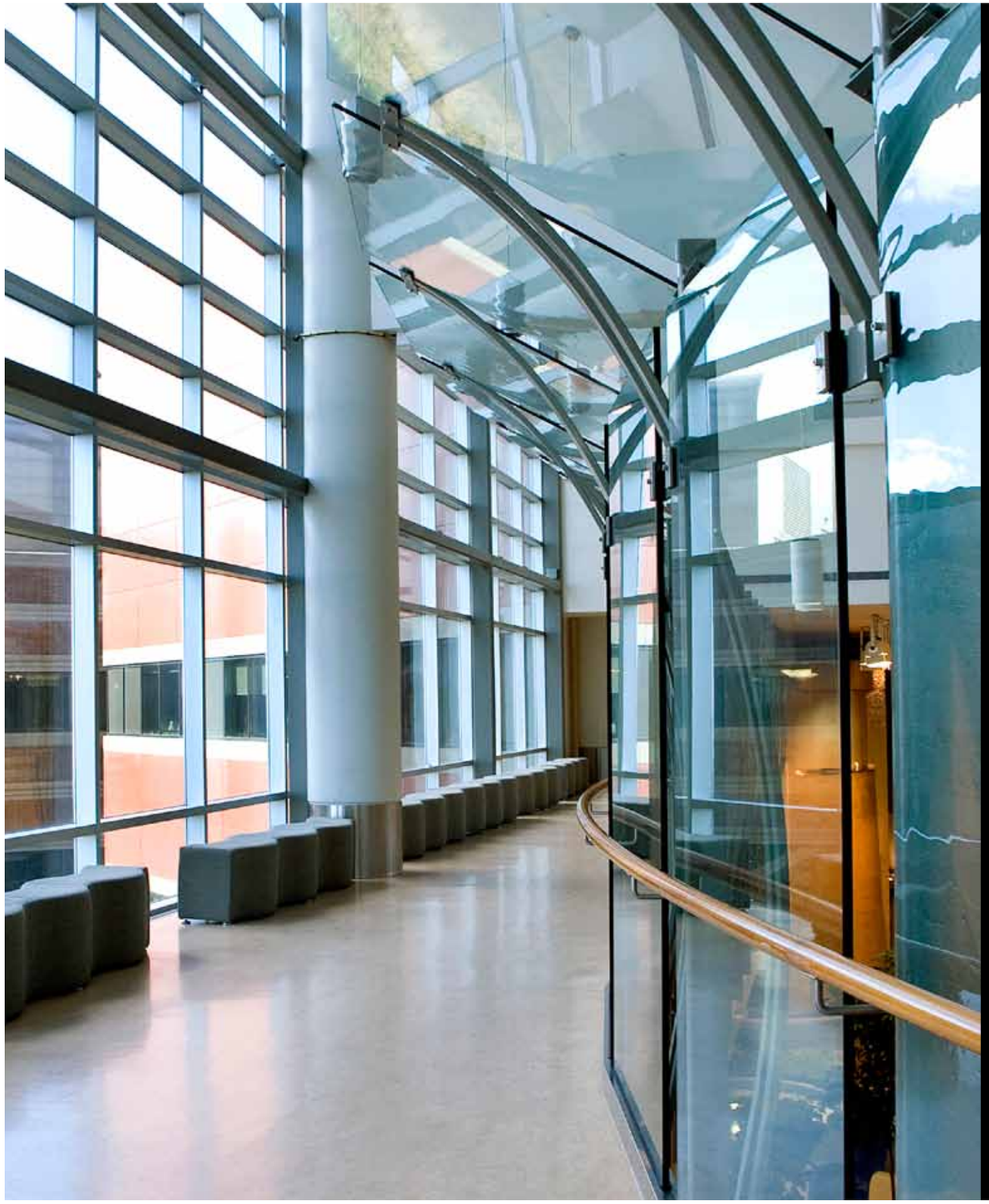
2011 Annual Report

CANADIAN VIGOUR CENTRE

Bridging Hearts and Minds to Enhance Cardiovascular Care



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 PROACT (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.

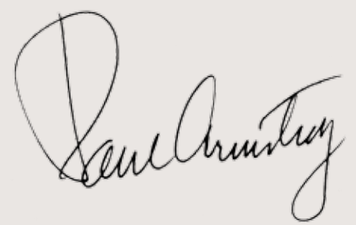
- Stimulated by the need for more efficient, cost effective and "smarter clinical trials", we have, in conjunction with our biostatistical group, begun to heavily invest in novel methodologies that will not only enhance the precision of our outcome estimates but potentially lead to more meaningful interpretation 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, Mission, and Core Values

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.

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.

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.

THE NEXT GENERATION OF RESEARCHERS

"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 —

CVC Activities and Services

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

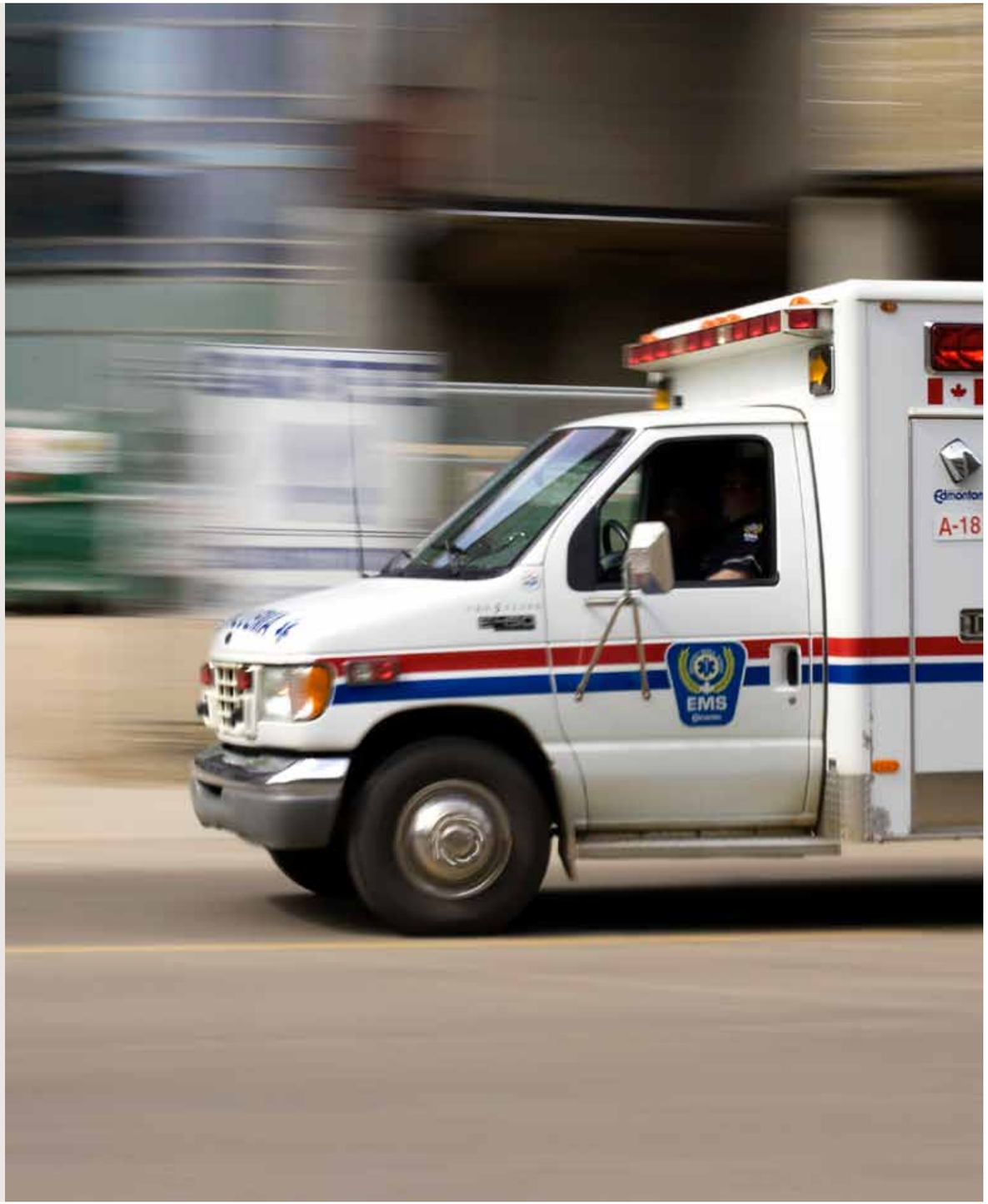
EGC Core Lab

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

Areas of Research Interest and Expertise

	THOUGHT LEADERSHIP	CLINICAL TRIAL MANAGEMENT	BIOSTATISTICS / EPIDEMIOLOGY	POPULATION HEALTH/OUTCOMES	CLINICAL REGISTRIES	HEALTH POLICY / ECONOMICS	MENTORING / EDUCATION	ECG CORE LABORATORY
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.

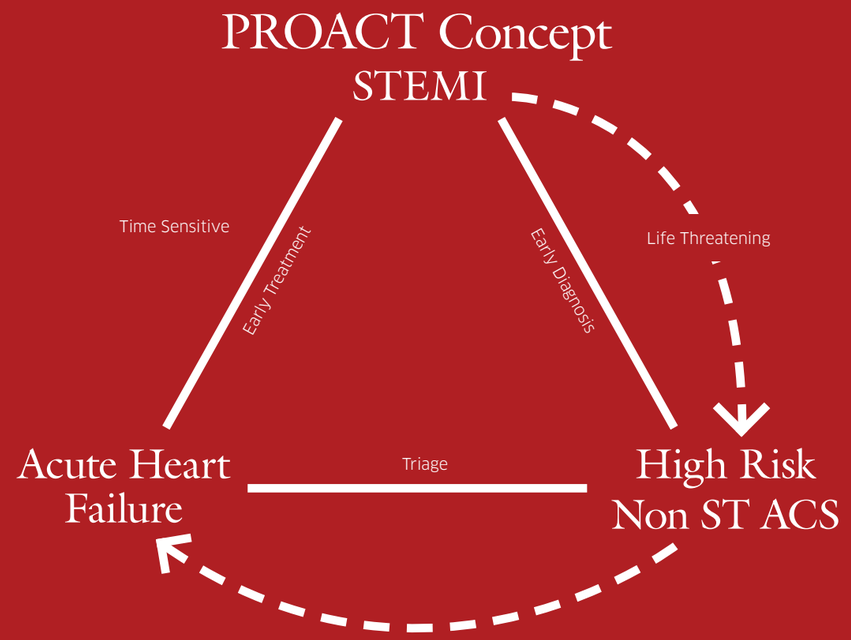
3) It served as a stepping stone for us to craft a four-centre Canadian feasibility trial, WEST (Which Early ST Elevation Myocardial Infarction Therapy), to address the relative efficacy and safety of mechanical versus pharmacologic reperfusion coupled with strategic mechanical co-intervention. WEST 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 PPCI.

4) Our findings have been an important underpinning of 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-ST elevation 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 triage 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: Sunil Sookram (University of Alberta Hospital); Dale Weiss (Emergency Medical Services, Edmonton Metro); Wayne Tymchak (University of Alberta); 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 ably supported though 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 paramedics 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 the 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

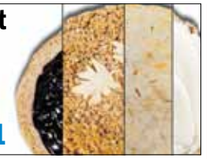
On September 27, 2011, Edmonton media were invited to see how the PROACT project puts a hospital laboratory into local ambulances, allowing patients with acute heart problems to receive a faster diagnosis and timelier treatment. Ten media outlets were in attendance as CVC faculty and staff answered questions and demonstrated the in-ambulance blood testing devices.

- From CBC news:
  http://www.cbc.ca/news/canada/edmonton/story/2011/09/27/edmonton-heart-attack-ambulance.html
- From The Edmonton Journal:
  See article on next page.
- Additional information in an international registry of clinical trials:
  http://clinicaltrials.gov/ct2/show/NCT01634425

EDMONTON JOURNAL

Arena vote expected by end of October / A3, A5

Pie contest headed for sweet finale
FOOD / E1



ESTABLISHED 1903 Breaking news at edmontonjournal.com * * WEDNESDAY, SEPTEMBER 28, 2011

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

JODIE SINNEMA
Journal Staff Writer
EDMONTON

With one drop of blood taken and tested in the back of an ambulance, University of Alberta researchers are hoping to transform care for heart patients across the country and abroad.

The researchers, led by cardiologist Dr. Paul Armstrong, are moving small diagnostic laboratories into 25 Edmonton ambulances to determine if a simple blood test done in the field could hasten treatment and save the lives of those having heart failure or a "silent" heart attack.

If the research proves successful, the new protocol could be expanded across Canada and beyond in the next two to three years to become the new way to treat some cardiac patients faster before they reach the hospital.

See AMBULANCE / A2

CANDACE ELLIOTT, THE JOURNAL

Dr. Robert Welsh, left; Dr. Paul Armstrong; Jannell Dawson, an emergency medical technician; and Dr. Justin Ezekowitz are working on a project that will examine new ways to treat patients suffering a heart attack or heart failure in an ambulance before they arrive at hospital.

INSIDE TODAY

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

AMBULANCE
Continued from A1

"We're changing the paradigm of care," said Armstrong, one of several cardiologists working with nurses, paramedics and others in this major trial. "If we can shave 55 to 60 minutes off the time we can get treatment in patients, we will save lives, we will shorten hospital stays and, of course, we would like to have our cake and eat it, too. Could this be cost effective in the end?"

Six years back, the same team enabled paramedics to do in-ambulance electrocardiograms that are beamed directly to the smartphone of an on-call doctor. That doctor can then diagnose a severe heart attack, when a blood clot has completely blocked the coronary artery and caused the heart muscle to die. With that diagnosis, the physician guides the ambulance team to immediately give a clot-busting drug to some patients instead of losing precious time driving to the hospital, then waiting for lab results. Other patients are delivered directly from the ambulance stretcher to the cardiac catheter lab, where a balloon is inserted into their artery to unplug the blockage.

The immediate, in-ambulance care for patients with severe heart attacks has saved one in 100 such patients, said Dr. Robert Welsh, a cardiologist who co-chairs the Vital Heart Protocol, developed here and now in place in different forms across Canada. Of the 750 people in central and northern Alberta who have these severe heart attacks, 250 to 300 are treated in the back of an ambulance.

The new research could help five times more patients: the 1,700 in the same catchment area who have acute heart failure each year and the 1,000 who suffer more mild heart attacks — sometimes called silent heart attacks, since the arteries are only partially blocked, limiting blood to a portion of the heart.

When such heart attacks occur, the heart emits markers that can be traced in one drop of blood.

During acute heart failure, the heart muscle stretches and sends out a hormone that can also be detected in the droplet.

During the first stage of the research, trained paramedics will deliver the confirmed lab results directly to the emergency doctor. That could save the 45 to 60 minutes it would normally take for a blood test to be done in the hospital, sent to a nearby lab and results delivered.

If that initial phase proves beneficial to patients, paramedics will then begin sending the blood results to an on-call physician via a smartphone. That physician can then guide the paramedic team to give treatment right away. Such heart attack patients can benefit from a substance that "puts grease on your platelets" to prevent worse clotting, Armstrong said.

Heart failure patients can be given something to reduce fluid in their lungs, thereby reducing the amount of work the heart has to do to pump blood.

The paramedics may also be counselled to drop off patients with milder heart attacks at the catheterization labs at the University or Royal Alexandra hospitals, where they would wait three to six hours to have a balloon inserted to clear the blockage. Normally, patients face a three- to four-day delay in hospital to access that lab, Welsh said.

He said overall, such expedited care could save the health system money by reducing hospital stays to two days for such patients instead of the usual five to seven.

"We know that if you treat people quickly, you can reduce their risk of dying by 60 to 70 per cent and you can also send them home without evidence of heart damage," Welsh said.

"If we succeed, these devices could easily go into ambulances across the province and across the country and, if it catches on, across the world. There's no reason this couldn't spread widely. It's an easy device to use."

The research project is funded with $225,000 from the University Hospital Foundation.

By mid-October, all 350 Edmonton-area paramedics will be trained on the device.

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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.

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.

Bueno H, Armstrong PW, Buxton MJ, Danchin N, Lubsen J, Roland E, Verheugt FW, Zalewski A, Jackson N, Komajda M, Steg PG on behalf of the Cardiovascular Round Table Clinical Trials ThinkTank participants The future of clinical trials in secondary prevention after acute coronary syndromes. Eur Heart J 2011 32: 1583-1589.

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 relative importance of each event but the likelihood that the recurrence of events is also of great clinical relevance. This article highlights how this methodology enhances the precision of outcome estimates and may lead to different and arguably more meaningful interpretation of the results. The relevance and importance of this approach was highlighted in the accompanying editorial by Kevin J. Anstrom, and Eric L. Eisenstein (Am Heart J 2011; 161:805=6). Importantly, this approach has now been incorporated in two upcoming trials.

Armstrong PW, Westerhout CM, Van de Werf F, Califf RM, Welsh RC, Wilcox RG, Bakal JA. Refining clinical trial composite outcomes: an application to the Assessment of the Safety and Efficacy of a New Thrombolytic-3 (ASSENT-3) trial. Am Heart J 2011; 161:848-54.

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.

Kaul P, McAlister FA, Ezekowitz JA, Bakal JA, Curtis LH, Quan H, Knudtson ML, Armstrong PW. Resource use in the last 6 months of life among patients with heart failure in Canada. Arch Int Med. 2011; 171(3):211-7

Effect of Nesiritide in Patients with Acute Decompensated Heart Failure

This first ever major trial of 7,500 patients with acute heart failure was key to CVC to developing a network of investigators across Canada interested in this crucially important, poorly understood and inadequately treated major clinical problem. Dr. Armstrong was privileged to be a member of the Executive Committee and Dr. Ezekowitz was the Canadian lead on the project and also responsible for developing some key mechanistic substudies that will enhance our understanding of patient care in this area and help drive the direction of future of research.

O'Connor CM, Starling RC, Hernandez AF, Armstrong PW, Dickstein K, Hasselblad V, Heizer GM, Komajda M, Massie BM, McMurray JJV, Nieminen MS, Reist CJ, Rouleau JL, Swedberg K, Adams KF Jr, Anker SD, Atar D, Battler A, Botero R, Bohidar NR, Butler J, Clausell N, Corbalán R, Costanzo MR, Dahlstrom U, Deckelbaum LI, Diaz R, Dunlap ME, Ezekowitz JA, Feldman D, Felker GM, Fonarow GC, Gennevois D, Gottlieb SS, Hill JA, Hollander JE, Howlett JG, Hudson MP, Kociol RD, Krum H, Laucevicius A, Levy WC, Méndez GF, Metra M, Mittal S, Oh BH, Pereira NL, Ponikowski P, Wilson WH, Tanomsup S, Teerlink JR, Triposkiadis F, Troughton RW, Voors AA, Whellan DJ, Zannad F, Califf RM. Effect of Nesiritide in Patients with Acute Decompensated Heart Failure. N Engl J Med 2011; 365:32-43 (accompanied by an editorial)

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).

Stebbins A, Mehta RH, Armstrong PW, Lee KL, Hamm C, Van de Werf F, James S, Toftegaard-Nielsen T, Seabra-Gomes R, White HD, Granger CB for the APEX AMI Investigators. 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. Circ Cardiovasc Interv.2010;3:414-422.

Peer Reviewed Publications 2011

1. Alherbish A, Charrois T, Ackman M, Tsuyuki R, Ezekowitz JA. **The prevalence of natural health product use in patients with acute cardiovascular disease.** PLoS-One 2011;6:e19623.

2. Al-Majed NS, Ezekowitz JA. **Cardiac resynchronisation therapy is efficacious in patients with mild heart failure symptoms.** Evid Based Med. 2011;16:138-139.

3. Al-Majed NS, McAlister FA, Bakal JA, Ezekowitz JA. **Meta-analysis: cardiac resynchronization therapy for patients with less symptomatic heart failure.** Ann Intern Med. 2011;154:401-412.

4. Armstrong PW, Boden WE. **Reperfusion paradox in ST-segment elevation myocardial infarction.** Ann Intern Med. 2011;155:389-391.

5. Armstrong PW, Westerhout CM, Van de Werf F, Califf RM, Welsh RC, Wilcox RG, Bakal JA. **Refining clinical trial composite outcomes: an application to the Assessment of the Safety and Efficacy of a New Thrombolytic-3 (ASSENT-3) trial.** Am Heart J. 2011;161:848-854.

6. Armstrong PW. **Aldosterone antagonists – last man standing?** N Engl J Med. 2011;364:79-80.

7. Bakal JA, Kaul P, Welsh RC, Johnstone D, Armstrong PW. **Determining the cost economic "Tipping Point" for the addition of a regional percutaneous coronary intervention facility.** Can J Cardiol. 2011;27:567-572.

8. Bueno H, Armstrong PW, Buxton MJ, Danchin N, Lubsen J, Roland E, Verheugt FW, Zalewski A, Jackson N, Komajda M, Steg PG on behalf of the Cardiovascular Round Table Clinical Trials ThinkTank participants . **The future of clinical trials in secondary prevention after acute coronary syndromes.** Eur Heart J. 2011;32:1583-1589.

9. Ezekowitz JA, Kaul, Bakal JA, Quan H, McAlister FA. **Trends in heart failure care: Has the incident diagnosis of heart failure shifted from the hospital to the emergency department and outpatient clinics?** Eur J Heart Fail. 2011;13:142-147.

10. French JK, Armstrong PW, Cohen E, Kleiman NS, O'Connor CM, Hellkamp AS, Stebbins A, Holmes DR, Hochman JS, Granger CB, Mahaffey KW (for APEX-AMI Investigators). **Cardiogenic shock and heart failure post–percutaneous coronary intervention in ST-elevation myocardial infarction: Observations from "Assessment of Pexelizumab in Acute Myocardial Infarction".** Am Heart J. 2011;162;89-97.

11. Gamble JM, Eurich 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.

12. Gharacholou SM, Lopes RD, Alexander KP, Mehta RH, Stebbins AL, Pieper KS, James SK, Armstrong PW, Granger CB. **Age and outcomes in ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention: Findings from the APEX-AMI Trial.** Arch Intern Med. 2011;171:559-567.

13. Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, Al-Khalidi HR, Ansell J, Atar D, Avezum A, Bahit MC, Diaz R, Easton JD, Ezekowitz JA, Flaker G, Garcia D, Geraldes M, Gersh BJ, Golitsyn S, Goto S, Hermosillo AG, Hohnloser SH, Horowitz J, Mohan P, Jansky P, Lewis BS, Lopez-Sendon JL, Pais P, Parkhomenko A, Verheugt FW, Zhu J, Wallentin L; the ARISTOTLE Committees and Investigators. **Apixaban versus warfarin in patients with atrial fibrillation.** N Engl J Med. 2011;365:981-992.

14. Hudson MP, Armstrong PW, O'Neill WW, Stebbins AL, Weaver WD, Widimsky P, Aylward PE, Ruzyllo W, Holmes D, Mahaffey KW, Granger CB. **Mortality implications of primary percutaneous coronary intervention treatment delays: Insights from the Assessment of Pexelizumab in Acute Myocardial Infarction Trial (APEX-AMI trial).** Circ Cardiovasc Qual Outcomes. 2011;4:183-192.

15. Huynh T, Birkhead J, Huber K, O'Loughlin J, Stenestrand U, Weston C, Jernberg T, Schull M, Welsh RC, Denktas AE, Travers A, Sookram S, Theroux P, Tu JV, Timmis A, Smalling R, Danchin N. **The pre-hospital fibrinolysis experience in Europe and North America and implications for wider dissemination.** JACC Cardiovasc Interv. 2011;4:877- 883.

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“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, collaborative 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 site network (more than 250 sites across Canada), comprised of over 440 principal investigators (PIs). A key indicator and metric of our operational success and our ability to deliver on our promise of quality to each of our stakeholders is our ability to recruit sites to participate in multiple, non-competing trials, and CVC is proud of the fact that over 200 PIs have participated in more than one clinical trial with CVC.

In 2011, the CVC provided project management, site management and monitoring for nine trials along with associated ancillary studies, some of which are Canadian driven and developed by our faculty. The Clinical Operations group, led by Tracy Temple, is comprised of experienced Project Leads, Site Management Coordinators, a monitoring lead, monitoring report reviewers and contracted monitors based regionally throughout the country.

Our Project Leads are responsible for managing and overseeing their projects in Canada, reporting internally to the Manager of Clinical Operations and reporting externally to 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, our 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 checks/ oversight 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 and 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 "Important Reference Documents on Conducting Clinical Research in Canada" was distributed to our entire Canadian site network (see appendix 4). The feedback has been very positive with the indication that this is an excellent resource.

A summary of the nine trials and associated ancillary studies the CVC provided Canadian clinical operations support for in 2011 are summarized in the following pages.

ASCEND-HF
Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure

Sponsored by Scios Inc, a Johnson & Johnson company, this phase III, randomized, double-blind, parallel-group, multicenter trial assessed the use of Nesiritide & standard treatment compared to placebo and standard treatment in patients with acute decompensated heart failure.

While ASCEND-HF completed enrollment and the results were presented in November 2010, the clinical operations work on the Canadian ancilliary and/or parallel studies associated with this project continued into 2011.

Dr. Ezekowitz was instrumental in the development and implementation of these ancillary and/or parallel studies, associated with the ASCEND-HF trial; (1) Respiratory Sub-study, (2) Climate Sub-study, (3) Early Process of Care/Registry Sub-study. Additionally, Padma Kaul, PhD, led the Canadian Health Economic ancillary study to examine the cost associated with the hospitalization of acute decompensated heart failure patients within Canada. These ancillary studies were further supplemented by a Canadian Heart Failure and Health Economic Registry, which retrospectively looked at the same patient population.

In August 2011, at the European Society of Cardiology Congress in Paris, France, Dr. Justin Ezekowitz's abstract for the Respiratory substudy "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.

EXSCEL
Exenatide Study of Cardiovascular Event Lowering

Sponsored by Amylin Pharmaceuticals, Inc. this trial is a pragmatic, long term, placebo-controlled, double-blinded trial which seeks to characterize the effects of Exenatide once weekly on cardiovascular(CV) -related outcomes in patients with type 2 diabetes when added to the current usual care for glycemic control in a standard care setting.

After some early delays, this study was approved by Health Canada and invitations were sent out to Canadian sites to determine their interest in December of 2011. Just over 1,600 patients have been enrolled globally with the majority from the United States. As we work through start up of 25 planned sites in Canada, an investigator training meeting will be planned and recruitment is expected to start in Canada in the second quarter of 2012.

The CVC is providing overall project management, site management and monitoring for EXSCEL. A unique collaboration has been established with Dr. Shaun Goodman, Associate Head of Cardiology at St. Michael's Hospital and Chair of the Department of Medicine at the University of Toronto as it relates to the operational aspects of this study. Dr. Goodman represents Canada as a thought leader and active member on the Operational Committee for the study. His operations team is collaborating on the site management responsibilities of this study with the CVC Clinical Operations Project Lead.

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 randomized. Canadian sites contributed a total of 1,106 subjects with 602 coming from sites managed by the CVC. Follow-up is currently expected to continue into 2014 as the trial accumulates the required events.

Dr. Armstrong is a member of the international Steering Committee. The CVC provides project management, site management and monitoring for over 30 Canadian sites.

PROACT

An Edmonton-region local initiative sponsored by the University Hospital Foundation and the Mazankowski 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.

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 (Penivacogin) 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 provided overall Canadian project management, site management and monitoring for the trial. Additionally, the CVC has worked closely with Dr. Christopher Buller, the Canadian member of the Steering Committee for this trial, who was based out of the Hamilton Health Sciences Centre at the time of this study.

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 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 enrollment 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 in Canada for this trial.

The CVC ECG Core Laboratory has been actively involved in the analysis 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 enrollment 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 issues/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 syndrome.

Following 30 months of recruitment, TRACER completed enrollment 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 NEXT GENERATION OF RESEARCHERS

"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, 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. To compare practice patterns and outcomes in Alberta with those in other Candian provices, we have acquired Canadian Institutes of Health Information 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 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. 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 groups such as Alliance for Canadian Health Outcomes Research in Diabetes (ACHORD) and the Alberta Kidney Disease Network (AKDN).

One of the major strengths of the CVC Outcomes group is its core of well-trained research personnel. We currently have three PhD biostatisticians, two analysts, and a database manager who are extremely well trained in linking clinical and administrative databases, developing and validating algorithms, conducting analyses, and identifying and developing new statistical methods for administrative data.

Selected Publications

1. **Van Diepen S,** Bakal J, McAlister FA, Ezekowitz JA. Mortality and re-admission of patients with heart failure, atrial fibrillation, or coronary artery disease undergoing non-cardiac surgery: An analysis of 38 047 patients. Circulation. 2011;124:289-296.
2. **Sandhu R,** Bakal J, Ezekowitz J and McAlister F. The epidemiology of atrial fibrillation in adults depends on locale of diagnosis. Am Heart J. 2011;161:986-992.
3. **Sandhu R,** Bakal J, Ezekowitz J and McAlister F. Risk stratification schemes, anticoagulation use and outcomes: the risk treatment paradox in newly diagnosed non-valvular atrial fibrillation. Heart. 2011;97:2046-2050.
4. Kaul P, Armstrong PW, Sookram S, Leung B, Brass N, Welsh RC. Temporal trends in patient and treatment delay among men and women presenting with ST-elevation myocardial infarction. Am Heart J. 2011;161:91-97.
5. **Gamble J-M,** Eurich 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.
6. Bakal JA, Kaul P, Welsh RC, Johnstone D, Armstrong PW. Determining the cost economic "Tipping Point" for the addition of a regional percutaneous coronary intervention facility. Can J Cardiol. 2011;27:567-572.

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(6):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 McAlister 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 clinics. They found that over this time period, an increasing number of patients were diagnosed as outpatients rather than in a hospital setting. (Eur J Heart Fail 2011;13(2):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, McAlister, 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)

ECG Core Laboratory

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 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 this procedure. The results of this process are then communicated to global investigative sites, providing timely feedback during the ongoing enrollment phase of the study.

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 6,085 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 (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 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.

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.

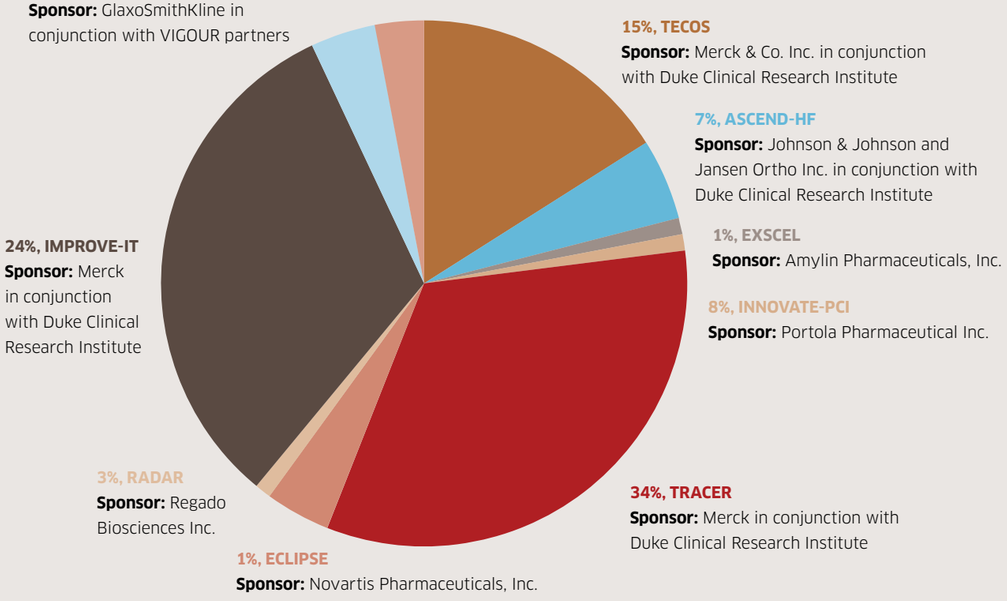
Also in 2011, additional in-house quality procedures were instituted. The core lab has a long history of assuring the accuracy and precision of ECG analysis through inter- and intra-reader variability and reliability testing, double data entry procedures, and hard copy and electronic storage and backup procedures. This year, with the assistance of the ECG readers and core lab assistants, detailed working processes were compiled for the STREAM study, ensuring that all staff follow the same procedures when dealing with important study information as well as assuring the audit preparedness of our lab.

Sources of Revenues

Clinical Trials

January - December 2011*
as % of Total Gross Trial Revenue

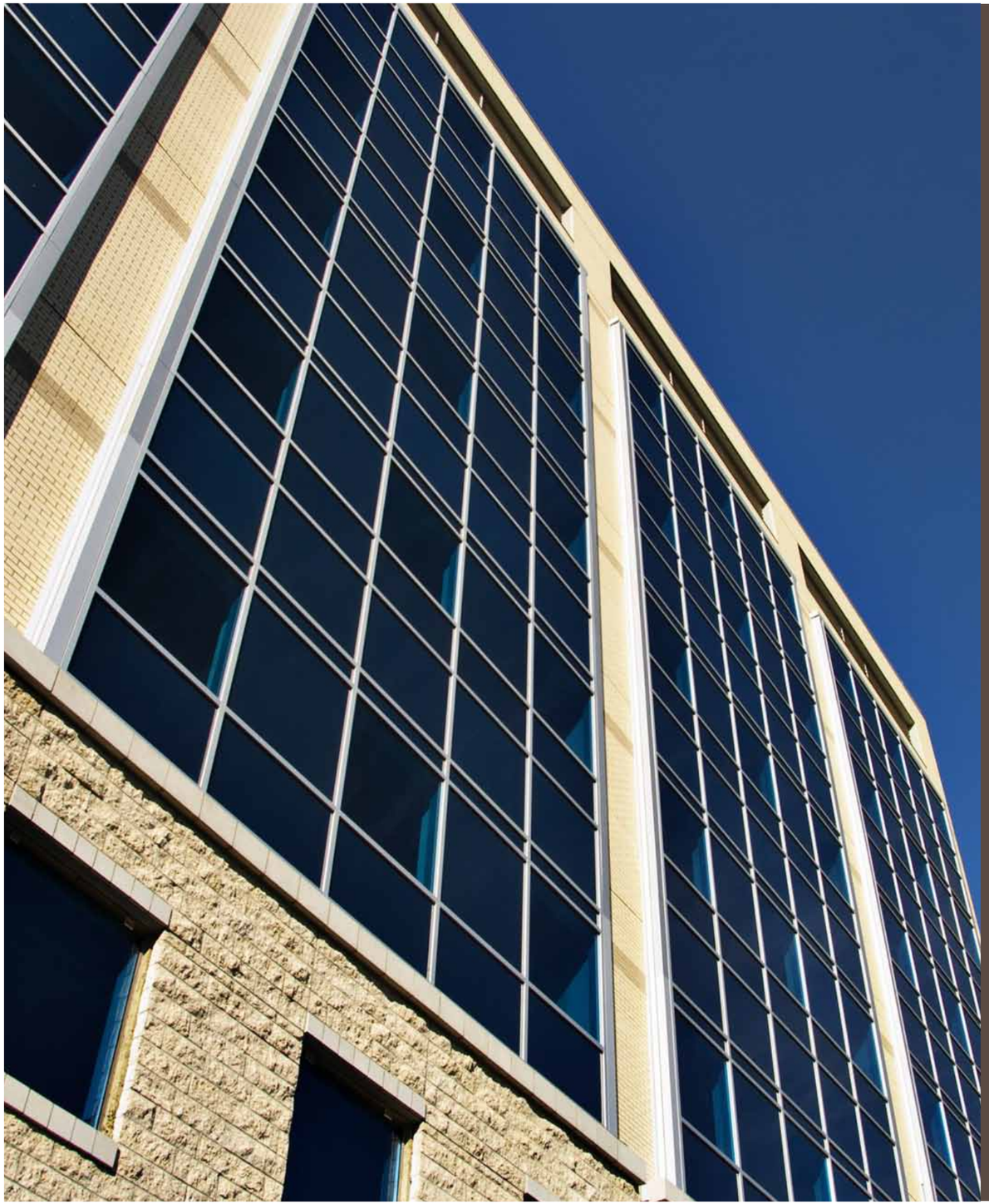
*In Canadian dollars, includes pass-throughs and exchange rate adjustments



Grants

(January - December 2011)

Project	Sponsor(s)	Grant Holders	Term
Providing Rapid Out of Hospital Acute Cardiovascular Treatment (PROACT)	Mazankowski Alberta Heart Institute and University Hospital Foundation	Paul Armstrong (PI), Justin Ezekowitz, Padma Kaul, Finlay McAlister, Robert Welsh	2010–2013
Tracking Gender Differences in Acute Coronary Syndromes: At the First Point of Care and Beyond	Canadian Institutes of Health Research	Padma Kaul (PI), Paul Armstrong, Michelle Graham, Colleen Norris, Robert Welsh	2008–2011
Team grant: Vascular complications associated with gestational diabetes mellitus in Alberta	Faculty of Medicine/Capital Health Emerging Research Team Grants Competition	E. Ryan (PI), Padma Kaul, S Davidge	2008–2011
Acute Heart Failure – Emergency Management	Canadian Institutes of Health Research	Justin Ezekowitz	2009 to 2012
Team Grant: Diastolic Heart Failure	Alberta Innovates- Health Solutions	Jason Dyck (PI), Todd Anderson, Justin Ezekowitz	2009–2014
Cardiac Chemoreceptors in Heart Failure	Heart and Stroke Foundation	Michael Stickland (PI), Justin Ezekowitz	2009–2012
Evaluating the impact of a Province Wide Disease Management Program on Heart Failure Outcomes in Alberta	Canadian Institutes of Health Research	Finlay A. McAlister (PI), Padma Kaul, Justin A Ezekowitz, H Quan	2010–2012



THE NEXT GENERATION OF RESEARCHERS

"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.

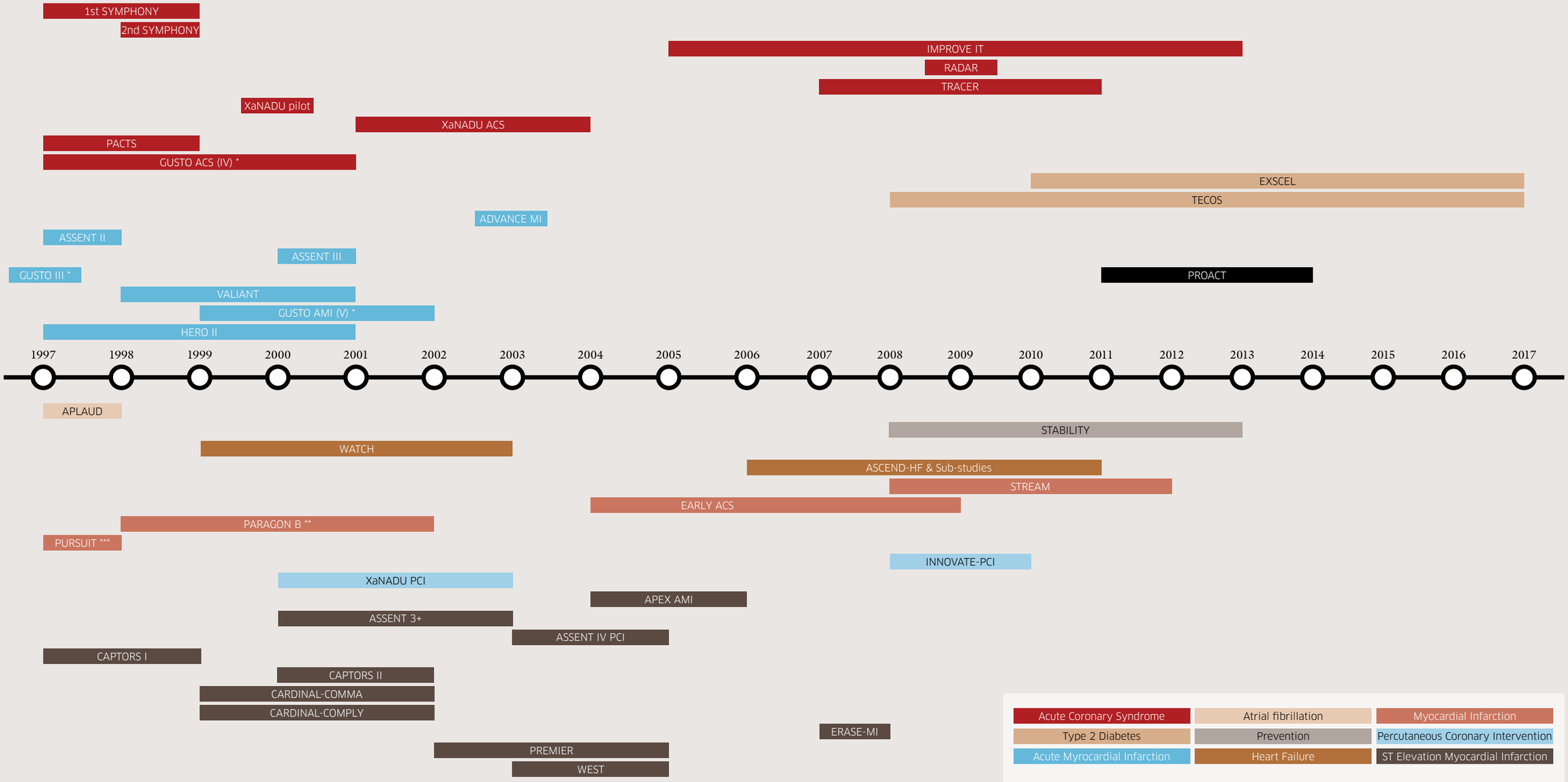
Frans Van de Werf, MD, PhD, Professor of Medicine, Chairman, Department of Cardiology, University Hospital Gasthuisberg and head Leuven Coordinating Centre (LCC), The University of Gasthuisberg, Leuven, Belgium

Lars Wallentin, MD, PhD, Professor of Cardiology, Institution 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

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 —

Faculty

Paul W. Armstrong, MD

Director, CVC
Distinguished University Professor, Division of Cardiology, University of Alberta

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.

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

Dr. Kaul is an epidemiologist and policy analyst by training and commits 75% of her time to research.

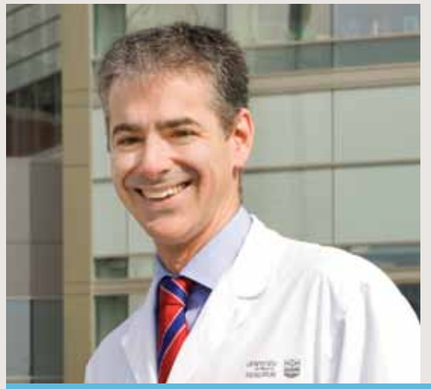
Her main research interests can be broadly classified into four areas:

- 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.

Faculty



Justin Ezekowitz, MBBCh, MSc

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 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.

Finlay A. McAllister, MSc, MD

Professor of Medicine, University of Alberta
Director, Patient Health Outcomes Research and Clinical Effectiveness Institute, University of Alberta
Senior Health Scholar, Alberta Innovates - Health Solutions (2010 - 2017)
Capital Health Chair in Cardiovascular Health Outcomes
Chair, Outcomes Research Task Force, Canadian Hypertension Education Program
Past-President, Canadian Society of Internal Medicine

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

- Outcomes research in hypertension, heart failure, perioperative 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.

Faculty

Robert Welsh, MD

Associate Professor, Division of Cardiology, University of Alberta
Interventional Cardiologist, Mazankowski Alberta Heart Institute
Director, Adult Cardiac Catheterization and Interventional Cardiology program
Co-Director, University of Alberta Chest Pain Program
Co-chair of Vital Heart Response
Co-chair of the Mazankowski TAVI program

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 (antithrombotic 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

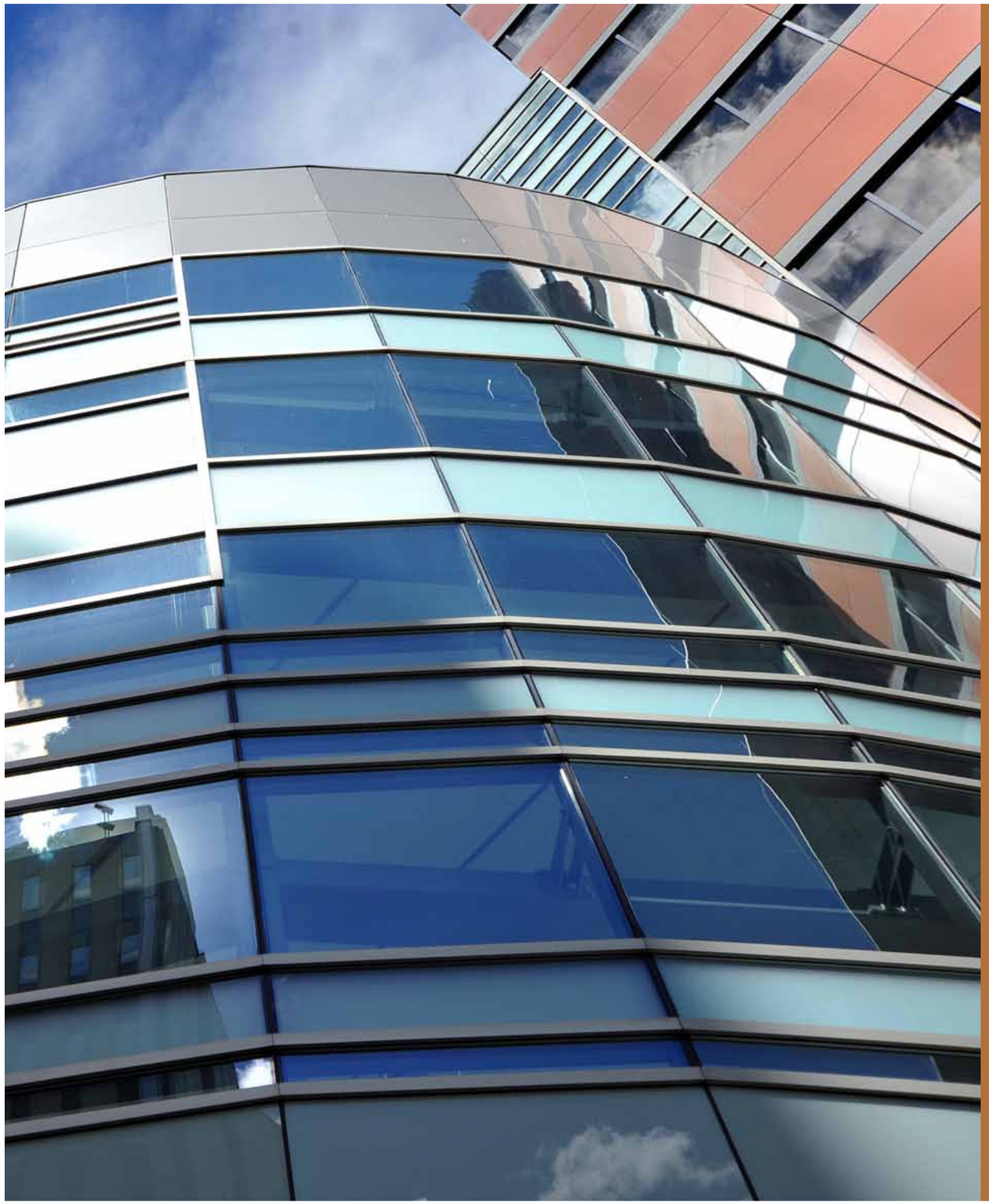
Hany Siha, MBBCh
Assistant Director, ECG Core Laboratory

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

Halina Nawrocki, RN
Lead Clinical Research Associate

Cynthia Westerhout, PhD
Assistant Director, Biostatistics

The CVC Team



THE NEXT GENERATION OF RESEARCHERS

"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 —

Appendices

Appendix 1
Media Clips

In the media

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

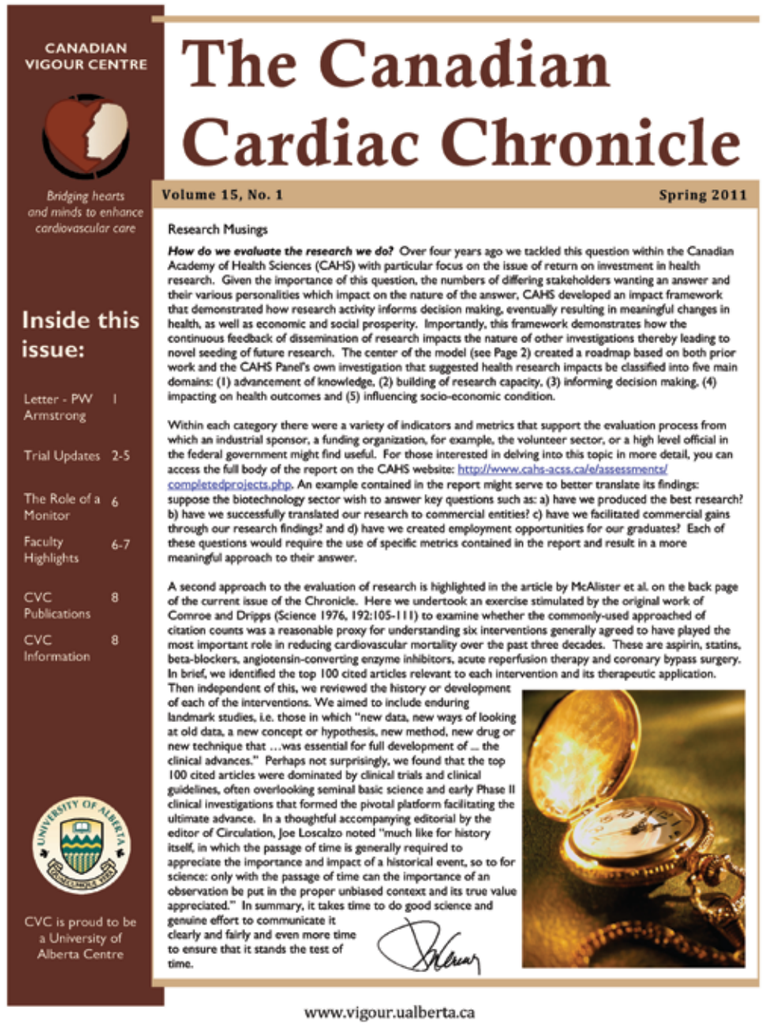
Hosted by Peter Mansbridge, this discussion among a panel of Canadian cardiovascular experts features CVC faculty members Dr. Paul Armstrong and Dr. Robert Welsh. Their overview examines how Canada is doing in the treatment of acute coronary syndromes and where improvement is needed with respect to time to treatment, drugs, equipment and facilities. View the full video session here: http://www.medscape.org/viewarticle/752383?src=0_mp_cmenl_0

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



CANADIAN VIGOUR CENTRE

Bridging hearts and minds to enhance cardiovascular care

Inside this issue:

CVC is proud to be a University of Alberta Centre

The Canadian Cardiac Chronicle

Volume 15, No. 1 Spring 2011

Research Musings

How do we evaluate the research we do? Over four years ago we tackled this question within the Canadian Academy of Health Sciences (CAHS) with particular focus on the issue of return on investment in health research. Given the importance of this question, the numbers of differing stakeholders wanting an answer and their various personalities which impact on the nature of the answer, CAHS developed an impact framework that demonstrated how research activity informs decision making, eventually resulting in meaningful changes in health, as well as economic and social prosperity. Importantly, this framework demonstrates how the continuous feedback of dissemination of research impacts the nature of other investigations thereby leading to novel seeding of future research. The center of the model (see Page 2) created a roadmap based on both prior work and the CAHS Panel's own investigation that suggested health research impacts be classified into five main domains: (1) advancement of knowledge, (2) building of research capacity, (3) informing decision making, (4) impacting on health outcomes and (5) influencing socio-economic condition.

Within each category there were a variety of indicators and metrics that support the evaluation process from which an industrial sponsor, a funding organization, for example, the volunteer sector, or a high level official in the federal government might find useful. For those interested in delving into this topic in more detail, you can access the full body of the report on the CAHS website: http://www.cahs-acss.ca/e/assessments/completedprojects.php. An example contained in the report might serve to better translate its findings: suppose the biotechnology sector wish to answer key questions such as: a) have we produced the best research? b) have we successfully translated our research to commercial entities? c) have we facilitated commercial gains through our research findings? and d) have we created employment opportunities for our graduates? Each of these questions would require the use of specific metrics contained in the report and result in a more meaningful approach to their answer.

A second approach to the evaluation of research is highlighted in the article by McAlister et al. on the back page of the current issue of the Chronicle. Here we undertook an exercise stimulated by the original work of Comroe and Dripps (Science 1976, 192:105-111) to examine whether the commonly-used approached of citation counts was a reasonable proxy for understanding six interventions generally agreed to have played the most important role in reducing cardiovascular mortality over the past three decades. These are aspirin, statins, beta-blockers, angiotensin-converting enzyme inhibitors, acute reperfusion therapy and coronary bypass surgery. In brief, we identified the top 100 cited articles relevant to each intervention and its therapeutic application. Then independent of this, we reviewed the history or development of each of the interventions. We aimed to include enduring landmark studies, i.e. those in which "new data, new ways of looking at old data, a new concept or hypothesis, new method, new drug or new technique that …was essential for full development of ... the clinical advances." Perhaps not surprisingly, we found that the top 100 cited articles were dominated by clinical trials and clinical guidelines, often overlooking seminal basic science and early Phase II clinical investigations that formed the pivotal platform facilitating the ultimate advance. In a thoughtful accompanying editorial by the editor of Circulation, Joe Loscalzo noted "much like for history itself, in which the passage of time is generally required to appreciate the importance and impact of a historical event, so to 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 summary, 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.

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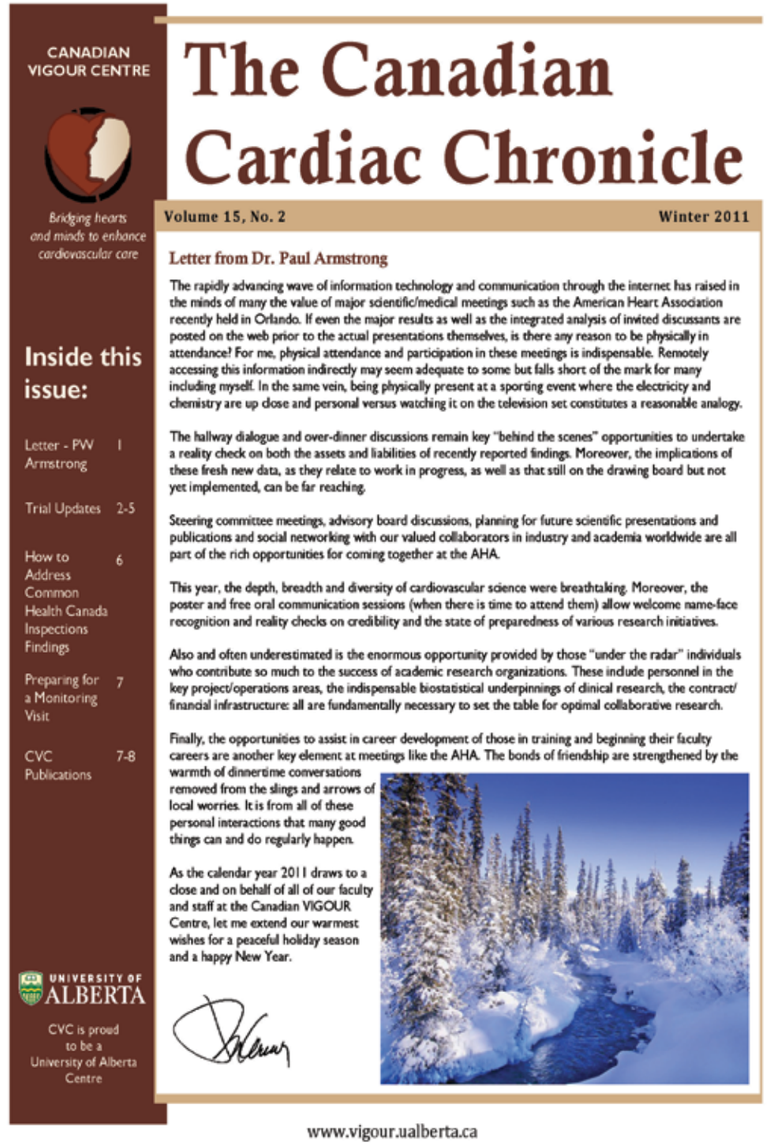


CANADIAN VIGOUR CENTRE

Bridging hearts and minds to enhance cardiovascular care

Inside this issue:

CVC is proud to be a University of Alberta Centre

The Canadian Cardiac Chronicle

Volume 15, No. 2 Winter 2011

Letter from Dr. Paul Armstrong

The rapidly advancing wave of information technology and communication through the internet has raised in the minds of many the value of major scientific/medical meetings such as the American Heart Association recently held in Orlando. If even the major results as well as the integrated analysis of invited discussants are posted on the web prior to the actual presentations themselves, is there any reason to be physically in attendance? For me, physical attendance and participation in these meetings is indispensable. Remotely accessing this information indirectly may seem adequate to some but falls short of the mark for many including myself. In the same vein, being physically present at a sporting event where the electricity and chemistry are up close and personal versus watching it on the television set constitutes a reasonable analogy.

The hallway dialogue and over-dinner discussions remain key "behind the scenes" opportunities to undertake a reality check on both the assets and liabilities of recently reported findings. Moreover, the implications of these fresh new data, as they relate to work in progress, as well as that still on the drawing board but not yet implemented, can be far reaching.

Steering committee meetings, advisory board discussions, planning for future scientific presentations and publications and social networking with our valued collaborators in industry and academia worldwide are all part of the rich opportunities for coming together at the AHA.

This year, the depth, breadth and diversity of cardiovascular science were breathtaking. Moreover, the poster and free oral communication sessions (when there is time to attend them) allow welcome name-face recognition and reality checks on credibility and the state of preparedness of various research initiatives.

Also and often underestimated is the enormous opportunity provided by those "under the radar" individuals who contribute so much to the success of academic research organizations. These include personnel in the key project/operations areas, the indispensable biostatistical underpinnings of clinical research, the contract/financial infrastructure: all are fundamentally necessary to set the table for optimal collaborative research.

Finally, the opportunities to assist in career development of those in training and beginning their faculty careers are another key element at meetings like the AHA. The bonds of friendship are strengthened by the warmth of dinnertime conversations removed from the slings and arrows of local worries. It is from all of these personal interactions that many good things can and do regularly happen.

As the calendar year 2011 draws to a close and on behalf of all of our faculty and staff at the Canadian VIGOUR Centre, let me extend our warmest wishes for a peaceful holiday season and a happy New Year.

www.vigour.ualberta.ca

Appendix 3

Beyond 2000

Appendix 4

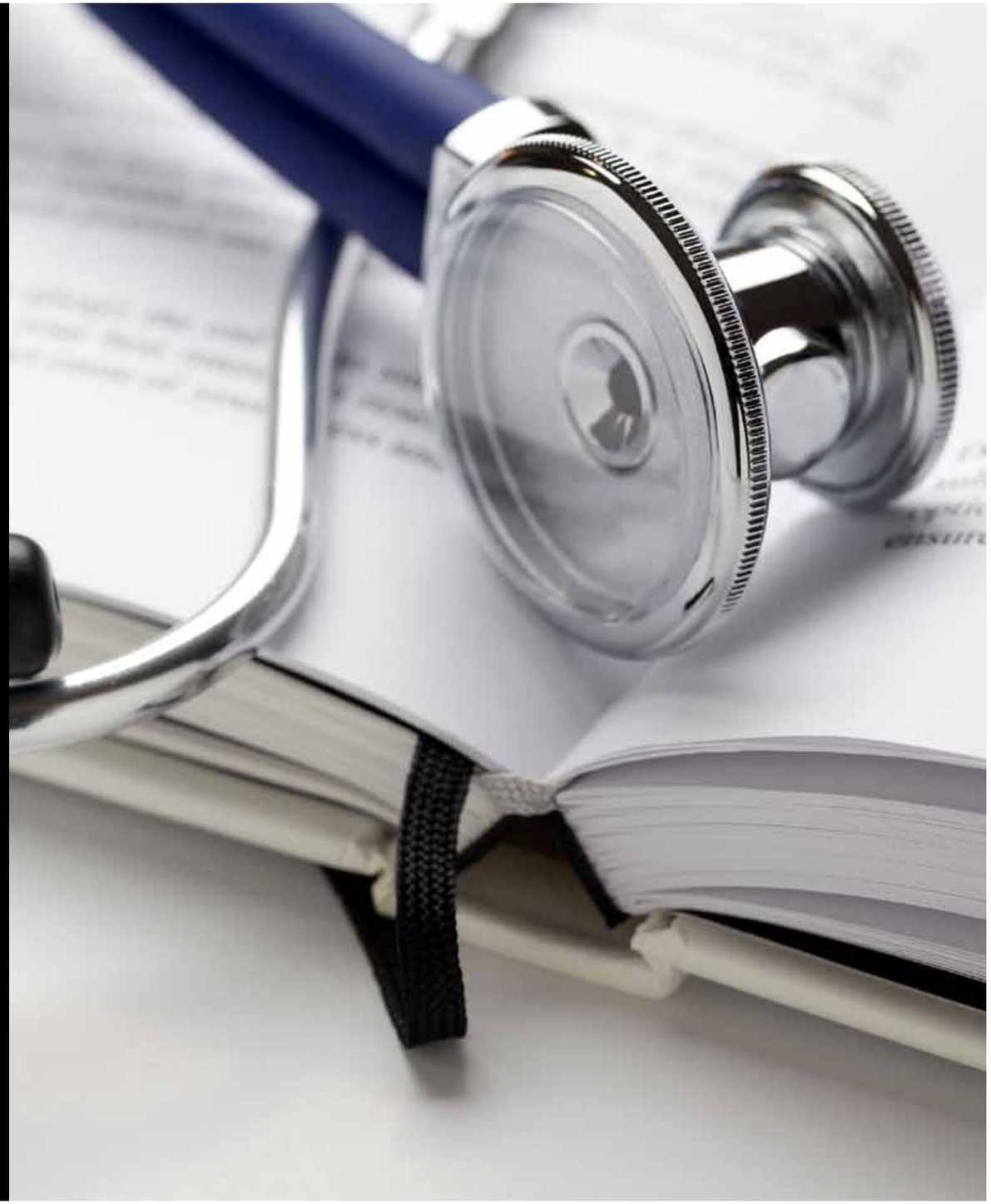
Important reference documents on Conducting Clinical Research in Canada

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;
- Dianne Payeur and Carla Price for their time and dedication required to produce this report;
- Kathy Watts and Bryan MacNeill 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.



UNIVERSITY OF ALBERTA

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