THE CANADIAN VIGOUR CENTRE

2015 Annual Report

The pulse
of promise.

The beat
of progress.

Table of Contents

Message from the Founding Director

Welcome to our 2015 annual report. Since the dawn of civilization, the creative elements of the human spirit have ensured the survival of the species. Hence adaptability has been an overarching feature of organizations "built to last" as so elegantly characterized by Jim Collins, the incisive management guru who also gave us the inspiring book *Good to Great*. In that book, a great organization is defined as … "one that delivers superior performance and makes a distinctive impact over a long period of time". In his essay on the Social Sectors that addresses this subject he reminds us that, unlike the profit-driven modus operandi of a business, the vision and mission are what drives the resource engine of not-for-profit organizations such as the Canadian VIGOUR Centre housed within the University of Alberta.

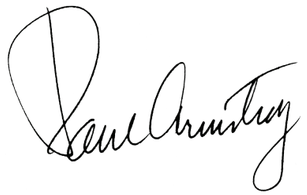
As you peruse the contents of this report you will note that we aspire to be a great organization. We focus herein on the creative achievements of our group that generate wealth in the broadest sense of the word. In that regard and as a learning organization, we subscribe to the insightful observations of Jim Rohn, a motivator/entrepreneur who said "Learning is the beginning of wealth. Learning is the beginning of health……Searching and learning is where the miracle process all begins." This quotation, like others that decorate our annual report, are meant to inspire us and we hope they do the same for our readers. Such captivating ideas from those who have gone before us illuminate our path forward and have now become part of a weekly tradition appearing on our internal website. Thirst for innovation is what begets learning. We at CVC understand that the status quo is unacceptable if we are to achieve our mission of enhancing cardiovascular health for current and future generations.

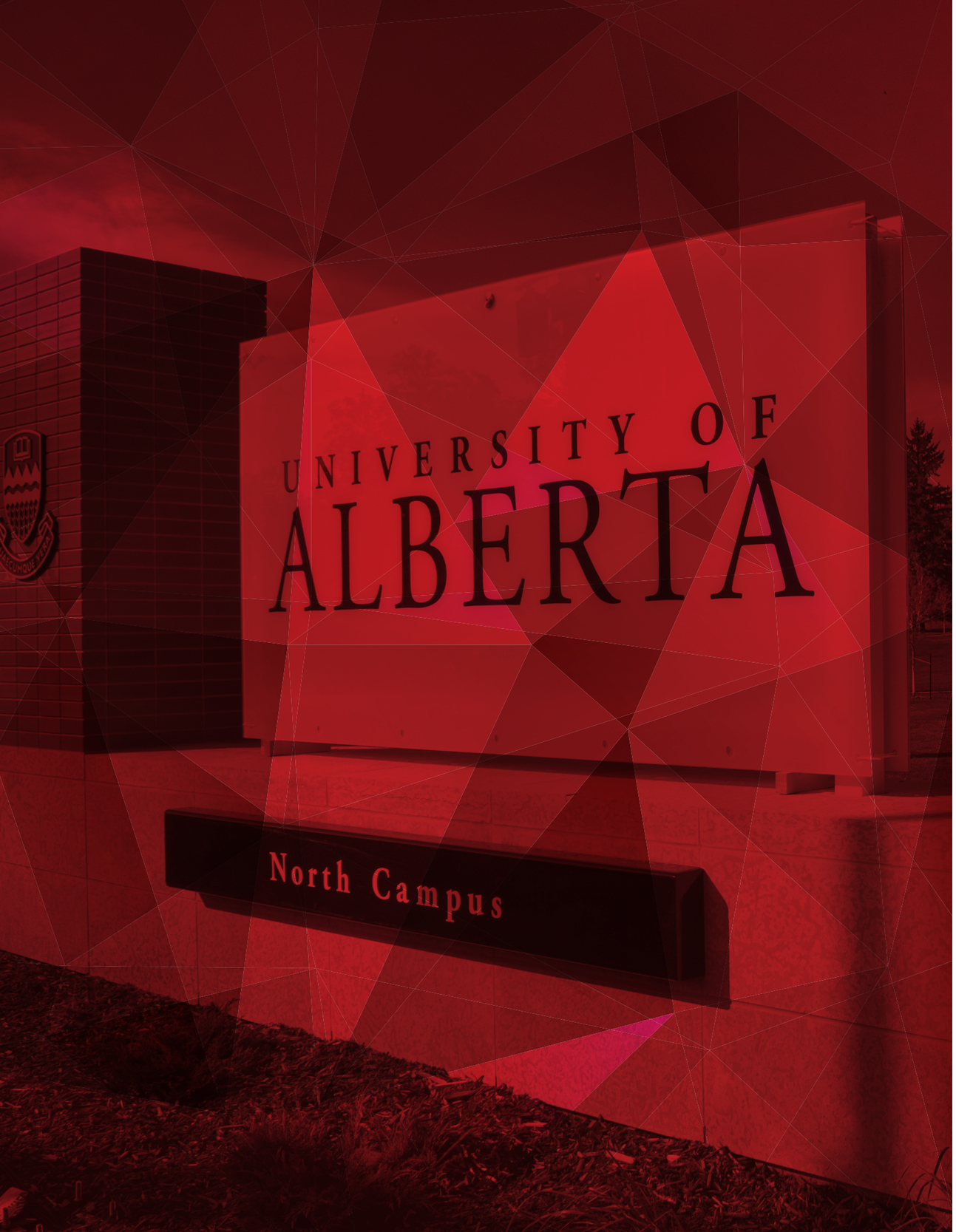
Our outstanding team is energetically committed to the CVC's vision and the goals as contained within our organizational compass depicted on page nine of this report. For me, this team represents family. As I listen to what they value about the CVC, it reflects the nobility of our cause of advancing CV care & health. They also know we will be responsive to their needs and ideas, and ensure that as individuals they can grow their careers and be part of an environment where there is an unquenchable thirst for innovation

At CVC we create "wealth" in several ways:

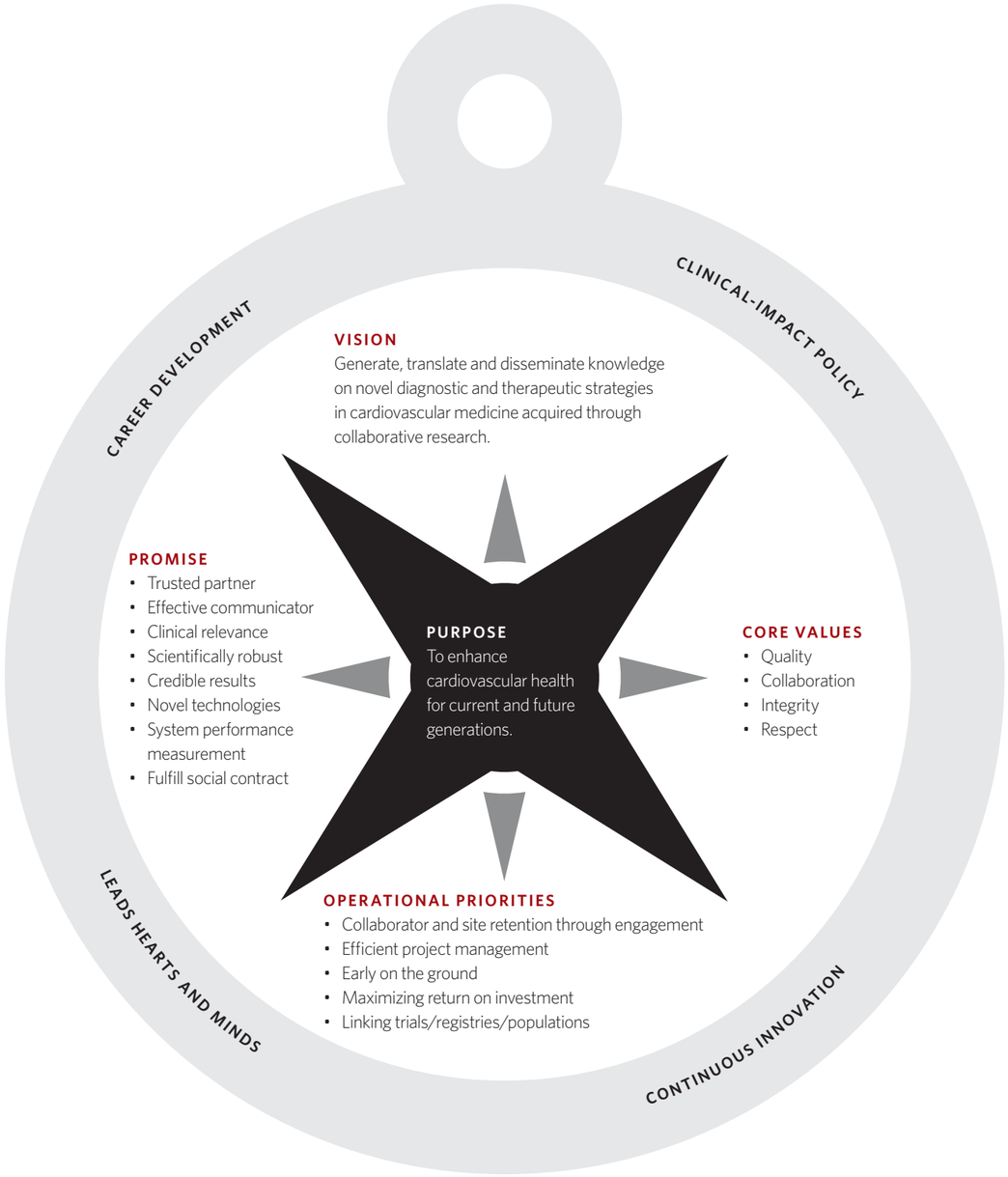
- Generating, translating and disseminating knowledge that influences the thoughts and actions of others through discovery of better ways to diagnose, treat and prevent cardiovascular disease.
- Evaluating how new approaches are incorporated into health care by performing registries that shine light on patterns of local and regional practices
- Understanding the lessons from large population health outcomes in Alberta that inform us whether outcomes that matter to our patients and citizens are headed in the right direction. Access to such data is critical for the work of CVC faculty members Padma Kaul and Finlay McAllister, which facilitates broad collaborative insights.
- Our faculty of thought leaders, biostatisticians and analysts, project leads and field monitors all contribute to our productivity so we can be an integral part of a learning health care system.
- The stellar reputation of our faculty and their track record of mentoring and training the next generation of health care professionals ensures that a steady stream of young bright minds come to learn along with us in our quest.
- Our finance and communications group are vital in ensuring we share our message through cataloguing the impressive and wide ranging list of peer reviewed publications, medical education events, quarterly Chronicles, and research colloquia we provide and which are highlighted not only in our annual report but also on our web site, www.vigour.ualberta.ca that we invite you to visit.
- Finally, at CVC we create and develop careers, provide and contract a diverse set of services and contribute substantially to our partners at the Northern Alberta Clinical Trials Research Centre for broader research investment.

We hope you enjoy reading more about who we are and what we do in the pages herein. We appreciate your interest and the support of so many friends and colleagues who make it possible for us to succeed.




UNIVERSITY OF
ALBERTA
North Campus

Compass


CAREER DEVELOPMENT
CLINICAL-IMPACT POLICY
LEADS HEARTS AND MINDS
CONTINUOUS INNOVATION
VISION
Generate, translate and disseminate knowledge on novel diagnostic and therapeutic strategies in cardiovascular medicine acquired through collaborative research.
PROMISE
• Trusted partner
• Effective communicator
• Clinical relevance
• Scientifically robust
• Credible results
• Novel technologies
• System performance measurement
• Fulfill social contract
PURPOSE
To enhance cardiovascular health for current and future generations.
CORE VALUES
• Quality
• Collaboration
• Integrity
• Respect
OPERATIONAL PRIORITIES
• Collaborator and site retention through engagement
• Efficient project management
• Early on the ground
• Maximizing return on investment
• Linking trials/registries/populations

Vision, Mission, Core Values

VISION

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

MISSION

Aligned with the University of Alberta and the Mazankowski Alberta Heart Institute (MAHI), our mission is to:

- Design, conduct, analyze and disseminate findings arising from novel clinical research
- Interrogate clinical trial, registry and population health data to evaluate outcomes, identify unmet needs and inform future basic and clinical research directions
- Identify, inspire and nurture the next generation of health researchers and professionals.

CORE VALUES

Quality
Aspire to the highest standard of work while respecting a balanced life perspective. Attract, mentor and retain high quality colleagues and collaborators with similar core values.

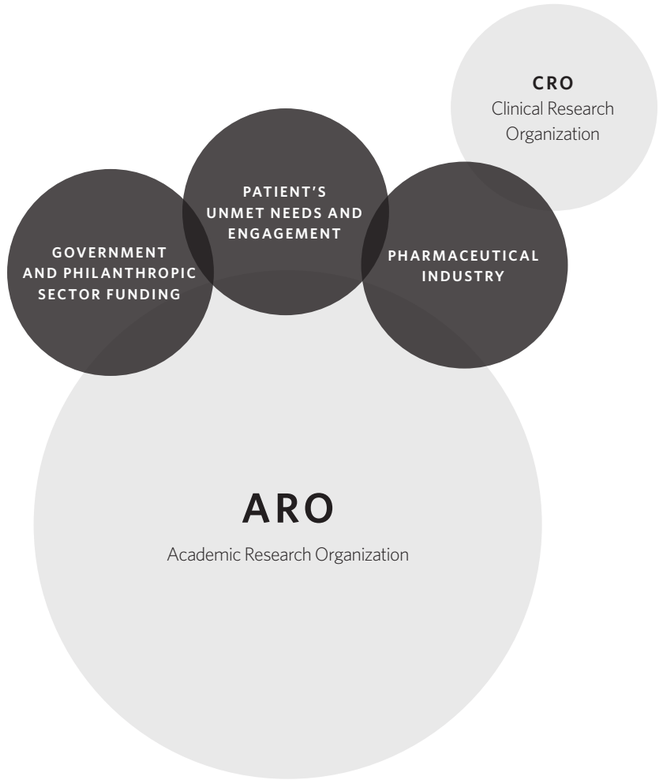
Collaboration
Promote and support an outstanding team that integrates a diversity of knowledge, experience, ideas, and skills supportive of our mission/vision.

Integrity
Perform our roles in an ethical framework which enhances our reputation an 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.

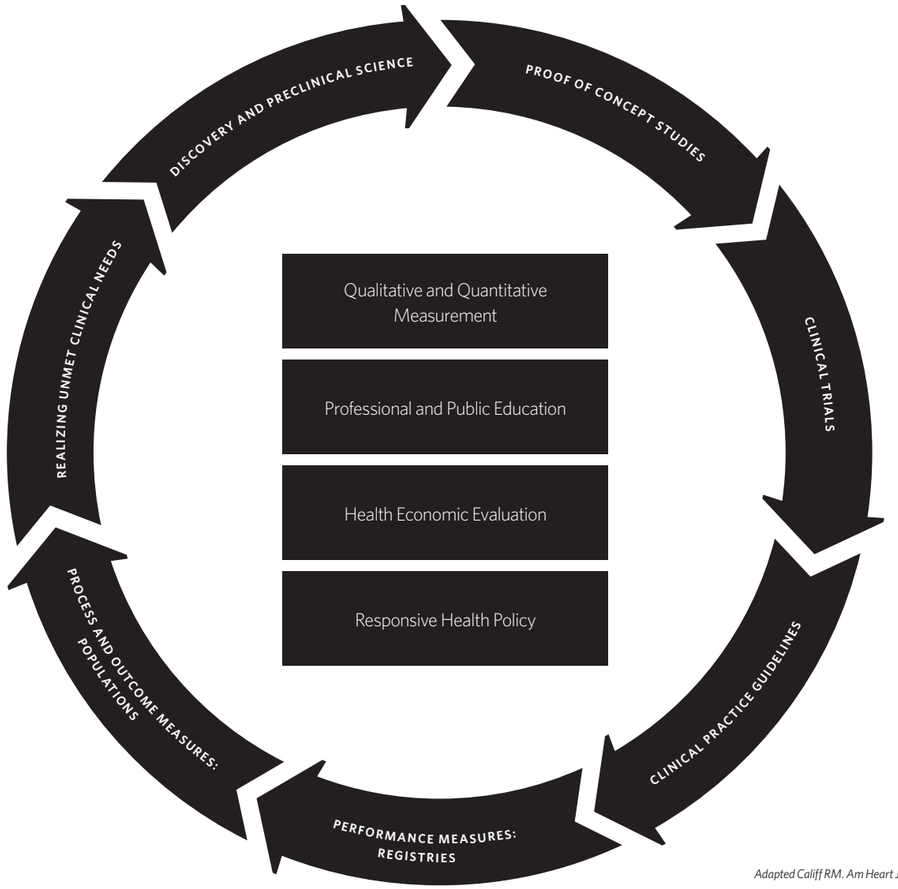
The Value Proposition of an ARO

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



Cycle of Quality

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



Adapted Califf RM. Am Heart J 2008

Our Year in Review

55

Publications that CVC's body of research produced

124

Principal Investigators participating in CVC managed trials

196

On-site monitoring visits that occurred in Canada

136

Global users accessing CVC's online collaborative platform

11

Industry and grant funded clinical trials underway

4,209

ECGs analyzed by CVC

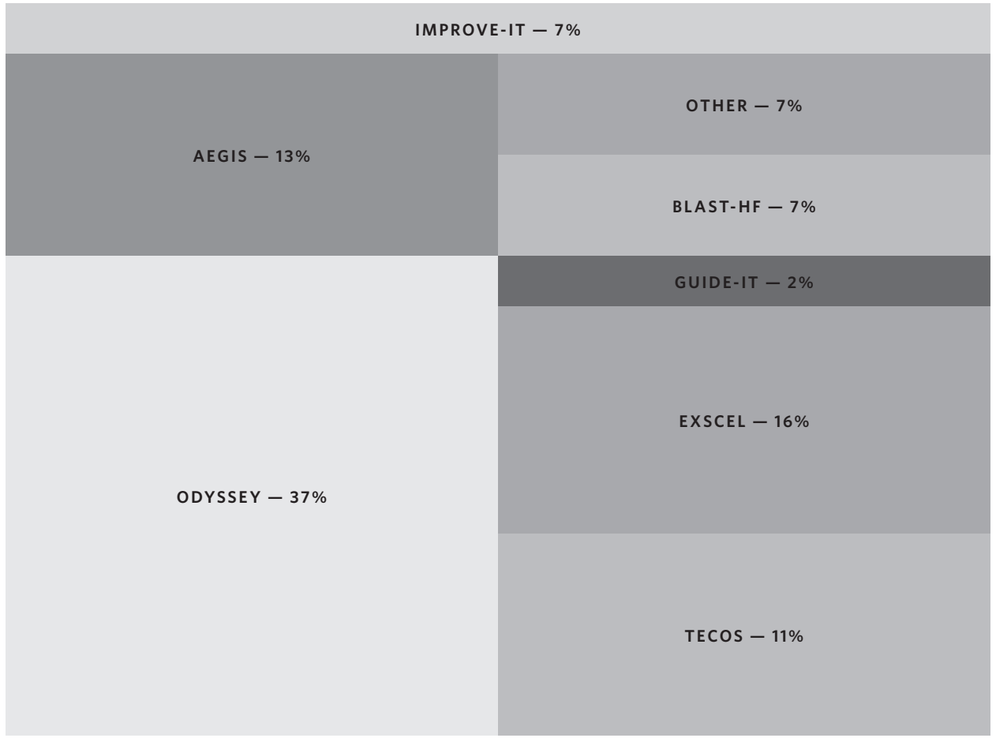
900,000+

Size of data repository reflecting health of Albertans with cardiovascular disease

Financial Summary

REVENUES FROM INDUSTRY-SPONSORED CLINICAL TRIALS AND EXPENSE RECOVERY

JANUARY 1, 2015 — DECEMBER 31, 2015



"An investment in knowledge pays the best interest."

—BENJAMIN FRANKLIN

Grants

PROJECT	SPONSOR(S)	GRANT HOLDERS	TERM	TOTAL GRANTED (CAD)
Providing Rapid Out of Hospital Acute Cardiovascular Treatment (PROACT-4)	Heart and Stroke Foundation	Justin Ezekowitz (PI) Padma Kaul Robert Welsh	2014-2017	$233,000
SODIUM HF	Canadian Institutes of Health Research	Justin Ezekowitz (PI)	2013-2017	$698,301
	University Hospital Foundation	Justin Ezekowitz (PI)	2015-2017	$200,000
Gestational Diabetes Mellitus (GDM) in Alberta	Canadian Institutes of Health Research	Padma Kaul (PI)	2014-2017	$278,139
HiLo-HF	Heart and Stroke Foundation	Justin Ezekowitz (PI)	2015-2016	$45,000
Identifying hospitalized heart failure patients who require a critical care admission	Heart and Stroke Foundation	Sean Van Diepen (PI) Justin Ezekowitz Padma Kaul Finlay McAlister Cynthia Westerhout	2015-2016	$42,000
Provincial and National Costs of Unnecessary Coronary Intensive Care Unit Admissions	University Hospital Foundation Medical Research Competition (UHFMRC)	Sean Van Diepen (PI) Justin Ezekowitz Padma Kaul Finlay McAlister David Zygun	2015	$29,975

Featured Publications

AHJ American Heart Journal

INCORPORATING PATIENT PREFERENCES INTO CLINICAL TRIAL DESIGN: RESULTS OF THE OPINIONS OF PATIENTS ON TREATMENT IMPLICATIONS OF NEW STUDIES (OPTIONS) PROJECT.

This study was our first effort at engaging patients in acquiring their perceptions on the importance of the various cardiovascular outcomes and complications of treatments that are commonly studied in clinical research trials. We used established interview administered surveys that included rating ranking, point allocation and tradeoff exercises in 52 adults. These were patients drawn from the outpatient clinical practices of cardiology colleagues at the University of Alberta Hospital. We were able to establish how they perceived different cardiovascular outcomes that follow a heart attack such as shock, heart failure, and recurrent heart attack. We then asked them to what extent they would be willing to accept a risk of bleeding and intracranial hemorrhage to reduce these consequences of heart attack. Because these "tradeoffs" are commonly undertaken by health professionals we were anxious to change the paradigm given we are entering an era when patient engagement and feedback in clinical care and research is increasingly important. This study is the first step on that new path and demonstrates its feasibility.

Outcomes, Health Policy and Managed Care

Incorporating patient preferences into clinical trial design: Results of the Opinions of Patients on Treatment Implications of New Studies (OPTIONS) project

Tania Stafinski, PhD,[a] Devidas Menon, PhD,[a] Alex Nardelli, MPH,[a] Jeff Bakal, PhD,[c] Justin Ezekowitz, MD,[c] Wayne Tymchak, MD,[b] Robert Welsh, MD,[c] Gabor Gyenes, MD,[b] and Paul W. Armstrong, MD[c] *Alberta, Canada*

Background Traditionally, clinical outcomes comprising composite end points in cardiovascular trials are assigned equal weights in statistical analyses. However, the importance of weighting outcomes according to their relative severity is now recognized. This study aimed to elicit patients' perceptions of the importance of cardiovascular outcomes and treatment complications and compare them with those of clinicians.

Methods and Results Interviewer-administered surveys, including rating, ranking, point-allocation and trade-off exercises, were conducted in 52 adults with confirmed coronary disease or previous myocardial infarction. Patients viewed "death" as the most severe cardiovascular outcome, followed by cardiogenic shock, congestive heart failure (CHF), and repeat myocardial infarction (re-MI), the same pattern observed in clinician responses in a previous study. Most patients were willing to accept a 3-fold increase in risk of systemic bleed (SB) or nonfatal intracranial hemorrhage (ICH) for a 20% reduction in risk of cardiogenic shock or 60% reduction in risk of CHF, but only a 2-fold increase in the risk of SB or ICH for a 20% reduction in risk of CHF or 60% reduction in risk of re-MI and no increase in risk of SB or ICH for a 20% reduction in risk of re-MI. Similar patterns were seen in a previous study of trade-offs in clinicians.

Conclusions Although patients' preferences appear to be comparable with those of clinicians, patients may be less willing than clinicians to tolerate potential treatment complications. The methods used in this study offer a feasible approach to incorporating patient preferences into cardiovascular trials and warrant further investigation in broader patient populations. (Am Heart J 2015;169:122-131.e22.)

Cardiovascular trials that compare different therapeutic interventions often consider several major clinical events, rather than a single outcome as the primary end point. These events, which include death, cardiogenic shock (CS), congestive heart failure (CHF), and nonfatal myocardial infarction (MI), may be combined to form a composite end point, where any one of them is counted as an end point. As a result, the event rate is increased, reducing the number of patients needed in a trial to detect a significant treatment effect. Although the use of composite end points in clinical trials has grown, they continue to generate debate among trialists.[1] This debate centers around the appropriateness of combining individual outcomes that vary widely in severity and difficulties in interpreting findings. However, in the case of cardiovascular trials, it has been argued that "death," "heart attack," and "stroke" are all "fairly grave."[2] Therefore, when measuring "time to first event" in such trials, the "first event" may be appropriately represented by any one of those comprising the composite end point. Furthermore, events receive the same weight because they are viewed as equally important. In recent years, this assumption has faced considerable criticism.[3] Although particular cardiovascular outcomes are all fairly grave, meaningful differences in their importance or seriousness compared with one another may still exist, and failure to capture those differences could lead to misinterpretations of trial findings.[4,5]

Early work exploring the relative importance of cardiovascular outcomes involved asking clinical trialists and health care providers to compare these outcomes using various methods, such as ranking, rating, and point allocation. The results showed that they were not of equal importance. For example, CS consistently received higher severity scores than CHF and MI (the gap was bigger for MI), suggesting that, when compared with CHF and MI, a reduction in its risk

From the [a]Health Technology & Policy Unit, School of Public Health, University of Alberta, Edmonton, Alberta, Canada, [b]Division of Cardiology, Mazankowski Heart Institute, University of Alberta, Edmonton, Alberta, Canada, and [c]Canadian VIGOUR Centre, University of Alberta, Edmonton, Alberta, Canada.

Submitted October 1, 2014; accepted October 1, 2014.

Reprint requests: Paul W. Armstrong, Canadian VIGOUR Centre, 2132 Li Ka Shing Centre for Health Research Innovation, University of Alberta, Edmonton, Alberta, Canada T6G 2E1.
E-mail: paul.armstrong@ualberta.ca

0002-8703

http://dx.doi.org/10.1016/j.ahj.2014.10.002

American Heart Association®
life is why™

VARIATION IN CRITICAL CARE UNIT ADMISSION RATES AND OUTCOMES FOR PATIENTS WITH ACUTE CORONARY SYNDROMES OR HEART FAILURE AMONG HIGH- AND LOW-VOLUME CARDIAC HOSPITALS.

Sean Van Diepen and other CVC colleagues have capitalized on access to Alberta Health Data in order to examine variations in critical care admission rates and outcomes on patients with two common and important entities, namely acute coronary syndromes and heart failure. They looked at "high and low volume" hospitals and carefully adjusted for comorbid conditions. They discovered that cardiac patients hospitalized in low volume hospitals were more frequently admitted to the critical care units of those institutions, had longer hospital stays despite lower and resource-intensive weighting, and concluded there were opportunities to standardize critical care utilization for these key entities. In our current health care system affected by increasing resource constraints, this type of research is especially helpful.

ORIGINAL RESEARCH

American Heart Association | American Stroke Association.

Variation in Critical Care Unit Admission Rates and Outcomes for Patients With Acute Coronary Syndromes or Heart Failure Among High- and Low-Volume Cardiac Hospitals

Sean van Diepen, MSc, MD; Jeffrey A. Bakal, PhD; Meng Lin, MSc; Padma Kaul, PhD; Finlay A. McAlister, MSc, MD; Justin A. Ezekowitz, MSc, MBBCh

***Background*—**Little is known about cross-hospital differences in critical care units admission rates and related resource utilization and outcomes among patients hospitalized with acute coronary syndromes (ACS) or heart failure (HF).

***Methods and Results*—**Using a population-based sample of 16 078 patients admitted to a critical care unit with a primary diagnosis of ACS (n=14 610) or HF (n=1467) between April 1, 2003 and March 31, 2013 in Alberta, Canada, we stratified hospitals into high (>250), medium (200 to 250), or low (<200) volume based on their annual volume of all ACS and HF hospitalization. The percentage of hospitalized patients admitted to critical care units varied across low, medium, and high-volume hospitals for both ACS and HF as follows: 77.9%, 81.3%, and 76.3% (P<0.001), and 18.0%, 16.3%, and 13.0% (P<0.001), respectively. Compared to low-volume units, critical care patients with ACS and HF admitted to high-volume hospitals had shorter mean critical care stays (56.6 versus 95.6 hours, P<0.001), more critical care procedures (1.9 versus 1.2 per patient, <0.001), and higher resource-intensive weighting (2.8 versus 1.5, P<0.001). No differences in in-hospital mortality (5.5% versus 6.2%, adjusted odds ratio 0.93; 95% CI, 0.61 to 1.41) were observed between high- and low-volume hospitals; however, 30-day cardiovascular readmissions (4.6% versus 6.8%, odds ratio 0.77; 95% CI, 0.60 to 0.99) and cardiovascular emergency-room visits (6.6% versus 9.5%, odds ratio 0.80; 95% CI, 0.69 to 0.94) were lower in high-volume compared to low-volume hospitals. Outcomes stratified by ACS or HF admission diagnosis were similar.

***Conclusions*—**Cardiac patients hospitalized in low-volume hospitals were more frequently admitted to critical care units and had longer hospitals stays despite lower resource-intensive weighting. These findings may provide opportunities to standardize critical care utilization for ACS and HF patients across high- and low-volume hospitals. **(*J Am Heart Assoc.* 2015;4: e001708 doi: 10.1161/JAHA.114.001708)**

Key Words: critical care • heart failure • acute coronary syndrome • hospital variation

Acute coronary syndromes (ACS) and decompensated heart failure (HF) are common hospital admission diagnoses, with 50% to 79% of ACS patients and 10% to 51% of HF patients being admitted to critical care units (CCU).[1–4] CCU beds comprise 5% to 10% of h.ospital beds in North America, but account for 20% to 35% of hospital costs.[5–7] A recent publication reported a wide variation between hospitals in the percentage of patients with HF who were triaged to the CCU in the United States.[8] Patients admitted to hospitals with the highest CCU admission rates were less likely to require critical care therapies (such as mechanical ventilation and intravenous vasoactive therapies), but there was no difference in in-hospital mortality. The authors hypothesized that in a for-profit healthcare system, the observed differences may have been due to economic considerations rather than patient considerations. However, an alternate hypothesis is that hospital expertise influences the decision to admit patients to critical-care areas. The lack of randomized trials supporting either individual interventions or management strategies that would require a CCU may contribute to considerable variation in clinical practice.

Canada has a single-payer not-for-profit healthcare system in which institutional economic considerations do not factor

From the Divisions of Cardiology (P.K., J.A.E.) and General Internal Medicine (F.A.M.), Department of Medicine, and Divisions of Critical Care and Cardiology (S.D.), and Canadian Vigour Center (S.D., J.A.B., M.L., P.K., F.A.M., J.A.E.), University of Alberta, Edmonton, Canada.

The interpretation and conclusions contained herein are those of the researchers and do not necessarily represent the views of the Government of Alberta. Neither the Government of Alberta nor the Alberta Health express any opinion in relation to this study.

Accompanying Figures S1 and S2 and Tables S1 through S5 are available at http://jaha.ahajournals.org/content/4/3/e001708/suppl/DC1

Correspondence to: Sean van Diepen, MSc, MD, 2C2 Cardiology Walter MacKenzie Center, University of Alberta Hospital, 8440-11 St. Edmonton, Alberta, Canada, T6G 2B7. E-mail: svp9@ualberta.ca

Received December 16, 2014; accepted February 5, 2015.

Featured Publications

American Heart Association®
life is why™

THE FUTURE OF CARDIOVASCULAR CLINICAL RESEARCH IN NORTH AMERICA AND BEYOND - ADDRESSING CHALLENGES AND LEVERAGING OPPORTUNITIES THROUGH UNIQUE ACADEMIC AND GRASSROOTS COLLABORATIONS.

In collaboration with our colleagues at the Duke Clinical Research Institute and Stanford University, we explored the threats and opportunities for the future conduct of clinical trials in North America. By focusing on the distinct and unique competencies of academic research organizations (AROs) such as the CVC, a series of strategies for best practices and optimization for future research has been defined. This sets a compelling path for us to move forward in this core function of our organization.

Curriculum in Cardiology

The future of cardiovascular clinical research in North America and beyond—addressing challenges and leveraging opportunities through unique academic and grassroots collaborations

Matthew T. Roe, MD, MHS,[a] Kenneth W. Mahaffey, MD,[b] Justin A. Ezekowitz, MBBCh, MSc,[c] John H. Alexander, MD, MHS,[a] Shaun G. Goodman, MD, MSc,[c,d] Adrian Hernandez, MD, MHS,[a] Tracy Temple, BScN, RN,[c] Lisa Berdan, PA, MHS,[a] Robert M. Califf, MD,[e] Robert A. Harrington, MD,[b] Eric D. Peterson, MD, MPH,[a] and Paul W. Armstrong, MD[c] *Durham, NC; Stanford, CA; Alberta, and Ontario, Canada*

Recent developments have highlighted the challenges facing cardiovascular clinical research in global contemporary practice, particularly in North America, including shifting priorities for drug development targets, increasing regulatory requirements, and expensive operational approaches for conducting randomized clinical trials. Nonetheless, emerging trends such as the consolidation of practices and hospitals into integrated health systems, the integration of electronic health records from thousands of practices into large data repositories to support prospective research studies, and streamlined operational approaches such as registry-based trials and risk-based monitoring have created numerous opportunities to disrupt the clinical research paradigm. Within this context, academic research organizations around the globe, particularly a strengthened collaboration of 3 established academic research organizations in North America, are uniquely positioned to promote and develop grassroots collaborations across all types of clinical practices, to delineate successful solutions to obstacles that limit clinical research initiatives, and to guide the future of cardiovascular research in the global research environment. (Am Heart J 2015;169:743-50.)

Almost 25 years ago, the first GUSTO clinical trial was conducted and set the then standard for large cardiovascular randomized controlled trials led from North America. Built by a loose confederation of global academic leaders, using a 3-page case report form and a grassroots network of thousands of clinical investigators, the GUSTO investigators enrolled close to 42,000 patients in just over 2 years, with most of the patients enrolled in North America.[1] This extraordinary effort not only delineated the superior reperfusion agent for acute ST-segment elevation myocardial infarction but also attracted many clinicians to incorporate clinical research into their daily practice and spawned well over 150 additional scientific publications that transformed our understanding of the pathophysiology, natural history, processes of care, impact of concomitant therapies, and international practice patterns for ST-segment elevation myocardial infarction. In addition, this unique clinical trial contributed to a significant expansion of cardiovascular academic collaborations across the globe that has been sustained for more than 2 decades.

Since then, the environment for cardiovascular clinical research has evolved considerably. On the positive side, advances in science have led to the discovery of thousands of molecules that have the potential to alter disease prognosis. In addition, technological innovations have significantly impacted the clinical research enterprise, accelerating evidence generation and providing unprecedented opportunities for new knowledge development, information exchange across all types of clinical practices, and the rapid dissemination and interpretation of study findings. However, repeated failures to move promising novel agents from the laboratory to the clinic likely reflect multiple causes including inadequate animal models of human disease, the challenge of building upon

From the [a]Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC, [b]Department of Medicine, Stanford University School of Medicine, Stanford, CA, [c]Canadian VIGOUR Centre, University of Alberta, Edmonton, Alberta, Canada, [d]Department of Medicine, University of Toronto, Toronto, Ontario, Canada, and [e]Duke Translational Medicine Institute, Duke University School of Medicine, Durham, NC.
James A de Lemos, MD, served as guest editor for this article.
Submitted November 12, 2014; accepted March 2, 2015.
Reprint requests: Matthew T. Roe, MD, MHS, 2400 Pratt St, Room 7035, Durham, NC 27705.
E-mail: matthew.roe@duke.edu
0002-8703

http://dx.doi.org/10.1016/j.ahj.2015.03.002

AHJ American Heart Journal

THE LONG-TERM EFFECTS OF DIETARY SODIUM RESTRICTION ON CLINICAL OUTCOMES IN PATIENTS WITH HEART FAILURE. THE SODIUM-HF (STUDY OF DIETARY INTERVENTION UNDER 100 MMOL IN HEART FAILURE): A PILOT STUDY.

Dietary sodium reduction in heart failure (HF) has been proposed and supported by multiple guidelines yet is based on little high-quality evidence; accordingly, there is a lack of consensus amongst guidelines on the recommended level of dietary sodium intake for patients with chronic HF. Justin Ezekowitz, Eloisa Colin-Ramirez and their colleagues completed a pilot randomized control trial (SODIUM-HF) and found that dietary sodium reduction in HF is feasible when an individualized and structured meal plan with close follow-up is provided to patients. Additionally, an achieved sodium intake less than 1500 mg/day at 6 months of follow-up was associated with reduced BNP levels, a surrogate prognostic marker, and improved quality of life in ambulatory patients with HF on optimal medical treatment. Larger randomized control trials with clinical outcomes as primary endpoints are required to support this recommendation and confirm a better prognosis associated to lower sodium intake in patients with HF.

Heart Failure

The long-term effects of dietary sodium restriction on clinical outcomes in patients with heart failure. The SODIUM-HF (Study of Dietary Intervention Under 100 mmol in Heart Failure): A pilot study

Eloisa Colin-Ramirez, BSc, PhD,[a,c] Finlay A. McAlister, MD, MSc,[b,c] Yinggan Zheng, MA, MEd,[c] Sangita Sharma, PhD,[a] Paul W. Armstrong, MD,[a,c,d] and Justin A. Ezekowitz, MBBCh, MSc[a,c,d,e] *Edmonton, Canada*

Aims To determine the feasibility of conducting a randomized controlled trial comparing a low-sodium to a moderate-sodium diet in heart failure (HF) patients.

Methods and Results Patients with HF (New York Heart Association classes II-III) were randomized to low (1500 mg/d) or moderate-sodium (2300 mg/d) diet. Dietary intake was evaluated using 3-day food records. The end points were changes in quality of life as measured by the Kansas City Cardiomyopathy Questionnaire (KCCQ) scores and B-type natriuretic peptide (BNP) levels from baseline to 6 months of follow-up presented as medians [25th, 75th percentiles]. Thirty-eight patients were enrolled (19/group). After 6 months, median sodium intake declined from 2137 to 1398 mg/d in the low-sodium and from 2678 to 1461 mg/d in the moderate-sodium diet group. Median BNP levels in the low-sodium diet group declined [216-71 pg/mL, $P = .006$), whereas in the moderate-sodium diet group, there was no change in BNP [171-188 pg/mL, $P = .7$; $P = .17$ between groups). For 6 months, median KCCQ clinical score increased in both groups [63-75 [$P = .006$] in the low-sodium diet group and 66-73 [$P = .07$] in the moderate-sodium group; $P = .4$ between groups). At 6 months, a post hoc analysis based on the dietary sodium intake achieved (> or ≤1500 mg/d) in all patients showed an association between a sodium intake ≤1500 mg/d and improvement in BNP levels and KCCQ scores.

Conclusions A dietary intervention restricting sodium intake was feasible, and achievement of this sodium goal was associated with lower BNP levels and improved quality of life in patients with HF. (Am Heart J 2015;169:274-281.e1.)

Chronic heart failure (HF) remains a major and growing public health problem. Approximately 1% to 2% of the adult population in developed countries have HF, with the prevalence rising to ≥10% among persons 70 years or older.[1] Despite advances in detection and treatment, HF carries a 5-year mortality rate of ~50% after diagnosis[2] and between 20% and 30% per year attend an emergency department or get hospitalized.[3] Pharmacologic and nonpharmacologic interventions that can further reduce morbidity and mortality for this important public health concern are clearly needed.

Heart failure is associated with neurohormonal activation and abnormalities in autonomic control that lead to sodium and water retention. Recognizing the importance of sodium balance in HF, it has been presumed that reducing dietary sodium intake in HF is a useful intervention.[4] However, observational[5-8] and experimental[9-17] studies evaluating the effects of sodium restriction in patients with HF have shown mixed results.[18] Accordingly, there is a lack of consensus among guidelines on the recommended level of dietary sodium intake for patients with chronic HF.[1,19-22]

We hypothesized that patients with HF after a low-sodium diet will have a reduction in B-type natriuretic peptide (BNP) levels and improvement in quality of life when compared with patients after a moderate-sodium diet. Accordingly, the ***main objective*** of this pilot study was to determine the feasibility of conducting a randomized controlled trial (RCT) comparing a low-sodium diet to a moderate-sodium diet. Secondarily, we explored whether there would be any changes in quality

From the [a]Medicine Department, University of Alberta, Edmonton, Canada, [b]Division of General Internal Medicine, University of Alberta, Edmonton, Canada, [c]Canadian VIGOUR Centre at the University of Alberta, Edmonton, Canada, [d]Division of Cardiology, University of Alberta, Edmonton, Canada, and [e]Heart Function Clinic, Division of Cardiology, University of Alberta, Edmonton, Canada.
Clinical Trial Identifier: Clinicaltrials.gov Identifier: NCT01480401.
Submitted September 12, 2014; accepted November 11, 2014.
Reprint requests: Justin A. Ezekowitz, MBBCh MSc, University of Alberta Hospital, 2C2 WMC, 8440-112 St, Edmonton, Alberta, Canada.
E-mail: joe2@ualberta.ca
0002-8703

http://dx.doi.org/10.1016/j.ahj.2014.11.013

Publications

AUTHORS	TITLE	JOURNAL
Butler CR, Savu A, Bakal JA, Toma M, Thompson R, Chow K, Wang H, Kim DH, Mengel M, Haykowsky M, Pearson GJ,Kaul P, Paternson I.	Correlation of cardiovascular magnetic resonance imaging findings and endomyocardial biopsy results in patients undergoing screening for heart transplant rejection.	*J Heart Lung Transplant.* 2015;34:643-650.
Abdel-Qadir H, Yan AT, Tan M, Borgia F, Piscione F, Di Mario C, Halvorsen S, Cantor WJ, Westerhout CM, Scheller B, Le May MR, Fernandez-Aviles F, Sánchez PL, Lee DS, Goodman SG.	Consistency of benefit from an early invasive strategy after fibrinolysis: a patient-level meta-analysis.	*Heart.* 2015;101:1554-1561.
Abualnaja S, Podder M, Hernandez AF, McMurray JJ, Starling RC, O'Connor CM, Califf RM, Armstrong PW, Ezekowitz JA.	Acute heart failure and atrial fibrillation: insights from the Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF) trial.	*J Am Heart Assoc.* 2015;4:e002092.
Al-Majed NS, Armstrong PW, Bakal JA, Hernandez AF, Ezekowitz JA.	Correlation between peak expiratory flow rate and NT-proBNP in patients with acute heart failure. An analysis from ASCEND-HF trial.	*Int J Cardiol.* 2015;182:184-186.
Armstrong PW.	The making of an author.	*Am Heart J.* 2015;169:446-447.
Bainey KR, Patel MR, Armstrong PW.	Evaluation of cardiac magnetic resonance as a surrogate in ST-segment elevation myocardial Infarction.	*Am J Cardiol.* 2015;115;1607-1614.
Clemmensen P, Roe MT, Hochman JS, Cyr DD, Neely ML, McGuire DK, Cornel JH, Huber K, Zamoryakhin D, White HD, Armstrong PW, Fox KA, Prabhakaran D, Ohman EM; TRILOGY ACS Investigators.	Long-term outcomes for women versus men with unstable angina/non-ST-segment elevation myocardial infarction managed medically without revascularization: insights from the targeted platelet inhibition to clarify the optimal strategy to medically manage acute coronary syndromes trial.	*Am Heart J.* 2015;170:695-705.
Colin-Ramirez E, Arcand J, Ezekowitz JA.	Estimates of dietary sodium consumption in patients with chronic heart failure.	*J Card Fail.* 2015;21:981-988.
Colin-Ramirez E, McAlister FA, Woo E, Wong N, Ezekowitz JA.	Association between self-reported adherence to a low-sodium diet and dietary habits related to sodium intake in heart failure patients.	*J Cardiovasc Nurs.* 2015;30:58-65.
Colin-Ramirez E, McAlister FA, Zheng Y, Sharma S, Armstrong PW, Ezekowitz JA.	The long-term effects of dietary sodium restriction on clinical outcomes in patients with heart failure. The SODIUM-HF (Study of Dietary Intervention Under 100 mmol in Heart Failure): A pilot study.	*Am Heart J.* 2015;169:274-281.

AUTHORS	TITLE	JOURNAL
Collins S, Storrow AB, Storrow AB, Albert N, Butler J, Ezekowitz JA, Felker GM, Fermann GJ, Fonarow GC, Givertz MM, Hiestand B, Hollander J, Lanfear D, Levy PD, Pang PS, Peacock WF, Sawyer DB, Teerlink J, Lenihan DJ.	Early management of patients with acute heart failure: state of the art and future directions: A consensus document from the SAEM / HFSA acute heart failure working group.	*Acad Emerg Med.* 2015;22:94-112.
Collins SP, Storrow AB, Levy PD, Albert N, Butler J, Ezekowitz JA, Felker GM, Fermann GJ, Fonarow GC, Givertz MM, Hiestand B, Hollander JE, Lanfear DE, Pang PS, Peacock WF, Sawyer DB, Teerlink JR, Lenihan DJ.	Early management of patients with acute heart failure: state of the art and future directions. A consensus document from the society of America acute heart failure working group.	*J Card Fail.* 2015;21:27-43.
Cornel JH, Tricoci P, Lokhnygina Y, Moliterno DJ, Wallentin L, Armstrong PW, Aylward PE, Clare RM, Chen E, Leonardi S, Van de Werf F, White HD, Held C, Strony J, Mahaffey KW, Harrington RA.	Glycoprotein iib/iiia receptor inhibitors in combination with vorapaxar, a platelet thrombin receptor antagonist, among patients with non-ST-segment elevation acute coronary syndromes (from the TRACER Trial).	*Am J Cardiol.* 2015;115:1325-1332.
Cowper PA, Pan W, Anstrom KJ, Kaul P, Wallentin L, Davidson-Ray L, Nikolic E, Janzon M, Levin LÅ, Cannon CP, Harrington RA, Mark DB.	Economic analysis of ticagrelor therapy from a U.S. perspective: results from the PLATO study.	*J Am Coll Cardiol.* 2015;65:465-476.
De Blois J, Kjellstrom T, Agewall S, Ezekowitz JA, Armstrong PW, Atar D.	The effects of climate change on cardiac health.	*Cardiology.* 2015;131:209-217.
DeVore AD, Hasselblad V, Mentz RJ, O'Connor CM, Armstrong PW, McMurray JJ, Ezekowitz JA, Tang WH, Starling RC, Voors AA, Califf RM, Hernandez AF.	Loop diuretic dose adjustments after a hospitalization for heart failure: insights from ASCEND-HF.	*Eur J Heart Fail.* 2015;17:340-346.
Ezekowitz JA, Welsh RC, Weiss D, Chan M, Keeble W, Khadour F, Sharma S, Tymchak W, Sookram S, Brass N, Knapp D, Koshy TL, Zheng Y, Armstrong PW.	Providing Rapid Out of hospital Acute Cardiovascular Treatment 4 (PROACT-4).	*J Am Heart Assoc.* 2015;4 pii:e002859.
Felker GM, Butler J, Collins SP, Cotter G, Davison BA, Ezekowitz JA, Filippatos G, Levy PD, Metra M, Ponikowski P, Soergel DG, Teerlink JR, Violin JD, Voors AA, Pang PS.	Heart failure therapeutics on the basis of a biased ligand of the angiotensin-2 type 1 receptor: rationale and design of the BLAST-AHF Study (Biased Ligand of the Angiotensin receptor Study in Acute Heart Failure).	*J Am Coll Cardiol Heart Fail.* 2015;3:193-201.

"The power of accurate observation is commonly called cynicism by those who have not got it." — GEORGE BERNARD SHAW

AUTHORS	TITLE	JOURNAL
Fordyce CB, Roe MT, Ahmad T, Libby P, Borer JS, Hiatt WR, Bristow MR, Packer M, Wasserman SM, Braunstein N, Pitt B, DeMets DL, Cooper-Arnold K, Armstrong PW, Berkowitz SD, Scott R, Prats J, Galis ZS, Stockbridge N, Peterson ED, Califf RM.	Cardiovascular drug development: Is it dead or just hibernating?	*J Am Coll Cardiol.* 2015;65:1567-1582.
Frolova N, Bakal JA, McAlister FA, Rowe BH, Quan H, Kaul P, Ezekowitz JA.	Assessing the use of international classification of diseases-10th revision codes from the emergency department for the identification of acute heart failure.	*JACC Heart Fail.* 2015;3:386-391.
Gershlick AH, Westerhout CM, Armstrong PW, Huber K, Halvorsen S, Steg PG, Ostojic M, Goldstein P, Carvalho AC, Van de Werf F, Wilcox RG.	Impact of a pharmacoinvasive strategy when delays to primary PCI are prolonged.	*Heart.* 2015;101:692-698.
Grodin JL, Perez AL, Wu Y, Hernandez AF, Butler J, Metra M, Felker GM, Voors AA, McMurray JJ, Armstrong PW, Califf RM, Starling RC, O'Connor CM, Tang WH.	Circulating kidney injury molecule-1 levels in acute heart failure: insights from the ASCEND-HF trial (Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure).	*JACC Heart Fail.* 2015;3:777-785.
Jolly SS, Cairns JA, Yusuf S, Meeks B, Pogue J, Rokoss MJ, Kedev S, Thabane L, Stankovic G, Moreno R, Gershlick A, Chowdhary S, Lavi S, Niemelä K, Steg PG, Bernat I, Xu Y, Cantor WJ, Overgaard CB, Naber CK, Cheema AN, Welsh RC, Bertrand OF, Avezum A, Bhindi R, Pancholy S, Rao SV, Natarajan MK, Ten Berg JM, Shestakovska O, Gao P, Widimsky P, Džavík V; TOTAL Investigators.	Randomized trial of primary PCI with or without routine manual thrombectomy.	*N Engl J Med.* 2015; 372:1389-1398.
Kaul P, Savu A, Nerenberg K, Donovan L, Chik C, Ryan E, Johnson J.	Impact of gestational diabetes mellitus and high maternal weight on the development of diabetes, hypertension and cardiovascular disease: a population-level analysis.	*Diabet Med.* 2015;32:164-173.
Kelly JP, Mentz RJ, Hasselblad V, Ezekowitz JA, Armstrong PW, Zannad F, Felker GM, Califf RM, O'Connor CM, Hernandez AF.	Worsening heart failure during hospitalization for acute heart failure: Insights from the Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF).	*Am Heart J.* 2015;170:298-305.

"Wonder is the beginning of wisdom."

— SOCRATES

AUTHORS	TITLE	JOURNAL
Khan R, Lopes RD, Neely ML, Stevens SR, Harrington RA, Diaz R, Cools F, Jansky P, Montalescot G, Atar D, Lopez-Sendon J, Flather M, Liaw D, Wallentin L, Alexander JH, Goodman SG; Apixaban for Prevention of Acute Ischemic Safety Events (APPRAISE)-2 Steering Committee and Investigators.	Characterising and predicting bleeding in high-risk patients with an acute coronary syndrome.	*Heart.* 2015;101:1475-1484.
Lincoff AM, Mehran R, Povsic TJ, Zelenkofske SL, Huang Z, Armstrong PW, Steg PG, Bode C, Cohen MG, Buller C, Laanmets P, Valgimigli M, Marandi T, Fridrich V, Cantor WJ, Merkely B, Lopez-Sendon J, Cornel JH, Kasprzak JD, Aschermann M, Guetta V, Morais J, Sinnaeve PR, Huber K, Stables R, Sellers MA, Borgman M, Glenn L, Levinson AI, Lopes RD, Hasselblad V, Becker RC, Alexander JH; REGULATE-PCI Investigators.	Effect of the REG1 anticoagulation system versus bivalirudin on outcomes after percutaneous coronary intervention (REGULATE-PCI): a randomised clinical trial.	*Lancet.* 2015;387:349-356.
Madan M, Halvorsen S, Di Mario C, Tan M, Westerhout CM, Cantor WJ, Le May MR, Borgia F, Piscione F, Scheller B, Armstrong PW, Fernandez-Aviles F, Sanchez PL, Graham JJ, Yan AT, Goodman SG.	Relationship between time to invasive assessment and clinical outcomes of patients undergoing an early invasive strategy after fibrinolysis for ST-segment elevation myocardial infarction: a patient-level analysis of the randomized early routine invasive clinical trials.	*JACC Cardiovasc Interv.* 2015;8:166-174.
McAlister FA, Jacka M, Graham M, Youngson E, Cembrowski G, Bagshaw SM, Pannu N, Townsend DR, Srinathan S, Alonso-Coello P, Devereaux PJ. J Thromb Haemost.	The prediction of postoperative stroke or death in patients with preoperative atrial fibrillation undergoing non-cardiac surgery: a VISION sub-study.	*J Thromb Haemost.* 2015;13:1768-1775.
McAlister FA, Youngson E, Bakal JA, Holroyd-Leduc J, Kassam N.	Physician experience and outcomes among patients admitted to general internal medicine teaching wards.	*CMAJ.* 2015;187:1041-1048.
McAlister FA, Youngson E, Padwal RS, Majumdar SR.	Similar outcomes among general medicine patients discharged on weekends.	*J Hosp Med.* 2015;10:69-74.
Mentz RJ, Hasselblad V, DeVore AD, Metra M, Voors AA, Armstrong PW, Ezekowitz JA, Tang WH, Schulte PJ, Anstrom KJ, Hernandez AF, Velazquez EJ, O'Connor CM.	Torsemide versus furosemide in patients with acute heart failure (from the ASCEND-HF Trial).	*Am J Cardiol.* 2015;117;404-411.

"You see things; you say, 'Why?' But I dream things that never were; and I say 'Why not?"

— GEORGE BERNARD SHAW

AUTHORS	TITLE	JOURNAL
Moe GW, Ezekowitz JA, O'Meara E, Lepage S, Howlett JG, Fremes S, Al-Hesayen A, Heckman GA, Abrams H, Ducharme A, Estrella-Holder E, Grzeslo A, Harkness K, Koshman SL, McDonald M, McKelvie R, Rajda M, Rao V, Swiggum E, Virani S, Zieroth S; Secondary Panel:, Arnold JM, Ashton T, D'Astous M, Chan M, De S, Dorian P, Giannetti N, Haddad H, Isaac DL, Kouz S, Leblanc M, Liu P, Ross HJ, Sussex B, White M.	The 2014 Canadian Cardiovascular Society Heart Failure Management Guidelines Focus Update: anemia, biomarkers, and recent therapeutic trial implications.	*Can J Cardiol.* 2015;31:3-16.
Nicolau JC, Bhatt DL, Roe MT, Lokhnygina Y, Neely B, Corbalán R, Leiva-Pons JL, Martinez F, Goodman SG, Winters KJ, Verheugt FW, Armstrong PW, White HD, Fox KA, Prabhakaran D, Ohman EM; TRILOGY ACS investigators.	Concomitant proton-pump inhibitor use, platelet activity, and clinical outcomes in patients with acute coronary syndromes treated with prasugrel versus clopidogrel and managed without revascularization: insights from the targeted platelet inhibition to clarify the optimal strategy to medically manage acute coronary syndromes trial.	*Am Heart J.* 2015;170:683-694.
Patel AB, Quan H, Welsh RC, Deckert-Sookram J, Tymchak W, Sookram S, Surdhar I, Kaul P.	Validity and utility of ICD-10 administrative health data for identifying ST- and non-ST-elevation myocardial infarction based on physician chart review.	*CMAJ Open.* 2015;3:413-418.
Reid R, Ezekowitz JA, Brown PM, McAlister FA, Rowe BH, Braam B.	The prognostic importance of changes in renal function during treatment for acute heart failure depends on admission renal function.	*PLoS One.* PMID:2015; 10:e0138579.
Roe MT, Mahaffey KW, Ezekowitz JA, Alexander JH, Goodman SG, Hernandez A, Temple T, Berdan L. Califf RM, Harrington RA, Peterson ED, Armstrong PW.	The future of cardiovascular clinical research in North America and beyond - addressing challenges and leveraging opportunities through unique academic and grassroots collaborations.	*Am Heart J.* 2015;169:743-750.
Sandhu RK, Hohnloser SH, Pfeffer MA, Yuan F, Hart RG, Yusuf S, Connolly SJ, McAlister FA, Healey JS.	Relationship between degree of left ventricular dysfunction, symptom status, and risk of embolic events in patients with atrial fibrillation and heart failure.	*Stroke.* 2015;46:667-672.
Sharma A, Ferguson C, Bainey KR.	Thrombocytopenia in acute coronary syndromes: etiologies and proposed management.	*Can J Cardiol.* 2015;31:809-811.
Sharma A, Khan JS, Bainey KR.	Preoperative stress tests-superfluous investigations resulting in excessive treatment delay: a teachable moment.	*JAMA Intern Med.* 2015;175:1610-1611.
Simpson J, Castagno D, Doughty RN, Poppe KK, Earle N, Squire I, Richards M, Andersson B, Ezekowitz JA, Komajda M, Petrie MC, McAlister FA, Gamble GD, Whalley GA, McMurray JJ; Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC).	Is heart rate a risk marker in patients with chronic heart failure and concomitant atrial fibrillation? results from the MAGGIC meta-analysis.	*Eur J Heart Fail.* 2015;17:1182-1191.
Stafinski T, Menon D, Nardelli A, Bakal J, Ezekowitz JA, Tymchak W, Welsh R, Gyenes G, Armstrong PW.	Incorporating patient preferences into clinical trial design: results of the Opinions of Patients on Treatment Implications of New Studies (OPTIONS) project.	*Am Heart J.* 2015;169:122-131.
Tang WH, Dupont M, Hernandez AF, Voors AA, Hsu AP, Felker GM, Butler J, Metra M, Anker SD, Troughton RW, Gottlieb SS, McMurray JJ, Armstrong PW, Massie BM, Califf RM, O'Connor CM, Starling RC.	Comparative assessment of short-term adverse events in acute heart failure with cystatin c and other estimates of renal function: results from the ASCEND-HF trial.	*JACC Heart Fail.* 2015;3:40-49.
Ter Maaten JM, Dunning AM, Valente MA, Damman K, Ezekowitz JA, Califf RM, Starling RC, van der Meer P, O'Connor CM, Schulte PJ, Testani JM, Hernandez AF, Tang WH, Voors AA.	Diuretic response in acute heart failure-an analysis from ASCEND-HF.	*Am Heart J.* 2015;170:313-321.
Thanh NX, Toye J, Savu A, Kumar M, Kaul P.	Health service use and costs associated with low birth weight-a population level analysis.	*J Pediatr.* 2015;167:551-556.
van Diepen S, Bakal JA, Lin M, Kaul P, McAlister FA, Ezekowitz JA.	Variation in critical care unit admission rates and outcomes for patients with acute coronary syndromes or heart failure among high- and low-volume cardiac hospitals.	*J Am Heart Assoc.* 2015;4. pii: e001708.
van Diepen S, Tricoci P, Podder M, Westerhout CM, Aylward PE, Held C, Van de Werf F, Strony J, Wallentin L, Moliterno DJ, White HD, Mahaffey KW, Harrington RA, Armstrong PW .	Efficacy and safety of vorapaxar in Non-ST-segment elevation acute coronary syndrome patients undergoing noncardiac surgery.	*J Am Heart Assoc.* 2015;4: e002546.
van Diepen S.	Is coronary intensive care unit volume a quality metric?	*J Am Heart Assoc.*2015;4:e002200.
Verma S, Goodman SG, Mehta SR, Latter DA, Ruel M, Gupta M, Yanagawa B, Al-Omran M, Gupta N, Teoh H, Friedrich JO.	Should dual antiplatelet therapy be used in patients following coronary artery bypass surgery? A meta-analysis of randomized controlled trials.	*BMC Surg.* 2015;15:112.
Wang X, Kindzierski W, Kaul P.	Comparison of transient associations of air pollution and AMI hospitalisation in two cities of Alberta, Canada, using a case-crossover design.	*BMJ Open.* 2015;5:e009169.

AUTHORS	TITLE	JOURNAL
Wang X, Kindzierski W, Kaul P.	Air pollution and acute myocardial infarction hospital admission in Alberta, Canada: a three-step procedure case-crossover study.	*PLoS One.* 2015;10:e0132769.
Westerhout CM, Bakal JA.	Novel approaches to composite endpoints in clinical trials.	*EuroIntervention.* 2015;11:122-124.
Wu C, McMurtry MS, Sandhu RK, Youngson E, Ezekowitz JA, Kaul P, McAlister FA.	Impact of rural residence on warfarin use and clinical events in patients with non-valvular atrial fibrillation: a Canadian population based study.	*PLoS One.* 2015 ;10:e0140607.
Yousef A, Simard T, Webb J, Rodés-Cabau J, Costopoulos C, Kochman J, Hernández-Garcia JM, Chiam PT, Welsh RC, Wijeysundera HC, García E, Ribeiro HB, Latib A, Huczek Z, Shanks M, Testa L, Farkouh ME, Dvir D, Velianou JL, Lam BK, Pourdjabbar A, Glover C, Hibbert B, Labinaz M.	Transcatheter aortic valve implantation in patients with bicuspid aortic valve: A patient level multi-center analysis.	*Int J Cardiol.* 2015;189:282-288.
Zordoky BN, Sung MM, Ezekowitz J, Mandal R, Han B, Bjorndahl TC, Bouatra S, Anderson T, Oudit GY, Wishart DS, Dyck JR; Alberta HEART.	Metabolomic fingerprint of heart failure with preserved ejection fraction.	*PLoS One.* 2015;10:e0124844.

Collaborative Mentoring

University of Toronto, University of Alberta, University of British Columbia

PARTICIPATING MENTORS
Shaun Goodman, Michael Farkouh, Paul Armstrong, Justin Ezekowitz, Robert Welsh, Andrew Krahn, John Cairns, John Mancini

PARTICIPATING MENTEES
Akshay Bagai, Jay Udell, Andrew Yan, Kevin Bainey, Sean van Diepen, Mustafa Toma, Chris Fordyce

In October 2013 during the Canadian Cardiovascular Society [CCS] Annual Scientific Meeting, Dr. Shaun Goodman hosted the inaugural Collaborative Mentoring meeting supported by the Polo Chair funds. Present at this meeting were representatives from the University of Toronto (including the Network for Innovation and Clinical Research [NICR]), the University of Alberta (including the Canadian VIGOUR Centre), and the University of British Columbia. This meeting was comprised of senior and junior faculty cardiologists from the three universities and together they developed a set of objectives for the Collaborative Mentoring program. The objectives (which were revised in 2015) are as follows:

1. Through a forum where clinical research opportunities can be shared among faculty members, address #2-#5;
2. To introduce developing clinicians conducting clinical research (mentees) to the lessons learned from established clinician scientists/leaders (mentors) in order to enrich their career development and enhance networking opportunities;
3. To facilitate developing faculty members in establishing goals, action plans and deliverables that would enable their academic success;
4. To bring together a community of developing and established clinician scientists in order to facilitate existing or planned Canadian clinical research activities; and,
5. To establish major unmet needs in clinical cardiovascular research in Canada and capitalize on opportunities that are best realized through creative collaboration.

Following the initial meeting, five virtual meetings occurred between 2014 and 2016 together with two additional face-to-face meetings in advance of the 2014 and 2015 Canadian Cardiovascular Congress meetings. A fourth meeting is planned for October 2016.

In addition to these meetings, several of the junior faculty members are now adjudicating clinical endpoints in a large cardiovascular outcomes trial as formal members of a Clinical Endpoint Committee in collaboration with the Duke Clinical Research Institute.

In the interview featured below, Dr. Goodman discusses the objectives of the Collaborative Mentoring program in more depth:

1. **Why is it important for senior clinicians to take on a mentorship role with their junior colleagues?**

   Mentoring provides senior clinicians with an ongoing opportunity to "give back". We've all been the beneficiaries of outstanding mentors who have shared their wisdom and experiences. Senior mentors helped all of us become comfortable in the academic environment, introduced us to key leaders and contacts and enhanced opportunities for networking in research areas of interest. Further, mentors have helped mentees to develop key goals and associated action plans, and provided encouragement, particularly when things (e.g., manuscripts, grant proposals, etc.) aren't successful. Perhaps most importantly, senior mentors can serve as role models for young mentees.

2. **During the collaborative mentoring meetings the junior clinicians have the opportunity to give short presentations about their area of clinical research interest. How do both the junior and senior clinicians benefit from this experience?**

   One unique opportunity that the mentoring meetings offer is sharing of ideas and perspectives beyond the four walls of one's own institution or university. We're blessed with senior mentors who are not just nationally, but also internationally recognized for their content expertise and experience in conducting clinical research. So we try to leverage this by exposing the junior clinicians to senior clinicians' perspectives. The mentors capitalize on the enthusiasm and ideas the young researchers bring to the table which often provides fresh input and an opportunity for rejuvenation.

3. **What is the role of creative collaboration at these meetings? Why is it important?**

   The Collaborative Mentoring initiative fosters an environment in which we can strengthen the cross-the-country relationships the Canadian VIGOUR Centre has worked hard to develop and maintain over the years while developing new ideas and engaging the "next generation" of Canadian clinical researchers. Hopefully we can work together to try and answer some important questions that aren't always addressed by a typical industry-initiated and sponsored study.

4. **One of the meeting objectives is to introduce junior faculty who are conducting clinical research to the lessons learned from established clinician scientists/leaders. What do you believe are the key lessons learned through your own experience conducting clinical research?**

   Persistence—there aren't too many truly "novel" ideas but if it's a good question, then stick with it! Don't wander too far from the bedside—important clinical questions present themselves every day, so listen to your patients and their families! Work hard but balance your time—being productive in research, like anything in life, requires a constant juggling of priorities! Publish—we have a responsibility to the patients we engage in our research and our collaborators for all of the time and effort and trust they have placed in us to get that information out in the peer-reviewed, public domain!

5. **Through your collaboration with the mentees what have you learned about their perspectives regarding the future of clinical cardiovascular research in Canada?**

   The future looks bright! Our mentees are excited, talented, and extremely capable individuals who simply need some protected research time, funding support, constructive criticism and positive feedback, and an occasional reminder to stay focused. If the senior mentors can offer some opportunities and guidance, there is no limit to what these mentees can accomplish.

Shaun Goodman

Trainees: The Next Generation of Health Researchers

The CVC continues its enthusiastic commitment to fostering a research environment conducive to disciplined academic inquiry and novel approaches to clinical questions and methodologies. We are pleased to offer research opportunities across a full spectrum of experience, education and backgrounds. CVC has provided research opportunities for undergraduates, medical students, and postdoctoral fellows from across Canada and from around the world. The hallmark of an academic research organization, CVC's mission remains steadfast in its dedicated efforts to inspire and nurture the next generation of health researchers.

In the following section, several of our young researchers discuss their research highlights and reflect upon their experience collaborating with the CVC faculty in 2015.

QENDRESA BEKA
MSc Student, Epidemiology

What would you say are your research highlights and personal achievements from 2015?
In 2015 I had the opportunity to present my research at a number of conferences and events. I presented at the Women and Children's Health Research Institute (WCHRI) Research Day and the School of Public Health's annual INSIGHTS event. I also had the opportunity to present results from two papers I have been working on at the 14th Symposium of the International Diabetes Epidemiology Group (IDEG). With IDEG I was awarded a trainee bursary to attend the meeting and participate in a diabetes epidemiology training course.

Why did you choose to work with your mentor(s)?
I chose to work with Dr. Kaul because I was very interested in her work with gestational diabetes (GDM) and was seeking a mentor who would guide me through my program. The Master's degree is unique because it acts as a link between course-based learning and academia. I knew I would be undergoing a steep learning curve and wanted a strong mentor to help me through the process.

What have you learned from working with your mentor(s)?
Dr. Kaul has guided me through the many steps of research, ranging from grant applications to analysis and reporting. Being relatively new to research, I appreciated Dr. Kaul's expertise with data analysis and presentation of results. Other members of the team, such as Ana Savu, also helped me navigate statistical programs and perform careful database linkage and analysis. Dr. Kaul also helped me with other skills that will carry on outside my Master's, such as effective writing, cross-disciplinary collaboration, and transitioning into post-academic pursuits.

PAUL BROWN
PhD Student, Medicine

What would you say are your research highlights and personal achievements from 2015?
I've been very fortunate to work on a number of topics that provide a real chance to influence the reporting of clinical trials. After months spent developing programming code, our work is coming to fruition; we had a paper on composite endpoints in heart failure accepted in the Canadian Journal of Cardiology. We are currently using the same code to evaluate other ideas, it is just the beginning.

What have you learned from working with your mentor(s)?
The questions I investigate are posed by my supervisor, Dr. Ezekowitz, and along the way my thinking is constantly calibrated and kept in check by our discussions. Thus I am brought up to speed–with what seems an endless literature –and can contribute far sooner than I otherwise could. Dr. Ezekowitz also flags papers I may be interested in or that I would benefit from reading.

DEBRAJ DAS
Resident, Internal Medicine

What would you say are your research highlights and personal achievements from 2015?
I was very fortunate to have worked with the VIGOUR group to publish an interesting paper associating meteorological events and decompensated heart failure using the ASCEND trial in the International Journal of Cardiology in the winter of 2014. With the help of VIGOUR I have continued working on novel and exciting research projects and have come one step closer in becoming an academic clinician scientist in Canada. Dr. Ezekowitz was also instrumental in helping me win the Sackett scholarship from the Canadian Stroke Prevention Network.

Why did you choose to work with your mentor(s)?
I was fortunate enough to work with Dr. Armstrong as a medical student all the way until I started my Internal Medicine residency training and wanted to shift gears in terms of research content. I was lucky enough to have Dr. Ezekowitz accept me as a trainee and support my personal and professional goals in becoming a cardiovascular clinician scientist. Dr. Ezekowitz has been a role model in every sense and has given me the foundation to develop a bright future in academic medicine.

What have you learned from working with your mentor(s)?
Dr. Ezekowitz has taught me that successful clinician scientists display an incredible amount of dedication and perseverance in addition to hard work. Dr. Armstrong taught me to never spread myself too thin, but to focus on the few things (both professional and personal) that excite you every time you wake up: this is the key to lifelong success.

SUMAN DHESI
Resident, Cardiology

What are some highlights from the research you have conducted in 2015? Additionally, are there any personal achievements or awards from 2015 you would like to highlight?
I presented my project on peripartum cardiomyopathy at the Mazankowski Cardiac Sciences Research Day and was awarded the Audrey Greenough-Norm Davies award for the best abstract presented by a Medical Resident. I also had the opportunity of presenting this work at Canadian Cardiovascular Congress and competed as a finalist for the Trainee Research Award.

Why did you choose to work with your mentor(s)?
Dr. Ezekowitz and Dr. Kaul are great mentors as they understand research methodology and what it takes to take a project from start to finish. Through working with them I have learned to present my work in a way such that the message is clear.

SHARRY KAHLON
Fellow, General Internal Medicine

What would you say are your research highlights and personal achievements from 2015?
My 2015 highlights included working with a group of researchers with extensive recognition and publications. My paper on "Association between frailty and 30-day outcomes after discharge from hospital" was published in the Canadian Medical Association Journal in 2015 with the support of my research supervisors. I also presented a poster at the Society of General Internal Medicine meeting.

Why did you choose to work with your mentor(s)?
Dr. McAlister is an exceptional and respected researcher. He is also a patient teacher who is able to guide research students with confidence and help them develop an understanding of the importance of publications in Medicine.

RABIA KASHUR
MSc Student, Medicine

What would you say are your research highlights and personal achievements from 2015?
The project that I am involved in addresses ethics in cardiovascular research; more specifically it assesses patients' comprehension to informed consent, the very tool that protects individuals' autonomy. PAC-VC uses a novel design in comparing two different methods of information delivery: written and verbal consent in the settings of acute and stable patient conditions.

I was selected among the finalists at the ACC Rockies resident research competition. In addition, I was successful in joining the internal medicine residency training program at the University of Calgary which will commence in the summer in 2016. As an international medical graduate, there are a limited number of seats to pursue clinical training and immense competition so it was very challenging to land a position in a clinical post graduate training program.

Why did you choose to work with your mentor(s)?
I consider Dr. Robert Welsh as a role model for any young person who is starting their career. He is an exceptional person whose footsteps one would want to follow to be a successful clinician, researcher, athlete, and health advocate. I have worked with him over the past two years and he has guided me to help achieve my goals. He is a cheerful, kind, open, visionary, humble and well balanced human and it has been a true honor to call him my supervisor.

"What lies behind us and what lies before us are tiny matters compared to what lies within us."

— RALPH WALDO EMERSON

What have you learned from working with your mentor(s)?
I have learned to always keep up a smile and be optimistic. Hard work always brings up results. There is always good in things no matter how bad they look, it is just that we have to find what we can use of it. We should never give up and that there are always better ways to do things.

JENELLE PEDERSON
MSc Student, Medicine

What would you say are your research highlights and personal achievements from 2015?
My thesis examined the prognostic value of current depressive symptoms in general medical inpatients, of which one of the top admitting diagnoses is heart failure. A major highlight was collecting data first-hand from patients and working alongside our team (supervising attendings, residents, nurse, and pharmacist) and the inpatient medical teams who supported our study –we prospectively enrolled 500 patients in just over a year. Primary data collection was a real grounding point, providing insight to patient experiences and acute care processes. In our recently published paper, we found that the presence of current depressive symptoms, but not a documented history of depression, predicted a 2-fold increased risk of short-term readmission or mortality independent of the current best risk prediction tools. This paper is a result of another major highlight, the collaboration that occurred over the last two years. From recruitment to publication, I gained invaluable support from our team and was awarded the Graduate Student Research Assistant Award as well as published the entirety of my thesis and collaborated on multiple co-authored publications, which were presented nationally and locally.

Why did you choose to work with your mentor(s)?
I was introduced to Dr. McAlister by my co-supervisor, who I had worked with as an undergraduate student. The project was a great fit in terms of skills I had and would gain by training under experienced outcomes researchers-clinicians. But beyond this, it really came down to how reasonable, transparent, and respectful those initial discussions were. This was true of interactions between Dr. McAlister and me, and interactions I witnessed between my two supervisors throughout my MSc. It was also apparent early on how genuinely each privilege teaching and learning.

What have you learned from working with your mentor(s)?
It is a rare opportunity to work closely with leading researchers. The mentorship provided by Dr. McAlister and my co-supervisor has been the best. Last year's CVC annual report aptly quotes Benjamin Franklin, "Tell me and I forget, teach me and I may remember, involve me and I learn". That's incredibly close to how I feel about my research experience. I was involved at each phase, from those first meetings to my own analyses and manuscript writing, and learned the research process from the ground up. Teamwork is an integral part of the research culture I experienced and it offered insight on engaging collaboration within a dynamic research team. Drs. McAlister and Majumdar challenged my reasoning and decision-making, teaching me to focus on methodological details and always to bring it back to research questions and the big picture. I am particularly thankful for many teaching moments and their critical appraisal or "red ink". At the same time, I felt supported and have gained a motivation to achieve my best work and pursue the highest standards.

JEYASUNDAR RADHAKRISHNAN
Postdoctoral Fellow

What would you say are your research highlights and personal achievements from 2015?
Majorly my research is on maternal and neonatal outcomes of gestational diabetes using Alberta's administrative health data. This project will build on and extend our understanding of gestational diabetes in Alberta, and provide valuable informative data for the rest of the country where this type of real-life data remains unavailable.

I am working on other cardiovascular projects too. For instance, we examined the impact of characteristics of the physician most responsible for care during a heart failure hospitalisation on mortality outcomes. The physician characteristics analysed were speciality (Cardiologist/Internist or other), experience level, sex, country of education, and whether the physician was fee-for-service or paid through an alternative payment plan. The results showed that physician characteristics do not appear to contribute significantly to variations in patient mortality outcomes in heart failure.

Why did you choose to work with your mentor(s)?
I have a background in physiotherapy, and some previous experiences in epidemiology and rehabilitation programs for patients with cardiovascular risk factors. Dr. Padma Kaul (epidemiology) and Dr. Roseanne Yeung (endocrinology) are my supervisors and Dr. Allyson Jones (physiotherapy) is my career mentor. This rare combination became possible at the University of Alberta and this completes all the gaps in my career interests. More than expected, it has been a great experience to work with these internationally recognized experts and I admire the working culture and environment at the CVC. I appreciate the learning opportunities every day and I am sure that this opportunity will make it easier to achieve my goals.

What have you learned from working with your mentor(s)?
It is a great opportunity to work at the CVC. My mentors have been assisting me in every possible way. I was given opportunities to work with the team of biostatistical experts to learn analytical techniques using new programs, supported in finding funding opportunities and preparing applications for grants, provided a teaching assistantship to improve my teaching skills, and given support to attend and present at conferences. Phil Jackson said "The strength of the team is each individual member and the strength of each member is the team." This idea is realized at the Canadian VIGOUR Centre and I am so proud to be here.

NARIMAN SEPEHRVAND
PhD Student, Experimental Medicine

What would you say are your research highlights and personal achievements from 2015?
Like all other CVC members, I am working on research projects related to cardiovascular diseases. We studied the factors that are related to testing for natriuretic peptides in patients presenting to emergency departments (ED) with acute heart failure (AHF). The findings are now published in the Canadian Journal of Cardiology and also featured in an interview by medicalresearch.com. I presented the findings on behalf of the investigators at the 2015 Canadian Cardiovascular Congress in Toronto, ON. These findings could help AHS-Laboratory services see the health and economic effects of their initiative of expanding the access to NP testing to all emergency departments in Alberta. For regions which are planning to introduce, extend or standardize their NP testing in the ED (e.g. other provinces of Canada as well as many European countries), the results may help them recognize and address the potential target groups (e.g. care providers who are more or less likely to order the test), patients groups that should be targeted for testing in the ED, and particular hospitals where other services (e.g. echocardiography) are not easily available.

We also published the findings of a sub-study of the Providing Rapid Out of Hospital Acute Cardiovascular Treatment 3 (PROACT-3) trial which was entitled "Alignment of Site versus Adjudication Committee-based diagnosis with patient outcomes" in Clinical Trials journal. The report addressed the important issue of the adjudication, which is now a routine part of randomized controlled trials.

During the last year, our main focus was to provide the pre-requisites for starting the HiLo-HF trial. The aim of this trial is to investigate the effect of a High versus Low setpoint of SpO2 on symptoms and clinical condition and patient outcome in patients presenting to emergency departments with AHF.

In 2015, with the invaluable support that I received from my mentor and all other CVC faculty, I was successful in receiving the Alberta Innovates-Health Solutions (AIHS) graduate studentship award and the CIHR-ICRH Travel Award.

Why did you choose to work with your mentor(s)?
Dr. Ezekowitz is a well-known investigator in the field of heart failure and he has contributed in many landmark studies in this specific field. I feel very lucky to be mentored by a person with that amount of impact. I also think that his way of mentorship is one of the best methods I have ever seen. He allocates a significant amount of time each week to mentoring his

"Only those who will risk going too far can possibly find out how far one can go."

— T.S. ELIOT

numerous trainees.

Besides Dr. Ezekowitz as my main supervisor, I also had the privilege of being mentored by one of best internationally-known cardiologists in the world, Dr. Armstrong, a man with great contributions in modern cardiology. So considering my genuine interest in Cardiology and in academic life, I believe this setting is the best to develop and pave my way to a successful academic life in the future.

What have you learned from working with your mentor(s)?
I have learned a lot from Dr. Ezekowitz about novel topics in the fields of heart failure management, biomarkers, risk scoring models and quality of life measures. In terms of research implementation, I have learned a lot about issues such as optimization of time-management, optimal utilization of available resources, productivity and continued performance feedback.

ABHINAV SHARMA
PhD Student, Medicine

What would you say are your research highlights and personal achievements from 2015?
Because of the connections established by my mentors, I am currently conducting research work at the Duke Clinical Research Institute. I have been working on a number of trial and registry databases including TECOS, HF-ACTION, and Get With the Guidelines. Through my work at the CVC and DCRI, I won the Heart Failure Society of America Young Investigator Grant and the Alberta Innovates Health Solutions Clinician Investigator Scholarship.

Why did you choose to work with your mentor(s)?
Dr. Justin Ezekowtiz has been an exceptional mentor. In addition to providing guidance on research, he has helped me understand the role of collaboration and developing research networks. He has provided me with many opportunities to participate in research and coauthor papers. Through his mentorship I have been able to win many awards including the Heart Failure Society of America Young Investigator Grant.

What have you learned from working with your mentor(s)?
I have learned many things while working with the faculty at CVC. The most important is that keeping an open dialogue and communication is key to ensuring successful, collaborative research.

JAY SHAVADIA
Fellow, Interventional Cardiology

What would you say are your research highlights and personal achievements from 2015?
Access site bleeding in STEMI intervention is associated with adverse patient outcomes. With the established safety of radial over femoral arterial access in primary PCI, and very limited data in patients undergoing a fibrinolytic pharmacoinvasive strategy, we sought to evaluate the prognostic utility of arterial access site in the early presenting, rapidly treated contemporary STEMI cohort enrolled within the STREAM trial. Our findings were aligned to those observed with primary PCI, and supported the utilization of radial over femoral access within the pharmacoinvasive strategy, especially in the higher risk rescue PCI cohort.

Why did you choose to work with your mentor(s)?
Having just completed a project with Dr. Armstrong, Gray Zheng and Cindy Westerhout the prospect of working with this team on my current project was irrefutable. As I had learned from the past, their mission was to see me succeed and achieve the goals and objectives I had set out to accomplish. Their open mindedness in thought process ensured that we had a view of the entire horizon, yet they also made sure that I never lost focus of the goals we had to meet. My research collaboration with the CVC has opened up networks, both locally and internationally, and has certainly paved the way to provide a rich blend in my interventional career.

ROBBIE SIDHU
Resident, Adult Cardiology

What would you say are your research highlights and personal achievements from 2015?
My personal highlights include receiving the ACC Rockies 2015 Resident Research award and being recognized by the American College of Cardiology in their Top 10 young author papers in Heart Failure for a paper entitled "Physician continuity improves outcomes for heart failure patients treated and released from the emergency department."

Why did you choose to work with your mentor(s)?
I chose to work with Dr. McAlister because of his breadth of experience in the field of heart failure and population outcomes research. His strong background in heart failure fit nicely with my research interests.

What have you learned from working with your mentor(s)?
Working with Dr. McAlister has been an invaluable experience. Apart from developing my clinical research skills, Dr. McAlister has been an excellent mentor to my career as a researcher. He has exposed me to a variety of research methodologies and has taught me an excellent approach to critical appraisal and formulating research questions. My work with Dr. McAlister and the CVC has been both motivating and fruitful.

DAT TRAN
PhD student, Health Services and Policy Research

What are some highlights from the research you have conducted in 2015? Additionally, are there any personal achievements or awards from 2015 you would like to highlight?
I have been doing a number of research projects during 2015. First, I evaluated the economic burden of heart failure hospitalizations in Canada. Heart failure is a chronic condition associated with significant morbidity and mortality, most prevalent among the elderly. It is the fourth most expensive condition in terms of hospitalization costs in Canada. We estimated that HF hospitalizations alone accounted for 0.8% of hospital spending in 2013. The manuscript is being reviewed at the Canadian Medical Association Journal Open. In addition, I have been working on other cardiovascular projects, such as evaluating hospitalization costs of congenital heart diseases in Canada, evaluating health services utilization and costs of syncope in Alberta, and benchmarking health outcomes and reperfusion strategy among ST-segment elevation myocardial infarction patients in Canada.

Why did you choose to work with your mentor(s)?
My primary supervisor at the School of Public Health is Dr. Arto Ohinmaa. I researched the possibility of having an additional mentor and found that Dr. Padma Kaul was a perfect fit to develop myself as an independent researcher. Both Drs. Ohinmaa and Kaul are experts in their fields who can guide the progress of my thesis project that evaluates health outcomes and costs of acute myocardial infarction in Canada.

What have you learned from working with your mentor(s)?
I have learned much from my mentors. For example, I have learned to do research and critically evaluate a research question or weigh its scientific value. I have also had the opportunity to study their writing style and learn about the process of presenting a scientific topic for clinical audiences. These skills are essential for me to develop as an independent researcher.

JACKSY ZHAO
MSc Student, Transitional Medicine
Resident, Adult Cardiology

What are some highlights from the research you have conducted in 2015? Additionally, are there any personal achievements or awards from 2015 you would like to highlight?
The research I am involved with looks at and compares outcomes in the heart failure and acute coronary syndrome patient populations using data from clinical registries. My current focus is on end of life outcomes in the advanced heart failure population. Our research aims to identify predictors of positive outcomes that can be translated to improve care for our patients with cardiovascular conditions.

Why did you choose to work with your mentor(s)?
I chose to work with Dr. Justin Ezekowitz as he is well known both nationally and internationally for advancing the field of clinical research in heart failure. Speaking with other trainees and cardiologists, they all describe Dr. Ezekowitz as a highly respected mentor, researcher, and clinician.

What have you learned from working with your mentor(s)?
Through working with Dr. Ezekowitz and Dr. Padma Kaul, I have developed a much better understanding of research design, methodology and data analysis. Instead of just providing me with the answers, they allowed me to figure things out on my own while guiding and supporting me along the way. As a result, I have gained invaluable skills that can be applied to future research endeavors. I am grateful to have Dr. Ezekowitz as a mentor as he provides sound research and career advice and is also a role model with qualities I aspire to emulate.

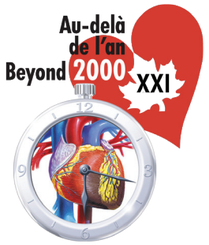
Beyond 2000

On October 25-26, 2015 CVC hosted the 21st Annual: Beyond 2000 symposia in Toronto in conjunction with the Canadian Cardiovascular Congress. Given the new guidelines allocated only two hours for the program we decided for the first time this year to hold two symposia. The first was directed towards our traditional New Concepts in Acute Coronary Syndrome topic, whereas the second addressed the unmet educational needs in the area of Heart Failure and Atrial Fibrillation. These programs were generously supported by unrestricted educational grants from AstraZeneca, Merck, Novartis, Servier and Bayer HealthCare. As has been our tradition with these events, we were pleased to have partnered with the Mazankowski Alberta Heart Institute and the University of Alberta in undertaking this venture.

In the Acute Coronary symposium we probed new avenues in ST elevation myocardial infarction, how to reduce residual remaining risk in such patients and the most appropriate use of contemporary antithrombotic and antiplatelet therapies. The symposium concluded with a futures look at how clinical trials in progress will likely affect medical practice.

The second symposium began with an assessment of novel therapeutic targets in heart failure likely to foster new drug development and included discussions around the best strategy for employing biomarkers In heart failure as well as how to integrate device therapy. The challenge of atrial fibrillation in heart failure and its implications for stroke was another major focus.

Both programs were very well received with strongly positive evaluations by the many registrants in attendance. A variety of post-event resource materials for both the ACS Symposium and the Heart Failure & Atrial Fibrillation Symposium that include interviews, recordings of the lectures, and presentation slides can be found at www.Beyond2000.org



New Concepts in Heart Failure and Atrial Fibrillation Presenters & Chairs: Michael McDonald, Paul Dorian, Justin Ezekowitz, Peter Mitoff, John McMurray, Adrian Hernandez, Paul Armstrong, John Eikelboom

CVC Clinical Trials Colloquium

On Sunday March 8, 2015 we held the 2nd Annual CVC Clinical Trials Colloquium in Banff, Alberta in collaboration with the ACC Rockies Meetings. Thanks to the support from our Canadian sponsors AstraZeneca, Amgen, Bayer, Eli Lilly, Novartis, Pfizer, and Sanofi, we were able to host this unique event and bring together representative investigators and study coordinators from 16 sites across the country (BC, AB, MB, ON, QC, NS, NL). This year's Colloquium was intended to build on last year with key objectives that included (I) gaining a better understanding of all aspects of clinical trial research and participation, (II) developing strategies for choosing and executing a clinical trial successfully, (III) gaining a better understanding of legal requirements for negotiating Canadian clinical trial site agreements, (IV) discussing opportunities to enhance the overall clinical trial experience at a site level, (V) engaging in open discussion with colleagues, sponsors and CVC as it relates to challenges in participation and execution of clinical trials. The Colloquium was expanded to not only include the main Colloquium session but also a Study Coordinator Workshop, and as part of the ACC Rockies Meeting, a Canadian VIGOUR Centre Workshop highlighting recent clinical trials results and opportunities.

Our morning agenda was ambitious but proved to be very informative. It covered the changing landscape in clinical trials, lessons learned, choosing trials wisely, costs, contract negotiations, investigator engagement, expectations and roles of the executive, steering committees and Data and Safety Monitoring Boards (DSMB) and finally, why we do clinical research. The discussion in the room generated some clear insights as it relates to each of these topics.

At last year's colloquium, contracts were cited as one of the major contributors to delays in the start-up of a clinical trial. In an effort to address this, we invited Marlon Rajakaruna, a lawyer/partner with Dentons Canada who has extensive experience in negotiating clinical trial agreements with sites, sponsors, ARO/CROs across Canada and around the world. He spoke about the contentious issues involving contracts and provided the best strategies for resolution.

In the afternoon we reconvened with the study coordinators and engaged in open sharing and discussion on ethics, electronic migration, training, recruitment strategies, audits, understanding why all the data is collected on the CRF, trial fatigue, and withdrawals and lost to follow up. As always our study coordinators were a wealth of knowledge and this session enabled them to share best strategies with each other, which not only reinforced what they perhaps were already doing, but also gave them some new strategies to take back to their site and work on implementing.

While all of our attendees know why they participate in clinical research, the colloquium served to remind us that clinical research gives us the opportunity to be leaders and champions in enhancing clinical practice and to beat the forefront of new technologies. Research not only offers us career satisfaction through intellectual curiosity but also provides opportunities for mentorship, collaboration, staff education and learning new skills. While it is clear that there are challenges that come with participating in clinical research, it is also evident that the benefits far outweigh the risks.

The Paul Armstrong Symposium

June 13, 2015 marked an extraordinary day for CVC and the University of Alberta when the Department of Medicine hosted a Festschrift to honor Paul Armstrong's 35 years of exemplary care, discovery and mentorship as a cardiologist and the recipient of the University of Alberta's 2014 University Cup. Borrowed from German the word Festschrift indicates an academic celebration in honor of a scholar.

The day featured presentations from four internationally renowned cardiologists whose professional lives were inextricably linked to Dr. Armstrong. It began with an overview of the Beginning of Fibrinolytic Drug Design to the Achievement of Optimal Reperfusion for ST Elevation Myocardial Infarction Patients by Frans Van de Werf, Professor of Cardiology from the University of Leuven in Belgium. This was followed by a "Big Theme" discussion of Medical Products Development by Robert Califf, formerly Professor of Cardiology and Vice Chancellor of Duke University and current Commissioner of the FDA in the United States, and Eric Peterson, Director of the Duke Clinical Research Institute who explored Novel Ways to do Clinical Trials and Health Outcomes. The academic component of the day was completed by Robert Harrington, Professor and Chair of the Department of Medicine at Stanford University who discussed how Biotech and Big Data Will Rule the World focusing on Google, Apple and IBM.

The day was capped by a gala celebratory dinner adroitly chaired by Peter Hamilton. The dinner featured tributes from several former trainees, colleagues and staff and included remarks from host, Barbara Ballermann, Chair of the Department of Medicine, Verna Yiu, Chief Medical Officer of Alberta Health Services and Richard Fedorak, Dean of the Faculty of Medicine and Dentistry.

CVC Directors - Justin Ezekowitz, Paul Armstrong, Shaun Goodman

Robert Harrington, Robert Califf, Paul Armstrong, Franz Van de Werf, Eric Peterson

CVC Staff - Jodi Parrotta, Tracy Temple, Devon Blanchette, Lyndsey Garritty, Melisa Spaling

Distinguished Visitors

In 2015, the faculty of the CVC had the privilege of hosting three outstanding, internationally renowned academics continuing a program generously sponsored by unrestricted educational grants from AstraZeneca and Novartis.

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

DR. MICHAEL J PENCINA
Director, Biostatistics & Bioinformatics,
Professor, Biostatistics & Bioinformatics,
Duke Clinical Research Institute

JUNE 2-3, 2015

- Cardiology Research Rounds: "How to Interpret Incremental Value of Biomarkers"
- Cardiology Divisional Rounds: "New US lipid Guidelines: Main Advances and Open Questions"

Michael Pencina, a well-known leader in biostatistics and the recently appointed Director of Biostatistics and Bioinformatics at the DCRI, shared his important work on assessing the incremental value of novel biomarkers. In an ever-increasing sea of biomarkers, traditional statistical tools such as the change in the c-index are no longer sufficient in identifying meaningful biomarkers. In response to this, Dr. Pencina and colleagues developed the net reclassification index. Dr. Pencina also discussed the practical implications of the new US Cholesterol Guidelines. When making treatment decisions according to 10-year risk of cardiovascular disease, he and his colleagues deduced that there would be a significant increase in the number of adults eligible for statins. His visit to the CVC strengthened the bond between clinical and biostatistics researchers in clinical cardiovascular research.

DR. ADRIAN HERNANDEZ
Associate Professor of Medicine, Duke University Medical Center
Director, Health Services and Outcomes Research
Faculty Associate Director, Duke Clinical Research Institute

OCTOBER 20-21, 2015

- Cardiology Research Rounds: "Blueprint to Save a Failing Research Market"
- Cardiology Divisional Rounds: "Changing Care, Changing Outcomes"

Adrian Hernandez, a leader in registry and clinical trial heart failure research, presented on the importance of revitalizing the discovery to clinical impact pipeline of the research enterprise. He highlighted the key economic and clinical need to drive research as well as the importance of the patient voice and engagement. He further described the efforts of groups in the United States working on the PCORI initiative for developing and implementing pragmatic clinical trials.

DR. SONIA ANAND
Associate Director, Population Health Research Institute
Director, Population Genomics Program, Department of Clinical Epidemiology and Biostatistics
Professor, Division of Cardiology, Department of Medicine
Associate Member, Department of Clinical Epidemiology & Biostatistics
McMaster University

DECEMBER 15-16, 2015

- Cardiology Research Rounds: "Ethnic Variations in Risk Factors and Burden of Cardiovascular Disease: How to prepare for the future?"
- Cardiology Divisional Rounds: "Early life origins of risk factors for cardiometabolic diseases"

We were pleased to host Dr. Sonia Anand in December 2015. She provided and insightful look at nature and nurture as part of a well-received Research Rounds entitled "Early life origins of risk factors for cardio metabolic diseases". At Cardiology Grand Rounds she addressed the subject of "Ethnic Variations in Risk Factors & Burden of Cardiovascular Disease: How to prepare for the future?" Her visit was co-hosted by Padma Kaul and Kevin Bainey and provided ample opportunities for faculty discussion and potential avenues for future collaboration.

Canadian Cardiac Chronicle

CVC is pleased to publish The Canadian Cardiac Chronicle, a quarterly newsletter that shares current trial information and upcoming projects that may be of interest to our site network.

The Chronicle also lists current publications by the CVC faculty, resulting from the projects and trials data we manage.

Posted on our website at www.vigour.ualberta.ca, the Chronicle is distributed to over 500 recipients, including our investigative sites, sponsors and international collaborators.

Adjudication of Clinical Endpoints—Why all the Fuss?

With the arrival of the fall, I find myself constantly "out on the road" participating in various national and international scientific sessions and meetings for ongoing and upcoming clinical trials. A frequent topic of conversation raised by busy study investigators and coordinators relates to the enormous amount of time and effort you are now exerting in studies in order to: identify all potential events, capture medical record information and related source documentation (that is often hard to obtain from other health care settings), provide narratives, and complete numerous forms while under the watchful eye of the trial operational leadership!

Indeed, the use of centralized committees to adjudicate clinical events (clinical endpoint or event committees; CECs) is common in large outcome trials, particularly for the assessment of nonfatal primary outcomes. Not surprisingly, site research staff are increasingly asking what is the rationale and value of this adjudication process (including the provision of source documentation) and why is it such a demanding task?

Earlier pivotal cardiovascular outcome trials (such as the ISIS-2 study, which established the role of ASA and fibrinolysis in the management of suspected acute myocardial infarction [MI]) did not, in fact, require central adjudication; however, these studies used all-cause mortality as the primary endpoint. Although no one is arguing for the need to adjudicate patient death itself, understanding the underlying cause (cardiovascular vs. non-cardiovascular) can be of added importance.

Since definitions for nonfatal events are generally heterogeneous and often times subjective, one reason for a central process of adjudication is to assist in assuring systematic application of the endpoint definitions used in the trial. This is particularly important when determination of nonfatal events, such as peri-procedural MI, can be challenging to sort out. For example, a patient presents with an ST-segment elevation MI and is randomized to receive a treatment aimed at preventing a second MI that can also potentially cause bleeding. If the patient then undergoes early stenting or coronary artery bypass surgery, how does one determine whether a recurrent MI has occurred when the troponin level continues to rise within the first 48 hours of the index event? Similarly, if the patient experiences some blood loss around the time of the procedure, how do we determine whether there was a clinically significant bleeding endpoint and can we attribute that adverse event to the randomized treatment or is it simply an expected complication for a patient undergoing revascularization? In addition, particularly in open-label trials, there is the possibility of systematic differential misclassification in determining the occurrence of events based on the patients' or investigators' belief that the experimental treatment is better or worse than the comparator. By assuring that the adjudication is done centrally, systematically, and blinded to treatment assignment, the CEC may provide protection against such differential misclassification. Regulatory authorities, including the U.S. FDA and Health Canada, derive confidence in the validity of trial results when central adjudication is performed and may therefore demand this approach before approving new treatments.

Investigators and coordinators have also noted a recent trend towards the use of "triggered" events whereby they receive a query regarding a possible endpoint even when they haven't indicated any event has occurred. For example, even if an MI form hasn't been completed by the local study team, the trial operational leadership may ask the site whether an MI might have happened. Indeed, a mild elevation of CK-MB following coronary stenting entered in the case report form as part of the systematic collection of all cardiac markers obtained during the patient's admission, may trigger a series of questions, requests

Featured Presentations

Reflecting the CVC's global reach and network of collaborators, this summary highlights some of the key national and international lectures and presentations that were delivered by CVC faculty members in 2015. The CVC's insights and impact are enhanced by these pursuits of knowledge translation and dissemination.

KEVIN BAINEY
San Francisco, California
Transcatheter Cardiovascular Therapeutics Conference - October 2015
Invited Speaker: A Practical Stenting Issue in Multivessel Disease: When and Where to Stop?

Montreal, Quebec
Montreal Live Symposium - June 2015
Invited Speaker: Culprit Only Versus Complete Revascularization in STEMI with Multi-vessel Disease

PAUL ARMSTRONG
Mumbai, India
Fellowship of the European Society of Cardiology, Mumbai Meeting of the Cardiologists - January 2015
Invited Speaker:
- Acute Coronary Syndromes: Lessons Learned & Roads Untraveled.
- Personalising Antiplatelet therapy in ACS.
- ST Elevation Myocardial Infarction 2015 – Contemporary Insights.

Mississauga, Ontario
Gauging the Guidelines – Cardiovascular: Which Road to Take? - February 2016
Keynote Lecture: The Challenge of Writing Guidelines.

San Diego, California
64th Annual Scientific Session & Expo, American Cardiology Conference - March 2015.
- Panelist in Special Session 46th Annual Louis F. Bishop Lecture: 25 Years of Acute Coronary Syndromes. A Paradigm for Collaborative Research and Training the Next Generation.
- Co-Chair: Late-Breaking Clinical Sessions Deep Dive

Kingston, Ontario
Southeast Ontario Academic Medical Organization (SEAMO) Innovation Showcase, Queen's University - May 2015
Keynote Speaker: Reflections of a Clinical Investigator.

New York City, New York
Icahn School of Medicine at Mount Sinai - June 2015.
Visiting Professorship Program: Acute Myocardial Infarction 2015: Reflections of a Clinical Investigator

ROBERT WELSH
Hamilton, Ontario
McMaster University/Hamilton Health Sciences - September 2015
Regional Cardiology Rounds: The Clinical Challenges of Treating your High Risk Cardiovascular Patients Incorporating Antithrombotic Therapy Into Secondary Prevention of ACS.

JUSTIN EZEKOWITZ
London, United Kingdom
European Society of Cardiology (ESC) Congress - August 2015
Invited Speaker:Management of Acute Heart Failure - The Current and Future Role of Biomarkers in Management.

Montreal, Quebec
Heart Failure Update - May 2015
Invited Speaker: Acute HF: What's New? Innovative Therapies for Heart Failure.

Canadian Heart Failure Society - May 2015
Invited Speaker: Targets for Therapy: Putting it All Together.

Seoul, South Korea
Korean Cardiology Society General Meeting - September 2015
Invited Speaker: Evidence Based Medications: From Guidelines to Practice

Korean Heart Failure Society Guidelines Meeting - September 2015
Invited Speaker:
- Heart failure: New Targets and Hormones of the Heart
- The Development of the CCS HF Guidelines

Kota Bharu, Malaysia
Hospital University Sains Malaysia - September 2015
Invited Speaker:
- Chronic HF: Current and future therapy.
- Canadian Heart Failure Guidelines: Development and Updates.

Vaughn, Ontario
State of the Heart - June 2015
Invited Speaker: Chronic and Reduced Heart Failure: Updates.

Ottawa, Ontario
Ottawa Heart Failure Research Conference - April 2015
Invited Speaker: Sodium in Heart Failure.

SEAN VAN DIEPEN
San Diego, California
The American College of Cardiology Scientific Sessions - March 2015
- Invited Speaker, Critical Care Workshop: Therapeutic Hypothermia: Who, When, Where.
- Panel Moderator: The Clinical and Angiographic Outcomes in Coronary Artery Bypass Surgery Using Grafts with Multiple Versus Single Distal Targets.

Toronto, Ontario
Canadian Cardiovascular Congress - October 2015
- Invited Speaker: ECMO Assisted Cardiopulmonary Resuscitation (eCPR) For In-Hospital Cardiac Arrest.
- Co-Chair: Critical Care Year in Review for the CICU Cardiologist.

Montreal, Quebec
Montreal Live Symposium - June 2015
Invited Speaker: Temperature Control in Out-of-Hospital Cardiac Arrest Patients with Cardiogenic Shock.

SHAUN GOODMAN
Mont Tremblant, Quebec
18th Tremblant Interventional Cardiology Meeting - February 2015
Invited Speaker: From Guidelines to Practice: Oral P2Y12 Therapy in Canadian Acute Coronary Syndrome Patients.

San Diego, CA
American College of Cardiology Annual Scientific Session - March 2015
- Poster Moderator: What's New in ACS?
- Invited Speaker: Logistical Challenges in STEMI, Ship and Drip (Facilitated Transfer to PCI Hospital).

Halifax, Nova Scotia
Atlantic Canada Cardiovascular Conference - May 2015
Invited Speaker: PCSK9 Inhibition Will Eliminate CAD by 2030!

Saint John, New Brunswick
New Brunswick Heart Centre Twenty-Fifth Annual Symposium on Current Perspectives in Cardiovascular Disease – September 2015
Invited Speaker: Management Challenges in ACS – From ER to Discharge.

London, United Kingdom
European Society of Cardiology Annual Congress - August 2015
Co-Chair, ESC Joint Canadian-Australian-United Kingdom Specialists Medical Round Table: Ongoing Cardiovascular Risk in Patients with a Prior Myocardial Infarction. Clinical Evidence and Discussion.

Toronto, Ontario
Canadian Cardiovascular Congress Year in Review - October 2015
Invited Speaker: A delicate balance between good and harm

Toronto, Ontario
Heart and Stroke Foundation Clinical Update - December 2015
Invited Speaker: Dual Oral Antiplatelet Therapy in Canadian Acute Coronary Syndrome Patients: Twice as Nice or Double the Trouble?

PADMA KAUL
Quebec City, Quebec
Canadian Perinatal Programs Coalition Annual Meeting - June 2015
Invited Speaker: Gestational Diabetes Mellitus in Alberta

Birmingham, United Kingdom
European Heart Rhythm Society Meeting - October 2015
Invited Speaker: Studying Outcomes and Costs of Patients Presenting to the Emergency Department with Syncope.

FINLAY MCALISTER
Mississauga, Ontario
Canadian Hypertension Congress - October 2015
Invited Speaker: Reducing cardiovascular risk in patients with hypertension: Moving beyond traditional models

Charlottetown, Prince Edward Island
Canadian Society of Internal Medicine Annual Meeting - October 2015
Invited Speaker: The Top 5 Papers by Canadian General Internists in the Past Year.

ARO Services

CVC Services and Activities

The Canadian VIGOUR Centre is recognized as a thought leader and valuable partner in cardiovascular research across all regions of Canada and amongst key centres around the world. Its track record of conducting, delivering and 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
- Defined 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 sub studies aimed at mechanistically informing primary clinical trial results
- Mentoring junior faculty, medical trainees, students and allied health professionals

CLINICAL TRIALS

- Investigator selection, qualification and recruitment
- Investigative site start-up and training
- Ensuring site regulatory compliance
- Project, Site, 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, 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

CLINICAL REGISTRIES

Vital Heart Response (VHR): R Welsh

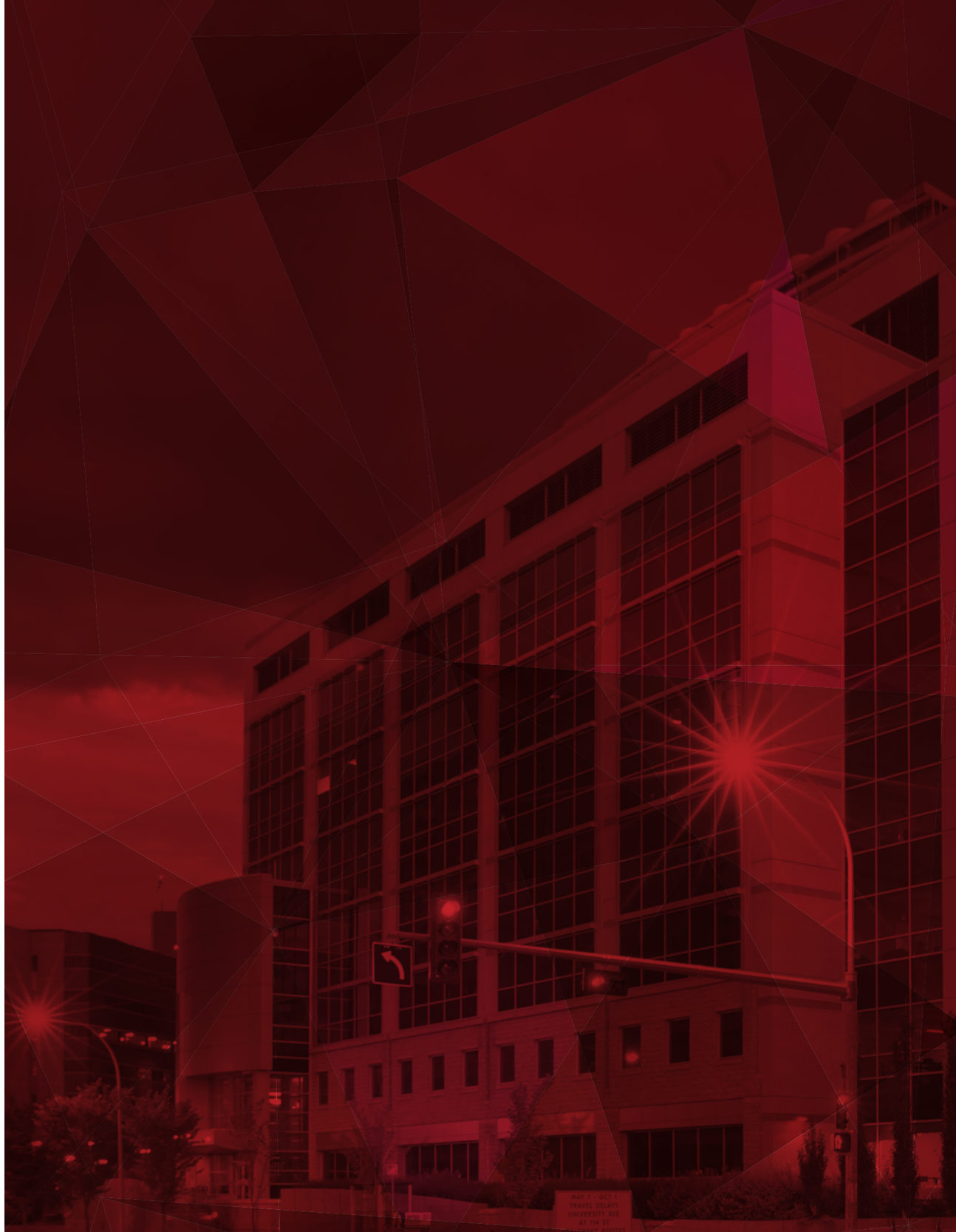
- Continuous Quality Improvement (CQI)
- Regional Collaboration
- Trials within registries e.g. PROACT
- Model for others

Acute Heart Failure (AHF): J Ezekowitz

- CIHR: inquiry regarding outcomes/ biomarkers
- Novel Interventions/trial

EGC CORE LAB

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



Clinical Trials

Our clinical trials team works hard to build and maintain strong relationships with our sites, sponsors and partners to deliver efficient, cost effective, and high quality clinical trials. In addition to the relationships we have built, we also attribute our success in the management of clinical trials to the hands on, collaborative team approach we provide to our sites, sponsors and partners which encompasses all aspects of our organization including our thought leadership, management board, project leadership, monitoring, biostatistics, health economics and administrative support teams.

We have a robust network of over 150 sites across Canada, with whom we have established relationships that have been built over many years as well as some new sites that we have been fortunate to recruit into a number of our recent studies. While we continue to focus on the operational management of phase II, phase III, and investigator initiated studies in acute coronary syndromes, lipid management, heart failure and diabetes, in 2015 we broadened our cardiovascular focus to include trials in cardiac surgery and transaortic valve replacement (TAVR). We are continuously seeking out novel and interesting studies to be involved in and are currently in the initial planning and negotiation stages for a few new projects in 2016.

Our clinical trials team is overseen by Tracy Temple, Assistant Director of Clinical Trials, who brings a background in cardiovascular nursing, project management and 16 years of clinical research experience with the Canadian VIGOUR Centre. We have a very experienced, diverse, knowledgeable and personable clinical trials team comprised of five Clinical Trial Project Leads, two Regulatory Support staff, a Lead Clinical Research Associate, eight regionally based Monitors, a Monitoring Report Reviewer and administrative support. Responsible for ensuring all operational aspects of the study run smoothly, our Clinical Trial Project Leads and Regulatory Support staff work closely with our sites to strive for quick and efficient start-up, high recruitment and retention of patients that meet the study criteria, data entry that is accurate and well maintained, and delivery on timelines as laid out from study start-up to study completion. As the primary contact for the Canadian sites, the Clinical Trial Project Leads have their fingers on the pulse of all aspects of the trial, which enables them to maintain a good understanding of the overall functioning of the study while closely monitoring trends and issues across Canada.

In addition to conducting source document verification, drug accountability and other required monitoring related tasks, the CVC monitors use their visits as a teaching opportunity to share lessons learned and ideas from other sites which are beneficial to their daily work and also help to ensure they are audit prepared. With an extensive background in monitoring and previous involvement in many audits and inspections throughout her career with the CVC, Halina Nawrocki has helped prepare many of our sites for upcoming inspections as well as shared lessons learned with our team and sites. With the ongoing support and expertise of our project and monitoring team and well prepared sites, all CVC monitored sites who underwent inspections in 2015 received compliant ratings.

The CVC is a strong advocate of continuing education for our staff and in addition to being ICH/GCP trained, many of our team members also hold or are working toward the CCRP designation with SoCRA or the CCRA designation with ACRP. We maintain a strong focus on training and quality and encourage our teams to share their knowledge, lessons learned, and expertise on an ongoing basis in their work with sites and sponsors to help build more efficient and cost effective clinical trials in Canada.

> "Medicine is the science of uncertainty and the art of probability."
>
> — WILLIAM OSLER

Tracy Temple , RN, BScN - Assistant Director, Clinical Trials

Amanda Carapellucci, BSc- Clinical Trials Project Lead

Lyndsey Garritty, BA - Clinical Trials Project Lead

Courtney Gubbels, BA-Clinical Trials Project Lead

Jodi Parrotta, MA - Clinical Trials Project Lead

Melisa Spaling, MEd - Clinical Trials Project Lead

Karin Kushniruk, RN, PhD - Clinical Trials Project Lead

Devon Blanchette - Regulatory Specialist

Halina Nawrocki, RN- Lead Clinical Research Associate

Paula Priest - Project Coordinator

Kris Reay - Administrative Assistant

Clinical Trials

AEGIS-I

Protocol #:	CSLCT-HDL-12-77
Sponsor:	CSL Behring LLC
Drug:	CSL112
Anticipated Timeline:	August 2013-2016
Trial Status:	Target enrollment reached

A Phase 2b, multicenter, randomized, placebo-controlled, dose-ranging study to investigate the safety and toleability of multiple does administration of CS112 in subjects with acute myocardial infarction.

40/1,200
(Canada/Global)
Patient enrollment target

25/1,258
(Canada/Global)
Patient enrollment achieved to date

8/184
(Canada/Global)
Number of sites participating

BLAST-HF

Protocol #:	CP027
Sponsor:	Trevena Inc.
Drug:	TRV027
Anticipated Timeline:	March 2014 - April 2016
Trial Status:	Database locked and closing out sites

Randomized, double-blind, placebo-controlled, dose ranging study to explore the efficacy of TRV027 in patients hospitalized for acute decompensated heart failure.

15/620
(Canada/Global)
Patient enrollment target

1/560
(Canada/Global)
Patient enrollment achieved

3/45
(Canada/Global)
Number of sites participating

EXSCEL

Exenatide **S**tudy of **C**ardiovascular **E**vent **L**owering

Protocol #:	BCB109
Sponsor:	AstraZeneca
Drug:	Exenatide
Anticipated Timeline:	May 2009 - June 2018
Trial Status:	Target enrollment reached now in patient retention stage

A randomized, placebo controlled clinical trial to evaluate cardiovascular outcomes after treatment with exenatide once weekly in patients with type 2 diabetes mellitus.

500/14,000
(Canada/Global)
Patient enrollment target

544/14,753
(Canada/Global)
Patient enrollment achieved to date

28/692
(Canada/Global)
Number of sites participating

GUIDE-IT

GUIDing **E**vidence Based Therapy Using Biomarker **I**ntensified **T**reatment in Heart Failure

Protocol #:	Pro00033097
Sponsor:	Duke Clinical Research Institute & Roche
Drug:	NA
Anticipated Timeline:	December 2012 - June 2017
Trial Status:	Actively enrolling

Determine the efficacy of a strategy of biomarker-guided therapy compared with usual care in high risk patients with left ventricular systolic dysfunction.

120/1,100
(Canada/Global)
Patient enrollment target

103/744
(Canada/Global)
Patient enrollment achieved to date

6/44
(Canada/Global)
Number of sites participating

IMPROVE IT

IMProved **R**eduction of **O**utcomes: **V**ytorin **E**fficacy **I**nternational **T**rial

Protocol #:	P04103
Sponsor:	Merck & Co. Inc.
Drug:	Vytorin
Anticipated Timeline:	March 2005 - March 2015
Trial Status:	Close out activities occurred in early 2015

A multicenter, double-blind, randomized study to establish the clinical benefit and safety of Vytorin (ezetimibe/simvastatin Tablet) vs. simvastatin monotherapy in high-risk patients presenting with acute coronary syndrome.

Note that the 500 for Canada is based on original projections and sample size and does not reflect modified sample size.

500/18,000
(Canada (CVC) /Global)
Patient enrollment target

602/18,142 COMPLETED
(Canada/Global)
Patient enrollment achieved

36/1,159
(Canada/Global)
Number of sites participating

LEVO-CTS

Protocol #:	TNX-LOV-01
Sponsor:	Tenax Therapeutics Inc.
Drug:	Levosimendan
Anticipated Timeline:	July 2014-October 2016 Canada: March 2015 - October 2016
Trial Status:	Actively enrolling

A double-blind, randomized, placebo-controlled study of Levosimendan in patients with left ventricular systolic dysfunction undergoing cardiac surgery requiring cardiopulmonary bypass.

50/760
(Canada/Global)
Patient enrollment target

32/322
(Canada/Global)
Patient enrollment achieved to date

10/64
(Canada/Global)
Number of sites participating

ODYSSEY OUTCOMES

Protocol #:	EFC11570
Sponsor:	Sanofi-aventis Recherche & Développement
Drug:	Alirocumab (SAR236553/REGN727)
Anticipated Timeline:	June 2012 - March 2018
Trial Status:	Target enrollment reached now in patient retention stage

A randomized, double blind, placebo-controlled, parallel-group study to evaluate the effect of Alirocumab SAR236553/REGN727 on the occurrence of cardiovascular events in patients who have already recently experienced an acute coronary syndrome.

340/18,000
(Canada/Global)
Patient enrollment target

361/18,313
(Canada/Global)
Patient enrollment achieved to date

38/1,263
(Canada/Global)
Number of sites participating

PROACT

Providing **R**apid **O**ut of Hospital **A**cute **C**ardiovascular **T**reatment

Sponsor:	Heart and Stroke Foundation, University Hospital Foundation & Mazankowski Alberta Heart Institute
Drug:	NA
Anticipated Timeline:	October 2011-August 2015
Trial Status:	Completed

Determine if early diagnosis and risk stratification acquired through pre-hospital clinical assessment, 12-lead electrocardiogram and point of care biomarkers will facilitate enhanced triage and treatment in patients with presumed non-ST elevation acute coronary syndromes (NSTEMI).

600 - CANADA ONLY
(Canada/Global)
Patient enrollment target

572 CANADA ONLY
(Canada/Global)
Patient enrollment achieved to date

LOCAL EDMONTON ONLY
(Canada/Global)
Number of sites participating

SODIUM-HF

Study **O**f **D**ietary **I**ntervention **U**nder 100 **M**MOL in **H**eart **F**ailure

Protocol #:	MOP130275
Sponsor:	CIHR grant
Anticipated Timeline:	December 2013-December 2017
Trial Status:	Actively enrolling

Multicenter clinical trial in ambulatory patients with chronic HF to evaluate the efficacy of a low sodium containing diet on a composite clinical outcome composed of of all-cause mortality, cardiovascular hospitalizations and cardiovascular emergency department visits.

1,000
(Canada/Global)
Patient enrollment target

157/167
(Canada/Global)
Patient enrollment achieved

14/16
(Canada/Global)
Number of sites participating

TECOS

Trial **E**valuating **C**ardiovascular **O**utcomes with **S**itagliptin

Protocol #:	082-04
Sponsor:	Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.
Drug:	Sitagliptin
Anticipated Timeline:	August 2008 - October 2015
Trial Status:	Database locked and sites closed

Randomized, placebo controlled clinical trial to evaluate cardiovascular outcomes after treatment with sitagliptin in patients with Type 2 diabetes mellitus and inadequate glycemic control.

481/14,000
(Canada/Global)
Patient enrollment target

549/14,745 COMPLETED
(Canada/Global)
Patient enrollment achieved to date

28/681
(Canada/Global)
Number of sites participating

Diabetes Comes of Age in Cardiovascular Medicine: The TECOS Study

By Paul W. Armstrong

The year 2015 marked the culmination of seven years of work on the TECOS trial (Trial Evaluating Cardiovascular Outcomes with SITAGLIPTIN), a large pragmatic international study designed to assess the impact of sitagliptin versus placebo on cardiovascular events. This intervention was added to usual diabetes care and undertaken in nearly 15,000 patients with type 2 diabetes who already had an established cardiovascular disease.

The TECOS trial was an academic collaboration involving the Duke Clinical Research Institute, the Canadian VIGOUR Centre and the Oxford Diabetes Trials Unit. The trial represented a unique collaboration between endocrinology and cardiology with three thought leaders from each specialty represented on the executive committee. Along with the sponsor, we crafted the protocol, oversaw the operations of the trial and then examined the results after an average follow up of three years in April of 2015. The results were presented at the American Diabetes Association in Boston in June 2015 and simultaneously published in the New England Journal of Medicine.

Much to our satisfaction and great relief, sitagliptin proved to be safe and effective in controlling glucose in these diabetic patients. Most importantly, it did not aggravate heart failure or other ischemic end points over the three years of follow up care as had been suggested previously with a number of diabetes drugs, including one within the class of Dipeptidyl Peptidase-4 Inhibitors (DPP-4 Inhibitors) where sitagliptin resides. Because diabetes is growing in epidemic proportion in association with obesity, and as such is a major cause of heart disease and stroke as well as kidney, eye and nerve damage, new therapies and approaches are desperately needed. This need demands new forms of collaboration such as occurred in the TECOS trial. We were very pleased to have engaged 26 sites across Canada who enrolled 549 patients, exceeding our enrollment goal. I wish to credit Tracy Temple and Lyndsey Garritty for their operational leadership so critical to this achievement and our collaborators across Canada who did an outstanding job.

Of particular interest in this trial was the issue of heart failure which was suggested as a potential hazard with a similar drug in the same class. Heart failure in diabetic patients is particularly harmful with a mortality double of that in non-diabetic patients, and has been characterized as "frequent, forgotten and often fatal". We were pleased to have had the opportunity to present this work to our Canadian colleagues at the Late Breaking Session of the Canadian Cardiovascular Society meeting in October 2015, as well as at a special investigator meeting in Toronto on that same occasion.

It is important to note that there are several other lessons to be learned from the large enriched database we have acquired. We are exploring, as one example, the question of osteoporotic based fractures that are known to be in excess in diabetes. Other questions include the impact on the elderly and the role of hypoglycemia in aggravating ischemic end points to name only a few. Since diabetes is so common, and a number of new agents are now in development, it is likely this patient population will be a target for future collaborative studies that are unquestionably enriched by novel collaborations as defined in the TECOS study.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes

Jennifer B. Green, M.D., M. Angelyn Bethel, M.D., Paul W. Armstrong, M.D., John B. Buse, M.D., Ph.D., Samuel S. Engel, M.D., Jyotsna Garg, M.S., Robert Josse, M.B., B.S., Keith D. Kaufman, M.D., Joerg Koglin, M.D., Scott Korn, M.D., John M. Lachin, Sc.D., Darren K. McGuire, M.D., M.H.Sc., Michael J. Pencina, Ph.D., Eberhard Standl, M.D., Ph.D., Peter P. Stein, M.D., Shailaja Suryawanshi, Ph.D., Frans Van de Werf, M.D., Ph.D., Eric D. Peterson, M.D., M.P.H., and Rury R. Holman, M.B., Ch.B., for the TECOS Study Group*

From the Duke Clinical Research Institute, Duke University School of Medicine, Durham (J.B.G., J.G., M.J.P., E.D.P.) and University of North Carolina School of Medicine, Chapel Hill (J.B.B.) — both in North Carolina; Diabetes Trials Unit, Oxford Centre for Diabetes, Endocrinology and Metabolism, University of Oxford, Oxford, United Kingdom (M.A.B., R.R.H.); Canadian VIGOUR Centre, University of Alberta, Edmonton, AB (P.W.A.) and St. Michael's Hospital, University of Toronto, Toronto (R.J.) — both in Canada; Merck, Kenilworth, NJ (S.S.E., K.D.K., J.K., S.K., P.P.S., S.S.); George Washington University Biostatistics Center, Rockville, MD (J.M.L.); University of Texas Southwestern Medical Center, Dallas (D.K.M.); Munich Diabetes Research Group, Helmholtz Center, Neuherberg, Germany (E.S.); and University of Leuven, Leuven, Belgium (F.V.W.). Address reprint requests to Dr. Holman at the Diabetes Trials Unit, Oxford Centre for Diabetes, Endocrinology and Metabolism, Churchill Hospital, Oxford OX3 7LJ, United Kingdom, or at rury.holman@dtu.ox.ac.uk.

*A complete list of members in the Trial Evaluating Cardiovascular Outcomes with Sitagliptin (TECOS) Study Group is provided in Supplementary Appendix 1, available at NEJM.org.

Drs. Green and Bethel contributed equally to this article.

This article was published on June 8, 2015, and updated on July 16, 2015, at NEJM.org.

N Engl J Med 2015;373:232-42.
DOI: 10.1056/NEJMoa1501352

ABSTRACT

BACKGROUND

Data are lacking on the long-term effect on cardiovascular events of adding sitagliptin, a dipeptidyl peptidase 4 inhibitor, to usual care in patients with type 2 diabetes and cardiovascular disease.

METHODS

In this randomized, double-blind study, we assigned 14,671 patients to add either sitagliptin or placebo to their existing therapy. Open-label use of antihyperglycemic therapy was encouraged as required, aimed at reaching individually appropriate glycemic targets in all patients. To determine whether sitagliptin was noninferior to placebo, we used a relative risk of 1.3 as the marginal upper boundary. The primary cardiovascular outcome was a composite of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for unstable angina.

RESULTS

During a median follow-up of 3.0 years, there was a small difference in glycated hemoglobin levels (least-squares mean difference for sitagliptin vs. placebo, −0.29 percentage points; 95% confidence interval [CI], −0.32 to −0.27). Overall, the primary outcome occurred in 839 patients in the sitagliptin group (11.4%; 4.06 per 100 person-years) and 851 patients in the placebo group (11.6%; 4.17 per 100 person-years). Sitagliptin was noninferior to placebo for the primary composite cardiovascular outcome (hazard ratio, 0.98; 95% CI, 0.88 to 1.09; P<0.001). Rates of hospitalization for heart failure did not differ between the two groups (hazard ratio, 1.00; 95% CI, 0.83 to 1.20; P=0.98). There were no significant between-group differences in rates of acute pancreatitis (P=0.07) or pancreatic cancer (P=0.32).

CONCLUSIONS

Among patients with type 2 diabetes and established cardiovascular disease, adding sitagliptin to usual care did not appear to increase the risk of major adverse cardiovascular events, hospitalization for heart failure, or other adverse events. (Funded by Merck Sharp & Dohme; TECOS ClinicalTrials.gov number, NCT00790205.)

PROACT-4: Moving Blood Tests into the Ambulance

By Justin Ezekowitz

Patients with chest pain are often seen first by an ambulance and taken directly to an emergency department where ECGs, blood tests and clinical evaluations occur in order to understand the source of their chest pain. The majority of this investigation is directed at the diagnosis of a heart attack. Recent advances in a biomarker called troponin have made this more rapidly and readily available and now even on smaller point-of-care (POC) devices. The PROACT-4 trial evaluated a strategy of testing troponin in the ambulance using a novel (POC) device. Paramedics in the Edmonton zone were able to obtain patient consent and randomize in the field. Using a small sample of blood, inserted into the mobile POC device, meant that the results of the heart test troponin could be available in less than 15 minutes. The trial was designed to be very pragmatic with broad inclusion criteria and few exclusion criteria. It also was designed to mimic the clinical practice of how paramedics and emergency department clinicians function.

This was truly a homegrown clinical trial that involved clinicians from each of the hospitals in Edmonton, paramedics across the zone and Alberta Health Services as partners in testing the strategy for patients with chest pain. Funding was received from the Heart and Stroke Foundation of Canada, the University Hospital Foundation, the Mazankowski Alberta Heart Institute and in-kind funding from Alberta Health Services together with Alere Inc. This partnership between the hospital and health system, ambulances, academics, industry, patients and clinicians is critical for the advancement of human health. This is where we as the Canadian VIGOUR Centre sit: at the interface.

After 18 months of enrollment, the education of hundreds of paramedics and inclusion of 601 patients, the trial was presented at the 2015 American Heart Association (AHA) Scientific Sessions in Orlando, Florida as a late breaking clinical trial presentation. The primary endpoint which was the time from an ambulance arrival on scene to the time the patient was discharged from the emergency department was shorter for those receiving the point of care troponin in the ambulance. Patients in the point of care troponin arm spent a median of 8.8 hours from ambulance to discharge; the usual care arm spent 9.1 hours for the same time. This was statistically significant and lead to detailed discussion on the clinical relevance. We were able to shorten the time to first troponin availability by nearly 100 minutes yet were not able to translate this full reduction to overall time. Furthermore, there were no differences in any of the secondary points which were traditional. We spent a fair amount of time thinking about the problem we were tackling and the data we collected so we had a look in greater detail at our results. First, we identified that we had enrolled a broad group of patients with chest pain and these were not low-risk patients. Second, we determined that some patients were not tested as intended (no troponin in the ambulance) and this may have led to the inability to demonstrate a greater time difference. Third, and what was the primary focus for the AHA discussant of our trial, was that we used a relatively sensitive troponin assay but not the newest high sensitive troponin. Finally, the majority of patients were discharged directly from the emergency department and this highlighted an important need to have an upfront troponin. Since most people were low risk and did not have an acute coronary syndrome, yet spent a large amount of time in emergency department, any methods to reduce this amount of 'dwell time' would lead to significant health care savings. Even within our clinical trial we estimated that 1500 hours of emergency department time would have been saved if troponin was done in the ambulance for all patients.

What does this mean overall? Broad engagement in a clinically relevant question with the right stakeholders engaged can lead to scientific advancement. As we answer one question we have raised several others, including further inquiries about system integration and POC biomarkers in the acute care environment. We look forward to answering these and other questions with you as a partner.

Active Principal Investigators

CVC has an extensive site network across Canada of principal investigators (PIs) who actively participate in CVC managed clinical drug trials, to meet patient enrollment targets. This map represents the locations of 124 principal investigators who were participating in ten (10) of the active clinical trials either coordinated by the CVC, or monitored by the CVC, in 2015. Nearly 50% of these sites have participated in more than one CVC managed clinical trial.

ECG Core Lab

The aim of our ECG Core Laboratory is to translate research results into clinically relevant applications. Using the ECG – a venerable but powerful biomarker – we can generate an improved understanding of the pathophysiologic processes involved in acute coronary syndromes (ACS), thereby enabling not only prediction of outcomes but also assessing effectiveness of treatment. These insights serve to further stimulate cardiovascular scientific research.

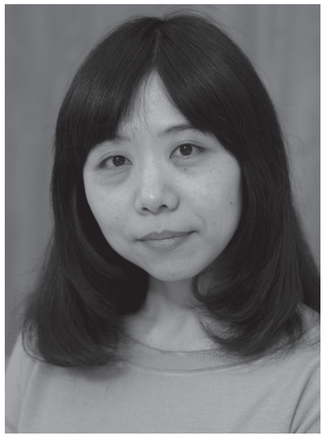
Key projects the ECG Core Lab is involved in include the Vital Heart Response and PROACT-4 studies.

The Vital Heart Response (VHR) project led by Dr. Robert Welsh is a regional initiative that aims to implement timely evidence-based reperfusion strategies to maximize the outcome of patients with ST-segment elevation myocardial infarction (STEMI). VHR project has enrolled 3,578 patients and the Core Lab has completed analysis of 3,333 patients (over 9,000 ECGs).

In 2015, the ECG Core Lab was also involved in PROACT-4, the fourth stage of the PROACT project. A key component of this study is timely recognition of acute cardiovascular patient presentations and how best to provide rapid early diagnosis and more efficient patient care. In 2015, 210 patients' ECGs were analyzed and this data will be examined in concert with acute biomarkers from patients with acute chest pain as well as those with shortness of breath and presumed heart failure.

The ECG Core Lab at the CVC continued its mandate of conducting quality analyses using clinical research data in 2015. The Core Lab has accumulated a wealth of experience and continues to serve as valuable resource and training ground for the next generation of talented researchers. To date ECGs from over 74,600 patients enrolled in studies around the world have been analyzed. This provides an excellent database for additional sub-studies, analyses and research.

Pushpa Jagasia, MD - Senior ECG Reader



Sheila Li, MSc - ECG Reader

Biostatistics

If "creativity is intelligence having fun" (acc. Albert Einstein), then the CVC Biostatistics Group had a year of good fun with a variety of statistical methods. Services provided by the Group include study design, 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.

POPULATION HEALTH LABORATORY

Drs. Anamaria Savu and Padma Kaul addressed the intersection of health and wealth among Canadians; specifically, the association between personal bankruptcy filing and acute myocardial infarction (AMI) rates from 2002 to 2009.[1] Cross-lagged structural equation models were used to assess this longitudinal relationship with adjustment for socioeconomic factors. As hypothesized, they observed that regions with higher rates of AMI were related with higher rates of bankruptcy.

Drs. Savu and Kaul also conducted an interrupted time series analysis to examine the relationship of the 2007 American Heart Association prophylaxis guidelines on infective endocarditis (IE) hospitalizations.[2] Based on the Canadian Institutes for Health Information discharge abstract database to identify all IE hospitalizations between 2002 and 2013, they found that the published guidelines did not change the rate of increasing IE hospitalizations.

CLINICAL TRIALS

The primary results of the PROACT-4 and SODIUM-HF trials were published with Mr. Yinggan (Gray) Zheng leading these analyses. In PROACT-4, patients were randomized to usual care (troponin testing in the emergency department) or point-of-care troponin testing, with the hypothesis tested that point-of-care troponin testing could expedite care for chest pain patients presenting in the emergency department and/or by ambulance.[3] Although there were no observed associations with outcomes, it demonstrated the opportunity to improve the process of care.

The SODIUM-HF pilot study was designed to test the feasibility of implementing a low-sodium dietary intervention in patients with heart failure and to assess the change of brain natriuretic peptide levels and quality of life (as per the Kansas City Cardiomyopathy Questionnaire) at six months.[4] Mr. Zheng and colleagues observed that improvements in these metrics were observed in patients who had achieved target dietary sodium levels.

Two secondary analyses of clinical trials highlight the use of emerging methodology and a unique clinical metric. First, the choice of arterial access site for percutaneous coronary intervention and its association with the risk of major bleeding was examined in acute coronary syndrome (ACS) patients enrolled in the TRACER trial.[5] Dr. Cynthia Westerhout was involved in this study, which used inverse probability weighting to account for the non-randomized selection of access site (transradial versus transfemoral access). And second, Dr. Westerhout and colleagues examined frailty, a rarely measured condition, in a large-scale ACS cohort from the TRILOGY-ACS trial.[6] Frailty was based on the Fried Score, which was self-reported at baseline in patients U65 years, and was associated with increased risk of cardiovascular death, MI, or stroke.

Cynthia Westerhout, PhD - Assistant Director, Biostatistics and Senior Research Associate

Yinggan (Gray) Zheng, MA, MEd - Senior Biostatistician

Wendim Alemayehu, PhD - Biostatistician

1 Savu A, Schopflocher A, Scholnick B, Kaul P. The intersection of health and wealth: association between personal bankruptcy and myocardial infarction rates in Canada. BMC Public Health 2015 16;31:

2 Mackie AS, Liu W, Savu A, Marelli AJ, Kaul P. Infective endocarditis hospitalizations before and after the 2007 American Heart Association prophylaxis guidelines Citation: CANADIAN JOURNAL OF CARDIOLOGY.

3 Ezekowitz JA, Welsh RC, Weiss D, Chan M, Keeble W, Khadour F, Sharma S, Tymchak W, Sookram S, Brass N, Knapp D, Koshy TL, Zheng Y, Armstrong PW. Providing Rapid Out of Hospital Acute Cardiovascular Treatment 4 (PROACT-4). J Am Heart Assoc. 2015;1;4(12).

4 Colin-Ramirez E, McAlister FA, Zheng Y, Sharma S, Armstrong PW, Ezekowitz JA. The long-term effects of dietary sodium restriction on clinical outcomes in patients with heart failure. The SODIUM-HF (Study of Dietary Intervention Under 100 mmol in Heart Failure): a pilot study. Am Heart J. 2015;169:274-281.

5 Dery JP, Mahaffey KW, Tricoci P, White HD, Podder M, Westerhout CM, Harrington RA, Chen E, Strony J, Van de Werf F, Ziada KM, Held C, Aylward PE, Armstrong PW, Rao SV. Arterial Access Site and Outcomes in Patients Undergoing Percutaneous Coronary Intervention With and Without Vorapaxar. Catheter Cardiovasc Interv. 2015 DOI: 10.1002/ccd.26335 [Epub ahead of print]

6 White HD, Westerhout CM, Alexander KP, Roe MT, Winters KJ, Cyr DD, Fox KA, Prabhakaran D, Hochman JS, Armstrong PW, Ohman EM; TRILOGY ACS investigators. Frailty is associated with worse outcomes in non-ST-segment elevation acute coronary syndromes: Insights from the TaRgeted platelet Inhibition to cLarify the Optimal strateGy to medicallY manage Acute Coronary Syndromes (TRILOGY ACS) trial. Eur Heart J Acute Cardiovasc Care. 2015 [Epub ahead of print].

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 continues to be actively involved in examining population-level 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. Accordingly, the CVC has one of the largest repositories of cardiovascular data at the University of Alberta. This repository currently includes data on approximately 6.5 million hospitalizations for 2.5 million Canadians, and data on hospitalizations, outpatient care, medications, and vital status for over 900,000 Albertans suffering from heart disease over the last decade. This data has been used to examine several research questions including socio-economic and urban/rural differences in access to treatment and outcomes; outcomes among vulnerable populations including 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.

The CVC population health data repository serves as a major resource for applied research training. This year, Drs. Van Diepen and Ezekowitz used data on 16,000+ Albertans with heart failure or acute coronary syndromes to examine variation in critical care unit admission rates and outcomes in high- and low-volume hospitals. Dr. Wu, Assistant Professor in Hematology at the University of Alberta and Dr. McAlister conducted a study involving 25,000+ patients with non-valvular atrial fibrillation to examine whether outcomes differed between those living in rural and urban areas in Alberta. Dr. Donovan, Clinical Associate Professor, University of Calgary and Dr. Kaul examined the prevalence and timing of screening for gestational diabetes in a cohort of 85,000+ women who delivered children between 2008 and 2012 in Alberta.

Padma Kaul, PhD - Director, Outcomes Research

Anamaria Savu, PhD - Biostatistician

Business Office

The business office is fundamental to the organizational and financial underpinnings of the CVC. Reviewing and negotiating contracts is one of its key tasks, alongside providing expert service in the areas of managing agreements, developing and tracking metrics, and executing invoices and site payments. Dedicated to financial stewardship, the business office prudently manages revenue and expense administration. It is also committed to the progress of information systems management, strategic planning, process improvement, and the promotion of learning and development initiatives. The business office is responsible for the creation and distribution of all marketing materials aimed at creating strong brand awareness that speaks to the mission and values of this organization. Finally, the office facilitates communications between the CVC and many institutional partners, which include, but are not limited to, Duke Clinical Research Institute (DCRI), Alberta Health Services (AHS), and Northern Alberta Clinical Trials and Research Centre (NACTRC). Our dedication to upholding strong partnerships with these institutions is essential to the day-to-day operations of the CVC.

Carla Price, BSc - Business and Research Administrator

Ellen Pyear, MA - Business and Operations Assistant

Oksana Grant, PCP - Business and Operations Assistant

"For medicine, the greatest surprises lie still ahead of us, but they are there waiting to be discovered or stumbled over sooner or later."

— LEWIS THOMAS

Faculty

Our CVC Faculty are internationally recognized as Thought Leaders in their respective areas of interest. They represent a unique and dynamic integration of clinical research. The approach begins by addressing unmet clinical needs through conducting rigorous clinical investigation and clinical trials of novel diagnostic and therapeutic interventions in selected areas of cardiovascular medicine. It extends from that pivot to the knowledge gained through detailed registries of all patients in areas of particular interest and relevance to public health, namely Acute Coronary Syndromes and Heart Failure. Our group has been especially keen to explore better ways of analyzing the responses of patients to interventions by modeling their outcomes over time, taking account of the relative value patients put on differing outcomes and their implications for quality of life and health care costs. Finally we are well positioned to study health care outcomes at a population level for all Albertans to assess how well new advances are being applied and whether they are making a meaningful difference.

PAUL W. ARMSTRONG, MD

- Founding Director, Canadian VIGOUR Centre
- Distinguished University Professor, Division of Cardiology, University of Alberta
- Formerly Chair of the Department of Medicine, University of Alberta
- Founding Director of TORCH (Tomorrow's Research Cardiovascular Health Professionals), a Strategic Training Program Initiative
- Founding President of the Canadian Academy of Health Sciences
- 2014 Recipient of the University Alberta Cup (the highest honour bestowed by the University on an individual who has achieved outstanding distinction in research, teaching and service)

Dr. Armstrong's research interests include:

- Development of novel methods to enhance clinical trial methodology
- Cardiovascular disease and its implications in the elderly
- Pathophysiology and novel therapeutic approaches of congestive heart failure
- Diagnosis and management of acute coronary syndromes. with emphasis on timely interventions

JUSTIN EZEKOWITZ, MBBCH, MSC

- Co-Director, Canadian VIGOUR Centre
- 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' research interests include:

- Testing the impact of drugs and processes of care for patients with acute heart failure
- Novel interventions for patients with chronic systolic and diastolic heart failure;
- The impact of comorbidities such as atrial fibrillation, anemia and hip fractures in patients with heart failure;
- Knowledge gaps for drugs and process of care in heart failure.

SHAUN GOODMAN, MD, MSC

- Co-Director, Canadian VIGOUR Centre
- Associate Head, Division of Cardiology, Department of Medicine, St. Michael's Hospital
- Heart & Stroke Foundation of Ontario (Polo) Chair and Professor, Department of Medicine, University of Toronto
- Adjunct Professor, Department of Medicine, University of Alberta

Dr. Goodman's research interests include:
Facilitating clinical trial, observational, and knowledge translation research in cardiovascular disease in Canada with a focus on:

- Diagnosis, management, and prognosis of acute coronary syndromes
- Optimal stroke prevention risk stratification and management in atrial fibrillation
- Primary and secondary prevention of cardiovascular disease.

KEVIN BAINEY, MD

- Assistant Professor and Interventional Cardiologist, Mazankowski Alberta Heart Institute, University of Alberta
- Director, Interventional Cardiology Fellowship Program, Mazankowski Alberta Heart Institute, University of Alberta

Dr. Bainey's research interests include:

- Optimizing reperfusion in ST-elevation myocardial infarction
- Ethnic-based clinical outcomes

PADMA KAUL, PHD

- Director, Outcomes Research, Canadian VIGOUR Centre
- 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

Dr. Kaul's research interests include:

- International differences in practice patterns and outcomes
- Sex differences in treatment and outcomes of cardiovascular disease
- Long term chronic disease implications for pregnancy related complications
- Issues related to access and delivery of care at a population level
- Health economics.

FINLAY A. MCALISTER, MD, MSC

- 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
- Past-Chair, Outcomes Research Task Force, Canadian Hypertension Education Program
- Past-President, Canadian Society of Internal Medicine

Dr. McAlister's 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

SEAN VAN DIEPEN, MD

- Assistant Professor of Critical Care Medicine, Division of Critical Care and Cardiology, University of Alberta
- Academic Cardiologist-Intensivist

Dr. Van Diepen's research interests include:

- Critical care cardiology
- Cardiovascular surgical care
- Cardiovascular risks of cardiac and non-cardiac surgery and heart failure

ROBERT WELSH, MD

- Professor, Division of Cardiology, University of Alberta
- Edmonton Zone Medical Director, Cardiac Sciences
- Interventional Cardiologist, Mazankowski Alberta Heart Institute
- Director, Adult Cardiac Catheterization and Interventional Cardiology program
- Vice-President, Canadian Association of Interventionla Cardiologists
- Co-chair of Vital Heart Response
- Co-chair of the Mazankowski TAVI Program

Dr. Welsh's research interests include:

- Acute Coronary Syndromes and Interventional Cardiology
- Cardiovascular disease and diabetes
- Exercise physiology and cardiac physiology
- Pre-hospital management of STEMI and the interaction of pharmacological (antithrombotic and fibrinolytic) and mechanical interventions (primary and rescue angioplasty)

Worldwide Collaborators

BRAZILIAN CLINICAL RESEARCH INSTITUTE
Sao Paulo, Brazil

C5 RESEARCH, CLEVELAND CLINIC
Cleveland, USA

DUKE CLINICAL RESEARCH INSTITUTE
Durham, USA

ESTUDIOS CLINICOS LATINOMERICA
Rosario, Argentina

GREEN LANE COORDINATING CENTER
Auckland, New Zealand

FLINDERS MEDICAL CENTRE
Adelaide, Australia

LEUVEN COORDINATING CENTRE
Leuven, Belgium

ICAHN SCHOOL OF MEDICINE, MOUNT SINAI
New York, USA

STANFORD CENTER FOR CLINICAL RESEARCH, STANFORD UNIVERSITY
Stanford, USA

UPPSALA CLINICAL RESEARCH CENTRE
Uppsala, Sweden

Acknowledgements

CVC gratefully acknowledges and thanks:

- the patients, for their willing participation in trials, they are the heroes of clinical research;
- the CVC faculty, external advisors and collaborators for their contributions and for providing ongoing research opportunities, we look forward to providing continued services and to future collaborations;
- the CVC staff and management for their dedication, professionalism, excellent contributions and ingenuity that enhances the quality of our research work;
- our trainees for their commitment and enthusiasm as the next generation of researchers;
- the sponsors and granting agencies, without their financial support these trials and educational activities would not be possible;
- the excellent work of Ellen Pyear and her colleagues Carla Price and Oksana Grant for their time and the dedication required to produce this report;
- AM/FM for the concept and design;
- photographers Mathew Martin and Stephen Wreakes for many of the images enclosed in this report;
- McCallum Printing Group Inc. for their service in printing this report and our Chronicle newsletter.

“You cannot swim for new horizons until you have courage to lose sight of the shore.”

— WILLIAM FAULKNER

CANADIAN VIGOUR CENTRE

Bridging Hearts and Minds to Enhance Cardiovascular Care

UNIVERSITY OF ALBERTA

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

vigour.ualberta.ca