<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTRODUCTION</td>
<td></td>
</tr>
<tr>
<td>Message From the Director</td>
<td>4</td>
</tr>
<tr>
<td>Our Vision, Mission, and Core Values</td>
<td>6</td>
</tr>
<tr>
<td>CVC Highlights</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>CVC ACTIVITIES, SERVICES AND REVENUE SOURCES</td>
<td></td>
</tr>
<tr>
<td>CVC Activities and Services</td>
<td>13</td>
</tr>
<tr>
<td>Areas of Research Interest and Expertise</td>
<td>14</td>
</tr>
<tr>
<td>Thought Leadership</td>
<td></td>
</tr>
<tr>
<td>A CVC Initiative: PROACT</td>
<td>16</td>
</tr>
<tr>
<td>Featured Publications</td>
<td>20</td>
</tr>
<tr>
<td>Peer Reviewed Publications 2011</td>
<td>22</td>
</tr>
<tr>
<td>Clinical Trial Operations</td>
<td>28</td>
</tr>
<tr>
<td>Population Health and Economic Outcomes</td>
<td>36</td>
</tr>
<tr>
<td>Biostatistical Analysis</td>
<td>38</td>
</tr>
<tr>
<td>ECG Core Laboratory</td>
<td>40</td>
</tr>
<tr>
<td>Sources of Revenues</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>CVC TEAM</td>
<td></td>
</tr>
<tr>
<td>Faculty</td>
<td>52</td>
</tr>
<tr>
<td>Key Personnel</td>
<td>58</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>APPENDICES</td>
<td>64</td>
</tr>
</tbody>
</table>

CVC PARTNERS, Collaborations and Experience
Worldwide Collaborations 46
CVC Trial Experience 48

CVC TEAM
Faculty 52
Key Personnel 58

APPENDICES 64
Message from the Director

I am delighted to provide this introductory overview to our 2011 Annual Report on behalf of our terrific faculty, operations team, biostatistical and population health outcome groups, ECG Core Laboratory and administrative staff who collaborate so effectively in helping us to achieve our mission. A few highlights follow:

- An exciting and home grown project called PROJECT (an acronym for Providing Rapid Out of Hospital Acute Cardiovascular Treatment) took flight in the fall of 2011. Building on our widely recognized success in acute STEMI care, and with the support of University Hospital Foundation and Mazankowski Alberta Heart Institute, we have extended the vision and reach of our pre-hospital program to other life threatening, time sensitive disorders, namely threatened heart attack and acute heart failure. This is a major collaborative effort involving our EMS system and colleagues in all the Edmonton hospitals that really does bring innovative research from CVC to our community. More details are contained in this annual report.

- As the prevalence of diabetes becomes of epidemic proportion and its role in the pathogenesis of coronary and diffuse vascular disease more clear, increasing emphasis on better control and treatment has emerged and with those, novel therapies have become available. Thus, in addition to the already established TECOS trial examining sitagliptin, we embarked on a new multinational pragmatic trial entitled EXSCEL which involves a GLP-1 analog formulated in a once weekly subcutaneous injection. This study, sponsored by Amylin Pharmaceuticals, will be done in conjunction with our good friend and colleague, Dr. Shaun Goodman from St. Michael’s Hospital and the University of Toronto, who is playing a lead role in Canada on the Operations Committee. He and his team will collaborate with CVC in managing this trial across Canada.

- We have continued to engage the next generation of cardiovascular health researchers, spanning the full spectrum of trainees from undergraduate physiology students planning to apply for a career in medicine, through to seasoned post graduate trainees in cardiology on the cusp of attaining their first independent faculty positions. A few of their experiences have been abstracted in quotations, sprinkled throughout this annual report. Many have benefited from access to the rich data warehouse that CVC stores that permits important subsidiary projects and questions to be addressed.

- As noted in one of our issues of the Canadian Cardiac Chronicle that is distributed internationally to all of our investigators, sponsors and research partners, we had a careful look this past year at how we evaluate the research we do. This is described in one of the featured publications herein. With thanks to leadership from Finlay McAlister and the able assistance of Heather Good, our administrative research assistant, we identified the top cited articles in the world’s literature relating to some of the key cardiovascular advances over the last few decades, namely aspirin, statins, ß-blockers, angiotensin-converting enzyme inhibitors, acute reperfusion therapy and coronary bypass surgery. Our work published in Circulation and cited extensively by a thoughtful accompanying editorial by the Circulation editor notes that “Much like for history itself, in which the passage of time is generally required to appreciate the importance and impact of an historical event, so, too, for science. Only with the passage of time can the importance of an observation be put in the proper unbiased context and its true value appreciated” In brief, it takes time to do good science and genuine effort to communicate it clearly and fairly and even more time to ensure that it stands the test of time. That speaks eloquently to one of our core values which is quality in all aspects of our work.

- Speaking of quality, Halina Nawrocki, our lead Clinical Research Associate, recognized when working with our participating centres across the country that a key resource was not readily available to them. She discerned a need to provide the guidelines and regulations which govern clinical research in a format that is easy to reference and which would enhance understanding and enable them to have a higher level of quality assurance at their institutions. Her suggestion to provide sites with a reference booklet was followed through by Tracy Temple, who manages our Clinical Operations group and Carla Price who compiled and distributed the reference manual entitled “Important reference documents on conducting clinical research in Canada”. This has been a hot item, which was exceedingly well received and appreciated. In fact, some sites have asked for additional copies and even invested in funding them.

- Stimulated by the need for more efficient, cost effective and “smarter clinical trials”, we have, in conjunction with our biostatistical group, begun to heavily invest in novel methodologies that will not only enhance the precision of our outcome estimates but potentially lead to more meaningful interpretation of the results. This, as well as our efforts with modeling in a dynamic process over the early phase of the index event of patients with acute coronary syndromes and heart failure, promises to provide exciting new footprints on the path to discovery.

- Finally, it is important to recognize the pioneering work of Finlay McAlister and Padma Kaul in the evaluation of population health and outcomes, effectively utilizing the Alberta Health and Wellness databases. One of many such examples that will inform our directions relates to the cost of care at the end of life for patients dying of heart failure. This disorder is unquestionably a “growth industry” and we need more compassionate and better approaches to its multidisciplinary management.

I hope you will digest the contents of this year’s annual report and join me in acknowledging the inspired contributions of our team as we continue to enthusiastically work towards enhancing the care of patients with cardiovascular disease.

Our work would not be possible without the financial support of many who are gratefully acknowledged throughout this report.

With kind regards,

Paul W. Armstrong, MD
Our 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.

Our 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.

Our Vision, Mission, and Core Values

Core Values

<table>
<thead>
<tr>
<th>Quality</th>
<th>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.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collaboration</td>
<td>Promote and support an outstanding team that integrates a diversity of knowledge, experience, ideas, and skills supportive of our mission/vision.</td>
</tr>
<tr>
<td>Integrity</td>
<td>Perform our roles in an ethical framework which enhances our reputation as honest, trustworthy and responsible.</td>
</tr>
<tr>
<td>Respect</td>
<td>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.</td>
</tr>
</tbody>
</table>
CVC Highlights
1997 - 2011

533,188
Number of unique patients accessible to CVC for population health research

188,862
Number of ECGs analyzed by CVC from 67,976 patients

18,000
Number of Canadian patients enrolled in CVC managed studies.

300
Number of publications CVC’s body of research has produced.

440
Number of Principal Investigators, from 250 Canadian sites, who have participated in CVC managed trials

44
Number of phase II and III clinical trials the CVC has managed.
“You start seeking to write a good paper and end up transformed in the way you approach, understand and organize research. This is the VIGOUR experience.

Working with Dr. Armstrong has changed the way I perceive research.

Many can teach how to write a paper but few can inspire your future outlook on research. The atmosphere of collegiality and devotion to science in this centre makes research an enjoyable and splendid experience.”

— Aws Alherbish, Cardiology Trainee —
The Canadian VIGOUR Centre is recognized as a valuable partner in cardiovascular research across all regions of Canada and amongst key leaders 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.

### 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 Trial Operations
- 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)

### 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
Areas of Research Interest and Expertise

- Acute Coronary Syndrome
- Heart Failure
- Pre-Hospital Emergency Medicine
- Prevention

- Experienced and proficient (includes current projects)
- Capacity for future projects / interest
Thought Leadership

A CVC Initiative: PROACT

Providing Rapid Out of Hospital Acute Cardiovascular Treatment

Ten short years ago, as was the case in other Canadian communities, Edmonton delivered ST-elevation myocardial infarction (STEMI) care after patient arrival to hospital. CVC and local leadership in a multi-national clinical trial (ASSENT 3+) of pre-hospital fibrinolysis galvanized us to transform STEMI care from the hospital to the home, workplace, or ambulance. This was only possible through an extraordinary collaborative effort involving emergency medical services, emergency physicians, cardiologists, and the community. Employing wireless technology, emergency personnel in the field were for the first time able to transmit 12-lead electrocardiograms via cell phone for physician assessment, thereby allowing pre-hospital diagnosis, triage, and treatment. This experience led to the establishment of the Vital Heart Response Program (VHR) that has transformed the care of STEMI patients in northern Alberta and provided several invaluable lessons.

1) We learned that pre-hospital pharmacologic therapy was both safe and effective and could be delivered by trained field EMS personnel.

2) An extraordinary 55 minute reduction in time to treatment was achieved as compared with a contemporaneous cohort of STEMI patients treated within the hospital.

3) It served as a stepping stone for us to craft a four-centre Canadian feasibility trial, WEST (Which Early ST Elevation Myocardial Infarction Therapy), to address the relative efficacy and safety of mechanical versus pharmacologic reperfusion coupled with strategic mechanical co-intervention. WEST suggested that an early strategic pharmacologic approach combining fibrinolysis with appropriate catheter co-intervention (emphasizing pre-hospital therapy) was effective, safe, feasible and similar to timely expert PCI.

4) Our findings have been an important underpinning to the STREAM (Strategic Reperfusion Early After Myocardial Infarction) study which has recently completed enrollment internationally as well as here in Canada. CVC has played a lead with the help of Robert Welsh and Cindy Westerhout, as well as our core ECG laboratory which is independently reviewing the key ECG parameters in STREAM. These results will be presented in the spring of 2013.

In the fall of 2011, a long standing transformative clinical research project known as PROACT commenced in the Edmonton region. This project builds on the success of our initial research in pre-hospital care for patients with ST-elevation myocardial infarction (STEMI) and the VHR program that coordinated STEMI care in a seamless and collaborative fashion. We embarked on a new initiative to extend the lessons learned to two other clinical syndromes. These were high risk non-STElevation acute coronary syndromes which actually are more common than STEMI and possess a greater disease burden and secondly, acute heart failure, for which new therapy is desperately needed. In both these latter syndromes, like STEMI, delay from symptom onset to hospital evaluation is significant and novel diagnostic biomarkers are now available to help at an earlier point in care to help decide on more accurate diagnosis, and to contribute to better risk stratification and ultimately best appropriate ImPACT and early care. Please refer to diagram on the following page.

Thanks to seed research funding from the University Hospital Foundation and the Mazankowski Alberta Heart Institute, and with the leadership of Justin Ezekowitz and Robert Welsh, we initiated a city-wide program involving the leaders from all hospitals as well as the emergency department: Suril Srikiram (University of Alberta Hospital), Dale Weiss (Emergency Medical Services, Edmonton), Metro), Wayne Tymchak (University of Alberta), Metro), Wayne Tymchak (University of Alberta), Delhi, William Keeble (Misericordia Hospital); Neil Brass (Royal Alexandra Hospital); Michael Chan (Royal Alexandra Hospital); Fadi Khadour (Sturgeon Community Hospital & Health Centre); Darren Knapp (Mazankowski Alberta Heart Institute) and Ken Woo (Grey Nuns Community Hospital). This effort is only supported through the project leadership of Ms. Courtney Bryden. One of the innovative features of this program is the installation of specialized biomarker meters that allow for measurement of cardiac troponin (a sensitive marker of myocardial injury) and brain natriuretic peptide (a sensitive marker of heart failure). Two hundred and fifty meters have been trained and 25 meters installed in the ambulances that facilitate the above-mentioned measurements. In this regard, collaboration with Alere Inc is another signal of the multiple collaborators that have joined to advance acute cardiac care.

We have ambitious objectives but through collaboration with health professions in the EMS system and elsewhere, we believe we can extend the success of our VHR program directed by Rob Welsh to other key areas and thereby make significant advances to the care of cardiovascular patients in Edmonton, Alberta and beyond.
In the News
On September 27, 2011, Edmonton media were invited to see how the PROACT project puts a hospital laboratory into local ambulances, allowing patients with acute heart problems to receive a faster diagnosis and timely treatment. Ten media outlets were in attendance as CVC faculty and staff answered questions and demonstrated the in-ambulance blood testing devices.

- From The Edmonton Journal: See article on next page.
- Additional information in an international registry of clinical trials: http://clinicaltrials.gov/cl2/show/NCT01634425

**PROACT Concept**

**STEMI**

Time Sensitive

Early Triage

Early Diagnosis

Life Threatening

Acute Heart Failure

High Risk

Non ST ACS

**AMBLANCE**

Conducted on A3

"We're changing the paradigm of care," said Milestone Health CEO Marc Aronson. "We're moving away from one-size-fits-all care in hospitals to more personalized treatment that can be delivered in your home." The PROACT project has a novel test that is currently being developed and has been approved for use by Health Canada for patients who present with acute heart failure. The test takes advantage of the fact that the time-sensitive period for delivering effective treatment is immediately after a heart attack. This is a significant departure from the traditional lab results, which can take hours to deliver. The PROACT test can deliver results in 10 minutes, allowing for immediate treatment to begin.

**Failure or a “silent” heart attack.**

"If you treat people quickly, you can reduce their risk of dying by 60 to 70 per cent," said Dr. Robert Welsh, left; Dr. Paul Armstrong; Jannell Dawson, right. "But if you delay, you can lose that window and the patient will die."

"We know that if you treat people quickly, you can reduce their risk of dying by 60 to 70 per cent," said Dr. Robert Welsh, left; Dr. Paul Armstrong; Jannell Dawson, right. "But if you delay, you can lose that window and the patient will die."

**If you treat people quickly, you can reduce their risk of dying by 60 to 70 per cent**

**Arena vote expected by end of October / A3, A5**

**City ambulances equipped with mini labs could save lives of heart patients**

**See AMBULANCE / A2**
The future of clinical trials in secondary prevention after acute coronary syndromes

Dr. Paul Armstrong was invited to participate in the European Society of Cardiology’s sponsored reflections on how to enhance the future direction of clinical trials as they relate to secondary prevention after acute coronary syndromes. The publication, derived from this important European Society of Cardiology initiative, provides several key strategies to improve research including the use of the weighted composite endpoint approach that has been championed by CVC as noted in the next featured article.

Refining clinical trial composite outcomes: an Application to the Assessment of the Safety and Efficacy of a New Thrombolytic-3 (ASSENT-3) trial

Because traditional research uses a time-to-first-event in a composite approach to the evaluation of new strategies, it fails to recognize not only the weighted composite endpoint approach that has been championed by CVC as noted in the next featured article.

The 2011 Annual Report of the Canadian VIGOUR Centre

Resource use in the last 6 months of life among patients with heart failure in Canada

In this Canadian perspective, the fundamental importance of resource utilization in the last 6 months of life amongst patients dying with heart failure is examined for the first time. This perspective was accompanied by a parallel U.S. article. This highlights the crucial health economics implications of cardiovascular care and the responsibility to appropriately evaluate these in a resource constraint in a publicly funded system such as exists in Canada.

A model for predicting mortality in acute ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention: Results from the Assessment of Pexelizumab in Acute Myocardial Infarction Trial

Using carefully collected data from nearly 6000 patients with ST-elevation myocardial infarction undergoing primary PCI, we developed a model that was practical for clinicians to assess patient outcomes using baseline clinical and novel ECG variables. Because the model identifies key factors affecting prognosis and enables quantification of risk stratification, it will be helpful in guiding clinical care as well as risk adjusting for future observational analysis. We were pleased that it was chosen as one of the “Most Important Papers in ST-Elevation Myocardial Infarction” by the journal Circulation: Cardiovascular Interventions (2011;4;e55-e66).

Featured Publications

CVC is pleased to highlight the following five publications from our faculty that reflect the breadth and reach of our collective research interests and efforts. We have provided brief executive summaries for each, but to reference the full publication, please see the following pages for a complete listing of all CVC’s publications for calendar 2011.


10. Ezekowitz JA, Kaul, Bakal JA, Quan H, McAlister FA. Patterns of care and outcomes differ for urban vs. rural patients with newly diagnosed heart failure, even in a universal health care system. Circ Heart Fail. 2011;4:317-323.


“I have had the great privilege to work with Dr. Armstrong’s VIGOUR group. Under the guidance of Drs. Kaul and Ezekowitz, I was very fortunate to complete a Master of Public Health degree in clinical epidemiology during my core cardiology residency training. It is usually a very challenging task to conduct productive and important epidemiological research; that being said, VIGOUR’s abundance of resources and ease of access to organized population data allowed me to accomplish just that. The experience I gained under the VIGOUR group has built a solid foundation for my future career as an academic cardiologist.”

— John Dmitry, Cardiology Trainee —
Clinical Trial Operations

CVC is dedicated to quality assurance and continually works with sites on timely and accurate data collection, collaboration, problem solving and audit preparedness. As an ARO, CVC routinely updates its Standard Operating Procedures (SOPs) and utilizes project management principles for quality assurance. CVC employs metrics to ensure that we deliver on commitments to our stakeholders and to identify areas for improvement.

CVC has access to an international group of clinical experts with experience in clinical research and access to a well-established network of Canadian sites. We have some bilingual staff/consultants and are sensitive to the linguistic and cultural characteristics of our collaborative partners. Our work in clinical trials is both informed and enriched by connectivity to regional, provincial and national registries and population outcomes databases.

To date, the CVC has participated in forty-four (44) cardiovascular clinical trials (Phase II and Phase III) and studies, with enrollment of over 284,830 patients globally, of which over 18,000 patients were from Canada. These patient enrollment figures consistently meet or exceed anticipated and representational enrollment relative to national populations of other countries around the world. CVC’s success in consistently meeting enrollment targets stems in large part from the strength of our relationships with our sponsors and academic partners. Additionally, they work closely with sites throughout the trial to answer questions related to the protocol, data, study drug, etc., to monitor trends and issues associated with the trial, to assess recruitment, to ensure data quality and integrity is maintained, and to track metrics to ensure project timelines and milestones consistently being met.

Our Site Management Coordinators work alongside the Project Leads to ensure regulatory is reviewed, logged and filed appropriately, to maintain databases with both demographic and trial related documentation, to assist sites through the start-up phase, and to communicate on a regular basis with the sites regarding recruitment, data and regulatory.

Part of the CVC’s ongoing project management includes periodic publication of The Canadian Cardiac Chronicle which is distributed to investigative sites, sponsors and international collaborators (Appendix 2 and http://www.vigour.ualberta.ca/).

Throughout 2011, our Clinical Operations team had a strong focus on quality. Quality measures including internal reviews on clinical trials, quality check/audit activities with our monitors during their visits, and increased tracking and metrics were implemented. Standard operating procedures (SOPs) were updated and new ones implemented. Ongoing internal training on the review of ICH-GCP guidelines and Health Canada and FDA regulations was an ongoing initiative throughout the year.

CVC also compiled a training tool for investigative personnel. This booklet, entitled ‘Contributions of peak expiratory flow to assessment of acute decompensated heart failure: Insights from ASCEND-HF’ was accepted and presented in the poster session. Additionally, Dr. Ezekowitz et al. had two abstracts ‘Acute heart failure: A comparison of preserved and reduced ejection fraction in the emergency department’ and ‘Acute heart failure: Canadian perspectives from an RCT and a registry’ generated from the Registry Data which were accepted for oral presentation at the Canadian Cardiovascular Congress held in October 2011 in Vancouver.

In addition to thought leadership, the CVC provided overall project management, site management and monitoring for this trial and for the associated ancillary studies in Canada.
An Edmonton-region local initiative sponsored by the University Hospital Foundation and the Mazankowski Alberta Heart Institute investigating novel proximal pathways for non-ST-elevation myocardial infarction and acute heart failure. This project initiated by Dr. Paul Armstrong, Dr. Justin Ezekowitz and Dr. Robert Welsh entitled PROACT is currently underway. PROACT is a randomized controlled trial designed to assess how the early diagnosis and risk stratification acquired through pre-hospital point of care biomarkers and paramedic assessment will facilitate enhanced triage and treatment in patients with presumed non-ST-elevation acute coronary syndromes or acute heart failure. Partnering with Alere-San Diego Discovery, this project involves collaboration with Edmonton Regional Hospitals, Edmonton Emergency Medical Services and involves pre-hospital point of care biomarkers including Troponin and BNP. The project aims to enroll approximately 1800 subjects over 18-24 months. For more information about PROACT, please refer to the feature on pages 16-19 of this report.

PROACT

Sponsored by Regado Biosciences, this is a randomized, partially-blinded, multicenter, active-controlled, dose-ranging study assessing the safety, efficacy and pharmacodynamics of the REG1 anticoagulation system compared to unfractionated Heparin or low molecular weight Heparin in subjects with acute coronary syndrome. Following thirteen months of patient recruitment which achieved 640 of the expected 800 patients from 5 countries, enrollment concluded unexpectedly in October 2010 due to a few serious adverse events requiring further investigation. It was determined that the data collected until recruitment was sufficient and the results of the trial were presented on April 3, 2011, by Dr. Thomas Povsic with the Duke Clinical Research Institute (DCRI) at the American College of Cardiology Congress (ACC) in New Orleans, Louisiana at the late breaking clinical trial session. The study revealed that at least 50% reversal is needed for hemostasis and that a reversal of 75% and 100% may result in less bleeding when compared to heparin. An exciting finding was that RB006 (Penilvasogin) with partial of complete reversal resulted in fewer ischemic events than heparin. The data from the trial supported further development of REG1 in clinical trials to assess the safety and efficacy of controllable anticoagulation.

Dr. Paul Armstrong sits on the Advisory Board. The CVC provides project management, site management and monitoring for over 30 Canadian sites.

Regado Biosciences

Sponsored by GlaxoSmithKline, this trial is a randomized, placebo-controlled, double-blind, parallel group, multicenter, event-driven clinical outcomes study of Darapladib versus placebo in subjects with chronic coronary heart disease to compare the incidence of major adverse cardiovascular events.

With the first patient randomized in December 2008 and the participation of 38 countries, enrollment progressed rapidly with 15,839 patients being enrolled over a 10 month period, which exceeded initial projections. After enrolling an expected 779 patients, Canadian enrollment was capped in August 2009. The CVC was responsible for the site start-up of 38 Canadian sites, and continues to provide ongoing regulatory maintenance in addition to working with the sponsor on patient retention strategies and standard of care reporting. Dr. Paul Armstrong is actively involved as a member of the Steering Committee on this trial. Currently, study management is focused on ensuring patients are retained in the trial and that their medical treatment is optimized such that the final result will be relevant to contemporary patient care. This trial is expected to meet the target number of Major Adverse Cardiovascular Events (MACE) in early 2013.

Sponsored by Merck & Co. Inc., this trial is a multicenter, double-blind, randomized study to establish the clinical benefit and safety of Vytorin (Ezetimibe/Simvastatin tablet) versus Simvastatin monotherapy in high-risk patients presenting with acute coronary syndrome (ACS).

Initiated in 2005, this is a phase IV study to evaluate the clinical benefit of Ezetimibe/Simvastatin combination compared with simvastatin in 18,000 stabilized acute coronary syndrome subjects worldwide. On July 8, 2010, the study completed enrollment with a total of 18,143 subjects worldwide. On July 8, 2010, the study completed enrollment with a total of 18,143 subjects worldwide. On July 8, 2010, the study completed enrollment with a total of 18,143 subjects worldwide.

Dr. Armstrong is a member of the international Steering Committee. The CVC provides project management, site management and monitoring for over 30 Canadian sites.
Sponsored by Boehringer Ingelheim, this trial is a comparison of the efficacy and safety of a strategy of early fibrinolytic treatment with Tenecteplase and additional antiplatelet and antithrombin therapy followed by catheterization within 6-24 hours of rescue coronary intervention versus a strategy of standard primary percutaneous coronary intervention (PCI) in patients with acute myocardial infarction within 3 hours of onset of symptoms.

With the commencement of enrolment in 2008, 1,632 patients have been enrolled globally with an anticipated final enrollment of 2000 by July 2012. As of December 2011, Canada contributed 90 patients from two pre-hospital sites and one community site.

Following the success of the CVC-initiated WEST trial, Dr. Armstrong was invited to participate in the Scientific Advisory Committee to develop this protocol which tests the use of pre-hospital therapy for acute myocardial infarction patients versus primary PCI. Additionally, he functions as the Co-Principal Investigator on the Executive Committee for STREAM.

Dr. Robert Welsh has been involved as the Canadian National Lead on the Steering Committee for this trial as well as participating as one of the active and recruiting sites in Canada. In collaboration with Dr. Paul Armstrong, he has developed and led a Canadian specific sub-study, “The Strategic Reperfusion Early After Myocardial Infarction (STREAM) anticoagulation with Enoxaparin vs. unfractionated Heparin in primary PCI sub-study.”

The CVC has provided overall project management, site management and monitoring for this trial.

With the commencement of enrolment in 2008, 1,632 patients have been enrolled globally with an anticipated final enrollment of 2000 by July 2012. As of December 2011, Canada contributed 90 patients from two pre-hospital sites and one community site.

Following the success of the CVC-initiated WEST trial, Dr. Armstrong was invited to participate in the Scientific Advisory Committee to develop this protocol which tests the use of pre-hospital therapy for acute myocardial infarction patients versus primary PCI. Additionally, he functions as the Co-Principal Investigator on the Executive Committee for STREAM.

Dr. Robert Welsh has been involved as the Canadian National Lead on the Steering Committee for this trial as well as participating as one of the active and recruiting sites in Canada. In collaboration with Dr. Paul Armstrong, he has developed and led a Canadian specific sub-study, “The Strategic Reperfusion Early After Myocardial Infarction (STREAM) anticoagulation with Enoxaparin vs. unfractionated Heparin in primary PCI sub-study.”

The CVC has provided overall project management, site management and monitoring for this trial.

The CVC ECG Core Laboratory has been actively involved in the analyses of ECGs for the STREAM study. This work is described later in this report.

Sponsored by Merck & Co. Inc., this is a randomized, placebo controlled clinical Trial to Evaluate Cardiovascular Outcomes after treatment with Sitagliptin (TECOS) in patients with Type 2 diabetes mellitus and inadequate glycemic control.

This trial has taken CVC into the therapeutic area of endocrinology which both broadened our site network and opened up a new area for clinical research. With a target enrolment of 14,000 patients globally, just over 10,600 had been recruited by the end of 2011 with a contribution of 444 patients from Canada’s 25 enrolling sites. Recruitment is expected to be completed at the end of May 2012 and initiatives are currently underway to bring on additional sites around the world, including in Canada, to meet this goal.

Dr. Paul Armstrong is a member of the Executive Committee for this trial. The CVC provides overall project management, site management and monitoring for TECOS. Additionally, a unique collaboration as it relates to site communications and trial site updates has been established between the CVC and Dr. Irene Hramiak, Professor of Medicine and Chair of Division of Endocrinology and Metabolism, University of Western Ontario.

Sponsored by Merck & Co. Inc., this trial is a multicenter, randomized, double-blind, placebo controlled study evaluating the safety and efficacy of adding a new thrombin receptor antagonist (Vorapaxar) to the standard of care for a minimum of 1 year in patients with non-ST-segment elevation acute coronary syndromes.

Following 30 months of recruitment, TRACER completed enrolment on June 9, 2010 with 12,642 patients enrolled globally from 812 sites, reflecting a Canadian contribution of 573 patients from 27 sites. The results of the trial were presented on Sunday, November 13, 2011, by Dr. Kenneth Mahaffey with the Duke Clinical Research Institute (DCRI) at the American Heart Association Meetings (AHA) in Orlando, Florida at the late breaking clinical trial session. (Published in the New England Journal of Medicine on November 13, 2011, the results showed:

When added to standard of care in patients with NSTE ACS and high use of aspirin and P2Y12 inhibition, vorapaxar did not significantly reduce the composite of CV death, MI, stroke, hospitalization for ischemia, or urgent revascularization, nor did vorapaxar reduce CV death, MI or stroke, nor did it significantly increase bleeding, including major bleeding, and intracranial hemorrhage.

In reflecting on these results and the balance of efficacy and risk, the second of the pair of large Phase III studies with vorapaxar (TRA-2P) is awaited with much interest and is expected to be presented at the American College of Cardiology Meetings in Chicago in March 2012.

The CVC provided overall project management, site management and monitoring for this trial. Recognizing that ECG changes are the basis for patient inclusion, and accurate ECG assessment was a critical component of this trial, the CVC’s ECG Core Lab was actively involved in assessing patients with negative markers to ensure they were enrolled in accordance with the protocol. Dr. Armstrong also serves an active member of the Executive Committee for TRACER.
“The endless amount of assistance and support offered by the CVC is amazing. Everyone at the CVC tried their best to facilitate any problems I faced. Through working with the CVC, I have learned how difficult things can be made possible by working as a team. In short, this has been a life-changing experience.”

— Nawaf Almajed, Master’s Student and Resident in Internal Medicine —
Population Health and Economic Outcomes

In the last decade over half a million Albertans have been diagnosed with heart disease, which accounts for the second highest number of deaths in the province annually. Ongoing technological advances in the treatment of acute coronary syndromes and heart failure make it essential to examine whether the use of these expensive drugs and devices is equitable and to assess their impact on current and future costs of cardiac care in Alberta.

The CVC Outcomes Group (led by Drs. Kaul, Ezekowitz and McAlister) has been actively involved in using health care administrative data to examine issues related to access, delivery, treatment, and outcomes of heart disease in Alberta and Canada. 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. Using administrative data received from Alberta Health and Wellness (AHW), the CVC Outcomes group has developed an integrated longitudinal database linking inpatient, 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. To compare practice patterns and outcomes in Alberta with those in other Canadian provinces, we have acquired Canadian Institutes of Health Research data on all acute care hospitalizations for these five conditions for the same time period. Our extensive portfolio of research projects based on these data includes examining the following: socio-economic and urban/rural differences in access to treatment and outcomes; outcomes among vulnerable populations such as 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. See accompanying list of selected publications.

Although administrative data have the strength of being population-based and are the best type of data for disease surveillance and health system evaluation, they are limited by their lack of clinical detail. Linking administrative databases to population-level clinical registries overcomes this limitation. In 2011, Dr Kaul received a Canadian Institutes of Health Research (CIHR) grant to link the Alberta Perinatal Health Program, a provincial clinical registry focused on the perinatal health of infants and their mothers to AHW administrative data. One of the major goals of this study is to examine the long-term cardiovascular health outcomes of mothers with gestational diabetes mellitus (GDM) and their children in Alberta.

A major goal of the CVC Outcomes group is to identify, inspire, and train junior faculty and students in the analysis of linked administrative healthcare databases. Trainees and junior faculty continue to feature prominently in our projects and manuscripts and are highlighted in bold in the accompanying list of selected publications.

Health outcomes research has been identified as an area of strong potential by the Faculty of Medicine and Dentistry: the Patient Health Outcomes Research and Clinical Effectiveness (PHORCE) Institute, directed by Dr Finlay McAlister is a Faculty of Medicine and Dentistry initiative to engage health outcomes researchers in collaborative, interdisciplinary health research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease research projects.

One of the major strengths of the CVC Outcomes group is its core of well-trained research personnel.

Selected Publications


5. Gamble JM, Durie DT, Ezekowitz JA, Kaul P, Quan H, McAlister FA. Patterns of care and outcomes differ for urban vs. rural patients with newly diagnosed heart failure, even in a universal health care system. Circ Heart Fail. 2011;4:317-323.

Biostatistical Analysis

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 mechanic 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. The CVC houses databases from 22 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 (over 2500 patients)
- ASCEND HF Registry (over 690 patients)
- PROACT Retrospective Cohorts (over 550 patients)

Academic Highlights

In 2011, the CVC 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.

Selected Publications

- Drs. Al-Majed (medical resident), McAlister, Bakal and Ezekowitz published a meta-analysis of cardiac resynchronization therapy in patients with less symptomatic heart failure. From the data published in 25 trials, they concluded that this therapy was beneficial in patients with reduced left ventricular ejection fraction, symptoms of heart failure and prolonged QRS, regardless of NYHA class. (Ann Intern Med 2011;154(8):401-12)
- Drs. Armstrong, Bakal and Westerhout developed a novel approach to analyzing composite endpoints, which are frequently used as the primary endpoint in cardiovascular trials, and applied this to data from the ASSENT-3 trial of over 6000 STEMI patients treated with fibrinolysis. (Am Heart J 2011;161:848-54) A complimentary editorial by Drs. Anstrom and Eisenstein also accompanied this article. (Am Heart J 2011;161(5):805-6)
- Drs. Ezekowitz, Kaul, Bakal and McAlisters examined trends in heart failure care from 1999 to 2007 in Alberta with particular interest in the location of the incident diagnosis of heart failure: hospital, emergency department or outpatient clinic. They found that over this time period, an increasing number of patients were diagnosed as outpatients rather than in a hospital setting. (Can J Cardiol 2011;27:142-7)
- Ethnic differences in one-year mortality were examined among white, Chinese and East Indian patients hospitalized with heart failure in Alberta between 1999 and 2005 by Drs. Kaul, McAlisters, Ezekowitz and Mishra. They observed higher 1-year mortality in Chinese patients compared to white patients, whereas there was no mortality difference among Indian and white patients. (Heart 2011;97(13):1048-53)
- In a pooled analysis of the CAPTIM and WEST trials by Drs. Westerhout, Welsh and Armstrong, a significant survival advantage within one year was observed in patients with early fibrinolysis when presentation delay was less than 2 hours compared to those undergoing primary PCI for STEMI. Beyond 2 hours, no treatment difference was observed. (Am Heart J 2011;161:283-90)
The aim of our ECG Core Laboratory is to translate research results into information useful for clinical application. Using the ECG parameters to generate an improved understanding of the pathophysiologic processes involved in ACS enables improvements in managing cardiac patients, prediction of outcomes, and further stimulates cardiovascular scientific research.

In 2011, the ECG Core Lab at the CVC continued its tradition 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 train the next generation of talented researchers.

To date, ECGs from over 67,976 patients, enrolled in studies around the world, have been analyzed. This provides a rich database for additional substudies, analyses and research. The main projects for the ECG Core Lab in 2011 included STREAM, PROACT, and PLATO, along with some additional local research projects.

The CVC ECG Core Laboratory continued with the analysis of ECGs for the Strategic Reperfusion Early After Myocardial Infarction (STREAM) trial. The examination of these ECGs includes 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). The Core Lab also provides central adjudication for patients with rescue PCI to determine whether they have met the clinical indication for infarct size in patients experiencing acute myocardial infarction (AMI). The Core Lab also provides central adjudication for patients with rescue PCI to determine whether they have met the clinical indication for infarct size in patients experiencing acute myocardial infarction (AMI). The Core Lab has accumulated a wealth of experience in its readers and continues to mentor and train the next generation of talented researchers.

As of the end of December 2011, at least one (and up to five) ECGs for 1,497 STREAM patients had been received, resulting in the analysis of a total 6,285 STREAM ECGs completed to that date. The STREAM study makes use of online technology for both the uploading and submission of ECGs; the investigative site is able to upload the electronic ECG photo file and once this process is complete, it is instantaneously available for download by ECG Core Lab staff at the CVC.

PLATO

PLATO (PLATelet Inhibition and Patient Outcomes), a study sponsored by AstraZeneca and was a large, prospective, multicenter, randomized, double-blind, event-driven trial comparing ticagrelor versus clopidogrel for reduction of 1-year cardiovascular events in patients with acute coronary syndrome with or without ST-segment elevation. The CVC ECG Core Lab was awarded the opportunity to systemically assess over 15,000 patients’ PLATO ECGs which provided us with unique opportunity to examine possible modulation of treatment effect via quantitative analyses of ST-T changes and Q wave duration between admissions and discharge ECGs. Moreover, PLATO allowed us to determine the relative contribution of the ECG in predicting the clinical outcome in the presence of the contemporary risk markers for refined prognostication and risk stratification of ACS patients. The ECG Core Lab team completed the analysis of 15,563 patient ECGs in 2010, and in 2011, this unique dataset provided new opportunities for insight into the PLATO study outcomes as well as helping to plan appropriate future studies. The first PLATO ECG Substudy was published in Circulation on December 16, 2011. In this paper, entitled “ST Elevation Acute Coronary Syndromes in PLATO: Insights from the ECG Substudy,” the researchers examined whether the relationship between the study treatment (ticagrelor versus clopidogrel) and vascular death/MI within one year was modified by the extent of ST shift on the baseline ECG and/or residual changes at discharge. Overall, there was no significant change in the benefit of ticagrelor according to these ECG metrics; however, the independent prognostic value of ST shift and resolution remained a consistently observed feature among ST-elevation ACS patients. This publication is the first to be generated from a tremendous undertaking of CVC’s ECG Core Laboratory and others are expected to follow.

PROACT

In 2011, the CVC received additional grant funding from the University Hospital Foundation to continue the PROACT project, which is detailed in an earlier section of this report. 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.

Other ECG Activities

Quality continues to be an important focus for the ECG Core Lab. To that end, the CVC ECG Core Lab designed and began a study in 2011, known as the J-Point Project, to establish optimal measurement points on ECGs with respect to feasibility, applicability and inter-observer agreement. In addition, the prognostic relevance of this measurement would be determined by correlating the data with outcomes measures from a large sample of clinical trial data from a previously completed study. 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 ongoing phase in which the intent is to test the inter-reader reliability on the application of the universal definition of myocardial infarction in a broad spectrum of acute coronary syndromes (ACS) patients.
Sources of Revenues

Clinical Trials
January - December 2011*

*In Canadian dollars, includes pass-throughs and exchange rate adjustments

Grants
(January - December 2011)

<table>
<thead>
<tr>
<th>Project</th>
<th>Sponsor(s)</th>
<th>Grant Holders</th>
<th>Term</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),</td>
<td>2010–2013</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Justin Ezekowitz, Padma Kaul,</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Finlay McAlister, Robert Welsh</td>
<td></td>
</tr>
<tr>
<td>Tracking Gender Differences in Acute Coronary Syndromes: At the First Point of Care and Beyond</td>
<td>Canadian Institutes of Health Research</td>
<td>Padma Kaul (P), Paul Armstrong, Michelle Graham, Colleen Norris, Robert Welsh</td>
<td>2008–2011</td>
</tr>
<tr>
<td>Team grant: Vascular complications associated with gestational diabetes mellitus in Alberta</td>
<td>Faculty of Medicine/Capital Health Emerging Research Team Grants Competition</td>
<td>E. Ryan (P), Padma Kaul, S Davidge</td>
<td>2008–2011</td>
</tr>
<tr>
<td>Acute Heart Failure - Emergency Management</td>
<td>Canadian Institutes of Health Research</td>
<td>Justin Ezekowitz</td>
<td>2009 to 2012</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>
</tr>
<tr>
<td>Cardiac Chemoreceptors in Heart Failure</td>
<td>Heart and Stroke Foundation</td>
<td>Michael Eckland (P),</td>
<td>2009–2012</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Justin Ezekowitz,</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>H Quan</td>
<td></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 (P), Padma Kaul, Justin A. Ezekowitz, H Quan</td>
<td>2010–2012</td>
</tr>
</tbody>
</table>

Sources of Revenues

Clinical Trials
January - December 2011*

*In Canadian dollars, includes pass-throughs and exchange rate adjustments

Grants
(January - December 2011)

<table>
<thead>
<tr>
<th>Project</th>
<th>Sponsor(s)</th>
<th>Grant Holders</th>
<th>Term</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),</td>
<td>2010–2013</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Justin Ezekowitz, Padma Kaul,</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Finlay McAlister, Robert Welsh</td>
<td></td>
</tr>
<tr>
<td>Tracking Gender Differences in Acute Coronary Syndromes: At the First Point of Care and Beyond</td>
<td>Canadian Institutes of Health Research</td>
<td>Padma Kaul (P), Paul Armstrong, Michelle Graham, Colleen Norris, Robert Welsh</td>
<td>2008–2011</td>
</tr>
<tr>
<td>Team grant: Vascular complications associated with gestational diabetes mellitus in Alberta</td>
<td>Faculty of Medicine/Capital Health Emerging Research Team Grants Competition</td>
<td>E. Ryan (P), Padma Kaul, S Davidge</td>
<td>2008–2011</td>
</tr>
<tr>
<td>Acute Heart Failure - Emergency Management</td>
<td>Canadian Institutes of Health Research</td>
<td>Justin Ezekowitz</td>
<td>2009 to 2012</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>
</tr>
<tr>
<td>Cardiac Chemoreceptors in Heart Failure</td>
<td>Heart and Stroke Foundation</td>
<td>Michael Eckland (P),</td>
<td>2009–2012</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Justin Ezekowitz,</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>H Quan</td>
<td></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 (P), Padma Kaul, Justin A. Ezekowitz, H Quan</td>
<td>2010–2012</td>
</tr>
</tbody>
</table>

Clinical Trials
January - December 2011*

*In Canadian dollars, includes pass-throughs and exchange rate adjustments

Grants
(January - December 2011)

<table>
<thead>
<tr>
<th>Project</th>
<th>Sponsor(s)</th>
<th>Grant Holders</th>
<th>Term</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),</td>
<td>2010–2013</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Justin Ezekowitz, Padma Kaul,</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Finlay McAlister, Robert Welsh</td>
<td></td>
</tr>
<tr>
<td>Tracking Gender Differences in Acute Coronary Syndromes: At the First Point of Care and Beyond</td>
<td>Canadian Institutes of Health Research</td>
<td>Padma Kaul (P), Paul Armstrong, Michelle Graham, Colleen Norris, Robert Welsh</td>
<td>2008–2011</td>
</tr>
<tr>
<td>Team grant: Vascular complications associated with gestational diabetes mellitus in Alberta</td>
<td>Faculty of Medicine/Capital Health Emerging Research Team Grants Competition</td>
<td>E. Ryan (P), Padma Kaul, S Davidge</td>
<td>2008–2011</td>
</tr>
<tr>
<td>Acute Heart Failure - Emergency Management</td>
<td>Canadian Institutes of Health Research</td>
<td>Justin Ezekowitz</td>
<td>2009 to 2012</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>
</tr>
<tr>
<td>Cardiac Chemoreceptors in Heart Failure</td>
<td>Heart and Stroke Foundation</td>
<td>Michael Eckland (P),</td>
<td>2009–2012</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Justin Ezekowitz,</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>H Quan</td>
<td></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 (P), Padma Kaul, Justin A. Ezekowitz, H Quan</td>
<td>2010–2012</td>
</tr>
</tbody>
</table>

Clinical Trials
January - December 2011*

*In Canadian dollars, includes pass-throughs and exchange rate adjustments

Grants
(January - December 2011)

<table>
<thead>
<tr>
<th>Project</th>
<th>Sponsor(s)</th>
<th>Grant Holders</th>
<th>Term</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),</td>
<td>2010–2013</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Justin Ezekowitz, Padma Kaul,</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Finlay McAlister, Robert Welsh</td>
<td></td>
</tr>
<tr>
<td>Tracking Gender Differences in Acute Coronary Syndromes: At the First Point of Care and Beyond</td>
<td>Canadian Institutes of Health Research</td>
<td>Padma Kaul (P), Paul Armstrong, Michelle Graham, Colleen Norris, Robert Welsh</td>
<td>2008–2011</td>
</tr>
<tr>
<td>Team grant: Vascular complications associated with gestational diabetes mellitus in Alberta</td>
<td>Faculty of Medicine/Capital Health Emerging Research Team Grants Competition</td>
<td>E. Ryan (P), Padma Kaul, S Davidge</td>
<td>2008–2011</td>
</tr>
<tr>
<td>Acute Heart Failure - Emergency Management</td>
<td>Canadian Institutes of Health Research</td>
<td>Justin Ezekowitz</td>
<td>2009 to 2012</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>
</tr>
<tr>
<td>Cardiac Chemoreceptors in Heart Failure</td>
<td>Heart and Stroke Foundation</td>
<td>Michael Eckland (P),</td>
<td>2009–2012</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Justin Ezekowitz,</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>H Quan</td>
<td></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 (P), Padma Kaul, Justin A. Ezekowitz, H Quan</td>
<td>2010–2012</td>
</tr>
</tbody>
</table>
“As a student of CVC, I take pride in this organization’s core values: integrity, respect, collaboration, and quality. Here, educating the next generation clinician-scientists is regarded as an integral mission. Dr. Armstrong strongly believes in active learning, so students are presented with the unique challenge of leading a research project from conception to publication.

The mentorship of Dr. Armstrong and support from everyone in CVC have been the perfect combination in orienting my career goal to academic cardiovascular medicine, and I am deeply grateful for this treasured experience.”

— Mike Bao, Undergraduate Student, Honours Physiology —
Worldwide Collaborations

External advisors

Robert M. Califf, MD, Vice Chancellor for Clinical Research, Duke University, Durham, NC
Christopher B. Granger, MD, Associate Professor of Medicine; Division of Cardiology; Director, Cardiac Care Unit, Duke University Medical Center, Durham, NC
Robert A. Harrington, MD, Professor, Division of Cardiology; Director, Duke Clinical Research Institute, Durham, NC
Kerry L. Lee, PhD, Professor of Biostatistics and Informatics, Duke University Medical Center, Durham, NC
P. Gabriel Steg, MD, Professor of Cardiology, Université Paris VII – Denis Diderot; Director, Coronary Care Unit, Hôpital Bichat – Claude Bernard, Paris, France; Director research team, Clinical Research in Atherothrombosis, INSERM U-698.
Frans Van de Werf, MD, PhD, Professor of Medicine, Chairman, Department of Cardiology, University Hospital Gasthuisberg and head Leuven Coordinating Centre (LCC), The University of Gasthuisberg, Leuven, Belgium
Lars Wallentin, MD, PhD, Professor of Cardiology, Institute of Medical Sciences Cardiology, University Hospital, Uppsala, Sweden
Harvey White, MB, Director of Coronary Care & Green Lane Cardiovascular Research Unit; Green Lane Cardiovascular Service, Auckland, New Zealand

Canadian VIGOUR Centre Edmonton, Canada
Duke Clinical Research Institute Durham, USA
Leuven Coordinating Centre Leuven, Belgium
Uppsala Clinical Research Centre Uppsala, Sweden
Canadian VIGOUR Centre Edmonton, Canada
Duke Clinical Research Institute Durham, USA
Leuven Coordinating Centre Leuven, Belgium
Uppsala Clinical Research Centre Uppsala, Sweden
Estudios Clinicos Latinoamérica Rosario, Argentina
Brazilian Clinical Research Institute São Paulo, Brazil
Trials Argentine Group Organization Buenos Aires, Argentina
Flinders Medical Centre Adelaide, Australia
Green Lane Coordinating Centre Auckland, New Zealand
National Health and Medical Research Council — Clinical Trials Centre Sydney, Australia

Brazilian Clinical Research Institute São Paulo, Brazil
Trials Argentine Group Organization Buenos Aires, Argentina
Flinders Medical Centre Adelaide, Australia
Green Lane Coordinating Centre Auckland, New Zealand
National Health and Medical Research Council — Clinical Trials Centre Sydney, Australia

Flinders Medical Centre Adelaide, Australia
Green Lane Coordinating Centre Auckland, New Zealand
National Health and Medical Research Council — Clinical Trials Centre Sydney, Australia
CVC Trial Experience
1997 - 2011

* Previous GUSTO I, IIA, IIB prior to CVC establishment as centre, although Armstrong lead PI on these trials
** PARAGON A, prior to CVC establishment as centre although Armstrong lead PI on this trial
*** PURSUIT commenced in 1995, prior to CVC’s establishment as a centre
PARADIGM commenced in 1995, prior to CVC’s establishment as a centre
"The Canadian VIGOUR Centre has played an instrumental role in my future goal to become a clinician scientist in Alberta. Not only has Dr. Armstrong and the CVC shown me the struggles and tremendous rewards of clinical research, I have gained a great deal of knowledge on how to manage a project from the initial research question to the final manuscript. VIGOUR has given me the support to jump start my medical career and the stepping stones towards a bright future."

— Debraj Das, Summer Student —
Dr. Armstrong’s principal investigative focus, involves the pathophysiology, diagnosis and management of acute coronary syndromes and congestive heart failure.

Having been principally involved in the introduction of novel fibrinolytic therapy to Canada over 20 years ago, he and his colleagues have spearheaded a comprehensive and transforming initiative to further enhance the care of patients with ST-elevation myocardial infarction given that you need time sensitivity on the one hand, and the failure of patients so afflicted to arrive at health care institutions in a timely manner on the other, so as to receive life-saving therapy. This concept is now being actively translated into other common and time-sensitive life-threatening conditions namely acute non-ST-elevation myocardial infarction and congestive heart failure.

Dr. Armstrong has had a lifelong commitment to the education and training of healthcare professionals. A number of his many former trainees, residents and research fellows have won research prizes and awards under his tutelage and have gone on to academic positions in Canada and internationally. His mentorship of trainees and faculty has been a key signature of his career and is recognized both nationally and internationally.

Dr. Kaul is an epidemiologist and policy analyst by training and commits 75% of her time to research. Her main research interests can be broadly classified into four areas:

- International differences in practice patterns and outcomes;
- Sex differences in treatment and outcomes of cardiovascular disease;
- Issues related to access and delivery of care at a population level; and
- Health economics.

A 2011 highlight of her research is illustrated in a publication in the Archives of Internal Medicine (see Featured Articles) which provides a Canadian perspective about the fundamental importance of resource utilization in the last six months of life amongst patients dying with heart failure. This article highlights the crucial health economics implications of cardiovascular care and the responsibility to appropriately evaluate these resource constraints in a publicly funded system such as exists in Canada. This article is accompanied by a parallel US article.

Dr. Kaul gratefully acknowledges the financial support from Alberta Innovates - Health Solutions.

Padma Kaul, PhD
Director, Outcomes Research, CVC
Associate Professor, Department of Medicine, University of Alberta
Adjunct Assistant Research Professor, Duke University Medical Center
Adjunct Associate Professor, School of Public Health, University of Alberta
Alberta Innovates – Health Solutions Population Health Investigator

Paul W. Armstrong, MD
Director, CVC
Distinguished University Professor, Division of Cardiology, University of Alberta

Faculty
Dr. Ezekowitz is passionate about trying to improve the outcomes of his patients with heart failure. He dedicates 75% of his time to clinical research to better understand this disease and to increase the amount of clinical evidence available to improve the process and quality of care for these patients.

Dr. Ezekowitz’ 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.

Dr. Ezekowitz has played a leadership role in major international trials. In 2011, one of these trials (ASCEND-HF) was concluded and the results published in the New England Journal of Medicine (see Featured Article). Arising from this work was a major substudy evaluating the role of shortness of breath and how best to assess it in heart failure research. Dr. Ezekowitz presented this work in Paris at the European Society of Cardiology “Contributions of Peak Expiratory Flow to Assessment of Acute Decompensated Heart Failure: Insights from ASCEND-HF” and the work is published in JACC.

Dr. Ezekowitz gratefully acknowledges the financial support from Alberta Innovates - Health Solutions, Canadian Institutes of Health Research, University Hospital Foundation and Mazankowski Alberta Heart Institute.

Dr. Finlay McAlister is a practising general internist. His research interests include:

• Outcomes research in hypertension, heart failure, periparative care, and coronary artery disease
• Clinical epidemiology methodology with a focus on evidence-based medicine and implementation of evidence at the bedside
• Methodology of trials and systematic reviews

Dr. McAlister gratefully acknowledges the financial support from Alberta Innovates - Health Solutions and the Capital Health Chair.
Dr. Welsh’s clinical research interests are focused:

• On the management of the full spectrum of Acute Coronary Syndromes and Interventional Cardiology in general.
• Understanding the implications and the interplay between cardiovascular disease and diabetes.
• Exploring exercise physiology and cardiac physiology.
• Designing and championing of various cardiovascular clinical trials including: the investigation of novel antiplatelet therapies in acute coronary syndromes; and pre-hospital management of STEMI and the interaction of pharmacological (anti thrombotic and fibrinolytic) and mechanical interventions (primary and rescue angioplasty) which are a major focus of his clinical research.

In 2011, Dr. Welsh and his team were involved in training over 200 paramedics to use new technology for the Providing Rapid Out of Hospital Acute Cardiovascular Treatment (PROACT) project which is aimed at manage patients prehospital with other life threatening acute heart disease including heightened risk of heart attack and heart failure.

Dr. Welsh gratefully acknowledges the financial support from University Hospital Foundation and Mazankowski Alberta Heart Institute.
Key Personnel

Dianne Payeur, B.Comm, MBA
Assistant Director

Yuling Fu, MD
Consultant, ECG Core Laboratory

Hany Siha, MBBCh
Assistant Director, ECG Core Laboratory

Tracy Temple, B.Sc., RN
Manager, Clinical Operations

Halina Nawrocki, RN
Lead Clinical Research Associate

Cynthia Westerhout, PhD
Assistant Director, Biostatistics
The CVC Team
I had the privilege to work with Dr. Armstrong and the VIGOUR group. It was an invaluable time of learning, filled with enthusiasm and support by all the members of the VIGOUR team. Clinical research could be a challenging and even intimidating experience for the beginner, yet I was fully supported and intellectually encouraged by Dr. Armstrong and Cindy Westerhout, which made my first taste of cardiovascular research exciting and very stimulating.

The CVC is an excellent media for planting the seeds of future researchers. The educational, professional and interpersonal atmosphere is the ultimate necessity for the motivation of trainees to continue on their research efforts and complete great projects."

— Olga Toleva, Cardiology Trainee —
Appendix 1

Media Clips

In the media

ACS 360°: The Canadian Perspective: The View from Inside CCC 2011, October 23, 2011:

Hosted by Peter Mansbridge, this discussion among a panel of Canadian cardiovascular experts, features CVC faculty members Dr. Paul Armstrong and Dr. Robert Welsh. Their overview examines how Canada is doing in the treatment of acute coronary syndromes and where improvement is needed with respect to time to treatment, drugs, equipment and facilities. View the full video session here: http://www.medscape.org/viewarticle/752383?

AHA 2011 Wrap-up, featured on Clinical Trial Results TV, November 15, 2011:

Dr. Armstrong was joined by colleagues Drs. Justin Ezekowitz, JF Tanguay and Shaun Goodman to review results of several important studies from a Canadian perspective. In this video, they discuss the findings of HOOPS, TRACER and ATLAS studies as well as the Canadian non-ASCEND Registry substudy. See the clip here: http://tv.clinicaltrialresults.org/play.php?submission_id=1095
Appendix 2

The Canadian Cardiac Chronicle

The Canadian Cardiac Chronicle

Volume 15, No. 1
Spring 2011

Inside this issue:
Letter: PM 1
Armstrong
Trial Updates: 3.1
This Issue: 6
Highlights: 6.7
CVC: 8
Publications: 8

Research Meeting
How does cardiovascular disease evolve? We discuss the role of inflammation and discuss what is known about the role of inflammation in cardiovascular disease.

Inflammation in Cardiovascular Disease

The Canadian Cardiac Chronicle

Volume 15, No. 2
Winter 2011

Inside this issue:
Letter: PM 1
Armstrong
Trial Updates: 5.5
How to Address: 6
CVC: 7.8
Publications: 8

Letter from Dr. Paul Armstrong
The rapidly evolving area of information technology and telecommunication through the Internet has resulted in the growth of many of the major scientific meetings such as the American Heart Association. Oddly, it seems the major media as well as the lay public is not aware of these developments. The 2011 Annual Report of the Canadian VIGOUR Centre focuses on the trends in the actual presentation of data. At times, this may be the case, whether it is an observed increase in the number of presentations in a particular area, or a decrease, or a combination of the two. It is always interesting to see how these developments affect the overall presentation of data.

The Canadian Cardiac Chronicle

www.vigour.ualberta.ca

CVC is proud to be a
Member of Alberta Centre

The 2011 Annual Report of the Canadian VIGOUR Centre
Appendix 3

Beyond 2000

New Concepts in Acute Coronary Syndromes
Beyond 2000 (XVII)

Held in association with the Canadian Cardiovascular Congress 2011

Nouveaux concepts dans les syndromes coronariens aigus Au-delà de l’an 2000 (XVII)

Symposium tenu en marge du Congrès 2011 de la Société canadienne de cardiologie

Ballroom B
Vancouver Convention Centre West Building
Vancouver, British Columbia

Sunday, October 23, 2011
07:55 – 12:00

This program has been reviewed and co-developed by the Canadian Cardiovascular Society for a maximum of 4 credits.

This event is an accredited group learning activity under Section 1 as defined by the Royal College of Physicians & Surgeons of Canada for the Maintenance of Certification program. It is approved by the Canadian Cardiovascular Society for a maximum of 4 credits. The accreditation program was co-developed with the Canadian Cardiovascular Society, University of Alberta, AstraZeneca Canada Inc, and Merck, and was planned to ensure the evidence presented is valid, objective and balanced.

Through an agreement between the American Medical Association and the Royal College of Physicians and Surgeons of Canada, the Canadian Cardiovascular Society designated this live educational activity for a maximum of 4 AMA PRA category 1 credits. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Appendix 4

Important reference documents on Conducting Clinical Research in Canada

ICH Guidelines
- E6 - Good Clinical Practice: Consolidated Guideline
- E2A - Clinical Safety Data Management Definitions and Standards for Expedited Reporting
- E8 - General Considerations for Clinical Trials

Health Canada
- Division 5 Regulations
- Extract from Regulatory Impact Analysis Statement

As of August 1, 2011

Compliments of the Canadian VIGOUR Centre
Acknowledgements

Special thanks to:

• 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;

• The trainees for their commitment, enthusiasm, creative insights and unique testimonials about their experiences, which we have cited throughout this report;

• Donnie Payeur and Carla Price for their time and dedication required to produce this report;

• Kathy Watts and Bryan Mackeill from WattsCommunications for the concept and design

• Photographers Pat Marston and Stephen Wreakes for many of the images enclosed in this report.

For further information about the Canadian VIGOUR Centre, or to view this report or our brochure digitally, please see our website at http://www.vigour.ualberta.ca.
The Canadian VIGOUR Centre is located on the campus of the University of Alberta in Edmonton, Alberta, Canada.

2-132 Li Ka Shing Centre for Health Research Innovation
University of Alberta
Edmonton, Alberta, T6G 2E1
Canada

Toll-free: 1 800 707 9098
Local: 780 492 8383
Fax: 780 492 0613

www.vigour.ualberta.ca