



Building a Brighter Future

2018 ANNUAL REPORT



Canadian **VIGOUR** Centre
Bridging Hearts and Minds

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“
As far as we can discern,
the sole purpose of human
existence is to kindle a light in
the darkness of mere being.

”

Carl Jung



Message from the Founding Director

Each year as I prepare an introductory message for our annual report on behalf of our great CVC team, I genuinely enjoy surveying the organizational accomplishments over the prior 12 months and contemplating what lies ahead on our path. Part of this exercise is selecting an annual theme that we perceive best reflects our organization's location in time and space. Given my personal joy of sailing, I am delighted that this year we are featuring a lighthouse on our cover. It beams radiantly our intent to be ***"Building a Brighter Future."***

To a sailor a lighthouse is usually a welcome sight, providing key navigational guidance and a path to a safe harbour and/or caution to avoid potential environmental hazards. Lighthouses are thought to have been first erected in ancient Egypt and then in Spain. They became especially prominent in the late 17th century to assist mariners crossing the English Channel. Incremental improvements in their structure, light sources, optics and lenses resulted in remarkable luminosity evident as far as 20 miles away. Although the arrival of GPS positioning has led to some decline in their prevalence, Canada has wisely maintained 50 staffed stations on its three coastlines, which are the coast guard's responsibility. Historically, lighthouses were - and still are - regarded as excellent examples of serving the public good.

It is exactly that spirit - elegantly phrased in Carl Jung's introductory quote - which drives our work at the CVC. We aim to serve the public good by enhancing cardiovascular health through creating, translating and disseminating new knowledge. As you peruse this report, please recognize that I have arbitrarily chosen only a scant six of the 126 peer-reviewed publications to feature. These are but a few examples of the great and

remarkable work our faculty and team of project leaders, biostatisticians and trainees are doing. Of particular note in 2018 was the completion of the important ODYSSEY OUTCOMES trial. This was led in Canada by our CVC team and championed by our Co-Director, Shaun Goodman, who also played a key role on the international executive committee. This work (described in more detail elsewhere in the report) defines the opportunity that a novel cholesterol-lowering drug provides in achieving a new standard of preventative care for cardiovascular (CV) disease.

To broaden our reach across the spectrum of CV disease, you will also notice in our annual report that we have welcomed two new cardiologists as associate CVC faculty. Roopinder (Rupi) Sandhu is an electrophysiologist with a special interest and expertise in atrial fibrillation: this disorder is increasingly common and her work dynamically intersects with heart failure, which has been a major focus of the CVC's work. Sean McMurtry's interests are in the vascular tree: aortic disease and peripheral arterial disease are understudied and constitute large unmet needs ripe for innovations. We anticipate their collaboration will enrich our mission.

Broadening our reach through enhanced east-west trans Canada collaborations and engaging developing cardiovascular clinician scientists has been another key 2018 initiative also addressed herein by Shaun Goodman (who plays a lead role). Although we are geographically a large country, a limited research community and a small cadre of young investigators reflect Canada's modest population. In 2016, we hatched the idea of a Canadian cardiovascular collaboratory to better position us to work together and enhance our global competitiveness.

The beam of light emitted by a lighthouse is not only broad and bright, but it also rotates to provide a wider field of vision. So too we will need to diversify the breadth and enhance the intensity of our focus on CV health and disease in the future. Some of the themes we will need to embrace in 2019 and beyond include: i) how to better engage patients and the public in our research, such that the design and outcomes measured are most meaningful for them, ii) how to exploit the coming electronic medical records (EMR) and opportunities to augment our intelligence and discern how to better align our therapies, and iii) how to preserve the integrity of Canada's health care system by pursuing research questions that really matter. This includes assessing those interventions and practices that result in the best outcomes and return on investment of our fellow taxpayers' dollars.

On behalf of our co-directors and the entire CVC team, I hope you find our 2018 accounting of CVC's progress illuminating. As always, we welcome comments and feedback from our many friends and colleagues around the globe. We relish the prospects of moving forward with your help in the future.



Paul W. Armstrong, MD
Founding Director





Vision, Mission, and Core Values

Vision

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

Mission

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

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

Core Values

Quality

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

Collaboration

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

Integrity

Perform our roles in an ethical framework, which enhances our reputation as honest, trustworthy and responsible.

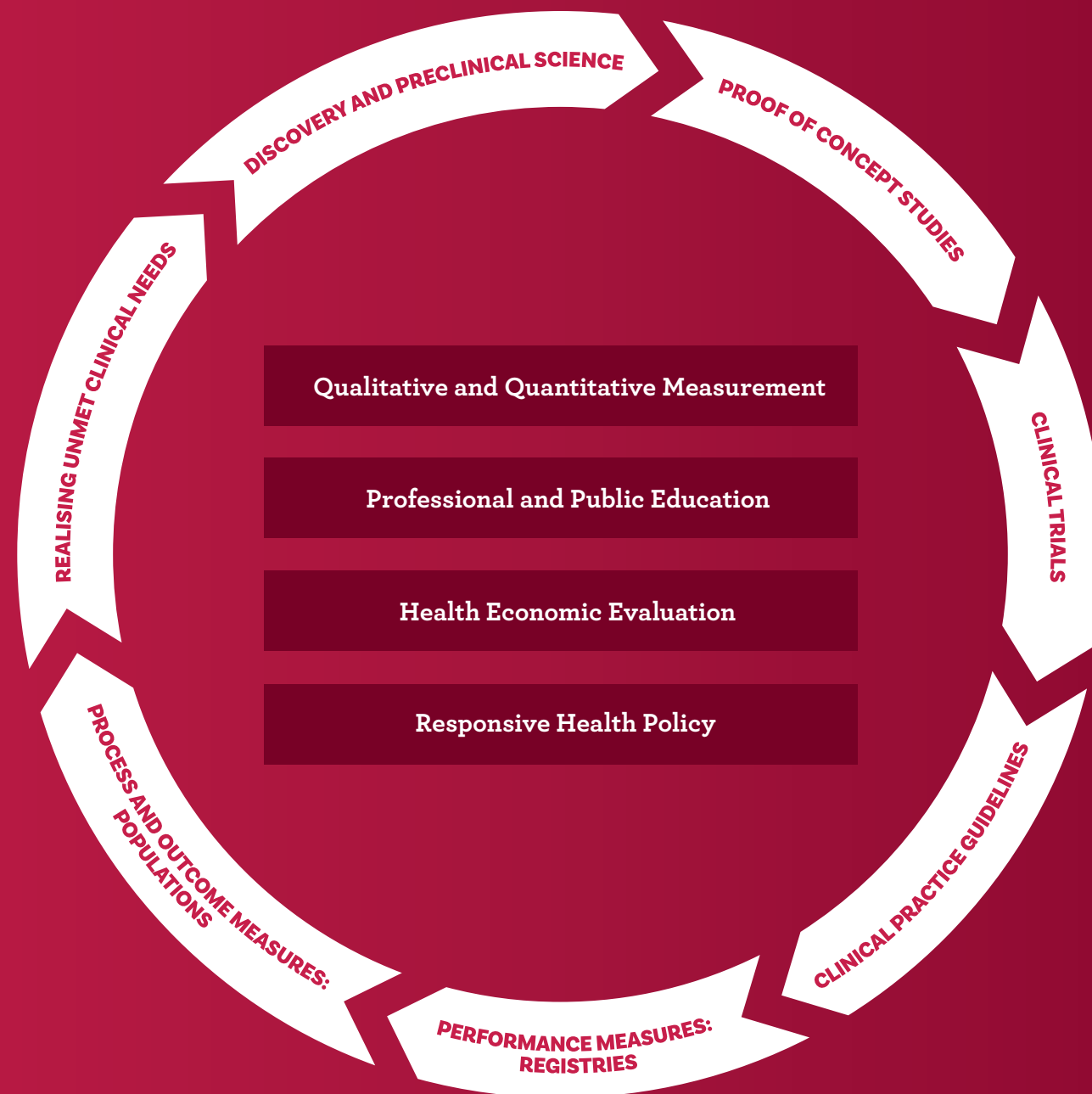
Respect

Create an innovative, engaging and inclusive work environment, appreciative of individual differences and contributions. Our workplace will be conducive 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 the right to publish its 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, thereby aiming 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, the 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.

2018 Year in Review



8

Industry-funded studies underway



39

Grant-funded projects underway on which CVC faculty members are principal or co-investigators



126

Publications produced by the CVC



127

Principal investigators participating in CVC-managed trials



194

On-site and remote monitoring visits conducted in Canada



2.5 Million

Canadians represented in CVC's data repository



90

Lectures and presentations given by the CVC faculty in Canada and abroad



7,775

Citations generated from CVC-authored papers published between 2014-2018



41

CVC faculty and staff members



231

Global users accessing the CVC's online collaborative platform



Introducing New Faculty

The CVC was pleased to introduce two new associate faculty members to our team in November.

Dr. Sean McMurtry is a clinician scientist and Associate Professor in the Division of Cardiology at the University of Alberta. He is engaged in basic and clinical research projects studying coronary artery disease, peripheral artery disease, venous thromboembolism and thoracic aortic disease.

Dr. Roopinder Sandhu is a cardiac electrophysiologist and Associate Professor in the Division of Cardiology at the University of Alberta. Her main research focuses involve gaining better understanding of atrial fibrillation epidemiology, identifying gaps in treatment and pursuing strategies to improve outcomes.

In the following interviews, Drs. McMurtry and Sandhu share more information about their individual backgrounds, research interests and new roles at the CVC.



M. Sean McMurtry, MD, PhD, FRCPC

What was your path to becoming a clinician scientist?

During my clinical training, I was fortunate to have two strong mentors, Drs. Stephen Archer and Evangelos Michelakis, who both inspired me to undertake formal research training. I completed a PhD on the experimental biology of pulmonary artery hypertension in the University of Alberta Clinical Investigator program, and during my subsequent time as a cardiology resident and vascular medicine fellow, also performed clinical research projects with other faculty. When I joined the faculty at the University of Alberta in 2007, it was clear that I would have a significant research commitment as part of my role.

How did you first become involved with the CVC? What specifically motivated you to join the CVC faculty?

My first exposure to the CVC was working with Dr. Paul Armstrong as cardiology resident. He is an inspiring figure who has built the strong and productive research enterprise that is the CVC. When the invitation came to join this very successful group, it became obvious that this would be an excellent opportunity for me to pursue.


What areas of clinical research interest you the most? How do you think these research interests align with the vision and mission of the CVC?

I trained in general cardiology and vascular medicine, so in addition to the common cardiac problems like acute coronary syndromes, heart failure and atrial fibrillation, I am interested in vascular problems like peripheral artery disease, acute aortic syndromes and venous thromboembolism. I am also interested in prevention, as well as sex differences in cardiovascular disease. Since no other CVC faculty has clinical expertise in the aforementioned vascular disorders, I bring a new skill set to the CVC that I am optimistic will expand the organization's scope and reach.

What are you most looking forward to in your first year as a new member of the CVC faculty?

I am most looking forward to developing substantive and productive relationships with the other faculty and staff of the CVC.





Roopinder Sandhu, MD, MPH

What was your path to becoming a clinician scientist?

My path to becoming a clinician scientist began during my first year of internal medicine training when I had the opportunity to be involved in my first research project titled “Prevalence of QRS Prolongation in a Community Hospital Cohort of Heart Failure Patients and Its Relation to Left Ventricular Systolic Dysfunction”. I was responsible for the literature review, data acquisition, data interpretation and writing the manuscript. This research was done under the mentorship of a master clinician and cardiologist who was conducting clinical research. This early experience not only fostered a passion for research, but it also provided me with an example of how research could be successfully integrated alongside my clinical interests. I went on to complete sub-specialty training in cardiology and cardiac electrophysiology (EP), and then a Masters degree in Public Health at Harvard. During this time, I continued to conduct research under the mentorship of exceptional clinician scientists.

How did you first become involved with the CVC? What specifically motivated you to join the CVC faculty?

I first became involved with the CVC prior to joining the Division of Cardiology when I had the opportunity to work on research with one of its faculty members, Dr. Finlay McAlister. We described the epidemiology of atrial fibrillation (AF) according to location of diagnosis, risk stratification schemes, and use of anticoagulation and outcomes in Alberta by using an AF cohort at the CVC, which had been developed by linking multiple administrative databases.

What areas of clinical research interest you the most? How do you think these research interests align with the vision and mission of the CVC?

The area of clinical research that interests me the most is arrhythmia (AF and syncope) health outcomes research, which includes gaining a better understanding of epidemiology, identifying gaps in treatment and pursuing strategies to improve outcomes. This research interest aligns itself well with the CVC’s strengths of conducting clinical trials, and population health and economic research. My clinical and research experience in EP provides an opportunity for the CVC to expand its research programs beyond heart failure, coronary artery disease, and critical care while simultaneously allowing for important collaborations with investigators in these areas where considerable overlap exists.

What are you most looking forward to in your first year as a new member of the CVC faculty?

I am most looking forward to being a member of and contributing to the successful team of investigators, statisticians, trainees and support staff at the CVC.



Featured Publications

One of the most tangible metrics of the CVC’s research is its contribution to peer-reviewed literature. The following publications represent the creative abilities and hard work of all the members of our team who contribute in many different ways to their production. This is not an easy task, and the scientific rigor necessary to convince editors and independent peer reviewers of the merit of our work requires talent, energy and perseverance - sometimes in the face of rejection.

We are proud of the 126 publications produced within the CVC’s body of research in 2018. Selecting just six was not easy, but their diverse topics and messages provide one window into our character and efforts.

If you would like to view a full list of the CVC’s publications from 2018, please visit thecvc.ca/publications.

1

Effects of Supplemental Oxygen Therapy in Patients With Suspected Acute Myocardial Infarction: A Meta-analysis of Randomised Clinical Trials.

Sepehrvand N, James SK, Stub D, Khoshnood A, Ezekowitz JA, Hofmann R.

Heart. 2018;104:1691-1698.

During his ongoing graduate training, Nariman Sepehrvand, in conjunction with his supervisor, Justin Ezekowitz, and other colleagues, undertook a systematic review of eight randomized clinical trials which included nearly 8,000 patients. They examined whether the use of supplemental oxygen administered in patients with suspected acute myocardial infarction was beneficial. Importantly, they found that neither the infarct size nor in-hospital or 30-day mortality was enhanced by the use of routine oxygen in this subset of patients. The bottom line of these cumulative observations is that despite the common use of supplemental oxygen, it appears not to have been associated with benefit. Given the cost of routine oxygen use and implications for care, they suggest a revaluation of this therapy be undertaken. This conclusion provides fertile opportunities for future research in which they are engaged.



Justin Ezekowitz, MBBCh, MSc



Nariman Sepehrvand, MD

2

Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome.

Schwartz GG, Steg PG, Szarek M, Bhatt DL, Bittner VA, Diaz R, Edelberg JM, Goodman SG, Hanotin C, Harrington RA, Jukema JW, Lecorps G, Mahaffey KW, Moryusef A, Pordy R, Quintero K, Roe MT, Sasiela WJ, Tamby JF, Tricoci P, White HD, Zeiher AM; ODYSSEY OUTCOMES Committees and Investigators.

N Engl J Med. 2018;379:2097-2107.

A publication of notable highlight in 2018 is the results of the ODYSSEY OUTCOMES trial. CVC Co-Director, Shaun Goodman, played a key role in this large international trial as a member of the executive committee, and the CVC undertook the trial management within Canada, contributing a total of 361 patients. ODYSSEY is a landmark research study proving that a new cholesterol-lowering agent — a monoclonal antibody called alirocumab — improves outcomes among patients who have had a previous acute cardiac event and who were already receiving high-dose conventional statin therapy. Importantly, this new agent is administered as an injection under the skin once every two weeks. Additional details about the ODYSSEY trial are provided by Dr. Goodman elsewhere in this report.



Shaun Goodman, MD, MSc

Population-level Incidence and Outcomes of Myocardial Infarction With Non-obstructive Coronary Arteries (MINOCA): Insights From the Alberta Contemporary Acute Coronary Syndrome Patients Invasive Treatment Strategies (COAPT) Study.

Bainey KR, Welsh RC, Alemayehu W, Westerhout CM, Traboulsi D, Anderson T, Brass N, Armstrong PW, Kaul P.

Int J Cardiol. 2018;264:12-17.

The acronym COAPT stands for Contemporary Acute Coronary Syndrome Patients Invasive Treatment Strategies, and is a pan-Alberta collaboration aimed at better understanding patients with acute coronary syndromes who undergo coronary angiography. This project was pioneered by Robert Welsh, who chairs a steering committee of contributors from across Alberta. In this publication, Kevin Bainey has analyzed patients who have myocardial infarction, yet they have little or no evidence of coronary arterial narrowing. This population, previously thought to have a benign prognosis, in fact turns out to have impaired 5-year outcomes as it relates to both cardiac mortality and recurrent myocardial infarction. As a crucial part of this study, the data were carefully derived and curated by senior author, Padma Kaul, who provides the team with key epidemiologic and biostatistical insights.



Kevin Bainey, MD



Robert Welsh, MD



Wendimagegn Alemayehu, PhD



Cynthia Westerhout, PhD



Paul W. Armstrong, MD



Padma Kaul, PhD

Frequency of Low-value Care in Alberta, Canada: A Retrospective Cohort Study.

McAlister FA, Lin M, Bakal J, Dean S.

BMJ Qual Saf. 2018;27:340-346.

Finlay McAlister and colleagues examined the use of clinical care in over three million Albertans between 2012 and 2015 in order to explore the frequency with which so-called low-value health services were employed. Although infrequent, they found the rate of such instances was approximately 5%. Especially revealing was the increased likelihood of these services for cervical cancer screening in women older than 65 and prostate antibody testing in men older than 75. In both of these instances little evidence exists to support their use. Importantly, they also found a pattern for this observation - namely that those in higher social economical brackets and seeing specialists were more likely to receive these investigations. As the cost of health care rises, these insights will be crucial in developing performance measures and exploring methods to translate standard of care guideline-based therapy to promote “de-intensification” of some areas of medicine. This is a good example of why access and careful analysis of “big data” in the health sector can influence health policy.



Finlay McAlister, MD, MSc

Use of Biomarkers to Predict Specific Causes of Death in Patients With Atrial Fibrillation: Insights From the ARISTOTLE trial.

Sharma A, Hijazi Z, Andersson U, Al-Khatib SM, Lopes RD, Alexander JH, Held C, Hylek EM, Leonardi S, Hanna M, Ezekowitz JA, Siegbahn A, Granger CB, Wallentin L.

Circulation. 2018;138:1666-1676.

In this innovative application of clinical trial biomarker data in patients with atrial fibrillation (AF), Abhinav Sharma (mentored by Justin Ezekowitz), while training at Duke University, explored which biomarkers acquired at the time of entry into the ARISTOTLE study were most likely to provide additional insight into patient outcomes. The patients with AF being studied received novel anticoagulation in order to prevent their well-known risk of stroke. The study group found that cardiac injury signaled by elevated troponin T (cTnT) was strongly associated with sudden death, whereas the cardiac stress marker, NT-proBNP, presaged death due to heart failure. By contrast, growth differentiation factor-15 (GDF-15) suggested an important association between deaths due to bleeding complications. These findings create new lines of evidence to better partition patients according to their baseline risk and identify novel targets to reduce their excess risk.



Justin Ezekowitz, MBBCh, MSc



Abhinav Sharma, MD

2018 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology Focused Update of the Guidelines for the Use of Antiplatelet Therapy.

Mehta SR, Baine KR, Cantor WJ, Lordkipanidzé M, Marquis-Gravel G, Robinson SD, Sibbald M, So DY, Wong GC, Abunassar JG, Ackman ML, Bell AD, Cartier R, Douketis JD, Lawler PR, McMurtry MS, Udell JA, van Diepen S, Verma S, Mancini GBJ, Cairns JA, Tanguay JF; members of the Secondary Panel.

Can J Cardiol. 2018;34:214-233.

The Canadian Cardiovascular Society (CCS) provides clinical practice guidelines for practitioners of cardiovascular medicine across Canada. This past year, they undertook an evaluation of how best to use antiplatelet therapy for patients with coronary heart disease, including those with recent acute myocardial infarction. The authors of these guidelines are chosen for their expertise and contributions to the field, and in this instance, three of our faculty (Kevin Baine, Sean McMurtry and Sean van Diepen) were chosen to participate and provide insight in this important area.

In this set of recommendations, the CCS focused on patients undergoing recent percutaneous coronary intervention, non-cardiac surgery and coronary bypass surgery, and addressed the thorny issues associated with concomitant anticoagulant/antiplatelet therapy in patients with complex cardiac disease. Importantly, these guidelines are a key national process that testify to the expertise of our engaged faculty members, and have a substantial impact on the clinical practice of many practitioners across the country.



Kevin Baine, MD



M. Sean McMurtry, MD, PhD, FRCPC



Sean van Diepen, MD



Faculty Presentations

Throughout the year, the CVC faculty shares their knowledge through lectures and presentations given across Canada and around the world. These activities reflect the global reach of the organization and our network of collaborators, and furthermore, illustrate that the CVC's impact and insights are enhanced by our faculty's pursuit of knowledge translation and dissemination.

- 1 Paul Armstrong
- 2 Kevin Bainey
- 3 Sean van Diepen
- 4 Justin Ezekowitz
- 5 Shaun Goodman
- 6 Padma Kaul
- 7 Finlay McAlister
- 8 Robert Welsh



The Next Generation of Health Researchers

The foundation of the CVC's mission is to enhance cardiovascular health for current and future generations, thereby fulfilling its contract with society. As a learning organization, one of the CVC's central tenets is to engage the next generation of health professionals in a culture of research that embraces curiosity, welcomes new ideas, and seeks to address key unanswered questions that are expected to alter the minds and behaviour of all those involved in health care delivery.

The CVC recognizes that research experience can be life changing whether it occurs during a summer studentship, an elective experience in clinical medicine, or through dedicated graduate or postdoctoral training. Whatever knowledge, skills or opportunities we provide to our trainees are inevitably returned to us bearing interest; this return on investment provides fresh and unbiased perspectives, challenges to accepted dogma, and is formulated with an energetic and enthusiastic willingness to learn.

Irrespective of an individual trainee's career plans, exposure to research galvanizes the development of a more critical mind, which can then be applied to the never ending search for better health solutions. An attitude of lifelong learning, coupled with a continuing commitment to remain engaged in the process of research – regardless of individual career destinations – is our aspiration for our research trainees.

In the following section, four of our summer students reflect upon their research highlights and experiences during their collaborations with the CVC in 2018.

Amy Du, BSc

Briefly describe your educational background and what program you are currently enrolled in.

My educational background is mostly based in science. I completed a Bachelor of Science degree with a major in biological sciences and a minor in psychology at the University of Alberta in 2018, and am now in my first year of medical school also at the University of Alberta.

What are your research highlights from your time at the CVC?

I have been very lucky to work on a number of interesting projects during my time at the CVC. During my first summer here, I worked on a project under the supervision of Dr. Justin Ezekowitz that examined how sacubitril/valsartan, a newly approved heart failure therapy, was being dosed and tolerated in general clinical practice compared to the PARADIGM-HF trial. A year and a half of ongoing work on this project culminated in the publication of my first lead-author manuscript, something that I am very grateful to have been able to do. I also had the opportunity to assist with the SODIUM-HF and FEAST-HF trials, and learned about the importance of non-pharmaceutical therapy in heart failure along the way.



What have you learned from working with your mentor at the CVC?

Not only did I learn about the logistics of conducting clinical research from Dr. Ezekowitz, he also showed me the tremendous impact great mentorship can have on a student. I am extremely appreciative of the amount of time that Dr. Ezekowitz took out of his weekly schedule to meet in person to discuss both research and my academic pursuits. In terms of research, he always found ways to keep me involved and expand my skill set, whether that meant getting me involved in different projects or allowing me to shadow him in clinic. Dr. Ezekowitz has also been a great academic support and source of encouragement through the end of my undergraduate degree into my first year of medical school.

How has your experience as a trainee at the CVC impacted your research or career goals?

I honestly wasn't too sure what to expect coming into the clinical research environment. However, in my past two and a half years as a trainee at the CVC, I have learned so much about clinical and translational research, and how crucial they are to medicine. Going forward in my career, I would love to split my time between research and clinical practice, and have a research group of my own.

What will you take away from this experience as you pursue your future goals?

I think my main takeaways from my time at the CVC would be recognizing the importance of research in advancing medicine, as well as the positive impact of committed mentorship on the next generation of physicians and researchers. I would definitely like to set aside time in the future that is dedicated to mentorship and teaching trainees.

Garrison Dyck

Briefly describe your educational background and what program you are currently enrolled in.

I completed my first year of a Bachelor's of Science degree with first-class standing, and currently am in my second year of a double major in biological sciences and psychology here at the University of Alberta.

What are your research highlights from your time at the CVC?

I had the opportunity to work on a few research projects during my time at the CVC. One of my highlights was contributing to a recently published journal article with Drs. Justin Ezekowitz and Nariman Sepehrvand, which investigates the validity of a diagnostic model for heart failure with preserved ejection fraction (HFpEF). It was a great opportunity to participate in the process of generating a journal article by observing how the research question was formed, developing methods of analyzing data, interpreting the results, contributing by writing a small component of the manuscript and eventually seeing the article getting published. The experience taught me a lot about the process of medical research as well as increased my knowledge of medical statistics and the difficulties in diagnosing and treating HFpEF. I was also given the chance to write a review paper about the potential of resveratrol in the treatment of heart failure and cardiovascular disease. It was an excellent project to work on as it also directly related to the clinical work I was involved with, which was assisting with recruiting patients for Dr. Ezekowitz's resveratrol and heart failure trial.

What have you learned from working with your mentor at the CVC?

I learned that medical research is complex, as it requires a huge amount of knowledge about the clinical condition being studied, a tremendous effort to collect the relevant data, and the capability to properly analyze the data that apply to the research question being asked. Through my collaboration with Dr. Ezekowitz on my review paper focusing on resveratrol, I was also able to research and expand my knowledge in regards to different cardiovascular diseases, such as atherosclerosis and its pathogenesis, as well as the effectiveness of alternative treatments to those cardiovascular diseases.

How has your experience as a trainee at the CVC impacted your research?

Dr. Ezekowitz was an especially good mentor as he was always available to answer my questions, involved me in multiple projects, respected my opinions and trusted me to work independently. This gave me confidence that I carried with me while conducting the research analysis and working on the two papers. In addition, my introduction to the vast amount of knowledge on cardiovascular diseases and their etiology will act as a foundation that will help me progress further on in cardiovascular research.

What will you take away from this experience as you pursue your future goals?

As I pursue my goal of becoming a medical doctor, I will certainly continue to respect the amount of effort needed to discover new treatments for disease and how important research is in the health care delivery system. Being able to work with a clinician-scientist provided me with a rare opportunity to observe and play a small role in the discovery of a potential new therapy and help advance this treatment into small scale clinical trials for validation. If I am successful in becoming a medical doctor, I will always respect medical researchers and the role that they play in caring for patients.

Anukul Ghimire, MSc

Briefly describe your educational background and what program you are currently enrolled in.

I am in my third year of the MD program here at the University of Alberta. Prior to medical school, I completed a Master of Science in cardiac sciences under the supervision of Drs. John Tyberg, Israel Belenkie, and Nowell Fine at the Libin Cardiovascular Institute in Calgary where I looked at cardiac mechanics in patients with heart failure and pulmonary hypertension. My ongoing enthusiasm for cardiovascular medicine has driven me to continue with research in the field, and has led me to work with Drs. Finlay McAlister and Justin Ezekowitz at the CVC.

What are your research highlights from your time at the CVC?

We recently received acceptance for our paper examining the prevalence and predictors of the recovery of ejection fraction in a community cohort of heart failure patients, for which I will have the privilege of being first-author, into the European Heart Journal. I have been fortunate to also be involved with other projects including the SODIUM-HF trial, PRECIS-2, and the Alberta HEART cohort study.

This summer, I worked with Dr. Ezekowitz on the cardiology inpatient service as part of my medical school rotation, during which I learned how research can be effectively translated to patient care and felt even more inspired to pursue a career in academic medicine in the future.

What have you learned from working with your mentors at the CVC?

My competency for the research process has

been greatly fostered through working with Drs. McAlister and Ezekowitz. Being directly involved in the literature search and figuring out how to generate novel questions has allowed me to practice the “art of researching”, through which I learned how to (1) ask important and notable questions as they apply to my patient population; (2) go back to the literature to identify the knowledge gaps; (3) develop a plan to tackle the question and fill the knowledge gaps; and (4) execute the plan while learning just how much there is to know on the matter.

How has your experience as a trainee at the CVC impacted your research or career goals?

I am now more inclined towards pursuing academic medicine and research in my future career. I have also developed a stronger interest for internal medicine and cardiology during my time with the CVC. Ultimately, I hope to have a profession in which I can continue to practice clinical medicine while also devoting time towards research and teaching.

What will you take away from this experience as you pursue your future goals?

One of the biggest take-aways for me is gaining an understanding of what it takes to be an effective mentor. Drs. McAlister and Ezekowitz have both been very encouraging and supportive mentors who have allowed me to gain as much experience and knowledge as I could during my time working with the CVC. In the later stages of my residency and in my future practice, I will be required to take on more leadership responsibilities; I hope to emulate these characteristics in my own role as a teacher and a mentor.



Junyi Mei, BSc

Briefly describe your educational background and what program you are currently enrolled in.

I am currently a second year medical student at the University of Manitoba. Prior to medical school, I completed a Bachelor of Science in anatomy and cell biology at McGill University.

What are your research highlights from your time at the CVC?

Over the summer, I worked on chart reviews for the Vital Heart Registry under Dr. Kevin Bainey’s mentorship. My project looked at outcomes of giving half-dose fibrinolytics to elderly patients with ST-elevation myocardial infarction compared to full-dose fibrinolytics or primary percutaneous coronary intervention. I also worked on drafting a statistical analysis plan for the project.

What have you learned from working with your mentor at the CVC?

Dr. Bainey was always accessible to provide guidance despite his busy schedule, and was always encouraging and patient in his mentorship. He provided opportunities for learning and inspired me with his passion for research. Having the opportunity to also observe his clinical work, Dr. Bainey showed me how it is possible to synergize both research and clinical work as a clinician scientist.

How has your experience as a trainee at the CVC impacted your research or career goals? What will you take away from this experience as you pursue your future goals?

My experience as a trainee at the CVC has given me insight into what it’s like to conduct clinical research and has deepened my passion for cardiology research. I have learned from working with the CVC team that research requires curiosity, patience, dedication and collaboration. As I continue with my medical studies, I’m excited to further develop my research skills and to work on more projects that will impact patient care.

B2K18 Symposium



B2K18 took place in the stimulating metropolis of Toronto on October 21, 2018, in conjunction with the Canadian Cardiovascular Congress (CCC). B2K continues to be one of the most highly attended sessions at the Congress each year. We were extremely gratified to have over 300 healthcare professionals attend the symposia, and are pleased at the overwhelmingly positive feedback we have received about the calibre of the program and its speakers.

B2K has evolved from its inception and we have now hosted two back-to-back webinars – the first on lipid lowering post-acute coronary syndrome (ACS), and the second on heart failure (HF) and atrial fibrillation (AF). These topics are highly relevant to our audience, and we are fortunate to attract a diverse group of both nationally and internationally renowned speakers. The B2K symposium and related webinars are generously supported by unrestricted educational grants from AstraZeneca, Novartis, Bayer, Sanofi, Servier and the Boehringer-Ingelheim Eli Lilly Alliance. As has been our tradition, we collaborated with the Canadian Cardiovascular Society (CCS) and the University of Alberta to undertake these ventures.



CVC Co-Director, Shaun Goodman, chaired the New Concepts in ACS symposium. The program began with a presentation by Dr. Gabriel Steg (Université Paris Diderot) on lipid-modifying treatment post-ACS. Thereafter, Dr. John Eikelboom (McMaster University) and Dr. Shamir Mehta (McMaster University) presented on the topic of oral antithrombotic therapy in coronary artery disease. Following that, Dr. Todd Anderson (University of Calgary) shared the top five ways to reduce the cost of cardiovascular care in Canada. Dr. Michael Heffernan (Oakville) then presented an ACS case that engaged both the audience and the panel.

The New Concepts in HF/AF symposium was chaired by CVC Co-Director, Dr. Justin Ezekowitz. It kicked off with a presentation by Dr. Faiez Zannad (Université de Lorraine) on the complex interaction between HF, diabetes, and kidney disease. Dr. Michael McDonald (University of Toronto) then took the stage to discuss the conundrums of device therapy in HF, followed by Dr. Alexander Dick (University of Ottawa), who shared his thoughts about which imaging tests should be used in HF and why. Dr. Carlos Morillo (University of Calgary) and Dr. Jeff Healey (McMaster University) enthusiastically

debated the statement that “all patients with HF and AF need cardioversion and/or a PVI attempt”; however, no clear victor could be declared! Dr. Richard Choi (Toronto) then presented a complex case that stimulated discussion amongst the audience and the panel.

One snapshot of feedback from the overall delegate ratings included the following statement:

“
This type of presentation
[is] worth its weight in
gold. Excellent session! The
presentations were clear and
concise. Thank you — excellent
and very helpful expertise.
”

The attendees responded positively toward the programming, and were particularly enthusiastic about the debate and case presentations.

Our B2K program will continue to progress through a series of CCS-accredited webinars, which capture several of the B2K18 presentations while also providing updates and dynamic cases with interactive features for all participants. These webinars provide continuing medical education opportunities for all interested health care professionals, and allow us to answer audience questions posed electronically during the meeting that could not be addressed during the B2K18 symposia. This year-long continuance and expansion of our meeting has generated extended exposure that has been enthusiastically received. We encourage you to visit <https://thecvc.ca/beyond-2000/webinar-series/> to explore the added value of this online resource.

Clinical Trials Colloquium

On February 25th, 2018, the CVC welcomed 13 sites from eight provinces to participate in the fifth annual CVC Clinical Trials Colloquium in Banff, AB. There were four primary objectives for this year's Colloquium:



1. Enhancing best practices for conducting clinical trials through open discussion, break-out sessions and sharing between sites;



2. Examining pragmatic, cost effective and innovative approaches to conducting clinical trials with the goal of understanding how these strategies may be effective in achieving desired outcomes;



3. Developing successful strategies for how to best engage patients in clinical trial research; and



4. Sharing and gaining knowledge from both current and past experiences in order to achieve success in all trial aspects of future research studies.



Facilitated by CVC Associate Director of Clinical Trials, Tracy Temple, and CVC Co-Directors, Drs. Shaun Goodman and Justin Ezekowitz, the Colloquium was an unique opportunity to exchange insights and experiences related to clinical trial research, ask important questions and collaborate on solutions through open discussion with colleagues.

In his opening remarks, CVC Founding Director, Dr. Paul Armstrong, imparted to us the idea that our future work must involve more personalized and transdisciplinary collaboration towards advancing medical research and practice. Dr. Shaun Goodman then led us through a review of some of the greatest challenges we face today in conducting clinical trials. We were pleased to welcome back our colleagues from Duke Clinical Research Institute (DCRI), Ty Rorick, Associate Director of Mega Trials, and Lisa Berdan, DCRI Director of Mega Trials. Ty led us in a case-study debate of the pros and cons of participating in a potential new trial, which served to highlight the top criteria for consideration by sites while deciding whether or not to participate. Dr. Justin Ezekowitz and Lisa Berdan then presented a comparison of traditional vs. pragmatic research designs. Out of this presentation, we received a glimpse of the current trends related to the use of electronic medical records (EMRs) in Canada. During a round-table discussion of innovative approaches to conducting clinical trials that was facilitated by Dr. Shaun Goodman and Tracy Temple, each site had the opportunity to share one idea they have implemented that has impacted the way they conduct research. We were inspired by both the multitude of exemplary ideas generated by the sites and the eagerness with which they

shared these pieces of knowledge with one another. Lisa Berdan and Ty Rorick then challenged us to step into the shoes of a research participant and consider how we might apply this perspective to keeping patients engaged in clinical research. We were once again impressed by the many creative solutions presented by sites that they use to make their patients feel like "research VIPs". Closing off the session, Drs. Shaun Goodman and Justin Ezekowitz led a group brainstorm about how to attract new investigators and sites to research, a topic that is always of interest to the CVC.

The valuable contributions of our investigators, coordinators and sponsors remain essential to the success of this unique learning opportunity. We strive each year to share the lessons learned from this small sample of our sites with our entire network in order to continuously improve the execution and outcomes of clinical trials in Canada. We hope that this information is of benefit to our sites and others as they develop innovative means of achieving best practice in clinical trial research.

Thank you to our sponsors Amgen Canada Inc., AstraZeneca, Bayer Inc., Boehringer-Ingelheim, CSL Behring, Novartis, BMS-Pfizer Alliance, Sanofi Canada Inc. and Servier; without their support, this important event would not have been possible! We are grateful every year for the opportunity to gain crucial insight into the perspectives of our sites and we look forward to continuing this tradition of collaboration at the CVC Colloquium for years to come.

Distinguished Visitor Series

In 2018, the faculty of the CVC had the privilege of hosting two outstanding, internationally renowned academics. The Distinguished Visitor Series is a continuing program generously sponsored by unrestricted educational grants from Bayer.

These visits are a highlight of our CVC academic year and allow for one-on-one faculty time and teaching of our cardiology and research trainees. The speakers provide a welcome look through the window at 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 education and research mission.



Sanjay Kaul, MD, FACC, FAHA

Professor of Medicine, David Geffen School of Medicine

Director, Cardiology Fellowship Training Program,
Cardiologist, Cedars-Sinai Medical Centre

March 7, 2018

- **Cardiology Divisional Rounds:** “Targeting Inflammation in Atherosclerosis: Has CANTOS Nailed It?”
- **Cardiology Research Rounds:** “Mitigating Cardiovascular Risk in Type 2 Diabetes with Antidiabetic Drugs: Evaluating the Strength of Evidence”

The CVC was enriched by a scintillating academic visit in March 2018 from Professor Sanjay Kaul from the David Geffen School of Medicine and Cedar-Sinai Medical Centre in Los Angeles, California. Dr. Kaul provided new insights into the role of inflammation in atherosclerosis at divisional rounds, and illuminated the strength of evidence for the role of new antidiabetic agents in mitigating cardiovascular risk. His well-known critical appraisal skills were in fine form during visits with the cardiology trainees and individual faculty members. His perceptive insights shared during a CVC research-in-progress session were also well received and capped a very successful distinguished visitor event.



Euan Ashley, BSc, MB ChB, DPhil

Professor of Medicine (Cardiovascular), Professor of Genetics, Professor of Biomedical Data Science and, by courtesy, of Pathology, Stanford University Medical Center

Co-Director, Clinical Genetics Program

Co-Director, Stanford Data Science Initiative

Founding Director, Center for Inherited Cardiovascular Disease

Director, Cardiopulmonary Exercise Testing Laboratory

October 10, 2018

- **Cardiology Divisional Rounds:** “Towards Precision Medicine”
- **Cardiology Research Rounds:** “From Single Cells to Populations in Cardiovascular Genetics”

Euan Ashley is a world leading clinician scientist with expertise on genetics and ‘big-data’ analytics. His visit began with a forward-looking discussion on precision medicine and real-world examples of this in action, as well as an exploration of near-term projects soon to be made public. His second presentation walked through the translation from a clinical scenario to the bench and back again, using a case example of how this can be achieved in medical practice. Finally, his interaction with the faculty and trainees was immensely valuable. These discussions provided perspective on ongoing and upcoming projects and data, and how they integrate with other collaborative projects.

Canadian Cardiovascular Research Collaboratory

An unmet need exists to strengthen synergies among Canadian researchers to expedite the discovery, evaluation, and application of emergent observational and clinical trial study, and application of emergent therapies and strategies of cardiovascular disease (CVD). Given a small critical mass of clinical CVD researchers who are widely spread across the country and vying for limited research funding in an increasingly competitive funding environment, there is an imperative to share and combine efforts.

We are excited to announce the establishment of the Canadian Cardiovascular Research Collaboratory (CCVRC), a new, virtual, clinical research network aiming to blend two fundamental elements – “collaboration” and the clinical “laboratory” – thereby providing novel opportunities for likeminded individuals to identify and study important unanswered questions and address unmet CV health care needs that would be challenging for a single centre to definitively evaluate. The CCVRC further aims to stimulate the growth of CV research in Canada by inspiring, nurturing, engaging, connecting, and mentoring the next generation of talented and committed CVD researchers.

Together with our partners at the University of Toronto, the CVC hosted a planning meeting (in March 2017 to explore the proposal for a Collaboratory) and two subsequent face-to-face meetings (in January 2018, supported in part by a Canadian Institutes of Health Research (CIHR; Institute of Circulatory and Respiratory Health [ICRH]) Planning and Dissemination Grant, and October 2018) of approximately 40 CV research colleagues. Participants benefitted from insights into clinical research and patient engagement provided by invited guest speakers Drs. Robert Howard, David Naylor, and Catharine Whiteside.

Five working groups were established: Prevention, Coronary Artery Disease, Heart Failure, Interventions/ Surgery and Population Health. These groups have undertaken environmental scans of research directions, and discussed key unmet health care needs and unanswered questions that would benefit from a trans-Canada systematic study. Such work is consistent with the four themes of CIHR-funded health research (biomedical, clinical, health services and social/ cultural/environmental/population health research and policy) and occurs across discovery science, clinical trials, observational studies (e.g., registries) and population health.

Reflections on the way forward, including discussion around mutually agreed upon areas of endeavor, continue to highlight the importance of informing and changing Canadian clinical practice through collaborative research that is focused on effective, timely, safe, equitable, patient-centered, and cost-effective treatments and interventions.



The Canadian Cardiac Chronicle

The Canadian Cardiac Chronicle is a newsletter published three times a year that includes information about the CVC's current trials, upcoming projects and events that might be of interest to our site network, and a list of recent publications from our team.

The Chronicle is available on the CVC website (www.thecvc.ca), and it is distributed to over 900 recipients, including investigative sites, sponsors and international collaborators.

The Canadian Cardiac
Chronicle

Volume 22, Issue No. 1

"Each man delights in the work that suits him best."
Odysseus in Homer's The Odyssey

As winter was quietly preparing to wrap up for this year, and spring unpacking its bags (in some parts of North America very slowly), one of the larger cardiovascular outcomes trials had been feverishly wrapping up and unpacking the data.

My colleague and co-director, Dr. Shaan Goodman, and CVC Project Leads Amanda, Jodi and Julianna, along with Regulatory Specialist Paula, led the Canadian effort from the CVC which included 38 sites, 361 patients, 29 cities and >100 investigators and site personnel from Canada. The trial was eagerly anticipated to support prior research in the area of chronic coronary artery disease progression as well as expand our knowledge on this patient population early after an acute coronary syndrome.


The ODYSSEY Outcomes results were presented at the American College of Cardiology meeting in Orlando, Florida in March, and disseminated via multiple avenues. Traditionally, the scientific exchange has relied on a presentation and often simultaneous publication of the same results in a leading medical journal. While important to disseminate efficiently, this can be challenging to get right with the vast amount of data available and many different explanations for a result covering many endpoints. To this end, the trial leadership of ODYSSEY Outcomes have taken a modicum of time to better relay the results that will stand the test of time, supported and explored by subsequent analyses.

How should the investigative team convey the results to the broader public and healthcare population? The ODYSSEY Outcomes results were disseminated to the investigative team via email, webinars, our CVC twitter feed ([CVC_UAlberta](https://twitter.com/CVC_UAlberta)), and local efforts to ensure dissemination to the


medical community at large. Knowledge translation, dissemination and exchange of scientific information is the bedrock of how advances are made both in discovery and implementation. Patients cannot benefit if the health system does not uptake the new information and transform this into practice - numerous examples exist such as the slow uptake of beta-blockers in heart failure, discontinuation of medications with no additional benefit or potential harm (e.g. some oral hypoglycemic medications) or de-adoption of historical unproven practices (morphine and oxygen in acute MI).


The scientific and clinical discourse has undergone many changes from simple lecture based didactic learning, lengthy book chapters in even heavier books, and published manuscripts to now add additional channels of learning such as webinars, live-streamed videos, twitter, and interactive chart audit. One can foresee that there may be a role for patient engagement in the design, delivery and dissemination of the results and thus this should be embraced.

An important shift is moving the scientific and clinical exchange from an asynchronous didactic exchange to one that is more interactive, inclusive and timely. We at CVC look forward to embracing this and measuring the change in clinical outcomes for our patients - we hope you will join us on this next odyssey.


Justin Ezekovitz
CVC Co-director

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The Canadian Cardiac
Chronicle

Volume 22, Issue No. 2

Patient Oriented Research: The Time is Now

Patient involvement in making medical decisions has been demonstrated to be an important contributor to treatment adherence, patient satisfaction, and health status. Thus, a large amount of literature exists which describes methods for improving health care provider patient communication and shared decision-making. However, while clinicians rely on evidence-based randomized trials and clinical practice guidelines to inform their recommendations to patients, very little information is available on patients' preferences for how best to involve them in the development and execution of the studies we collectively work on.

The Canadian VIGOUR Centre (CVC) has been exploring how best to engage patients in clinical research, including as part of our developing national initiative - the **Canadian Cardiovascular Research Collaboratory (CCVRC)**. I recently met with Dr. Catharine Whiteside, Executive Director of Diabetes Action Canada, the **Strategy for Patient-Oriented Research (SPOR)** Network in Diabetes and Related Complications. Dr. Whiteside kindly shared the SPOR patient engagement framework they have developed, which advocates for "putting patients first". One of the key approaches identified by the SPOR group is patient involvement across the entire spectrum of research initiatives, including: engagement in the identification of important unanswered questions; collaboration in study development (including methodology, shared trial leadership and decision-making and, communication related to study progress and results.

Similar patient engagement initiatives are underway in the United States. For example, the **Patient Focused Medicines Development (PFMD)** group notes that "simply enrolling and following patients as passive research subjects in a clinical trial does not rise to the level of patient engagement. Instead, patients should be treated as valued and valuable partners whose input, advice, and guidance is sought and implemented throughout these processes". Indeed, PFMD makes a key distinction between patients and partners: "A patient is a person who needs, awaits, and receives medical treatment and care. In contrast, a partner is a person who wants, co-designs, and co-delivers medical treatment and care. In order to commit to more meaningful partner engagement in medicines

development, we must invest more time to listen, involve them in finding solutions through co-creation, and engage in constant communication with them throughout the development lifecycle."

What are we at the CVC doing in light of this highly anticipated change? In collaboration with our academic research organization (ARO) partner, the **Duke Clinical Research Institute (DCRI)**, the CVC is coordinating the Canadian component of a randomized clinical trial where patient engagement is a key priority. The Apo A-I Trest Reducing in Ischemic Syndrome (AEGIS-II) trial is a large, international, multicenter Phase 3 trial infusing intravenous apolipoprotein (Apo) A-I (CSL112) to reduce cardiovascular events in acute coronary syndrome (ACS) patients. In AEGIS-II, the CVC and DCRI are committed to ensuring a high-quality, efficient, patient-centered trial by: (1) developing a trial that is feasible and minimally burdensome for participants; (2) increasing enrollment rates by proactively addressing barriers to recruitment and improving study communications and materials; and, (3) driving higher rates of retention and protocol adherence through enhanced value and improved participant experience. Recognizing that patients are our partners in research, not our subjects, we are aiming to engage participants in the conduct, oversight, and dissemination activities of the trial. For example, there is a Canadian representative (enrolled in the phase 2 AEGIS-I trial) on the AEGIS-II Participant Advisory Group, who will help provide input on the informed consent process, recruitment and retention strategies, tactics, and materials, anticipated participant experience (having themselves had a recent ACS and/or been part of AEGIS-I), and the conduct of the study related to optimizing participant comfort and convenience in the context of the protocol requirements. While this is simply a first step towards more optimal patient-oriented research, we hope that listening, co-creating, communicating, and collaborating with our partners will lead to better engagement and more impactful clinical trial results.


Shaan Goodman
CVC Co-director

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The Canadian Cardiac
Chronicle

Volume 22, Issue No. 3

"In God we trust, all others must bring data."
- W. Edwards Deming


The familiar adage is attributed to W. Edwards Deming an American statistician considered the father of modern quality management. He advocated that data measurement and analysis were fundamental to attaining superior performance.

Yet in 2018 we are living in a new world where the search for truth is sometimes derailed by opinions and "alternative facts". The convincing and consistent metrics from multiple and credible sources supporting climate change are disputed and largely ignored in some prominent quarters. Denial of the facts raising false fears about vaccinations causing autism has led to unnecessary measles outbreaks. Public health now and in the future is at risk. In part this relates to the deluge of electronic information rapidly disseminated from non-credible sources making facts and opinions difficult to separate. Junk science abounds, arising from obscure websites or journals without critical standards. Health misinformation is especially problematic and has recently been defined (Chow et al JAMA 2018) as "a health related claim of fact that is currently false due to a lack of scientific evidence. This misinformation may be abundant on social media and some evidence has linked the sharing of misinformation with health-related knowledge, attitudes, and beliefs." Such misinformation finds willing receptors among advocacy groups doubtful of scientific advances that contravene well established prior cultural beliefs. They especially resonate within information silos where these beliefs are reinforced and unchallenged by a more balanced and objective context.


As an academic research organization (ARO) we strive for high quality, best performance and work hard to measure indices that accurately reflect this aspiration. The data acquired by our collaborating investigators and research sites are subject to careful auditing and oversight by our sponsors, regulatory bodies, and ourselves. Site visits, timely submission and careful data entry coupled with quality checks happen at every step leading to the final results. These are replicated and independently confirmed so there is absolute accountability for all subjects and their outcomes. At the end of this fastidious process we are confident the results are correct, reliable and trustworthy. This is what science is meant to achieve.


Working in a university environment - which in large part is publicly funded in Canada - we have a special responsibility to earn and maintain public trust. In presenting our work and ideas we must avoid hyperbole and find a balance between hopefulness and reality while striking a responsible tone. We also need to root out scientific fraud and acknowledge that this does occur in exceptional circumstances. I believe these are ultimately detected and corrected in the best scientific traditions. Enhancing scientific literacy is part of our core responsibility. We need to externally validate social media sources of information and resist the temptation to further disseminate "shaky" claims. One of the most gratifying presentations I gave in 2018 was to high school students where I explained why we need the next generation to join in the search for new knowledge through scientific inquiry that contributes to human health. There is more for all of us to do here and this will be part of my New Year's resolutions.

At this special time of year and on behalf of our splendid team at CVC, we send you our very best wishes for a Happy Christmas, Hanukkah or other celebrations. Take time to enjoy the comfort, joy and restorative power afforded by your family and friends. We look forward to collaborating with you on illuminating the path of discovery that will lead to better cardiovascular health in 2019.


Paul W. Armstrong
CVC Founding Director

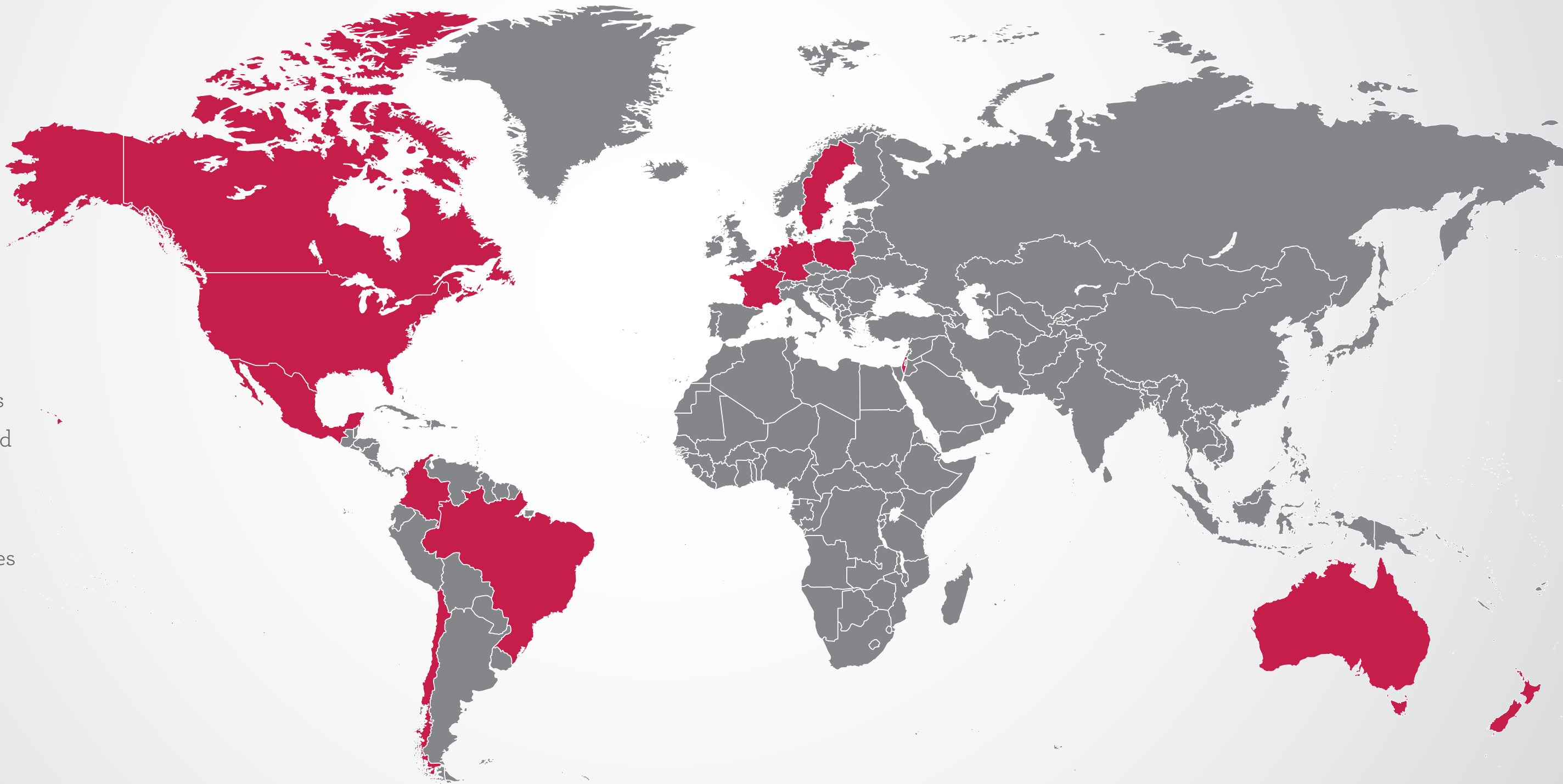
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- ✦ Mexico
- ✦ Netherlands
- ✦ New Zealand
- ✦ Poland
- ✦ Sweden
- ✦ United States





Services and Activities

The Canadian VIGOUR Centre provides a wide range of services supporting worldwide improvements in health outcomes, and has an exemplary track record supporting cardiovascular, population and economic-health outcomes research. Our organization has led or participated in clinical trials that have had seminal impacts on outcomes for patients with cardiovascular disease, and has developed clinical data registries informing on prognostic models, treatment guidelines and outcomes.

Biostatistics

- Consultation on design of research protocols/studies
- Statistical analysis plans, database specifications and data management
- Data analysis using SAS and R
- Generation of statistical tables, figures, listings and interpretation of findings
- Execution of advanced statistical methods

Clinical Data Registries

CVC Clinical Data Registries contain data on patients that are critical for informing treatment guidelines, prognostic models, and describing temporal trends in therapies and outcomes.

Alberta HEART: J. Ezekowitz, P. Kaul, F. McAlister

- Seeks a better understanding of patients having, or at risk of developing, heart failure (HF)
- Data include history, lab, imaging, medications used, diagnoses, mortality and demographics
- Informs on targeted therapies and diagnostic tests, with a focus on patients with HF and preserved ejection fraction

Alberta CoAPT: R. Welsh, K. Bainey, P. Kaul, P. Armstrong

- Evaluates short (30 day) and long term (1 year) outcomes for patients with Acute Cardiac Syndromes (ACS)
- Data include anatomical and clinical entries in the APPROACH database (Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease), post-ACS interventions, medications used, outpatient and inpatient diagnoses, physician claims and mortality
- Informs on outcomes for patients with ACS, regional variations, medication efficacy and costs of each therapeutic strategy

Acute Heart Failure – Emergency Management (AHF-EM): J. Ezekowitz, F. McAlister

- Seeks a better understanding of outcomes for patients with acute heart failure presenting at Edmonton emergency departments (EDs)

- Data include lab, imaging, medications used, ejection fraction, outpatient and inpatient diagnoses, mortality, and demographics
- Informs on outcome differences (e.g., self-presenting versus via emergency medical services (EMS), admitted versus discharged home)
- Develops prognostic models based on presentation mode, admittance, treatment, etc.
- Predict outcomes at time of (i) ambulance attendance, (ii) ED-presentation and (iii) discharge home from or admittance to hospital

Vital Heart Response (VHR): R Welsh, K. Bainey

- Seeks an understanding of ST-Elevated Myocardial Infarction (STEMI) Patients from Edmonton, including those who activated the Vital Heart Response system (pre-admission EMS-administered anti-platelet therapies)
- Data include entries from the Vital Heart Response registry, inpatient diagnoses and electrocardiogram data from the CVC ECG Core lab
- Continuous quality improvement in STEMI patients
- Informs on contemporary use of novel antiplatelet therapies in patients with STEMI, and informs on clinical outcomes

Clinical Trials

- Project, site and data management
- Negotiation and oversight of site contracts and payments
- Site/investigator and selection recruitment
- Investigative site start-up and training
- Communication/collaboration with all trial-related stakeholders
- Site regulatory compliance, data collection and query resolution
- Clinical monitoring and adverse-event reporting
- Creation and dissemination of newsletters and trial-related communications

Core Labs

ECG Core Lab

- ECG reading/analysis; collecting and tracking of ECG tracings
- Pathophysiological, prognosis and outcomes assessments
- Data management (collection, entry and quality control)
- Informing trial design
- Monitoring protocol adherence
- ECG-based admissibility criteria (for clinical trials and registries)

Food Record Core Lab

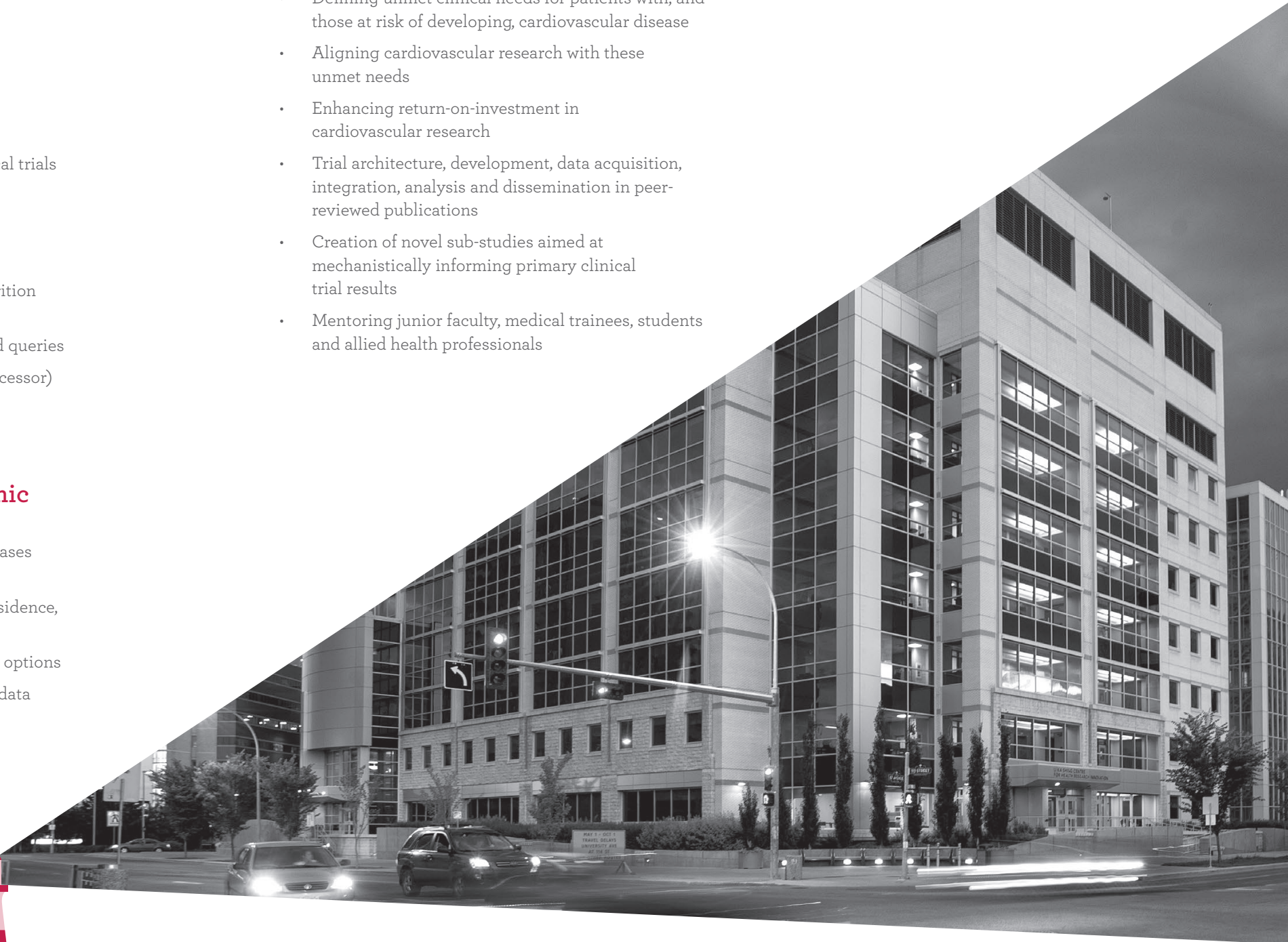
- Receiving, tracking and analyzing Food Records in Food Processor, a powerful nutrition analysis software
- Initiating and following up on Food Record queries
- Entering Food Record data (from Food Processor) into REDCap for site access and use

Population Health and Economic Outcomes

- Analyzing healthcare administrative databases (CIHI, Alberta Health, etc.)
- Linking health outcomes to urban/rural residence, socioeconomic group, etc.
- Comparing cost-effectiveness of treatment options
- Collection of resource utilization and cost data
- Clinical registry development

Thought Leadership

- Expert advice on cardiovascular disease, treatment guidelines and population health
- Promoting research characterized by quality, scholarship and integrity
- Defining unmet clinical needs for patients with, and those at risk of developing, cardiovascular disease
- Aligning cardiovascular research with these unmet needs
- Enhancing return-on-investment in cardiovascular research
- Trial architecture, development, data acquisition, integration, analysis and dissemination in peer-reviewed publications
- 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

With over 20 years of experience in clinical trial operations for phase II/III/IV and investigator initiated studies, our team brings the knowledge and skills needed to deliver a high quality and well-executed trial from study start-up to closeout. Having worked with over 460 Canadian site investigators, which are representative of more than 230 institutions across Canada, we not only have the knowledge and expertise to understand their capabilities, but have also developed ongoing collaborations and relationships with them. This relationship enables us to approach the best sites who can deliver the right patients for the study. As an academic research organization, all of our clinical trials include the involvement of at least one of our faculty members who, as practicing physicians, are able to relate to the role of the investigator and site.

We have a very experienced, diverse, knowledgeable and personable clinical trials team comprised of a senior project manager, a quality assurance and regulatory compliance lead, clinical trial project leads, regulatory specialists, a monitoring lead, regionally based monitors and administrative support. At a senior project management level, we work directly with the study leadership and sponsor to coordinate all efforts related to the study executive and steering committees. Our clinical trial project leads and regulatory specialists are responsible for ensuring all operational aspects of the study run smoothly. They work closely with our sites to strive for rapid 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.

Our team is adaptable and flexible, recognizing the differing requirements for each project. In addition to routine on-site monitoring, our monitors, as well as our in-house teams, have experience implementing and working with both risk-based, and central and/or remote monitoring approaches. The CVC monitors conduct source document verification, drug accountability and other required monitoring-related tasks, while also utilizing visits as a teaching opportunity to share lessons learned and ideas from other sites. The advice and suggestions are beneficial to the daily work of site personnel, and also help to ensure sites are audit prepared.

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.

Our clinical trials team works hard to establish 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.



Left to right: Jodi Parrotta, Tracy Temple, Paula Priest, Kalli Belseck, Courtney Gubbels, Kate Dawson, Melisa Spaling, Kris Reay, Karin Kushniruk, Lyndsey Garritty

Monitoring Team (not pictured)

- Corrina Boyd
- Lyne Cantin
- Valerie Carr
- Halina Nawrocki
- Linda Tardif

Clinical Trials and Registries

Trial: AEGIS-II

Study Title: A phase 3, multicenter, double-blind, randomized, placebo-controlled, parallel-group study to investigate the efficacy and safety of CSL112 in subjects with acute coronary syndrome

Protocol #: CSL112_3001

Sponsor: CSL Behring LLC

Drug: CSL112

Anticipated Timeline: August 2017 - May 2022

Study Purpose: The primary objective of this study is to evaluate the efficacy of CSL112 on reducing the risk of major adverse cardiac event (MACE) (cardiovascular death, myocardial infaction, or stroke) from the time of randomization through 90 days in subjects with acute coronary syndrome (diagnosed with ST-elevation myocardial infarction (STEMI) or non-STEMI).

Trial Status: Start-Up



Trial: GALILEO

Study Title: Global multicenter, open-label, randomized, event-driven, active-controlled study comparing a rivaroxaban-based antithrombotic strategy to an antiplatelet-based strategy after transcatheter aortic valve replacement (TAVR) to optimize clinical outcomes

Protocol #: 17938

Sponsor: Bayer AG

Drug: Rivaroxaban, Acetylsalicylic acid, Clopidogrel

Anticipated Timeline: September 2015 - August 2018

Study Purpose: To assess whether a rivaroxaban-based anticoagulation strategy, following successful transcatheter aortic valve replacement (TAVR), compared to an antiplatelet-based strategy, is superior in reducing death or first thromboembolic events. To assess the primary bleeding events of the rivaroxaban-based strategy, following TAVR, compared to an antiplatelet based strategy, following TAVR.

Trial Status: Close-Out



Trial: FEAST-HF

Study Title: Heart failure, fiber and the gut microbiome: A randomized controlled trial

Protocol #: N/A

Sponsor: University of Alberta Hospital Foundation

Drug: Acacia gum

Anticipated Timeline: July 2018 - January 2020

Study Purpose: To assess whether dietary supplementation with acacia gum reduces heart failure related biomarkers (NT-proBNP and ST2) and how the gut microbiome responds to dietary supplementation with acacia gum in patients with heart failure.

Trial Status: Recruiting



Trial: HEART-FID

Study Title: A randomized, double-blind, placebo-controlled study to investigate the efficacy and safety of Injectafer® (ferric carboxymaltose) as treatment for heart failure with iron deficiency

Protocol #: 1VIT15043

Sponsor: Luitpold Pharmaceuticals, Inc.

Drug: Ferric Carboxymaltose (Injectafer®)

Anticipated Timeline: February 2017 - January 2021

Study Purpose: The primary objective of this study is to determine the efficacy and safety of iron therapy using intravenous ferric carboxymaltose, relative to placebo, in the treatment of participants in heart failure with iron deficiency and with a reduced ejection fraction.

Trial Status: Recruiting



Trial: HiLo-HF Pilot

Study Title: High versus Low SpO2 oxygen therapy in patients with acute Heart Failure - Pilot
Protocol #: N/A
Sponsor: Heart and Stroke Foundation, Alberta Innovates Health Solutions
Drug: N/A
Anticipated Timeline: January 2017 - March 2018
Study Purpose: The primary objective of this pilot trial is to determine whether inpatients presenting to the emergency department with symptoms suggestive of acute heart failure, who receive supplemental oxygen adjusted at either a high (SpO2>96%) or low (SpO2 range 90-92%) oxygen saturation level, leads to greater reduction in N-terminal-proBNP at 72 hours.
Trial Status: Close-Out



Trial: HiLo-HF Registry

Study Title: High versus Low SpO2 oxygen therapy in patients with acute Heart Failure - Registry
Protocol #: N/A
Sponsor: Heart and Stroke Foundation, Alberta Innovates Health Solutions
Drug: N/A
Anticipated Timeline: November 2016 - July 2019
Study Purpose: The primary objective of this registry is to determine the usual oxygen saturation levels in patients presenting to the emergency department with symptoms suggestive of acute heart failure, routine practice of oxygen therapy in those patients and whether the use of high versus low level of supplemental oxygen is associated with worse clinical outcomes.
Trial Status: Close-Out



Trial: ODYSSEY Outcomes

Study Title: 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 recently experienced an acute coronary syndrome
Protocol #: EFC11570
Sponsor: Sanofi-aventis Recherche & Développement
Drug: Alirocumab (SAR236553/REGN727)
Anticipated Timeline: June 2012 - March 2018
Study Purpose: To compare the effect of alirocumab with placebo on the occurrence of cardiovascular events (composite endpoint of coronary heart disease death, non-fatal myocardial infarction, fatal and non-fatal ischemic stroke, unstable angina requiring hospitalization) in patients who have experienced an acute coronary syndrome event 4 to 52 weeks prior to randomization, and are treated with evidence-based medical and dietary management of dyslipidemia.
Trial Status: Close-Out



Trial: SODIUM-HF

Study Title: Study Of Dietary Intervention Under 100 Mmol in Heart Failure
Protocol #: N/A
Sponsor: Canadian Institutes of Health Research, University Hospital Foundation
Drug: N/A
Anticipated Timeline: December 2013 - 2019
Study Purpose: To evaluate the long-term effects of a low-sodium containing diet on a composite clinical outcome composed of all-cause mortality, cardiovascular hospitalizations or cardiovascular emergency department visits in patients with heart failure.
Trial Status: Recruiting



Trial: STREAM-II

Study Title: **S**T^rategic **R**eperfusion in elderly patients **E**arly **A**fter **M**yocardial infarction
Protocol #: LRD.2016.STREAM2
Sponsor: Leuven
Drug: Tenecteplase, Clopidogrel
Anticipated Timeline: September 2016 - June 2020
Study Purpose: In elderly patients ≥ 60yrs with acute ST-elevation myocardial infarction randomized within three hours of onset of symptoms, the efficacy and safety of a strategy of early fibrinolytic treatment with half-dose tenecteplase and additional antiplatelet therapy with a loading dose of 300 mg clopidogrel, aspirin and coupled with antithrombin therapy followed by catheterisation within 6-24 hours or rescue coronary intervention as required, will be compared to a strategy of primary percutaneous coronary intervention with a P2Y12 antagonist and antithrombin treatment according to local standards.
Trial Status: Recruiting



Trial: VICTORIA

Study Title: **V**er**I**cigua**T** gl**O**bal study in subjects with heart failure with **R**educed eject**I**on fr**A**ction
Protocol #: MK-1242-001
Sponsor: Merck, Bayer
Drug: Verciguat, Placebo
Anticipated Timeline: May 2016 - December 2020
Study Purpose: Randomized parallel-group, placebo-controlled, double-blind, event-driven, multi-centre pivotal phase III clinical outcome trial of efficacy and safety of the oral sGC stimulator vericiguat in subjects with heart failure with reduced ejection fraction.
CVC Role: Executive/Steering Committee, thought leadership and senior project management only

Trial: VICTORIA-HF Registry

Study Title: **V**er**I**cigua**T** gl**O**bal study in subjects with heart failure with **R**educed eject**I**on fr**A**ction
Protocol #: N/A
Sponsor: Merck , Bayer
Drug: N/A
Anticipated Timeline: March 2017 - June 2019
Study Purpose: The main objective of the study is to describe the baseline characteristics, practice patterns and in-hospital clinical outcomes of patients hospitalized for chronic heart failure with reduced ejection fraction at select North American sites.
Trial Status: Close-Out



Trial: VITALITY-HFpEF

Study Title: A randomized parallel-group, placebo-controlled, double-blind, multi-center trial to e**V**aluate the eff**I**cacy and safe**T**y of the or**A**L sGC st**I**mulator vericigua**T** to improve ph**Y**sical functioning in activities of daily living in patients with heart failure and preserved ejection fraction (VITALITY-HFpEF)
Protocol #: BAY 1021189/19334
Sponsor: Bayer, Merck
Drug: Verciguat, Placebo
Anticipated Timeline: February 2018 - January 2020
Study Purpose: To evaluate the efficacy of vericiguat 10 mg and 15 mg in comparison to placebo on improving physical functioning from baseline to week 24.
CVC Role: Study Chair/Steering Committee, thought leadership and senior project management only

ODYSSEY Outcomes

By Shaun Goodman

Patients who have had an acute coronary syndrome (ACS) are at high risk for recurrent ischemic cardiovascular (CV) events. We sought to determine whether alirocumab, a fully human monoclonal antibody to proprotein convertase subtilisin-kexin type 9 (PCSK9), would improve CV outcomes after an ACS in patients receiving high-intensity statin therapy.

In collaboration with the Duke Clinical Research Institute (DCRI) and other international academic partners, we conducted a multicenter, randomized, double-blind, placebo-controlled trial involving almost 19,000 patients (including 361 from 38 Canadian centres) who had an ACS 1 to 12 months earlier, had a low-density lipoprotein (LDL) cholesterol level of at least 1.8 mmol/L, a non-high-density lipoprotein (non-HDL) cholesterol level of at least 2.6 mmol/L, or an apolipoprotein B level of at least 80 mg/dL, and were receiving statin therapy at a high-intensity dose or at the maximum tolerated dose. Patients were randomly assigned to receive the PCSK9 inhibitor, alirocumab, subcutaneously at a dose of 75-150 mg or matching placebo every two weeks. The dose of alirocumab was adjusted under blinded conditions to target an LDL cholesterol level of 0.6 to 1.3 mmol/L.

The primary end point was a composite of death from coronary heart disease, nonfatal myocardial infarction, fatal or nonfatal ischemic stroke, or unstable angina requiring hospitalization. After a median duration

follow-up of 2.8 years, the primary end point occurred in 9.5% of the alirocumab group and in 11.1% of the placebo group (a statistically significant 15% relative reduction). All-cause mortality was also lower in the alirocumab group compared to the placebo group (3.5% vs. 4.1%; a 15% relative reduction). The incidence of adverse events was similar in the two groups, with the exception of local injection-site reactions (3.8% in the alirocumab group vs. 2.1% in the placebo group). Thus, among patients who had a previous ACS and who were receiving high-intensity statin therapy, the risk of recurrent ischemic CV events was lower among those who received alirocumab than those who received the placebo.

This treatment is now available by prescription in Canada and offers a safe and effective way forward for high-risk patients who cannot otherwise achieve Canadian guideline-recommended target cholesterol levels with statin and/or other lipid-lowering therapies.





ECG Core Laboratory

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, thereby enabling not only prediction of outcomes, but also assessing effectiveness of treatment. These insights serve to further stimulate cardiovascular scientific research.

The ECG Core Laboratory's key project in 2018 was the Vital Heart Response (VHR) study. The VHR-1 and VHR-2 projects, led by Dr. Robert Welsh, are 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) utilizing a pre-hospital approach. VHR has enrolled over 3,000 patients and the Core Laboratory has completed analysis of over 4,000 ECGs done by our ECG reader, Eric Ly. The use of VHR registry-acquired ECGs and the biostatistical analyses performed by Yinggan (Gray) Zheng provide unique insights and often validation from “real world” patients as it relates to the original findings from our clinical trials.

The STREAM-2 (Strategic Reperfusion in Elderly Patients Early After Myocardial Infarction) study began enrolling patients in Canada in 2018. STREAM-2 will build upon the important foundation laid by the first STREAM study in which the ECG Core Laboratory played a critical role. As in the first study, STREAM-2 ECGs will be analyzed for ST deviation (to determine area at risk) and resolution (as a marker of myocardial reperfusion) and QRS Score (for infarct size) in patients experiencing acute myocardial infarction. The Core Laboratory provides central adjudication for patients with rescue percutaneous coronary intervention (PCI) to determine whether the clinical indications for the procedure were met. The objectives of this study are to compare the efficacy and safety of a pharmaco-invasive reperfusion strategy with primary PCI in elderly STEMI patients, and to compare the incidence of intracranial hemorrhage (ICH) and non-ICH major systemic bleeding in these elderly STEMI patients who receive pre-hospital clopidogrel as an adjunct to half-dose tenecteplase. The study is currently underway.

The ECG Core Laboratory continues its mandate of conducting quality analyses using clinical research data. To date, ECGs from over 75,000 patients enrolled in studies around the world have been analyzed. This provides an excellent database for additional sub-studies, analyses and ‘big-data’ research.

Left to right: Kevin Bainey,
Yinggan (Gray) Zheng, Eric Ly



Biostatistics

The collaborative spirit is at the heart of impactful clinical research, and CVC Biostatistics serves as an active collaborator in such endeavours. By applying statistics to understanding biology, medicine and health, we work with clinical collaborators to develop research questions, design studies, refine measurements, plan and analyze data, and translate findings into knowledge and action. CVC Biostatistics has extensive experience in working with both population-based data and those from randomized clinical trials, as well as with data generated at all levels: locally, nationally and internationally.

Pragmatic trial design is increasingly prevalent; one of those being registry-based RCTs. The Comparison of Angiotensin-Converting Enzyme Inhibitor (ACEi) and Angiotensin Receptor Blocker (ARB) Management Strategies Before Cardiac Surgery (COMPACT) pilot trial, which sought to evaluate the feasibility of (dis) continuation of ACEi or ARB in patients undergoing on-pump cardiac surgery, was reported by [Yinggan \(Gray\) Zheng, MA MEd](#) and colleagues in 2018.¹ This pilot trial was based on the Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH) registry, which collected patient demographics, procedural details and clinical outcomes. Although some key data were either not collected or were collected for other (non-research) purposes, the use of pragmatic trial design in the pilot or feasibility stage provides an efficient pathway to deeper exploration.

In 2018, [Wendimagegn Ghidey Alemayehu, PhD](#) and colleagues applied different lenses to ambulance resources for patients with confirmed and suspected cardiovascular disease in Alberta. In a registry of hospitalized patients with acute coronary syndrome, there

were apparent differences in the activation of ground ambulance services according to sex and, to a lesser extent, ethnic background.² In a separate study, patients presenting to emergency departments (ED) in Edmonton and Calgary with suspected cardiovascular disease were examined for factors related to ambulance use, with specific interest in the travel distance between the ED and the patient's home.³ Among the several patient factors associated with ambulance use, patients travelling longer distances were more likely to have activated ambulance services. In both studies, working with the measurement of ethnicity (through surname-based algorithms) and travel distance (through the geographic information system) provides both opportunities and challenges in answering the clinical research questions in population-based cohorts.

National hospitalization data from the Canadian Institute of Health Information were analyzed by [Anamaria Savu, PhD](#) and colleagues when examining inter-provincial differences in the burden of comorbidities and subsequent outcomes in patients with syncope.⁴ In this understudied population, the identified heterogeneity across provinces may encourage a national approach to better serve these patients.

Health care resource utilization has been a keen interest at the CVC, and work from [Dat Tran, PhD](#) (who completed his doctoral studies in 2018 and was awarded the Gold Medal from the Dean of the School of Public Health)⁵ and [Sunjidatul Islam, MBBS, MSc](#) (who joined the CVC in 2018)⁶ highlight this. Using population-based cohorts in Alberta, resource utilization among patients with acute myocardial infarction and congenital heart disease was characterized, and findings from these



Left to right: Yinggan (Gray) Zheng, Anamaria Savu, Cynthia Westerhout, Wendimagegn Alemayehu
Not pictured: Sunjidatul Islam

studies may help to shape future resource allocation in these patients.

CVC Biostatistics is also committed to generating methods-based research and participating in broader discussions on the future of clinical research. At the 2018 Joint Statistical Meeting in Vancouver, BC, [Wendimagegn Ghidey Alemayehu, PhD](#) presented his work on latent class analysis as an approach to identify diagnostic subgroups of heart failure in the Alberta Heart Failure Etiology and Analysis Research Team (Alberta HEART) study.⁷ Acknowledging and accounting for the role of missing or uncertain data was found to be an important consideration in refining the diagnosis of heart failure.

Sharing of clinical trial data is one of the terms of reference for clinical research that is evolving at a quickening pace. In a commentary published in *JACC Heart Failure* by [Cynthia Westerhout, PhD](#) and colleagues, the current roster of assets and challenges related to data sharing was outlined with historic and ongoing experiences from academic research organizations in clinical cardiovascular research.⁸ Among the assets, making data from clinical trials (and arguably also, other sources of health data) available to the next generation of biostatisticians and clinical investigators is

valuable in their training and advancement. Also, the opportunity for biostatisticians from both sides of the data sharing process to learn from one another and promote high-quality, reliable analysis will be a positive contribution to advancing clinical research, and ultimately patient health.

¹ van Diepen S, Norris CM, Zheng Y, Nagendran J, Graham MM, Gaete Ortega D, Townsend DR, Ezekowitz JA, Bagshaw SM. Comparison of Angiotensin-Converting Enzyme Inhibitor and Angiotensin Receptor Blocker Management Strategies Before Cardiac Surgery: A Pilot Randomized Controlled Registry Trial. *J Am Heart Assoc.* 2018;7:e009917. doi: 10.1161/JAHA.118.009917. PMID: 30371293.

² Bailey KR, Alemayehu W, Gupta AK, Bowker SL, Welsh RC, Kaul P. Ethnic and Sex Differences in Ambulance Activation Among Hospitalized Patients with Acute Coronary Syndromes: Insights from the Alberta Contemporary Acute Coronary Syndrome Patients Invasive Treatment Strategies (COAPT) Study. *Int J Cardiol.* 2018;272:33-39. doi: 10.1016/j.ijcard.2018.08.035. PMID: 30119915.

³ Sepehrvand N, Alemayehu W, Kaul P, Pelletier R, Bello AK, Welsh RC, Armstrong PW, Ezekowitz JA. Ambulance Use, Distance and Outcomes in Patients With Suspected Cardiovascular Disease: A Registry-based Geographic Information System Study. *Eur Heart J Acute Cardiovasc Care.* 2018;2048872618769872. doi: 10.1177/2048872618769872. PMID: 29652166.

⁴ Abulhamayel A, Savu A, Sheldon RS, Kaul P, Sandhu RK. Geographical Differences in Comorbidity Burden and Outcomes in Adults With Syncope Hospitalizations in Canada. *Can J Cardiol.* 2018;34:937-940. doi: 10.1016/j.cjca.2018.04.011. PMID: 29960620.

⁵ Tran DT, Welsh RC, Ohinmaa A, Thanh NX, Kaul P. Resource Use and Burden of Hospitalization, Outpatient, Physician, and Drug Costs in Short- and Long-term Care After Acute Myocardial Infarction. *Can J Cardiol.* 2018;34:1298-1306. doi.org/10.1016/j.cjca.2018.05.022. PMID: 30170782.

⁶ Islam S, Kaul P, Tran DT, Mackie AS. Health Care Resource Utilization Among Children With Congenital Heart Disease: A Population-Based Study. *Can J Cardiol.* 2018;34:1289-1297. doi: 10.1016/j.cjca.2018.06.011. PMID: 30205987.

⁷ Alemayehu W, Westerhout CM, Dyck JR, Anderson T, Ezekowitz JA. A Latent Class Analysis to Identify Subgroups of Heart Failure Under Missingness And/Or Uncertainty in the Indicator Variables. Poster Presentation: Section on Statistics in Imaging. Joint Statistical Meeting (JSM), Vancouver, British Columbia, CA. August 1, 2018.

⁸ Armstrong PW, Mentz RJ, Westerhout CM. Traveling the Interstices of Data Sharing. *JACC Heart Fail.* 2018;6:533-535. doi: 10.1016/j.jchf.2018.02.003. PMID: 29655824.

Population Health and Economic Outcomes

The CVC is actively involved in examining population-level issues related to access, delivery, treatment, and outcomes of heart disease in Alberta and Canada. Healthcare 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. The integrated system of health care delivery in Alberta, with one centralized provider and one payer, has facilitated the linking of inpatient, outpatient (including emergency department), ambulance, pharmaceutical and laboratory data at the patient level. The volume of data generated by linking the health care databases to environment, census and other databases has brought us into the wider realm of 'big-data'.

The following publications exemplify how population health research at the CVC is working towards accomplishing its goals of research training, international collaboration and knowledge dissemination. Six of our trainees had seven first-authored publications based on research conducted using population health databases. Thomas Roston (PhD, Translational Medicine, current) examined the incidence of syncope in pediatric patients presenting to emergency departments in Alberta¹; while Ahmed Abulhamayel (cardiology resident) examined, for the first time, geographical differences in comorbidity burden and outcomes in adults hospitalized with syncope in Canada.² Dat Tran (PhD, Health Policy and Management, 2018) and Sunjidatul Islam (MSc, Epidemiology, 2016) used data from the population-health data repository to estimate the economic burden, including hospitalization, outpatient, physician services and drug costs, of patients with acute myocardial infarction and congestive heart failure in Alberta, respectively.^{3,4} As a follow-up to Dr. Sean van Diepen's earlier examination of interprovincial differences in critical care unit (CCU) admission rates for patients hospitalized for acute coronary syndromes or

heart failure in Canada⁵, Dr. Sanam Verma (cardiology fellow) examined whether CCU utilization and outcomes differed across teaching and community hospitals.⁶ Finally, Qendresa Beka (MSc, Epidemiology, 2017), used the longitudinal Alberta Pregnancy-Birth cohort to examine the history of mood or anxiety disorders and risk of gestational diabetes mellitus (GDM)⁷, as well as the development of perinatal mental illness in women with GDM.⁸

International collaboration is a central tenet of the CVC. In 2018, we had a unique opportunity to collaborate with colleagues from Italy, Denmark and the United States to provide evidence on a topic of considerable controversy. There is a paucity of data and conflicting evidence on the prevalence of pulmonary embolism in patients with syncope. As a result of this international collaboration, our study was able to evaluate data from over 1.5 million patients in the four countries who presented to the emergency department with syncope. The study found that pulmonary embolism was identified in less than 1% of patients with syncope, suggesting that although it should be considered at first evaluation, not all patients warrant a diagnostic algorithm to exclude it, and that the algorithm may increase false-positive results and overtreatment, resulting in more adverse events.⁹

At a more local level, Alberta Contemporary Acute Coronary Syndrome Patients Invasive Treatment Strategies: Impact on Clinical Outcomes and Health Care Resources (the Alberta COAPT Study), is a collaboration among researchers across the province to utilize the integrated population-health data in Alberta to examine practice variations and outcomes in ACS.¹⁰ Dr. Kevin Bainey and colleagues used the COAPT data to examine ethnic and sex differences in ambulance activation among hospitalized patients with ACS, and examine the incidence and outcomes of myocardial infarction patients who present with non-obstructive coronary arteries.¹¹



Left to right: Linn Moore, Anamaria Savu, Padma Kaul

¹Roston TM, Tran DT, Sanatani S, Sandhu R, Sheldon R, Kaul P. A Population-Based Study of Syncope in the Young. *Can J Cardiol*. 2018;34:195-201. doi: 10.1016/j.cjca.2017.12.006. PMID: 29407009.

²Abulhamayel A, Savu A, Sheldon RS, Kaul P, Sandhu RK. Geographical Differences in Comorbidity Burden and Outcomes in Adults With Syncope Hospitalizations in Canada. *Can J Cardiol*. 2018;34:937-940. doi: 10.1016/j.cjca.2018.04.011. PMID: 29960620.

³Tran DT, Welsh RC, Ohinmaa A, Thanh NX, Kaul P. Resource Use and Burden of Hospitalization, Outpatient, Physician, and Drug Costs in Short- and Long-term Care After Acute Myocardial Infarction. *Can J Cardiol*. 2018;34:1298-1306. doi: 10.1016/j.cjca.2018.05.022. PMID: 30170782.

⁴Islam S, Kaul P, Tran DT, Mackie AS. Health Care Resource Utilization Among Children With Congenital Heart Disease: A Population-Based Study. *Can J Cardiol*. 2018;34:1289-1297. doi: 10.1016/j.cjca.2018.06.011. PMID: 30205987.

⁵van Diepen S, Tran DT, Ezekowitz JA, Zygun DA, Katz JN, Lopes RD, Newby LK, McAlister FA, Kaul P. The High Cost of Critical Care Unit Over-Utilization for Patients With NSTEMI ACS. *Am Heart J*. 2018;202:84-88. doi: 10.1016/j.ahj.2018.05.003. PMID: 29906667.

⁶Verma S, Kaul P, Lin M, Ezekowitz JA, Zygun DA, Fordyce CB, Wang TY, McAlister FA, van Diepen S. Acute Coronary Syndromes and Heart Failure Critical Care Units Utilization and Outcomes in Teaching and Community Hospitals: A National Population-Based Analysis. *Can J Cardiol*. 2018;34:1365-1368. doi: 10.1016/j.cjca.2018.07.419. PMID: 30269834.

⁷Beka Q, Bowker SL, Savu A, Kingston D, Johnson JA, Kaul P. History of Mood or Anxiety Disorders and Risk of Gestational Diabetes Mellitus in a Population-Based Cohort. *Diabet Med*. 2018;35:147-151. doi: 10.1111/dme.13543. PMID: 29120506.

⁸Beka Q, Bowker S, Savu A, Kingston D, Johnson JA, Kaul P. Development of Perinatal Mental Illness in Women With Gestational Diabetes Mellitus: A Population-Based Cohort Study. *Can J Diabetes*. 2018;42:350-355.e1. doi: 10.1016/j.jcjd.2017.08.005. PMID: 28943221.

⁹Costantino G, Ruwald MH, Quinn J, Camargo CA, Dalggaard F, Gislason G, Goto T, Hasegawa K, Kaul P, Montano N, Numé A-, Russo A, Sheldon R, Solbiati M, Sun B, Casazza G. Prevalence of Pulmonary Embolism in Patients With Syncope. *JAMA Intern Med*. 2018;178:356-362. doi: 10.1001/jamainternmed.2017.8175. PMID: 29379959.

¹⁰Bainey KR, Alemayehu W, Gupta AK, Bowker SL, Welsh RC, Kaul P. Ethnic and Sex Differences in Ambulance Activation Among Hospitalized Patients with Acute Coronary Syndromes: Insights From the Alberta Contemporary Acute Coronary Syndrome Patients Invasive Treatment Strategies (COAPT) Study. *Int J Cardiol*. 2018;272:33-39. doi: 10.1016/j.ijcard.2018.08.035. PMID: 30119915.

¹¹Bainey KR, Welsh RC, Alemayehu W, Westerhout CM, Trabelsi D, Anderson T, Brass N, Armstrong PW, Kaul P. Population-Level Incidence and Outcomes of Myocardial Infarction With Non-Obstructive Coronary Arteries (MINOCA): Insights From the Alberta Contemporary Acute Coronary Syndrome Patients Invasive Treatment Strategies (COAPT) Study. *Int J Cardiol*. 2018;264:12-17. doi: 10.1016/j.ijcard.2018.04.004. PMID: 29655952.

Diabetes and Childhood Obesity

By Padma Kaul

The causes of being overweight or obese in childhood are multifactorial. Children who are born large are more likely to be larger in childhood. Maternal weight and maternal diabetes status during pregnancy are established risk factors for having large for gestational age (LGA) infants. However, little is known about the relative contribution of LGA and maternal diabetes during pregnancy in relation to the risk of being overweight or obese in early childhood.

Using the unique longitudinal Alberta Pregnancy-Birth cohort that links data from multiple sources (see figure), this study examined whether maternal diabetes in pregnancy or LGA was a more important contributor to excess weight in childhood. The study also examined whether breast-feeding modulated these associations.

A total of 81,226 children born in the Calgary Zone between 2005 – 2013, for whom height and weight measurements were available at their pre-school immunization visit (at age 4 – 6 years), were categorized according to maternal diabetes status (no diabetes, gestational diabetes mellitus (GDM) and pre-existing diabetes) and birth weight (appropriate for gestational age (AGA) or LGA). Children who were reported as not having received any breast-milk at 5 months of age were considered not to have been breast-fed. World Health Organization age-sex specific criteria were used to identify children who were overweight/obese at pre-school age.

The rate of being overweight/obese at pre-school age ranged from 20.5% in the control group of AGA children born of mothers with no diabetes to 42.9% in the GDM/LGA group. The adjusted attributable risk percent for LGA alone (39.4%) was significantly higher than that for maternal GDM (16.0%) or pre-existing diabetes alone (15.1%); the risk for the combinations of GDM/LGA and pre-existing diabetes/LGA were 50.1% and 39.1%, respectively. Breast-feeding was associated with a lower likelihood of being overweight/obese in childhood in all groups except GDM/LGA and pre-existing diabetes/LGA.

These findings suggest that LGA is a stronger marker for risk of being overweight/obese in early childhood, compared with maternal diabetes during pregnancy. Women who are planning to become pregnant need to be advised about risk factors for LGA, such as maternal weight and dysglycaemia during pregnancy. Further research into the components of breast milk and infant feeding practices of mothers with diabetes is required to identify reasons why breast-feeding was not associated with lower overweight/obesity outcomes in mothers with diabetes who had LGA children.

Population Health Data, Alberta, Canada (pop 4.1 million)



Alberta Pregnancy-Birth Cohort							
Inpatient	Outpatient	Drugs	Physician Claims	Labs	Birth Registry	Immunization Data	Vital Status
Dx, procs, LOS	ED use; specialty clinics	Drugs	Follow-up care; provider factors	Bio-markers	Birth details	Breastfeeding; pre-school BMI	Mortality
Unique Patient Identifier							



Left to right: Lisa Soulard, Leah Luoma, Karen Mellor, Oksana Grant, Ellen Pyear

Business Operations

The business office is fundamental to the organizational and financial underpinnings of the CVC. Reviewing and negotiating contracts is one of its key tasks, along with 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 development and distribution of all marketing materials aimed at creating strong brand awareness that speaks to the mission and values of the organization. Additionally, the office manages the CVC's website and social media portfolio, and provides visual design support to our staff and faculty for a variety of projects.

Finally, the office facilitates communications between the CVC and many institutional partners. Our dedication to upholding strong partnerships with these institutions is essential to the day-to-day operations of the CVC.

Academic Research Administration

The Academic Research Administrator (ARA) is involved in the development and management of investigator initiated academic research projects. The ARA coordinates and facilitates proposal development, from identifying potential funding sources, drafting proposals and critical review of project design, through to editing and final polish. For research projects underway, the ARA manages ethics submissions, reporting to stakeholders, and knowledge translation by way of manuscript development, graphical abstract design, and data visualizations for various presentation formats.

Faculty

The CVC Faculty are internationally recognized as Thought Leaders in their respective areas of interest, and they collectively represent a diverse field of clinical research. Our faculty are passionately dedicated to advancing the frontiers of cardiovascular science through several domains:

- **Clinical Trials** – architecture, operational management, analysis and interpretation
- **Registry Development** – creative insights into the process of care of acute coronary syndromes and congestive heart failure
- **Large Population Databases** – informing the impact of research on practice, and pointing towards unmet needs and future directions

Our faculty plays a pivotal role in linking new knowledge to the community, understanding the implications on health outcomes, embracing the quality feedback loop, and discovering science through clinical trials registries and population outcomes. The CVC faculty is deeply engaged in identifying, nurturing, and mentoring the health professionals and leaders of tomorrow by grounding them in the discipline of cardiovascular research.





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
- Chair of the Alberta Institute of Health Economics (IHE) Board of Directors
- 2014 Recipient of the University Cup, the University of Alberta capstone award for outstanding contributions in teaching, research and service
- 2014 Recipient of the Margolese National Heart Disorders Prize, awarded annually to a Canadian who has made outstanding contributions to the treatment, amelioration or cure of heart disease
- Recognized in 2018 as an Officer of the Order of Canada, in acknowledgement of "his contributions to the advancement of cardiology, notably for his pioneering research in acute cardiac care, and for his leadership in health care institutions"

Dr. Armstrong's research interests include:

- Development of novel methods to enhance clinical trial methodology
- Cardiovascular implications of diabetes and aging
- 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
- Professor, Division of Cardiology, University of Alberta
- 2017 Appointed Member, Royal Society of Canada College of New Scholars, Artists and Scientists

Dr. Ezekowitz' research interests include:

- Testing the impact of drugs, existing care, and processes of care for patients with acute and chronic heart failure
- Novel interventions for patients with chronic heart failure
- Non-pharmacologic interventions such as dietary sodium or altering the gut microbiome, and existing tools such as biomarkers for discovery or prognosis
- Population health outcomes and interventions
- Clinical trial design and endpoints



Shaun Goodman, MD, MSc

- Co-Director, Canadian VIGOUR Centre
- Adjunct Professor, Department of Medicine, University of Alberta
- 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

Dr. Goodman's research interests include:

Facilitating collaborative clinical trial, observational, and knowledge translation research in cardiovascular disease in Canada with a focus on:

- Diagnosis, management, and prognosis of stable coronary artery disease and acute coronary syndromes
- Secondary prevention of cardiovascular disease
- Optimal stroke prevention risk stratification and management in atrial fibrillation



Kevin Bainey, MD

- Director, ECG Core Lab, Canadian VIGOUR Centre
- Interventional Cardiologist, Mazankowski Alberta Heart Institute
- Assistant Professor, Division of Cardiology, University of Alberta
- Director, Interventional Cardiology Fellowship Program, Mazankowski Alberta Heart Institute, University of Alberta
- Co-Director of the ACS working group for Alberta Health Services Cardiovascular Health and Stroke Strategic Clinical Network

Dr. Bainey's research interests include:

- Optimizing reperfusion strategies in ST-elevation myocardial infarction
- Population health outcomes in acute coronary syndromes



Sean van Diepen, MD

- Academic Cardiologist-Intensivist, University of Alberta Hospital
- Co-Director, Coronary Intensive Care Unit, University of Alberta Hospital
- Assistant Professor, Critical Care Medicine, Division of Critical Care and Division of Cardiology, University of Alberta
- Associate Editor, American Heart Journal

Dr. van Diepen's research interests include:

- Critical care cardiology
- Cardiovascular surgical care
- Critical care resource utilization



Padma Kaul, PhD

- Director, Outcomes Research, Canadian VIGOUR Centre
- 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, delivery, and costs of care at a population level



Finlay McAlister, MD, MSc

- General Internist, University of Alberta Hospital
- Professor, Division of General Internal Medicine, University of Alberta
- Adjunct Professor, School of Public Health, University of Alberta
- Director, Patient Health Outcomes Research and Clinical Effectiveness Institute, University of Alberta
- Lead, Alberta SPOR (Support for Patient Oriented Research) Data Platform
- Senior Health Scholar, Alberta Innovates - Health Solutions (2010 - 2017)
- Alberta Health Services Chair in CV Outcomes Research
- 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



M. Sean McMurtry, MD, PhD, FRCPC

- Clinician Scientist, Mazankowski Alberta Heart Institute
- Associate Professor, Division of Cardiology, University of Alberta
- Medical Director, Anticoagulant Management Service, University of Alberta

Dr. McMurtry's research interests include:

- Thoracic aortic disease
- Venous thromboembolism
- Coronary artery disease
- Sex differences in cardiovascular disease



Roopinder Sandhu, MD, MPH

- Cardiac Electrophysiologist, Division of Cardiology, University of Alberta
- Associate Professor, Division of Cardiology, University of Alberta
- Visiting Scientist, Brigham and Women's Hospital, Boston
- Director, Edmonton Cardiac Arrhythmia Trials (ECAT) group

Dr. Sandhu's research interests include:

- Arrhythmia health services and outcomes research
- Atrial fibrillation
- Cardiac implantable devices
- Syncope



Robert Welsh, MD

- Interventional Cardiologist, Mazankowski Alberta Heart Institute
- Professor, Division of Cardiology, University of Alberta
- Edmonton Zone Clinical Department Head, Cardiac Sciences
- Director, Adult Cardiac Catheterization and Interventional Cardiology Laboratory
- Co-Director and Co-Founder, University of Alberta Chest Pain Program
- Co-Chair and Founder, Vital Heart Response Program
- Co-Chair, Acute Coronary Syndromes Committee
- Co-Chair, Transcatheter Aortic Valve Implantation (TAVI) Program, Mazankowski Alberta Heart Institute

Dr. Welsh's research interests include:

- Acute coronary syndromes and interventional cardiology
- Atherosclerotic cardiovascular disease
- Cardiovascular disease and diabetes
- Exercise physiology and cardiac physiology
- Pre-hospital management of ST-elevation myocardial infarction, and the interaction of pharmacological (antithrombotic and fibrinolytic) and mechanical interventions (primary and rescue angioplasty)





Collaborators

The CVC has forged strong partnerships with a number of institutions and centres around the world in the pursuit of novel research directions and the advancement of cardiovascular research. The CVC takes great pride in our relationships with these collaborators, who are internationally recognized leaders in the advancement of cardiovascular research.

The map illustrates the CVC’s worldwide network of collaborators.

APPLIED HEALTH RESEARCH CENTRE, UNIVERSITY OF TORONTO
Toronto, Canada

BRAZILIAN CLINICAL RESEARCH INSTITUTE
Sao Paulo, Brazil

C5 RESEARCH, CLEVELAND CLINIC
Cleveland, USA

CHARITÉ – UNIVERSITÄTSMEDIZIN BERLIN
Berlin, Germany

DUKE CLINICAL RESEARCH INSTITUTE, DUKE UNIVERSITY
Durham, USA

GREEN LANE COORDINATING CENTRE
Auckland, New Zealand

ICAHN SCHOOL OF MEDICINE, MOUNT SINAI
New York, USA

INOVA HEART AND VASCULAR INSTITUTE, INOVA FAIRFAX HOSPITAL
Falls Church, USA

LEUVEN COORDINATING CENTRE, UNIVERSITY OF LEUVEN
Leuven, Belgium

LIBIN CARDIOVASCULAR INSTITUTE OF ALBERTA
Calgary, Canada

NATIONAL UNIVERSITY HEART CENTRE, NATIONAL UNIVERSITY OF SINGAPORE
Singapore

PERFUSE STUDY GROUP, HARVARD MEDICAL SCHOOL
Boston, USA

PETER MUNK CARDIAC CENTRE, UNIVERSITY HEALTH NETWORK
Toronto, Canada

SAMU URGENCES DE FRANCE
Pontoise, France

SOUTH AUSTRALIAN HEALTH AND MEDICAL RESEARCH INSTITUTE
Adelaide, Australia

STANFORD CENTER FOR CLINICAL RESEARCH, STANFORD UNIVERSITY
Stanford, USA

THE HEART AND STROKE RICHARD LEWAR CENTRE OF EXCELLENCE, UNIVERSITY OF TORONTO
Toronto, Canada

UPPSALA CLINICAL RESEARCH CENTRE, UPSALA UNIVERSITY
Uppsala, Sweden

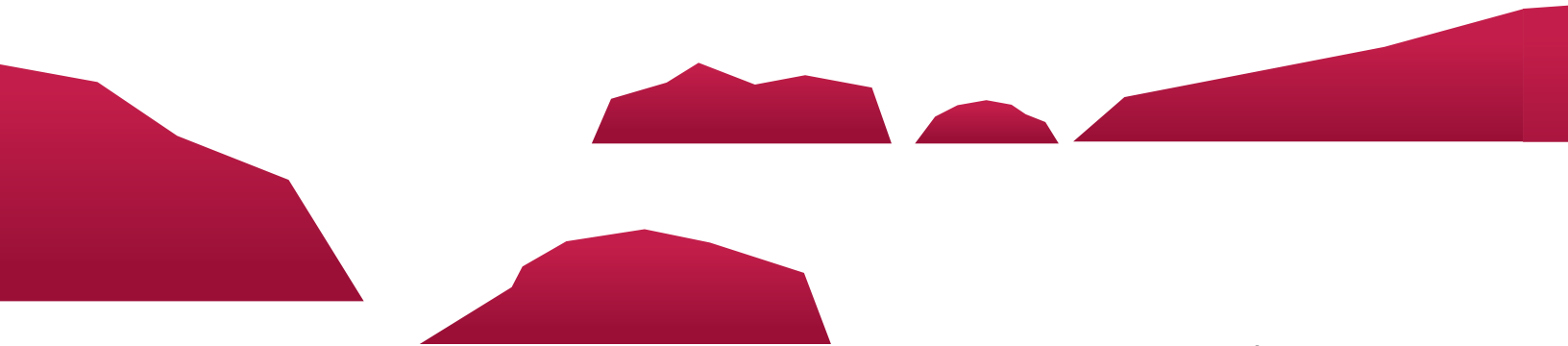
Acknowledgements

CVC gratefully acknowledges and thanks:

- The patients, for their willing participation in our trials and registries. They are the true heroes of clinical research and we honor their volunteer spirit.
- The CVC faculty, external advisors and collaborators for their enriching contributions and for providing ongoing research opportunities. We look forward to providing continued support and to future collaborations in advance of our mission.
- The CVC staff and management for their outstanding dedication, professionalism, excellent contributions and ingenuity, which enhances the quality of our research work.
- Our trainees for their commitment, ideas and enthusiasm. You are the next generation of researchers and health care providers.
- The sponsors and granting agencies; without their generous financial support our research and educational activities would not be possible.
- The excellent work of our communications group (Ellen Pyear, Lisa Soulard, Kate Dawson, Leiah Luoma and Kris Reay) for their time and the dedication required to produce this report.
- The team at AM/FM for the concept and design.
- Photographer, Richard Seimens, for the group photos of our staff and faculty enclosed within this report.







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