous studies based on clinical trial or population-based data, utilizing a variety of statistical techniques. These ranged from survival analysis and meta-analysis to a novel analysis of composite endpoints in STEMI trials (i.e., weighted composite endpoint). The latter has garnered increased interest from various stakeholders and remains a key area of research. In keeping with a key component of the CVC mandate, members of the biostatistics team contribute to mentoring the next generation of cardiovascular researchers. They work closely with medical students, residents and other junior researchers to explain the statistical techniques used and their interpretation.
The CVC Outcomes Group (led by Drs. Kaul, Ezekowitz and McAlister) has been actively involved in building the crosswalk between trials, registries, and populations. A prime example of this is our work on the Acute Study of Nesiritide in Decompensated Heart Failure (ASCEND-HF) trial. The trial enrolled 7141 patients internationally, including 465 Canadians at 31 sites in six Canadian provinces. However, randomized controlled trials (RCT) are often limited by their generalizability to the broader non-trial population. To provide a context for the trial, Dr. Ezekowitz and colleagues designed a complementary Canadian registry of 697 patients from a subset of eight sites (three community hospitals and five tertiary care hospitals). Dr. Kaul and colleagues in turn extended the comparison to heart failure hospitalizations at all acute care hospitals in all Canadian provinces (except Quebec) using data from the Canadian Institutes of Health Information (CIHI). The result was, for the first time, we were able to describe the difference in the characteristics of clinical trial patients and the population at large living with acute heart failure in Canada. The dichotomy of observed outcomes in the trial and population-level data highlighted the important role that each plays in observational studies and informing clinical practice.

Administrative databases have become a cornerstone in the process of assessing performance and providing feedback to improve quality of health care delivery at a population-level. This is exemplified by the work by Dr. McAlister and colleagues examining the changes in heart failure outcomes after the implementation of the Alberta Cardiac Access Collaborative (ACAC), a province-wide initiative to increase access to specialized heart failure clinics after hospital discharge. Based on administrative data received from Alberta Health, the CVC Outcomes group has developed an integrated longitudinal database linking inpatient, outpatient (including emergency department), physician office, pharmaceutical claims, registry, vital statistics and census data for all Alberta residents with heart failure, acute coronary syndromes, non-acute ischemic heart disease, cardiac arrhythmias and congenital heart disease between 1999 and 2009 in Alberta. Using these data, Dr. McAlister was able to demonstrate that the ACAC increased specialized heart failure clinic access and was associated with a statistically significant improvement in 30-day post-discharge mortality/readmission rates.

The CVC continues to expand our data repository of clinical registries and provincial and national healthcare administrative databases. Our extensive portfolio of research projects based on these data includes examining the following: socioeconomic and urban/rural differences in access to treatment and outcomes; outcomes among vulnerable populations such as women, the elderly, and ethnic minorities; the association of risk factors and use of evidence-based therapies on long-term outcomes; impact of alternative levels of care; resource utilization and costs of care; validity and reliability of disease coding; and novel methods to risk stratify patients. These research objectives are completely aligned with the Canadian Institutes of Health Research funded Alberta SPOR Support Unit.
The business office is fundamental to the organizational and financial underpinnings of the CVC. Reviewing and negotiating contracts is one of its key tasks, alongside providing expert service in the areas of managing agreements, developing and tracking metrics, and executing invoices and site payments. Dedicated to financial stewardship, the business office prudently manages revenue and expense administration. It is also committed to the progress of information systems management, strategic planning, process improvement, and the promotion of learning and development initiatives.

The business office is responsible for the creation and distribution of all marketing materials aimed at creating strong brand awareness that speaks to the mission and values of this organization. Finally, the office facilitates communications between the CVC and many institutional partners, which include, but are not limited to, Duke Clinical Research Institute (DCRI), Alberta Health Services (AHS), and Northern Alberta Clinical Trials and Research Centre (NACTRC). Our dedication to upholding strong partnerships with these institutions is essential to the day-to-day operations of the CVC.
Faculty

Our CVC Faculty are internationally recognized as Thought Leaders in their respective areas of interest. They represent a unique and dynamic integration of clinical research. The approach begins by addressing unmet clinical needs through conducting rigorous clinical investigation and clinical trials of novel diagnostic and therapeutic interventions in selected areas of cardiovascular medicine. It extends from that pivot to the knowledge gained through detailed registries of all patients in areas of particular interest and relevance to public health, namely Acute Coronary Syndromes and Heart Failure.

Our group has been especially keen to explore better ways of analyzing the responses of patients to interventions by modeling their outcomes over time, taking account of the relative value patients put on differing outcomes and their implications for quality of life and health care costs. Finally we are well positioned to study health care outcomes at a population level for all Albertans to assess how well new advances are being applied and whether they are making a meaningful difference.
Acknowledgements

CVC gratefully acknowledges and thanks:

• The patients, for their willing participation in trials, they are the heroes of clinical research.
• the CVC faculty, external advisors and collaborators for their contributions and for providing ongoing research opportunities, we look forward to providing continued services and to future collaborations;
• the CVC staff and management for their dedication, professionalism, excellent contributions and ingenuity that enhances the quality of our research work;
• our mentees for their commitment and enthusiasm as the next generation of researchers;
• the sponsors and granting agencies, without their financial support these trials and educational activities would not be possible;
• Dianne Payeur, Carla Price, and Ellen Pyear for their time and the dedication required to produce this report;
• Kathy Watts and Bryan MacNeill from Watts Communications for the concept and design;
• Photographer Stephen Wreakes for many of the images enclosed in this report;
• McCallum Printing Group Inc. for their service in printing this report and our Chronicle.