ANNUAL REPORT

Canadian **VIGOUR** Centre

Bridging Hearts and Minds

2017

The future belongs to those who see it coming.

Janus is the ancient Roman god of beginnings and transitions. He has historically been depicted as a god with two faces — one looking backward, and the other looking forward. To recognize the 20th anniversary of the Canadian VIGOUR Centre (CVC), we look to Janus as a symbol of our organization's strength. The CVC continues to evolve by learning from the lessons of the past and building strategic directions for the future.

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Message From the Founding Director

Welcome to our 2017 annual report! As we celebrate our 20th anniversary at the Canadian VIGOUR Centre (CVC), it seems a propitious time to reflect on our organization's development, evolution and direction. Seeking inspiration on such an occasion, as I write this on a wintery Sunday afternoon, I am drawn back to my ancient Roman friend Janus. As the god of beginnings and transitions, he is often represented as a god with two faces - one which looks backwards and the other forwards. His spirit exactly captures what floods my mind on this anniversary.

What gives an organization lasting value? First off, it needs to have an inspiring vision and mission. This should be noble and timeless so that there is no equivocation as to why it exists. Second, its core values should reflect the things that matter to good people, namely mutual respect, unimpeachable integrity, unrelenting pursuit of quality and an outward looking and generous collaborative spirit. To attract outstanding faculty and staff, such as those who grace the pages of this report, the organization needs to have an unquenchable thirst for innovation (often driven by dissatisfaction with the status quo), a willingness and desire to lead and the intent to impact health policy by finding better health care solutions. Add a healthy dollop of career development strategies and presto... you have all the ingredients necessary to attract and grow a wonderful group of people who, as a synergistic team, can make great things happen!

Walk with me for a moment as we travel through the genesis of a research publication that constitutes one key metric of our progress. These come from the faculty's creative ideas, often in collaboration with others. Translating a research grant or protocol needs careful building and then editing by talented administrative staff who help give these ideas life. For ideas to be sound and feasible, they need careful planning by rigorous analysts and biostatisticians. The best ideas go nowhere if there is no fuel to drive them, and so our business and finance group is critical in the budgeting and funding elements. Execution of all of this planning cannot happen without our project team, who deftly operationalize all of the delicate details. Our monitors, or troops in the field in every region of Canada, provide needed evaluation that we are doing what we said we would do, and if not, why not? To complete the cycle of quality, as is evident in the list of selected publications herein, the access to large population health data requires analytical sophistication and the ability to understand "big data". Along this great journey, we engage trainees of many differing stripes, so they can learn with us as we move forward while growing their careers and taking part in the adventure and the presentations and publications that follow.

It has been said *"Those who do not remember the past are condemned to repeat it"* (George Santayana). As the Founding Director, I have made more mistakes than my two accomplished Co-Directors and three talented Associate Directors combined! Hence, I work hard on influencing us to avoid repeating too many of those as we move ahead in these exciting times. In preparing to celebrate this 20th anniversary, I recently conversed with one of our original and prior project leads about her early experience at the CVC. She reported that in my original letter offering her a job I wrote, *"Welcome aboard... It should be a great ride!"* This proved to be correct as I reflect on the remarkable transformation in cardiovascular care over the past two decades. The major improvement in outcomes of our patients with acute and chronic coronary disease, as well as those with heart failure, would not have occurred without research. It has been immensely gratifying for us at the CVC to be so deeply involved in this extraordinary and welcome shift in cardiovascular health.

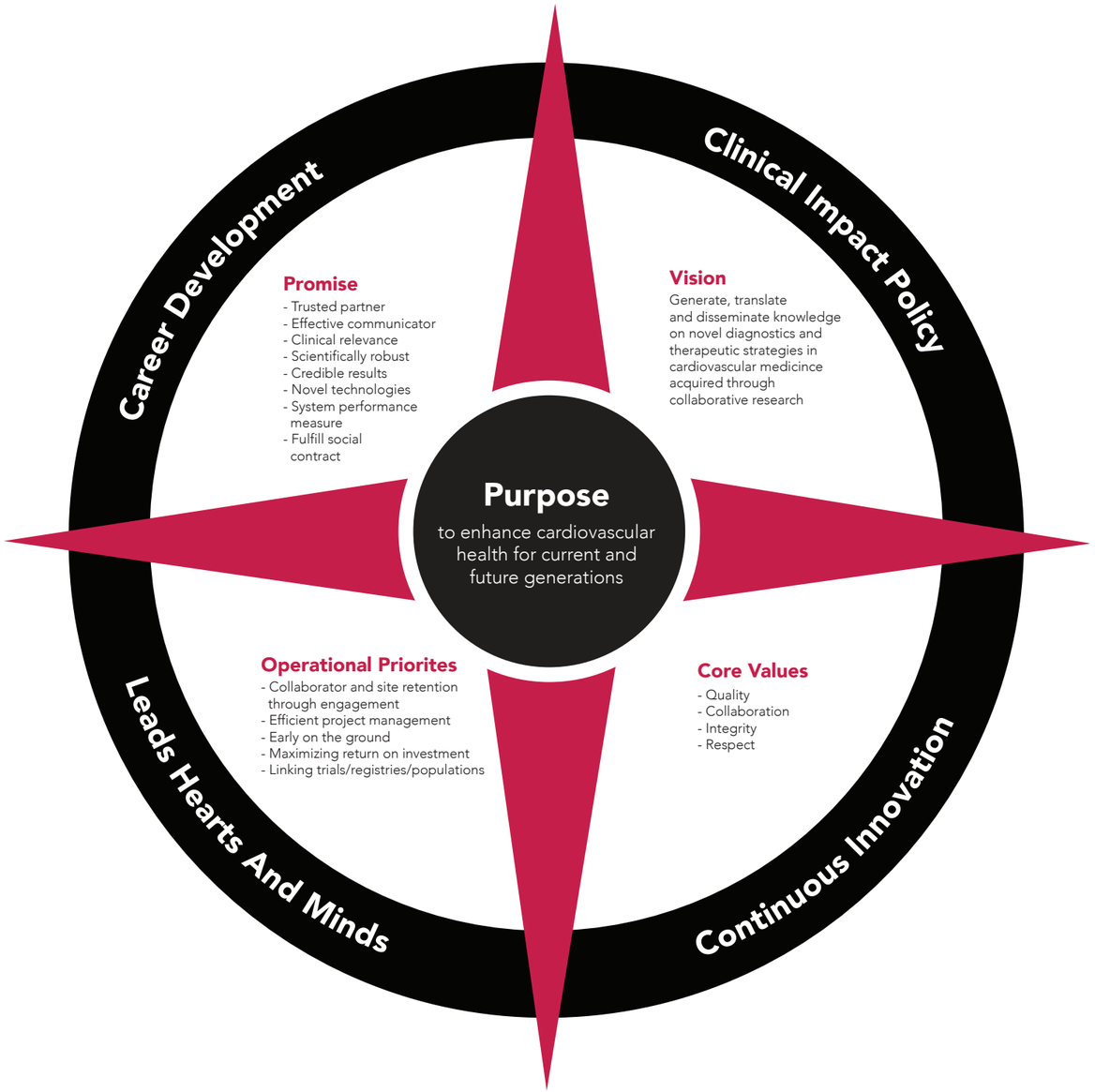
Yet the other face of our old friend Janus encourages us to look ahead at the key unmet needs of our patients, their families and their family's families. There are many of these. Cardiovascular disease remains the most prevalent chronic non-communicable disease worldwide with a lifetime risk exceeding 60% of the population. Fortunately, a remarkable array of new tools ranging from stem cells, pharmacogenomics, precision medicine, big data and artificial intelligence have emerged that promise to facilitate the search for new solutions. Recruiting the best and brightest young people to participate in this enterprise is the key to our future success.

In 2016 we identified key strategic initiatives for the organization, and we have continued to refine these throughout the past year. These initiatives are rooted in our engagement in regional, national, and international collaborations, honouring our teaching and mentoring legacy, enhancing our contributions to the quality cycle of research, and leading innovations in CV research. To galvanize these objectives the faculty and leadership convened in June 2017 to explore bold ideas that would inform our future directions. An internal deep dive into CVC operations has also encouraged us to set long-term targets on our strategic pathway.

We at the CVC intend to be here to continue bridging hearts and minds to enhance cardiovascular care. I wish to acknowledge the creative expertise of Ellen Pyear, Lisa Soulard and Oksana Grant in preparing this report as well as our CVC team's extraordinary work in 2017 about which the Co-Directors and I are both proud and exceedingly grateful. We hope you enjoy this annual report and would welcome any feedback, which can be directed to **thecvc@ualberta.ca.**

Paul W. Armstrong, MD
- Founding Director

Compass



Vision, Mission, and Core Values

Vision

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

Mission

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

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

Core Values

Quality

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

Collaboration

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

Integrity

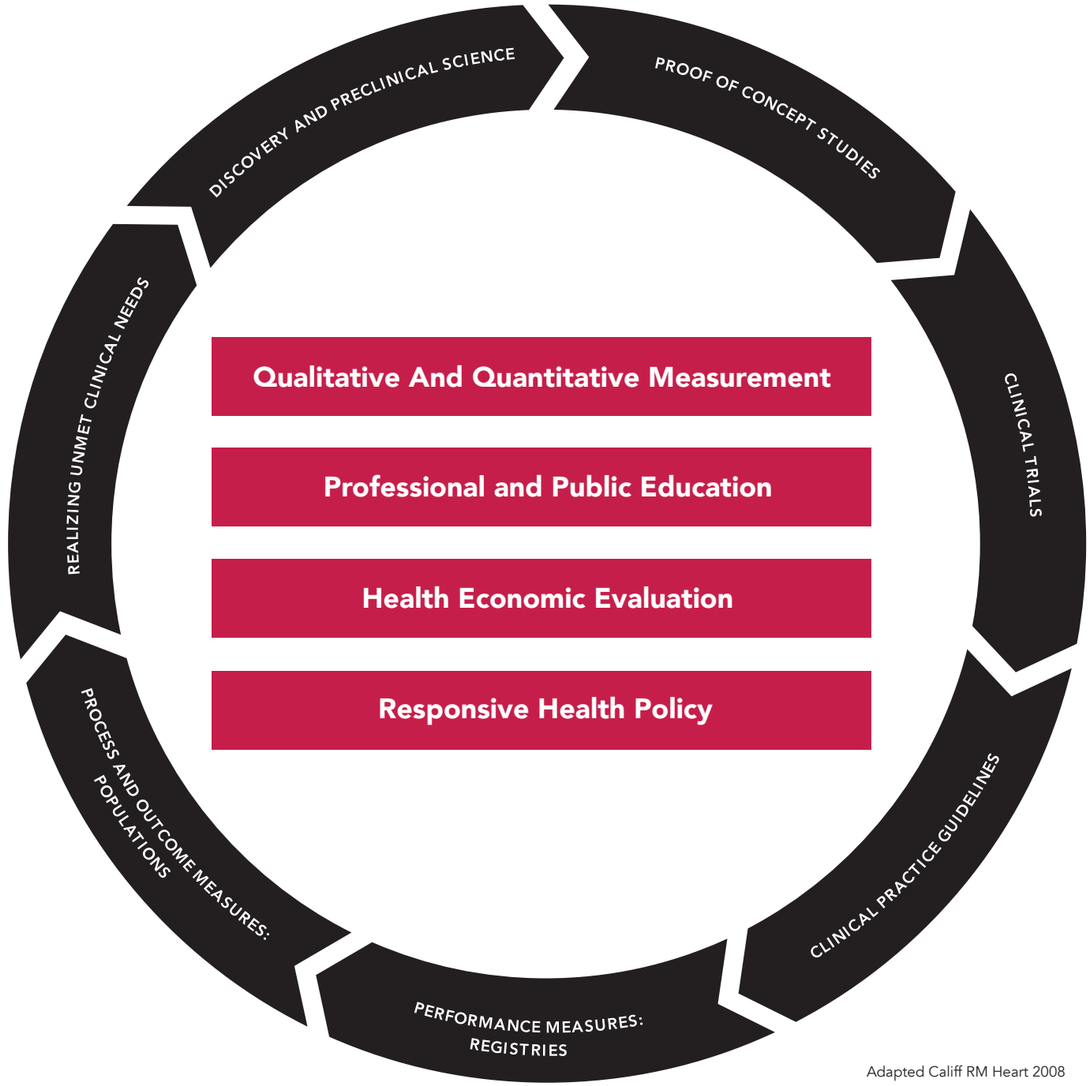
Perform our roles in an ethical framework which enhances our reputation as honest, trustworthy and responsible.

Respect

Create an innovative, engaging and inclusive work environment, appreciative of individual differences and contributions. Our workplace will be conductive to personal growth and development that is aligned with our overall mission.

The Value Proposition of an ARO

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



Adapted Califf RM Heart 2008

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 is 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.

2017 Year in Review

9
Industry-funded studies underway

36
Grant-funded projects underway on which CVC faculty members are Principal or Co-Investigators

131
Publications produced by the CVC's body of research

117
Principal Investigators participating in CVC-managed trials

224
On-site and remote monitoring visits that occurred in Canada

2.5 Million
Canadians represented in the CVC's data repository

59
Lectures and presentations given by the CVC faculty in Canada and abroad

7702
Citations generated from CVC-authored papers published between 2013-2017

41
CVC faculty and staff members

177
Global users accessing the CVC's online collaborative platform

Insights from CVC Cornerstones

In recognition of the 20th anniversary and in the spirit of Janus, Roman god of beginnings and transitions, we are highlighting three CVC team members who have had, and will continue to have, a major impact on the evolution of the organization. Dr. Padma Kaul, Ms. Tracy Temple, and Dr. Cynthia Westerhout have been foundational parts of the CVC since its early days. Their dedication, leadership, and innovative spirit are fundamental to the continued success of the CVC.

In the following series of interviews, they each reflect upon the experiences and insights they have gained during their time with the CVC.

Dr. Padma Kaul joined the CVC in 1998 and is a faculty member and the Director of Outcomes Research.

How did you first come to work at the CVC, and what specifically interested you about the CVC prior to joining the organization?

In 1998 I was studying for my PhD in the Department of Epidemiology at the University of Alberta, and took a course with Weiching Chang, who at the time was working as the principal Biostatistician with Paul Armstrong. At the end of the course Weiching asked if I would be interested in doing a research assistantship with Paul and his group, and it was an opportunity I was keen to take on. I worked very closely with Paul, Weiching, and Yuling Fu, and while the work was very challenging, it was ultimately a very rewarding experience. The whole process of joining the CVC was very fortuitous but twenty years later I am still with the organization.

What have you learned from your time working at the CVC?

In many ways my time at the CVC has shaped much of my learning experience to date. Almost everything I know about cardiovascular research can be attributed to the work I have done with Paul and other colleagues at the CVC. This knowledge and experience has allowed me not only to develop new research questions in the area of cardiovascular epidemiology, but has also given me the confidence to take on new projects in lesser studied areas.

There was also much I learned from working directly with Weiching and Yuling. In particular, they taught me the importance of reviewing the accuracy and consistency of numbers. This is something that has stuck with me, and I now expect the same level of accuracy and consistency from my own students and trainees.

During your time at the CVC what has been your most valuable experience?

Perhaps the most valuable experience I have had with the CVC was the opportunity to pursue a post-doctoral fellowship with Dr. Daniel Mark at Duke University in North Carolina. I had just finished my PhD prior to going, and to work alongside Dan and others at DCRI really opened my horizons. Paul was instrumental in me pursuing this opportunity and to date it is still one of the most valuable professional experiences I have had.

The CVC's core values are collaboration, quality, integrity and respect. Can you speak to how you see one of these values reflected in the work being done at the CVC?

Collaboration is at the core of the work we do at the CVC. By design, the faculty at the CVC work closely together on projects, but the relationships we build and foster with external organizations is particularly key to our success. We are increasingly trying to build relationships at a local level, and this is especially important for population health research which has an Alberta and Canada centric focus.

How would you summarize your experience with the CVC to those who might be interested in working with the organization?

If you are serious about research and are an individual who is driven and looking for a lifelong learning process, the CVC is the place for you. If you bring an intellectual curiosity and enthusiasm, the organization will provide all the necessary resources to help you succeed.

Ms. Tracy Temple joined the CVC in 2000 and is the Associate Director of Clinical Trials.

How did you first come to work at the CVC, and what specifically interested you about the CVC prior to joining the organization?

One of the key things that interested me in the organization was the linkage to the University of Alberta. I was also drawn to the opportunity to change practice and care of patients through clinical trials/research. I had been working as a Registered Nurse at that time so the chance to see the development of medications and put them into practice with patients was very interesting to me. Another aspect that was attractive to me was the global reach of the CVC at that time, and specifically the VIGOUR (**V**irtual Coord**i**nating Centre for **G**lobal Collab**o**rative Cardiovasc**u**lar **R**esearch) group collaboration.

What have you learned from your time working at the CVC?

One of the main things I have learned is the importance of each clinical trial and the impact it can have on changing practice and the care of patients. During the time I have worked at the CVC there have been trials that are successful and others that are not so successful, but you ultimately learn something from each trial and patient population.

The importance of our team is another thing I have learned during my time at the CVC. By building a strong and cohesive team that works well together, we have the ability to be creative and innovative, and produce the high quality of work we strive for. On a similar note, I have learned much about the significance of building and maintaining strong relationships with our sites, partners, sponsors and collaborators. These connections are a key piece of our identity at the CVC, and they speak to how we've grown as an organization. Over the last 17 years I have had the opportunity to develop many lifelong connections, professional relationships and friendships which I highly value.

During your time at the CVC what has been your most valuable experience?

Since joining the CVC I have been involved in over 25 clinical trials, and I've had the opportunity to work with several industry sponsors, organizations and partners. This experience has given me a unique perspective on the operational aspects of running a clinical trial, and the variety of approaches that are taken.

Over time, and through each experience, I have been able to pull value from every clinical trial I have been involved in and then bring it to the next trial or project. The importance of continuing to learn from the past, evolve, be innovative, and be willing to adapt to your changing environment is a valuable experience that I have learned and continue to learn while working at the CVC.

The CVC's core values are collaboration, quality, integrity and respect. Can you speak to how you see one of these values reflected in the work being done at the CVC?

It is tough to choose just one because when you step inside the walls of the CVC you can see how each of these core values are represented in our people and our interactions. Through my position at the CVC, I have had the opportunity to work with and be inspired by everyone throughout our organization, and each person brings something unique and different to the team. By recognizing the special talents, diversity and knowledge of each individual that makes up the CVC team, you can see the important role collaboration holds within our organization.

How would you summarize your experience with the CVC to those who might be interested in working with the organization?

It takes someone very special to work at the CVC. The expectations at our organization are high, but that is because when things leave the door they are delivered with the highest quality in mind. Ultimately, those high expectations drive us to always strive for and produce a quality result in everything we do.

The CVC is also very supportive of investing in its people and continuing to enhance their knowledge by providing opportunities for learning and development. If you are willing to embrace new projects and push yourself, there are many opportunities for growth within the organization. Our Founding Director, Dr. Paul Armstrong, has been key to this process over the years as he continuously challenges us to be our best while encouraging personal growth and learning.

Dr. Cynthia Westerhout joined the CVC in 2000 and is the Associate Director of Research and Strategic Planning.

How did you first come to work at the CVC, and what specifically interested you about the CVC prior to joining the organization?

When I was a Master's student I had the same supervisor (Prof. L. Duncan Saunders) as Dr. Kaul when she was finishing her PhD. In 2000, Dr. Kaul had secured a University Hospital Foundation (UHF) grant to look at the utilization of abciximab in Alberta using the APPROACH registry, and the opportunity to work on this project came along at a time when I was looking for a thesis project. I wasn't really familiar with the CVC as an entity at the time, but cardiovascular research was an interest during my undergrad so it seemed like a good match for my background in biomedical sciences, epidemiology and cardiology.

What have you learned from your time working at the CVC?

I think the most important thing I've learned is how research works in practice. During my undergraduate science degree I learned scientific method, but until you're practicing, you don't realize the length of time and number of people involved in generating new evidence. It was an eye-opening experience to realize that it takes a variety of people and different skill sets to make it all happen.

I've also learned about the benefits of working within a smaller organization. The CVC has always been very good at recruiting and retaining very strong people, and that has led to great relationships both internally and externally. There are a lot of excellent opportunities at the CVC that I don't think are necessarily possible at other centres. In that way I would consider our organization small but mighty.

During your time at the CVC what has been your most valuable experience?

As I was finishing my master's degree, I learned of a scholarship, sponsored by the Dutch government, that promoted an opportunity to work or study in the Netherlands. Dr. Armstrong at the time was a member of the Executive Committee for the GUSTO-IV ACS trial, and he connected me with the primary investigator (PI) for the trial, Prof. Maarten Simoons, and Dr. Eric Boersma, both based at Erasmus Medical Centre (Rotterdam, NL). Through this connection, I went to the Netherlands to work for a year and that experience turned into pursuing my PhD. From that time on I became more integrated in the CVC, working more closely with Dr. Armstrong, and had the opportunity to foster strong relationships in both centres. Recognizing the immense value of secondary analyses of clinical trial data also stems from this experience. Overall, this impactful experience set the trajectory for my career.

The CVC's core values are collaboration, quality, integrity and respect. Can you speak to how you see one of these values reflected in the work being done at the CVC?

I think respect is the most obvious one for me, particularly since I came to the organization as a non-MD researcher. I've observed in other groups where biostatisticians function more as a service rather than a partner in research. From the very early days, the CVC has been dedicated to ensuring that biostatisticians are at the table as contributing members, and I see this as a sign of respect for the contributions we make to the clinical cardiovascular research. This also speaks to collaboration, and the role of that core value within our organization.

How would you summarize your experience with the CVC to those who might be interested in working with the organization?

The expectations are high and one should be prepared for a lot of hard work, but the rewards and recognition for this certainly follow. One of the best things about the organization is the types of people it brings you into contact with, both internally and externally. To the latter, my collaboration with centres like DCRI, Leuven CC, Uppsala CR, and Rotterdam, just to name a few, has been really rewarding and beneficial to both sides. The CVC has a longstanding tradition of strong relationships built on high-quality work and a shared vision. I've also always appreciated the organization's emphasis on pursuing individual interests, as well as their continued support for further educational and growth opportunities.

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 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 131 publications produced within the CVC's body of research in 2017. Selecting a handful of five 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 2017, please visit **thecvc.ca/publications.**

Finding the Right Balance Between Precision Medicine and Personalized Care.

McAlister FA, Laupacis A, Armstrong PW.

CMAJ. 2017; 189:E1065-E1068.

In this thoughtful viewpoint, Dr. Finlay McAlister reflects on one of the most important emerging trends in contemporary medicine. He cautions us about the excitement generated from the reductionist trends provided by "precision medicine", which draws from increasingly detailed molecular characterization of disease states using the molecular characterization to better individualize diagnostics, prognostics and therapeutics. He then indicates that better health outcomes necessitate a more holistic approach (i.e. "personalized medicine") requiring clinical skill. This places the individual person at the centre and takes heed of their environment, culture and beliefs.

Hospital Variation in Treatment and Outcomes in Acute Coronary Syndromes: Insights From the Alberta Contemporary Acute Coronary Syndrome Patients Invasive Treatment Strategies (COAPT) Study.

Bainey KR, Kaul P, Armstrong PW, Savu A, Westerhout CM, Norris CM, Brass N, Traboulsi D, O'Neill B, Nagendran J, Ali I, Knudtson M, Welsh RC.

Int J Cardiol. 2017;241:70-74.

This work represents the first publication of the COAPT group, a true trans-Alberta network that brings together cardiovascular specialties from across the province. Dr. Kevin Bainey, with the able analytical insights of Dr. Padma Kaul and key support from Dr. Robert Welsh and others, discovered that there was significant variation in treatment of acute coronary syndromes in a large cohort of over 14,000 patients. Importantly, this also appeared to be related to differences in 1-year clinical outcomes, thus suggesting that closer evaluation of care variations is warranted.

Composite End Points in Clinical Research: A Time for Reappraisal.

Armstrong PW, Westerhout CM.

Circulation. 2017; 135:2299-2307

In this invited review in Circulation, Dr. Cynthia Westerhout and Dr. Paul Armstrong provide new insights and a rationale for how future clinical trials could be better composed. They suggest this could maximize trial efficiency and anticipate that the emerging big data revolution may provide an even broader scope of outcomes than ever before. They further propose that leading associations of healthcare professionals, patient engagement groups, journal editors, and regulatory agencies collaborate to establish more uniformly accepted calibration of clinical end-point definitions, and their relative significance, by weighting them in a more meaningful sense.

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

2017 Comprehensive Update of the Canadian Cardiovascular Society Guidelines for the Management of Heart Failure.

Ezekowitz JA, O'Meara E, McDonald MA, Abrams H, Chan M, Ducharme A, Giannetti N, Grzeslo A, Hamilton PG, Heckman GA, Howlett JG, Koshman SL, Lepage S, McKelvie RS, Moe GW, Rajda M, Swiggum E, Virani SA, Zieroth S, Al-Hesayen A, Cohen-Solal A, D'Astous M, De S, Estrella-Holder E, Fremes S, Green L, Haddad H, Harkness K, Hernandez AF, Kouz S, LeBlanc MH, Masoudi FA, Ross HJ, Roussin A, Sussex B.

Can J Cardiol. 2017; 33:1342-1433.

Guidelines are a key source of advice for clinical practitioners and heart failure is a common health care issue that consumes massive resources. The CVC is proud that our Co-Director, Dr. Justin Ezekowitz, chaired this key initiative based on his broad clinical and research experience. Hence, he is the lead author of this new edition of the national heart failure guidelines sponsored by the Canadian Cardiovascular Society.

CJC Canadian Journal of Cardiology
Journal canadien de cardiologie

"I joined the CVC in 1997, applied survival analysis in my research, and extended it to dynamic modeling and multilevel analysis. The CVC pioneered early treatment of ST-elevation MI patients by paramedics, and according to my daughter Solene, an emergency nurse in Courtenay, B.C., our cutting-edge treatment had been put into practice at her hospital. I retired in 2007 to a life of critical and philosophical writings, yet it's heartening that CVC research makes a real difference in practice."

- Wei-Ching Chang, Adjunct Professor of Medicine, University of Alberta

Relationships Between Baseline Q Waves, Time From Symptom Onset, and Clinical Outcomes in ST-Segment-Elevation Myocardial Infarction Patients: Insights From the Vital Heart Response Registry.

Zheng Y, Bainey KR, Tyrrell BD, Brass N, Armstrong PW, Welsh RC.

Circ Cardiovasc Interv. 2017 Nov;10: pii: e005399.

This work illustrates a key link between our prior clinical trial work and its applicability to a much broader population studied in the VITAL Heart Response (VHR) registry. The VHR registry was founded by Dr. Robert Welsh and represents a cooperative effort from physicians across Edmonton who care for patients with acute ST elevation myocardial infarction. This research is important because it confirms –using an analysis conducted by Yinggan (Gray) Zheng- that it is possible to determine the prognosis using a simple ECG signal. This provides insight into how much damage has occurred, and influences early therapeutic choices.

Circulation
Cardiovascular Interventions
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Interprovincial Differences in Canadian Coronary Care Unit Resource Use and Outcomes.

van Diepen S, Lin M, Ezekowitz JA, McAlister FA, Lee DS, Goodman SG, Armstrong PW, Kaul P.

Can J Cardiol. 2017; 33:166-169.

Dr. Sean van Diepen collaborated closely with Dr. Padma Kaul, and others in our CVC group, to undertake this interesting and important trans-Canada look at the use of critical care bed resources. He found significant threefold variation in coronary care unit (CCU) admission rates across provinces for patients hospitalized with acute coronary syndromes and heart failure. A majority of patients admitted to the CCU did not receive critical care therapies in the first two days of hospital admission. These findings suggest new opportunities to enhance guidelines for CCU admission practices.

CJC Canadian Journal of Cardiology
Journal canadien de cardiologie

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 insights and impact are enhanced by our faculty's pursuit of knowledge translation and dissemination.

The following is a selection of the key presentations given by our faculty members in 2017.

Paul W. Armstrong, MD

CAD Conference 2017
– Mumbai, India
September 2017

Meet the Legend: Acute Myocardial Infarction 2017: Reflections of a Clinical Investigator

This keynote address was provided to approximately 300 Indian cardiologists in Mumbai, India. This is an annual meeting held in conjunction with the European Society of Cardiology that engages a distinguished international faculty. Dr. Paul W. Armstrong was honored as a legend for his work in acute myocardial infarction and presented with a Ganesh which is known as "the elephant-headed god of wisdom and learning, as well as the remover of obstacles, and consequently the sign of auspiciousness".

Kevin Bainey, MD

Canadian Cardiovascular Congress (CCS) 2017
– Vancouver, Canada
October 2017

Canadian Cardiovascular Society Guidelines for the use of Antiplatelet Therapy

Dr. Kevin Bainey served as a panel member during a workshop on the CCS Guidelines for the use of Antiplatelet Therapy (APT). The update to the APT guidelines incorporates new evidence on how to optimize APT use. Topics include optimal duration of dual APT (DAPT) after percutaneous coronary intervention (PCI), management of DAPT in patients undergoing PCI who also require oral anticoagulation (atrial fibrillation, venous thrombo-embolic disease, prosthetic heart valves, left ventricular thrombus), peri-operative DAPT management (non-cardiac surgery, elective/semi-urgent CABG surgery) and how and when to switch between APT agents.

"In my short time at the CVC, I have been intensely affected by the team Dr. Armstrong has meticulously assembled. To see such a driven, creative and innovative group constantly endeavoring to better not only themselves, personally and professionally, but to also go to extraordinary lengths to help improve processes and outcomes in health care is inspiring. It is truly heartening to be part of a team that has, and will continue, to leave such a profound legacy in cardiovascular research."

- Lisa Soulard, Executive Assistant to Dr. Paul W. Armstrong

Sean van Diepen, MD

American Heart Association Scientific Sessions 2017
– Anaheim, United States of America
November 2017

Contemporary Management of Cardiogenic Shock

This was a formal presentation of the American Heart Association's (AHA) Scientific Statement on Cardiogenic Shock, for which Dr. Sean van Diepen was the first author. This scientific statement on cardiogenic shock summarizes the epidemiology, pathophysiology, causes, and outcomes of cardiogenic shock; reviews contemporary best medical, surgical, mechanical circulatory support, and palliative care practices; advocates for the development of regionalized systems of care; and outlines future research priorities.

Shaun Goodman, MD, MSc

Sunnybrook Health Sciences Centre Contemporary Cardiac Care Conference – Toronto, Canada
November 2017

PCSK9 Inhibitors and Cardiovascular Outcomes

This presentation covered the current unmet clinical need in Canada for safe and effective lipid-lowering treatment, the updated Canadian Cardiovascular Society (CCS) guidelines outlining the important of risk assessment, risk stratification, and treatment considerations, and the potential role for proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors. The CVC has managed the Canadian component of the ODYSSEY Outcomes trial, comparing the PCSK9 inhibitor alirocumab to placebo in post-acute coronary syndrome patients at high risk of recurrent cardiovascular events; the design and potential impact of the highly anticipated results of this study were discussed.

Justin Ezekowitz, MBBCh, MSc

65th Annual Scientific Meeting of the Cardiac Society of Australia and New Zealand (CSANZ) – Perth, Australia
August 2017

• Guided Therapy (GUIDE-IT)
• Sacubitril in Canada
• Sodium and HF

This series of invited talks was an opportunity to discuss three different programs: research in progress (the Canadian Institutes of Health Research and University Hospital Foundation funded SODIUM-HF trial), just completed research (the NIH funded GUIDE-IT trial) and the heart failure guidelines developed by the Canadian Cardiovascular Society. These presentations gave Dr. Justin Ezekowitz, representing the CVC's broader research community, the opportunity to explore unanswered questions and further collaboration with investigators in Australia and New Zealand. Additionally, immediate knowledge translation and dissemination about guiding therapy using advanced biomarkers was featured throughout the discussion of a trial lead by our colleagues at the DCRI, and for which the CVC and Canadian sites played a key role. Finally, it is not often we have the honor to 'show-off' our Canadian guidelines abroad, which hit the right balance of science and practicality, and stem from the hard work of the Canadian heart failure community.

Padma Kaul, PhD

Western Canadian Universities Big Data Health Conference
– Banff, Canada
September 2017

Prescription Drug use During Pregnancy and Long-Term Health Outcomes in the Mother and Child

The Western Canadian Universities Big Data Health Conference (WCUC) is a partnership between the universities of British Columbia, Alberta, Calgary, Saskatchewan, and Manitoba. The primary goal of the first WCUC was to foster collaboration between the Western Canadian medical schools in the area of big data and precision medicine. Dr. Padma Kaul received one of the four seed grants that were awarded to promote cross-jurisdiction collaborative research projects, and presented the study design and analytical framework of the project at the conference.

Finlay McAlister, MD, MSc

Canadian Society of Internal Medicine Annual Scientific Meeting (CSIM) - Toronto, Canada.
November 2017

Heart Failure Management in 2017

CSIM is the national meeting for Canadian General Internists. Dr. Finlay McAlister was invited to give this workshop to update attendees on the Canadian Cardiovascular Society Heart Failure guidelines and to discuss complicated heart failure cases.

Robert Welsh, MD

European Association of Percutaneous Coronary Interventions (EUROPCR)
– Paris, France
May 2017

Novel Ways to Reduce Atherothrombotic Burden in Interventional Cardiology

The Euro PCR, occuring annually in Paris, France, is the largest international interventional cardiology meeting. Dr. Robert Welsh's presentation was part of a session on New Antithrombotic Treatment Strategies in Interventional Cardiology. This session is a key symposium with an accomplished international faculty.

The Next Generation of Health Researchers

The foundation of the CVC 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 research culture that embraces curiosity, welcomes new ideas and seeks to address key unanswered questions that are likely to alter the minds and actions of all those involved in health care delivery.

The CVC recognizes that a research experience can be life changing, whether during a summer studentship, an elective experience in clinical medicine, or through dedicated graduate or postdoctoral training. Whatever we provide to our trainees is inevitably returned to us bearing interest: this return on investment provides fresh and unbiased thinking, 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 that can then be applied to the unending search for better health solutions. An attitude of lifelong learning, coupled with a continuing commitment to remain engaged in the process of research – irrespective of individual career destinations – is our aspiration for research trainees.

In the following section, two of our young researchers and their respective CVC mentors discuss the important role of mentorship and collaboration.

Nariman Sepehrvand, MD

PhD Candidate
Department of Medicine, University of Alberta

What would you say are your research highlights and personal achievements from 2017?

In terms of research highlights, we had good progress in patient recruitment for the HiLo-HF trial, which is a pilot trial on the efficacy of supplemental oxygen therapy in patients with acute heart failure. I also presented the findings of the Emergency Heart failure Mortality Risk Grade (EHMRG) validation study at the European Society of Cardiology (ESC) congress in Barcelona, Spain, which was selected as the best poster in the acute heart failure section. The ESC congress attendance also sparked collaboration with some of the key experts on the issue of supplemental oxygen therapy in the setting of acute myocardial infarction, which later led to a meta-analysis study on that topic. Publishing two research papers and two book chapters in fields related to my previous projects are some other achievements I had in 2017.

Why specifically were you interested in working with Dr. Justin Ezekowitz?

That decision goes back to 2014 when I started my PhD here at University of Alberta. Every year since then, I come to the same conclusion that this was one of the best decisions I have made. Dr. Ezekowitz is a world-renowned clinician-scientist in the field of heart failure, but most importantly he is a great mentor. It is wonderful to see how he manages to allocate a substantial amount of time each week to all of his students/trainees to guide them and provide them with advice that is essential to their success in conducting research projects.

What is the most important lesson or piece of advice you have learned from your mentor, and why?

As a person who is intrigued by every aspect of medicine and science, I might get easily distracted by different ideas and one of the most important lessons I learned from Dr. Ezekowitz is that not every topic is worth our time and effort. A continuous quest for new ideas and skills, hard work and effective time-management are some of his key qualities that I try to emulate.

Why is mentorship so important within a research environment?

I think mentorship is important in every aspect of life, from personal decisions to career goals. However, academic life and the research environment have complexities that are difficult for a person to confront alone. Accessing the invaluable experiences of established academicians can help us to surpass those challenges successfully. A strong mentor-mentee relationship can pave the way for a junior researcher to learn required skills, build collaborative networks and to eventually become a successful member of the scientific community.

Justin Ezekowitz, MBBCh, Msc

Co-Director, Canadian VIGOUR Cente
Professor, Division of Cardiology, University of Alberta
Director, Heart Function Clinic, Mazankowski Alberta Heart Institute

When you were a trainee, was there a specific mentor or learning experience that impacted you?

I have been extremely privileged to have had exceptional mentorship throughout my training and career. I'd like to recognize that my early mentors Drs. Greg Korbutt and Ray Rajotte, both at the University of Alberta involved in diabetes research, gave me insight into research in a welcoming and generous environment that almost made me want to do more basic science research. My second set of mentors when I was doing my internal medicine training were Drs. Clyde Yancy and Mark Drazner. Both elucidated that one could be a clinician scientist and educator, and they showed me a path forward for Cardiology and specifically heart failure research. Finally, when I landed at the University of Alberta, I could not have been more privileged to have Drs. Paul Armstrong and Finlay McAlister as my mentors, as they have helped shape my career into what it is. I'm also reminded, in a good way, that mentorship needs to be lifelong.

Why is it important for you to help mentor the next generation of health researchers?

In the same way that I received mentorship that provided me with the environment, tools and excitement to go into research, I too want to provide that experience. We never know where the next great idea or researcher will come from and it's important to have a legacy that is well beyond what we individually can achieve.

What have been some of the highlights of working with Dr. Nariman Sepehrvand in 2017?

The highlight is simply working with such a bright young mind with so much enthusiasm and energy, as well as creative ideas. This year saw the start of a few major projects and I have really stayed out of the way as he continues to exceed expectations. One could say that the highlight was the year overall. I look forward to the future of things he will achieve and to continuing to learn from him.

What are the key factors for a successful working relationship between a mentor and a trainee?

I think it's critical that both are engaged in working together over a long period of time as it does take a while for these relationships to develop. A very typical way to think about being a mentor - which has been written about extensively - is that a mentor needs to be a teacher, friend, advisor, and role model. That means that there needs to be trust, mutual respect and an openness to delivering and receiving information and feedback. It's both an art and a science.

Michael Raco, MD

Fellow, Interventional Cardiology

What would you say are your research highlights and personal achievements from 2017?

I have been working on a research project involving temporal trends in heart failure and mortality for ST-elevation myocardial infarction (STEMI) patients. I was excited to have this project accepted at the American College of Cardiology (ACC) Annual Scientific Session and Expo, and I am currently working on a manuscript for this project as well. I was also thrilled to be accepted into the interventional cardiology fellowship at the University of Alberta, where I will be learning coronary interventions under the guidance of Dr. Bainey.

Why specifically were you interested in working with Dr. Kevin Bainey?

Dr. Bainey embodies the ideal qualities of a great mentor and leads by example. He is a busy clinical interventional cardiologist who also dedicates a significant amount of time to research, as well as training both interventional cardiology fellows and general cardiology residents. He has a career that I hope to emulate.

What is the most important lesson or piece of advice you have learned from your mentor, and why?

Dr. Bainey has taught me that research involves curiosity, passion, and commitment. You must have the curiosity to generate unanswered questions regarding a subject that ignites passion. This passion will drive your commitment in seeing a project through to completion.

Why is mentorship so important within a research environment?

Mentors are vital in their role of providing guidance and support, delivering constructive criticism, and inspiring personal and professional growth in order to facilitate future success.

"I joined the CVC in 2007 after I had just finished my secondary education in a foreign country, and now I am a citizen of this country that I call home. Over the past decade I have witnessed the CVC's success and my own personal growth as well. Analyzing complex data, attending weekly research meetings, revising returned papers, and learning new vocabulary are just some of the experiences I have enjoyed during my first ten years with the CVC, and I look forward to the years to come. I guess you could say the chemistry is right."

- Yinggan (Gray) Zheng, Senior Biostatistician

Kevin Bainey, MD, MSc

Director, ECG Core Lab, Canadian VIGOUR Centre
Interventional Cardiologist, Mazankowski Alberta Heart Institute
Assistant Professor, Division of Cardiology, University of Alberta

When you were a trainee, was there a specific mentor or learning experience that impacted you?

There is no question that Paul W. Armstrong has had an immense impact on both my learning experience and enthusiasm for clinical research. His mentorship has undoubtedly shaped the path of my career today.

Why is it important for you to help mentor the next generation of health researchers?

Honestly, it is difficult for me to think of myself as a mentor at this point in my career. However, with the support and guidance of my colleagues at the CVC, I can help introduce the next generation of trainees to the merits of health research.

What have been some of the highlights of working with Dr. Mike Raco in 2017?

Mike Raco has displayed a strong sense of enthusiasm and commitment for his clinical research, which is refreshing to see in a cardiology trainee. His acknowledgment of limitations is certainly a highlight, as is his willingness to learn from others.

What are the key factors for a successful working relationship between a mentor and a trainee?

It is important for a mentor and trainee to maintain regular communication in an open and non-threatening environment. I do believe this strengthens the relationship and builds trust. While clinical duties can become demanding, designating specified times to meet face-to-face and review projects is absolutely paramount. Having an agenda prepared is often helpful recognizing the importance of reviewing progress and documenting minutes (useful tip I received from my mentor). Finally, reflection on goals achieved and future opportunities helps cultivate an ongoing interest for research which I do believe provides a sustainable and effective working relationship.

Michael Raco, MD

Kevin Bainey, MD, MSc

Distinguished Visitors

In 2017, the faculty of the CVC had the privilege of hosting two outstanding, internationally renowned academics. The Distinguished Visitors series is a continuing program generously sponsored by an unrestricted educational grant 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 window on the global state of cardiovascular medicine as it relates to career choices for trainees and potential future directions for meaningful research. They constitute a seminal part of our educational and research mission.

Lesley H. Curtis, PhD

Professor of Medicine
Director, Centre for Population Health Sciences,
Duke University School of Medicine
Director, Center for Pragmatic Health Systems Research,
Duke Clinical Research Institute

May 10, 2017

- **Cardiology Divisional Rounds:** "Making good on the promise of the EHR for research: Experience from a national clinical research network (PCORnet)"
- **Cardiology Research Rounds:** "The realities of real-world data"

The CVC and the University of Alberta Division Of Cardiology welcomed Dr. Lesley Curtis as a distinguished visitor in May 2017. Her visit began with an insightful Divisional Rounds on how data from Electronic Health Records (EHR) are being employed for research purposes by the national Patient-Centered Clinical Research Network (PCORnet) in the US. This was followed by a thought-provoking Research Rounds on the opportunities and challenges offered by real-world healthcare data.

Steven R. Steinhubl, MD

Director, Digital Medicine
Scripps Translational Science Institute,
Associate Professor, Department of Molecular Medicine
The Scripps Research Institute

October 11, 2017

- **Cardiology Divisional Rounds:** "What Is Digital Medicine and How Will It Change the Practice of Cardiology?"
- **Cardiology Research Rounds:** "The All of Us Precision Medicine Research Program"

In October of 2017, our faculty and Division of Cardiology was delighted to host Dr. Steven Steinhubl, the Director of Digital Medicine at the Scripps Research Institute in California. His innovative insights into the future of digital medicine were tremendously well received by our faculty, given the major advances in this arena and the impending Alberta electronic medical record. His forward-looking perspective was also shared in a research round that communicated the advances in mobile health and devices that offer new opportunities to make more informed choices in future patient care and clinical research.

Beyond 2000 XXIII

Vancouver provided a splendid setting for our 23rd annual Beyond 2000 symposia, which was held on October 23, 2017 in conjunction with the Canadian Cardiovascular Congress. This event continues to be one of the most highly attended sessions at the Congress each year. We were extremely gratified that approximately 500 registered healthcare professionals attended the symposia, and also pleased at the overwhelmingly positive feedback we received about the caliber of the program and the speakers.

We now undertake two back-to-back events –the first on Acute Coronary Syndromes (ACS) and the second on Heart Failure and Atrial Fibrillation (HF/AFib). These topics are highly relevant to our audience and we are fortunate to attract a diverse group of both national and internationally renowned speakers. These programs were generously supported by unrestricted educational grants from AstraZeneca, Merck, Novartis, and Bayer, and, as has been our tradition, we partnered with the Canadian Cardiovascular Society, the Mazankowski Alberta Heart Institute and the University of Alberta in undertaking this venture.

The New Concepts in ACS symposium was co-chaired by CVC Co-Director Shaun Goodman. The program began with a presentation by Dr. Gregory Schwartz, of the University of Colorado, on secondary prevention with lipid modifying therapy. Thereafter preferred therapies for secondary prevention in stable CAD, 21st century ACS care pathways, and hot button issues in ACS were featured.

The New Concepts in HF/AFib symposium was co-chaired by CVC Co-Director Justin Ezekowitz. It kicked off with a presentation by Dr. Scott Solomon from Harvard Medical School on current concepts in classifying and managing heart failure. This was followed by a lively debate on whether or not old school therapies have a continuing role in patients with heart failure, sinus rhythm and left ventricular dysfunction. Other topics included a look at contemporary treatment strategies in diabetes and an overview of hot button issues in HF/AFib.

A few snapshots from the overall delegate ratings include; "Very well presented and timely. Right length of time per speaker. Interesting cases and discussion. The program is always very valuable for knowledge translation. Great presentations, very informative! Excellent!" The registrants were very positive of the programming and particularly enthusiastic about the debates and case presentations.

Our program has been further enriched for both attendees and those unable to be present through the creation of a website, which provides year-round access to speaker slides and in-depth video interview discussions on symposium topics. We also have begun employing this vehicle to answer some of the many audience questions posed electronically during the meeting that could not be addressed at the time. This living legacy of our meeting has generated extended exposure that has been enthusiastically received. We encourage you to visit **www.beyond2000.org** to determine for yourself the added value of this online resource library that we intend to continue.

Clinical Trials Colloquium

On March 12, 2017, the CVC welcomed 12 Canadian sites, representing seven provinces across Canada, to participate in the 4th Annual CVC Clinical Trials Colloquium in Banff, AB. The three primary objectives were as follows:

1. **Work together to enhance best practices in conducting clinical trials locally and across Canada through an open forum discussion and sharing among clinical trial sites, the CVC and industrial sponsors.**

2. **Establish and understand the roles and responsibilities of the investigators in clinical trials and what investigator oversight means within the context of clinical research expectations and regulations.**

3. **Share and gain knowledge from current and past clinical trial experiences in order to achieve success in all aspects of future clinical research studies.**

Our agenda was centered on the following four topics; feasibility, legal aspects of clinical research agreements, audits, and investigator oversight. Facilitated by CVC Associate Director of Clinical Trials, Tracy Temple, and CVC Co-Directors, Drs. Shaun Goodman and Justin Ezekowitz, this was a unique opportunity to ask questions, strategize on solutions, and share, through an open discussion with colleagues, insights on clinical research at their sites.

Our CVC Founding Director, Dr. Paul Armstrong, inspired the group with his opening remarks, which reminded us of the importance of quality and why we do clinical research. We were pleased to welcome back Ty Rorick, Associate Director of Mega Trials with the Duke Clinical Research Institute (DCRI), who challenged us to think about feasibility throughout the lifetime of a project. One key element of this discussion was understanding the importance of ascertaining all clinical events and safety throughout a patient's participation in a study, with the ability to access and review electronic medical records (EMR). Marlon Rajakaruna, a partner at Dentons who brings extensive legal knowledge as it relates to clinical trial research agreements, shared his insights on the top ten risks found within clinical research and confidentiality agreements. With the help of Lisa Berdan, Director of Mega Trials at DCRI, Tracy Temple along with our sponsor and site representatives were able to have a robust discussion based on their first-hand experience with audits from the FDA, Health Canada and sponsors. Finally, Dr. Shaun Goodman reminded us that investigator oversight remains one of the most important aspects of participating in clinical research. This topic is embedded in all aspects of our Colloquium, and continues to be an ongoing theme in our communications with sites.

Recognizing that we can only bring a small group of sites to the Colloquium each year, we make ongoing efforts to disseminate key information to others through the Chronicle newsletter, word of mouth from attendees, and communications with our project teams and monitors. We hope that this information continues to highlight the importance of choosing participation in trials wisely, mitigating risk with clinical trial site agreements through legal consultation, preparedness for audits and inspections, and most importantly, ensuring you are an involved and informed investigator.

Without the support of our Canadian sponsors, (AstraZeneca, Amgen, Bayer, Novartis, Pfizer/BMS Alliance, and Sanofi) we would not have been able to offer this unique opportunity. We always appreciate hearing from our sites across Canada and look forward to continuing the Colloquium in the years ahead.

The Canadian Cardiac Chronicle

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

The Chronicle is available on our website (**thecvc.ca**), and it is distributed to over 600 recipients, including investigative sites, sponsors and international collaborators.

Volume 21, No. 1 — Spring 2017

In This Issue:

Joined by our colleagues from the Duke Clinical Research Institute (DCRI), the Canadian VIGOUR Centre (CVC) recently held the **4th Annual CVC Clinical Trials Colloquium** in conjunction with the annual ACC Rockies Continuing Medical Education meeting in Banff on Sunday, March 12th. A special thanks to Dr. Robert Welsh for another successful ACC Rockies conference and the opportunity to link the Colloquium to this important event.

Principal investigators (PIs) and study coordinators (SCs) from 12 sites and 7 provinces, together with medical representatives from Canadian pharmaceutical, met to discuss regulatory, ethical, operational, and legal issues related to, and share their experiences and best practices in, conducting clinical trials.

One of the key objectives of this year's Colloquium was to enhance the understanding of PI roles and responsibilities in clinical trials and what PI oversight means in the context of clinical research expectations and regulations. The results of a pre-Colloquium survey of participating sites suggested that 75% of sites had experienced an audit, and among those that had previously undergone inspections by regulatory authorities (Health Canada and the U.S. Food and Drug Administration), PI oversight was a frequent area of scrutiny.

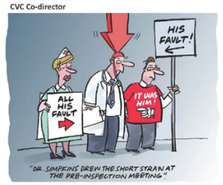
As indicated by the U.S. FDA Code of Regulations and International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH; i.e., Good Clinical Practice [GCP])—and highlighted in a recent DCRI PI Oversight document shared with you—the PI is the leader of the local clinical research team and assumes complete responsibility for the safe and successful execution of the protocol.

This includes **a number of responsibilities and duties** that can only be accomplished when the **PI is an active and engaged leader in the conduct of the trial**: (1) protocol knowledge; (2) oversight of the patient consent and randomization process; (3) trial follow-up, study drug compliance, and patient retention procedures; (4) complete ascertainment of suspected trial endpoints and adverse events; (5) local ethics board reporting; (6) reporting of significant GCP issues; (7) resolution of Corrective Action Plans (CAPs) put in place when issues are identified during trial conduct; and, (8) participation in monitoring activities.

This exhaustive (and sometimes exhausting!) list of PI responsibilities clearly demands a local oversight plan, including defined responsibilities, awareness and good communication (e.g., weekly reviews with the study coordinator), involvement of sub-investigators, frequent engagement with, and providing ongoing access to, study coordinators and patients. Thus, in the face of a high likelihood that your clinical trial oversight will be examined under the microscope, the Scouts Canada motto **"Be Prepared"** offers up some good advice!

Shaun

Shaun Goodman
CVC Co-director



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Volume 21, Issue No. 2

CANADA 150

The first sentence of every novel should be: **Trust me, this will take time but there is order here, very faint, very human**.

- In the Skin of a Lion, Michael Ondaatje

It comes as no surprise that this Chronicle arrives around the longest day of the year. The longest day, June 20th, will see nearly 18 hours of light in Edmonton – so, there is no limit to getting outside and enjoying the summer! Some of you are working equally long hours in your pursuit of clinical care or research activities and recognize that it can't always be done in a day, or sometimes, even in a year.

The 150th year celebration for Canada, starting on July 1st, is an opportunity for us all to reflect on Canadian contributions to existing pivotal research, as well as those discoveries that are still to come. Similar to Canada's history, research has to incorporate many changes over time, introduce adjustments where needed, and adapt to the environment while staying committed to the overarching goals we initially set out to test. Over the past 150 years, Canada has seen many challenges and we have recognized the importance of inclusivity, adapting to change, and ensuring that we remain committed to the goals set forth a long time ago. Importantly, Canada holds a unique place in the world and we value our friendships with our collaborators outside of Canada. Without our international friends and neighbours, we cannot achieve our collective goals.

Like the longest day of the year, the pathway from a research hypothesis regarding a molecule in a lab or a patient encounter resulting in an unanswered clinical question to the completion of a pivotal phase III clinical trial is similarly long (but measured in years). It often takes over 10 to 15 years to develop and refine a concept that we are all engaged in testing. Sometimes, this process can be much shorter; we look for these rapid, early wins when we are deciding what should be pursued and how it may impact human health. To that end, clinical research requires commitment over multiple years in order to continually train and re-educate teams with new techniques that advance how we all perform research. The commitment of patients participating in studies that can often run over multiple years also deserves consideration. It is this commitment (e.g., staying on therapy, coming back to the clinical research site, blood work, and repeat imaging) that I have to admire of our patient volunteers; we should make sure we express this when we see them each and every time.

The overall health of our research and clinical teams is often forgotten. I'd like to encourage you to make sure you are eating healthy, sticking to a minimum of 150 minutes per week of exercise, and maintaining your work/life balance. Get outside; you've earned it.

Justin Ezekowitz
CVC Co-director

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Volume 21, Issue No. 3

Composite Outcomes in Clinical Trials – What Happened to All-Cause Mortality as the Sole Endpoint?

Clinical trials, particularly in cardiovascular (CV) medicine, have improved the lives of patients in Canada and worldwide. As a consequence, a marked decline in mortality from CV disease in developed countries has made it increasingly challenging to demonstrate potential benefits of new, effective treatments when the primary outcome of a clinical trial is based on mortality alone. Thus, the era of large (e.g., n=42,000), simple (e.g., 4-page informed consent and 3-page case report forms) and efficient (e.g., 30-day follow-up post card given to patients surviving hospitalization to mail to the coordinating center) clinical trials like the first GUSTO study completed in 1993, have long since ended. Recognizing that surrogate outcomes may be misleading (recall the "suppress the premature ventricular complex PVC" approach that resulted in increased mortality with anti-arrhythmic therapies in the duet of CAST trials), clinical trial innovators like Califf, Topol, Braunwald, Cannon and others advocated for combining mortality with other nonfatal events to minimize the number of endpoints (and patients and time it would take) to evaluate new strategies and treatments.

However, as nicely discussed in a recent White Paper published in Circulation (2017;135:2299–2302) by our CVC Founding Director (Dr. Paul Armstrong) and Associate Director, Research & Strategic Planning (Dr. Cynthia Westerhout), despite the benefits in trial efficiency from combining events into a single composite outcome, "... this method assumes uniform directionality of each component, does not distinguish the relative clinical significance of each, and counts only the first occurrence of any event in the final tally within a conventional time to first event analysis." The most common current analytic approach assigns an equal "value" across all event types within the composite end point: thus, patients typically have a component of lesser severity than death as their first event conventional time to composite event analyses in trials. Further, unlike all-cause mortality, non-fatal events—even something like myocardial infarction (MI)—may be under-reported and are defined differently across studies.

In an attempt to address some of these limitations, Drs. Armstrong and Westerhout, in collaboration with Dr. Jeffrey Bakal (Lead, Health Research Methods and Analytics at the University of Alberta SPOR Data Platform) have proposed differentially weighting event types, with input from experienced trialists, clinicians, and patients themselves to derive a relative weighting system for individual patient outcome. They further point out that, even after differential weights within event types such as MI or stroke are accounted for, variability exists within each endpoint category with respect to clinical impact. For example, the clinical significance of an MI defined by a small troponin rise is likely different than a larger MI complicated by heart failure, and yet conventional analysis would "count" these two ends of the MI spectrum as being the same. Thus, additional attempts at grading the severity of individual end points within an event type—"weighting the weights"—may provide even greater discrimination between interventions that might not otherwise have been initially apparent.

Of note, the U.S. Food and Drug Administration (FDA) has recently chosen to restrict regulatory labeling of the recommended indication for empagliflozin in its label for diabetes to the reduction in CV death but not the primary composite of CV death, MI, or stroke. While both the former and the latter were statistically significantly lower with empagliflozin vs. placebo in the outcome-based EMPA-REG trial, MI and stroke were not. It will be

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Volume 21, Issue No. 4

The leaves are off the trees, there is snow on the ground and Canadian Thanksgiving has receded into the distance in our rear view mirror. The winter solstice beckons and heralds both Christmas and the coming holiday season. Reflecting on this year that is passing and the new one looming ahead has always been a meaningful time for me. Counting my many blessings and appreciating the extraordinary privileges afforded to those of us engaged in the search for new and better solutions in health care is an integral part of that process. We must never take for granted the freedom to pursue our ideas that is only limited by our energy, talents and dedication.

For us at the Canadian VIGOUR Centre 2017 is a special year since it marks the 20th anniversary of the first **Canadian Cardiac Chronicle** that was distributed to our many colleagues and friends across Canada and around the world. In that original issue, we reported on the successful completion of GUSTO 3 (comparing reteplase to rTPA in STEMI) and PURSUIT (which evaluated eptifibatide in Non STE ACS). We also eagerly anticipated the arrival of ASSENT 2, SYMPHONY and GUSTO 4 as novel projects in development. In preparing to celebrate this 20th anniversary, I tracked down and spoke to one of our original project leads about the history of the CVC. She reported that in my original letter offering her a job I wrote, "Welcome aboard… It should be a great ride!" It has indeed been a great ride and the transformation in cardiovascular care over the past two decades has been truly remarkable.

The major improvement in outcomes of our patients with acute and chronic coronary disease as well as those with heart failure have been directly related to the fruits of research. It has been immensely gratifying to participate in this extraordinary and welcome shift in cardiovascular health. So too has been this journey decorated by several hard-won learnings and many wonderful collaborations that we have developed in every corner of the globe thereby enriching our professional lives.

Yet the unmet needs of our patients, their families and their family's families continue. New diseases and new insights into old diseases that we once mistakenly thought we understood keep us humble and catalyze us to do better. We have come to the stark realization that it is one thing to discover a new medicine or technique and quite another to ensure that it can be applied in an efficient and timely manner. Many of the major causes of CV morbidity and mortality remain unknown and we are grappling with an epidemic of obesity and diabetes. The costs of clinical trials has risen enormously and the administrative burden to undertake them has similarly grown. Our health care systems are groaning under burden of accelerating costs and we are being appropriately challenged to participate in finding value for investment. Fortunately a remarkable panoply of new tools ranging from stem cells, pharmacogenomics, precision medicine, big data and artificial intelligence have emerged that hold much promise in the search for new solutions. Recruiting the best and brightest young people to participate in this enterprise is the key to our future success.

On behalf of our great team at CVC let me send out very best wishes to all of you for a Happy Christmas, Hanukah or whatever you choose to celebrate in the days ahead. Take time to enjoy the warmth and company of your family and friends and recharge your batteries for the year ahead. We look forward to collaborating with you on the path to discovery and better cardiovascular health in 2018.

Paul W. Armstrong

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The Canadian Cardiac Chronicle newsletter is distributed to 600+ people in 14 countries

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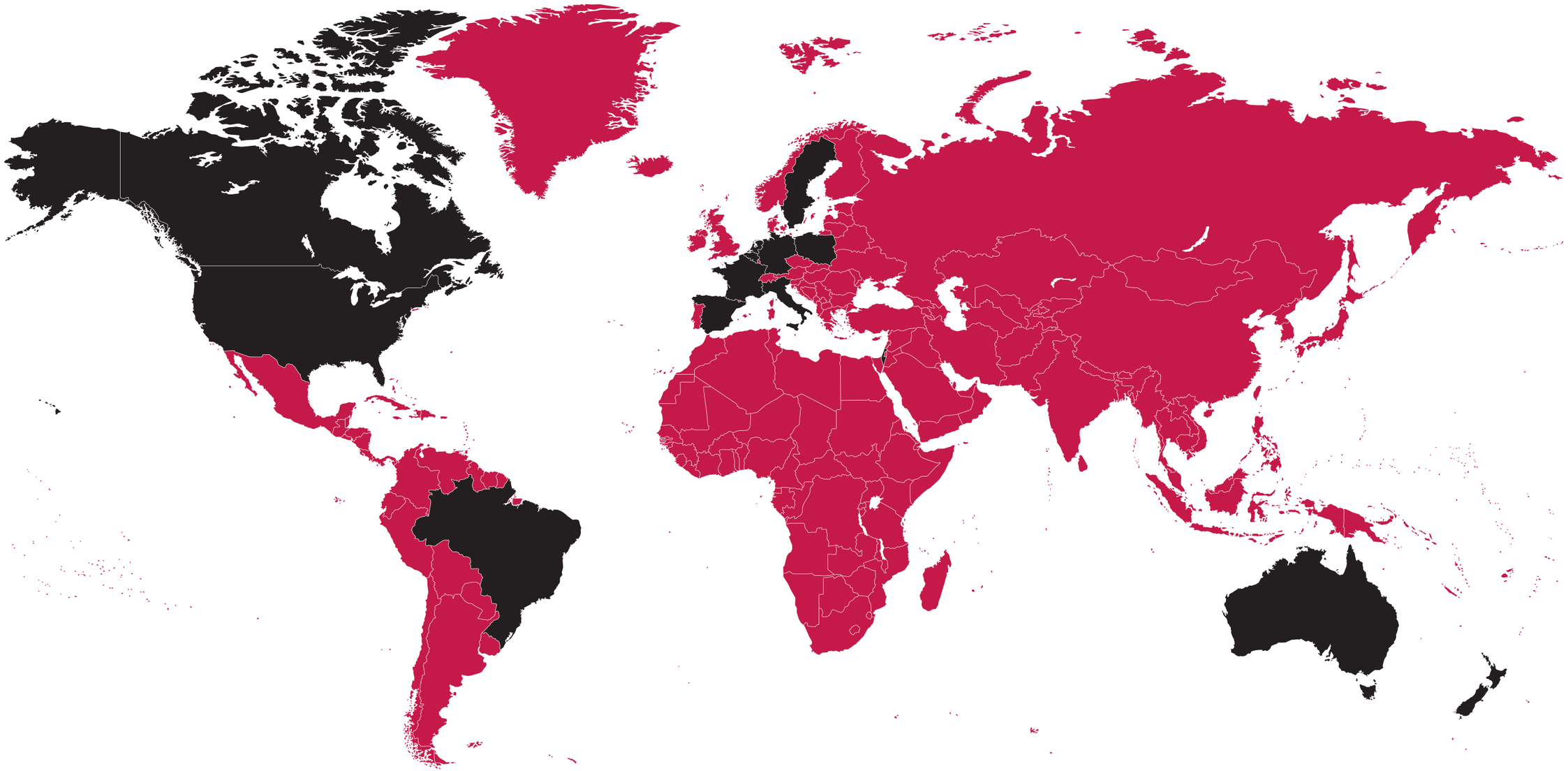


CVC Services and Activities

The CVC 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.

Thought Leadership

- Expert advice on cardiovascular disease, treatment guidelines, 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

Population Health & Economic Outcomes

- Analyzing healthcare administrative databases (CIHI and 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

Biostatistical Analysis

- 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

EGC 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)

Clinical Trials

- Project, site, and data management
- Negotiation and oversight of site contracts and payments
- Site/investigator 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

Clinical Data Registries

CVC Clinical Data Registries contain data on patients that is 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 diastolic HF

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 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

"In 2004, the CVC provided me with my first serious job. That first job turned into over a decade of unique experiences in challenging positions that compelled me to learn and innovate every day, supported by a team of talented and experienced colleagues. It is the culture of lifelong learning and the relationships built that I will continue to value most from my time with the CVC."

- Carla Price, Former Interim Assistant Director, Operations

Clinical Trials

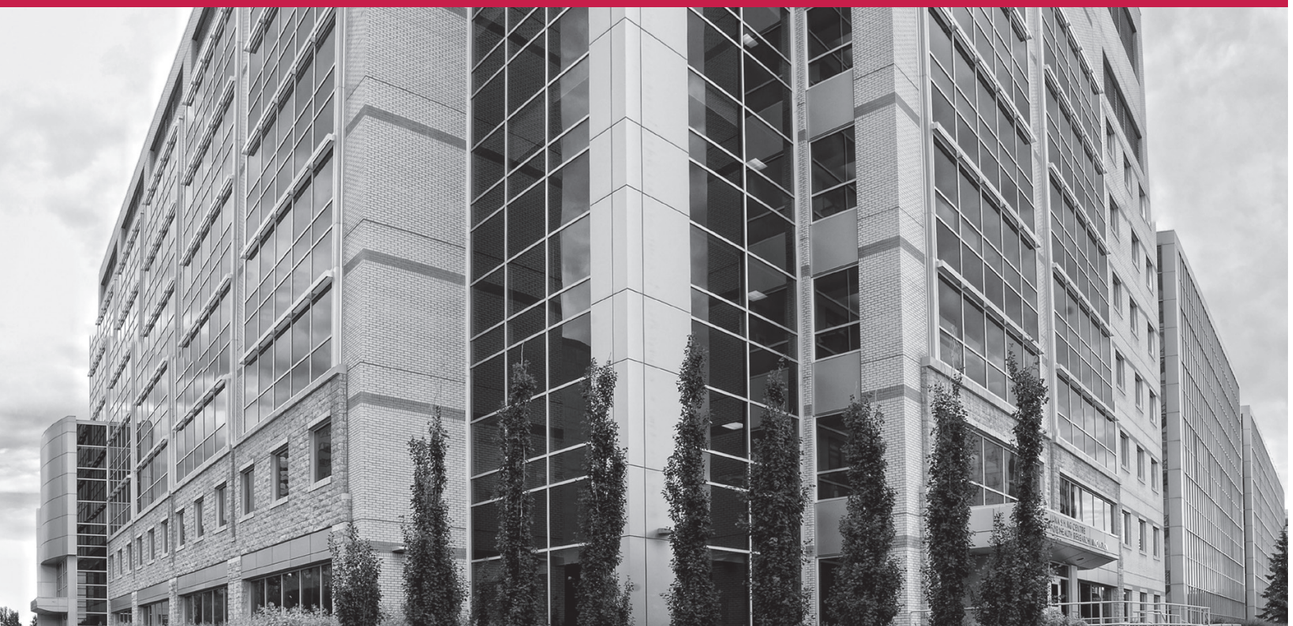
With over 20 years of experience in Clinical Trial Operations for Phase II/III/IV and investigator initiated studies, our team brings the expertise and knowledge to deliver a high quality and well executed trial from study start-up to closeout. Having worked with over 460 Canadian Site Investigators 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 risk based, central and/or remote monitoring approaches. The CVC monitors conduct source document verification, drug accountability and other required monitoring related tasks, while also utilizing their 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 they 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.



Tracy Temple, RN, BScN
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Kate Dawson, BSc
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Paula Priest
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Kris Reay
- Administrative Assistant

Melissa Spaling, MEd
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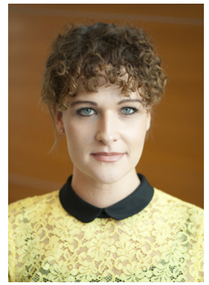

Julianna Wozniak, MSc
- Clinical Trials Project Lead

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- Clinical Trials Project Lead

Monitoring Team

Corrina Boyd, RN – Monitoring Lead
Lyne Cantin, RN, BSc, MBA – Clinical Research Associate
Valerie Carr, BN, RN – Clinical Research Associate
Halina Nawrocki, RN – Clinical Research Associate
Francine Nole, RN – Clinical Research Associate
Linda Tardif, RN – Clinical Research Associate
Paula Tiller, BN, RN – Clinical Research Associate

Clinical Trials and Registries

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 MACE (CV death, MI, or stroke) from the time of randomization through 90 days in subjects with ACS (diagnosed with STEMI or NSTEMI).
Trial Status:	Study start-up

Patient Enrollment Target (Canada/Global)
> 600/17,400

Patient Enrollment Achieved to Date (Canada/Global)
0/0

Number of Sites Participating (Canada/Global)
0/0

EXSCEL

Study Title:	**Ex**enatide **S**tudy of **C**ardiovascular **E**vent **L**owering Trial: A Trial To Evaluate Cardiovascular Outcomes After Treatment With Exenatide Once Weekly In Patients With Type 2 Diabetes Mellitus
Protocol #:	BCB109
Sponsor:	AstraZeneca, Amylin Pharmaceuticals, LLC
Drug:	Exenatide
Anticipated Timeline:	May 2009 - June 2017
Study Purpose:	This study will compare the impact of including exenatide once weekly in addition to usual care vs. usual care without exenatide on major cardiovascular outcomes as measured by the primary composite endpoint of cardiovascular-related death, nonfatal myocardial infarction (MI), or nonfatal stroke.
Trial Status:	Trial closed

Patient Enrollment Target (Canada/Global)
500/14,000

Patient Enrollment Achieved to Date (Canada/Global)
544/14,753

Number of Sites Participating (Canada/Global)
28/692

GALILEO

Study Title:	**G**lobal Study Comparing a riv**A**roxaban-based Antithrombotic Strategy to an antip**L**atelet-based Strategy After Transcatheter aort**I**c va**L**ve r**E**placement to **O**ptimize Clinical Outcomes
Protocol #:	17938
Sponsor:	Bayer
Drug:	Rivaroxaban, Acetylsalicylic acid, Clopidogrel
Anticipated Timeline:	September 2015 - August 2018
Study Purpose:	To assess whether a rivaroxaban-based anticoagulation strategy, following successful TAVR, compared to an antiplatelet-based strategy, is superior in reducing death or first thromboembolic events (DTE). To assess the primary bleeding events (PBE) of the rivaroxaban-based strategy compared to an antiplateletbased strategy, following TAVR.
Trial Status:	Target enrollment reached, now in patient retention stage

Patient Enrollment Target (Canada/Global)
90/1,520

Patient Enrollment Achieved to Date (Canada/Global)
61/1,522

Number of Sites Participating (Canada/Global)
10/140

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 (IV) ferric carboxymaltose (FCM), relative to placebo, in the treatment of participants in heart failure with iron deficiency and with a reduced ejection fraction.
Trial Status:	Actively enrolling

Patient Enrollment Target (Canada/Global)
300/3,014

Patient Enrollment Achieved to Date (Canada/Global)
5/164

Number of Sites Participating (Canada/Global)
8/113

HiLo-HF Pilot

Study Title:	**Hi**gh versus **Lo**w SpO2 oxygen therapy in patients with acute **H**eart **F**ailure - 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 (ED) with symptoms suggestive of Acute Heart Failure (AHF), 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:	Actively enrolling

Patient Enrollment Target (Canada)
50

Patient Enrollment Achieved to Date (Canada)
39

Number of Sites Participating (Canada)
1

HiLo-HF Registry

Study Title:	**Hi**gh versus **Lo**w SpO2 oxygen therapy in patients with acute **H**eart **F**ailure - 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 ED with symptoms suggestive of AHF, 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:	Actively enrolling

Patient Enrollment Target (Canada)
200

Patient Enrollment Achieved to Date (Canada)
55

Number of Sites Participating (Canada)
1

LEVO-CTS

Study Title:	A Double-Blind, Randomized, Placebo-Controlled Study of Levosimendan in Patients With Left Ventricular Systolic Dysfunction Undergoing Cardiac Surgery On Cardiopulmonary Bypass
Protocol #:	TNX-LVO-01
Sponsor:	Tenax Therapeutics Inc.
Drug:	Levosimendan
Anticipated Timeline:	March 2015 - April 2017
Study Purpose:	To evaluate the efficacy of levosimendan compared with placebo in reducing the co-primary endpoints of composite of all-cause death (Day 30) or use of mechanical assist (IABP, LVAD, or ECMO((Day 5), or the composite endpoint of all-cause death (Day 30), perioperative MI (Day 5), need for dialysis (Day 30), or use of mechanical assist (IABP, LVAD, or ECMO)(Day 5) in subjects with reduced LVEF undergoing cardiac surgery on CPB.
Trial Status:	Trial closed and presented

Patient Enrollment Target (Canada/Global)
144/760

Patient Enrollment Achieved to Date (Canada/Global)
165/884

Number of Sites Participating (Canada/Global)
10/62

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 (CHD) death, non-fatal myocardial infarction (MI), fatal and non-fatal ischemic stroke, unstable angina requiring hospitalization) in patients who have experienced an acute coronary syndrome (ACS) event 4 to 52 weeks prior to randomization and are treated with evidence-based medical and dietary management of dyslipidemia.
Trial Status:	Target enrollment reached now in patient retention stage

Patient Enrollment Target (Canada/Global)
340/18,000

Patient Enrollment Achieved to Date (Canada/Global)
361/18,927

Number of Sites Participating (Canada/Global)
38/1,263

SODIUM-HF

Study Title:	**S**tudy **O**f **D**ietary **I**ntervention **U**nder 100 **M**MOL in **H**eart **F**ailure
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 clincial outcome composed of all-cause mortality, cardiovascular hospitalizations or cardiovascular emergency departmetn visits in patients with heart failure.
Trial Status:	Actively enrolling

Patient Enrollment Target (Canada/Global)
1,000

Patient Enrollment Achieved to Date (Canada/Global)
357/478

Number of Sites Participating (Canada/Global)
16/23

STREAM-II

Study Title:	**ST**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 ≥ 70yrs with acute ST-elevation myocardial infarction randomised within 3 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 PCI with a P2Y12 antagonist and antithrombin treatment according to local standards.
Trial Status:	Actively recruiting in other countries; Not yet recruiting in Canada

Patient Enrollment Target (Canada/Global)
30/600

Patient Enrollment Achieved to Date (Canada/Global)
0/4

Number of Sites Participating (Canada/Global)
1/65

VICTORIA

Study Title:	**V**er**IC**igua**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 (HFrEF).
CVC Role:	Executive/Steering Committee, Thought leadership and Senior Project Management only

VICTORIA-HF Registry

Study Title:	Vericiguat in Participants With Heart Failure With Reduced Ejection Fraction (HFrEF)
Protocol #:	N/A
Sponsor:	Merck, Bayer
Drug:	N/A
Anticipated Timeline:	March 2017 - January 2021
Study Purpose:	The main objective of the study is to describe the baseline characteristics, practice patterns and in-hospital clinical outcomes of patients hospitalised for chronic HFrEF at select North American sites.
Trial Status:	Start-up

Patient Enrollment Target (Canada/Global)
750/2,000

Patient Enrollment Achieved to Date (Canada/Global)
0/0

Number of Sites Participating (Canada/Global)
0/0

ECG Core Laboratory

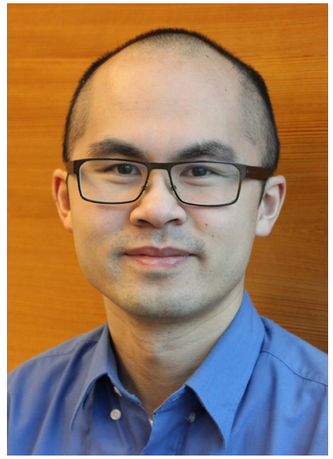
The aim of our ECG Core Laboratory is to translate research results into clinically relevant applications. Using the ECG – a venerable but powerful biomarker – we can generate an improved understanding of the pathophysiologic processes involved in acute coronary syndromes (ACS), thereby enabling not 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 2017 was the Vital Heart Response (VHR) study. The VHR-1 and VHR-2 project, led by Dr. Robert Welsh, is a regional initiative that aims to implement timely evidence-based reperfusion strategies to maximize the outcome of patients with ST-segment elevation myocardial infarction (STEMI) utilizing a pre-hospital approach. VHR has enrolled over 3,000 patients and the Core Laboratory has completed analysis of over 4,000 ECGs by our ECG reader Eric Ly. The use of VHR registry-acquired ECGs and the biostatical 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.

Preparations began in 2017 for the STREAM-2 (**ST**rategic **R**eperfusion in Elderly Patients **E**arly **A**fter **M**yocardial Infarction) study. 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 (AMI). The Core Laboratory will also provide 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 will be to compare the efficacy and safety of a pharmaco-invasive reperfusion strategy with primary PCI in elderly STEMI patients, and also to compare the incidence of intracranial and non-ICH major systemic bleeding in these elderly STEMI patients who receive pre-hospital clopidogrel as an adjunct to half-dose TNK. The study is currently underway.

The ECG Core Laboratory also continued 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.

Kevin Bainey, MD
- Director, ECG Core Lab



Eric Ly, BHK
- ECG Reader

Biostatistics & Research Administration

"The goal is to turn data into information, and information into insight."
—Carla Fiorina

CVC Biostatistics contributed significantly to the CVC's research activities in 2017, ranging from supporting students, developing investigators and CVC Faculty, to advancing novel statistical approaches in the construction and analysis of clinical endpoints. Services provided by CVC Biostatistics include study design, data management, development of statistical analysis plans and database specifications, programming expertise in SAS and R, generation of statistical tables, figures and listings and interpretation of findings, and consultation and execution of advanced statistical methods. CVC Biostatistics has extensive experience in working with both population-based data and those from randomized clinical trials, and data generated at all levels: locally, nationally, and internationally.

The provincial and national linked administrative databases served as the sources for several important papers published in 2017. Dr. Anamaria Savu and colleagues interrogated the Alberta data when examining the association of age with mortality among more than 34,000 heart failure (HF) patients hospitalized between 2002 and 2014. This analysis provided contemporary evidence in an understudied cohort, the young (<45 years old) HF patient, revealing that adverse events were frequent, and more than 10% died within one year.[1]

As part of his doctoral studies, Dr. Dat Tran and colleagues reported a 10-year review on the quality of care for acute myocardial infarction (AMI) in Canada.[2] Using data from the Canadian Institute of Health Information, patients hospitalized for AMI between 2004 and 2013 were followed for mortality and readmission within 30 days. There were few changes in these quality metrics after percutaneous coronary intervention (PCI), and modest improvements made in those undergoing coronary artery bypass grafting (CABG). Interprovincial differences were apparent, signalling the opportunity for improved pan-Canadian coordination of AMI care and the need to set benchmarks for AMI-specific PCI- and CABG-related quality metrics.

The Alberta Heart Failure Etiology and Analysis Research Team (HEART) program provided the bases to prospectively evaluate established criteria for HF with preserved ejection fraction.[3] Dr. Wendimagegn Ghidey Alemayehu and colleagues applied an established criteria to identify said patients in this uniquely data-rich cohort. The likelihood ratios for these criteria were deemed to be below the standards necessary for definitive diagnosis, signalling the need for better criteria.

A validation of the value of the Q-wave on the electrocardiogram, a biomarker of the evolving state of AMI, was published by Yinggan (Gray) Zheng and colleagues.[4] This important work validated this concept tested earlier by these authors in several clinical trial cohorts in the 'real world setting' of an AMI registry. They observed that the presence of the Q-wave provided more insight than the conventional metric of time to treatment in the association with adverse in-hospital events.

Novel Approaches to Clinical Endpoints

The CVC authored several papers in 2017 acknowledging a growing discomfort in the use of composite endpoints in the evaluation of cardiovascular therapies. Dr. Cynthia Westerhout and Dr. Paul Armstrong outlined in detail the challenges, but yet, increasing use, of composite endpoints in cardiovascular research.[5] A potential way forward will be to engage multiple stakeholders, including patients, clinicians, healthcare providers and pharmaceutical regulators, in the valuation of event types within a composite endpoint and incorporating these as weights into the analysis of new therapeutic agents or strategies. Similarly, doctoral student, Dr. Paul Brown published two important papers with Dr. Justin Ezekowitz in the pursuit to better characterize clinical endpoints in HF. One reviewed the existing approaches and proposed a new metric, the probability index, billed as intuitive, easy-to-calculate, and applicable across various composites.[6] The second paper demonstrated the value of simultaneous modelling of multiple event types (i.e., multi-type events models versus a standard composite endpoint alone) in the analysis of HF readmissions.[7]

[1] Wong CM, Hawkins NM, Ezekowitz JA, Jhund PS, Savu A, MacDonald MR, Kristensen SL, Petrie MC, McMurray JJV, McAlister FA, Kaul P. Heart Failure in Young Adults Is Associated With High Mortality: A Contemporary Population-Level Analysis. *Can J Cardiol.* 2017;33:1472-1477.

[2] Tran DT, Welsh RC, Ohinmaa A, Thanh NX, Bagai A, Kaul P. Quality of Acute Myocardial Infarction Care in Canada: A 10-Year Review of 30-Day In-Hospital Mortality and 30-Day Hospital Readmission. *Can J Cardiol.* 2017;33:1319-1326.

[3] Ezekowitz JA, McAlister FA, Howlett J, Alemayehu W, Paterson I, Belenkie I, Oudit GY, Kaul P, Dyck JR, Anderson T; Alberta HEART Investigators. A prospective evaluation of the established criteria for heart failure with preserved ejection fraction using the Alberta HEART cohort. *ESC Heart Fail.* 2017 doi:10.1002/ehf2.12200.

[4] Zheng Y, Bainey KR, Tyrrell BD, Brass N, Armstrong PW, Welsh RC. Relationships Between Baseline Q Waves, Time From Symptom Onset, and Clinical Outcomes in ST-Segment-Elevation Myocardial Infarction Patients: Insights From the Vital Heart Response Registry. *Circ Cardiovasc Interv.* 2017 Nov;10(11). pii: e005399. doi: 10.1161/CIRCINTERVENTIONS.117.005399.

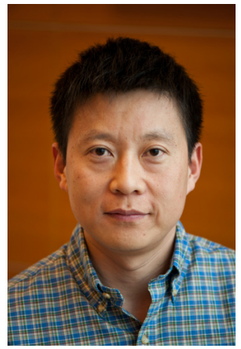
[5] Armstrong PW, Westerhout CM. Composite End Points in Clinical Research: A Time for Reappraisal. *Circulation.* 2017;135:2299-2307.

[6] Brown PM, Ezekowitz JA. Composite End Points in Clinical Trials of Heart Failure Therapy: How Do We Measure the Effect Size? *Circ Heart Fail.* 2017;10. pii:e003222.

[7] Brown PM, Ezekowitz JA. Multitype Events and the Analysis of Heart Failure Readmissions: Illustration of a New Modeling Approach and Comparison With Familiar Composite End Points. *Circ Cardiovasc Qual Outcomes.* 2017; pii: e003382.

Biostatistics Team

Cynthia Westerhout, PhD
- Associate Director, Research & Strategic Planning



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

Wendimagegn Alemayehu, PhD
- Biostatistician

Research Administration Team

Richard Rothery, PhD
- Academic Research Administrator

Lisa Soulard
- Executive Assistant to Dr. Paul Armstrong

Population Health & 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 ED), 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".

An example of how population health research is working towards accomplishing the CVC's goals of research training, international collaboration, and knowledge dissemination, is our work examining heart failure incidence in younger patients. Heart failure is traditionally considered a disease of the elderly; however, recent studies from Sweden and Denmark have shown a reduction in heart failure in the elderly, and an increase in its incidence in younger patients. Using population-health data, Dr. Chih Wong, a trainee from the University of Glasgow, several international colleagues, and Drs. Justin Ezekowitz, Finlay McAlister, and Padma Kaul from the CVC examined age-specific incidence and outcomes of heart failure in Alberta.[1] The study confirmed previous reports of declining incidence of heart failure in the elderly, but found that the increase in the disease in the young was restricted to men alone. In an accompanying editorial, Drs. Koon Teo and Hisham Dokainish suggested that these contrasting trends in older versus younger patients may be due to differences in the underlying causes of heart failure: more traditional risk factors such as hypertension, diabetes and coronary artery disease in the elderly and causes such as congenital heart disease and cardiomyopathy in younger patients.[2]

In the modern era of cost conscious medicine, clinical management decisions must account for risks and benefits of new therapies and consider them in the context of short and long-term resource consumption. The CVC therefore uses empirical data from the population-health data repository to develop prediction models to estimate the current and future economic burden of cardiovascular disease on the Alberta and Canadian health care systems. In addition to the impact of interventions on mortality and morbidity, there is increasing interest in assessing their impact on patient reported outcomes such as health-related quality of life (HRQoL).

In 2017, the CVC's contribution to the field of health economics are exemplified by the following two publications. In the first study, Dr. Sean van Diepen and colleagues examined interprovincial differences in critical care unit (CCU) admission rates for patients hospitalized for acute coronary syndromes (ACS) or heart failure (HF) in Canada.[3] Historically, CCUs were implemented as monitoring units for patients at high arrhythmogenic risk. However, many cardiology ward beds are now equipped with telemetry capabilities, obviating the need for CCU stays. Using Canadian Institutes of Health Information (CIHI) data, the study examined CCU admission rate among 220,759 patients hospitalized for ACS or HF between April 1, 2007 and March 31, 2013. The overall CCU admission rate was 33% and varied significantly across provinces. A majority (59%) of patients admitted to the CCU did not receive any critical care therapies within 2 days. The correlation between CCU admission rates and risk-adjusted mortality, at the province level, was low. These findings highlight the need for national CCU admission criteria designed to reduce variability and improve health care resource use and outcomes.

In the second study, Dr. Andrew Mackie, a pediatric cardiologist at the University of Alberta, worked with the CVC to examine the cost of hospitalizations for congenital heart disease (CHD) in Canada.[4] The prevalence of CHD is rising, particularly among adults with complex lesions. Both cardiac and non-cardiac complications are common in this high-risk population. The impact of these factors on hospitalization costs are not well described. Using CIHI data from April 1, 2004 and March 31, 2014, we found that CHD costs increased from $99.7 million in 2004 to $121.2 million in 2014, a 21.6% increase. Total costs were higher for children compared with adults, however, the cost increase was greater in adults than in children, with adults accounting for 38.2% of costs in 2004 vs 45.8% in 2013. Costs increased most among adults with complex CHD.

[1]Wong CM, Hawkins NM, Ezekowitz JA, Jhund PS, Savu A, MacDonald MR, Kristensen SL, Petrie MC, McMurray JJV, McAlister FA, Kaul P. Heart Failure in Young Adults Is Associated With High Mortality: A Contemporary Population-Level Analysis. *Can J Cardiol.* 2017;33:1472-1477.

[2]Teo KK, Dokainish H. Heart Failure in Transition: Is It Really Better to Be Younger? *Can J Cardiol.* 2017 Nov;33:1455-1456.

[3]van Diepen S, Lin M, Ezekowitz JA, McAlister FA, Lee DS, Goodman SG, Armstrong PW, Kaul P. Interprovincial Differences in Canadian Coronary Care Unit Resource Use and Outcomes. *Can J Cardiol.* 2017;33:166-169.

[4]Mackie A, Tran DT, Marelli A, Kaul P. Cost of Congenital Heart Disease Hospitalizations in Canada: A Population-Based Study. *Can. J. Cardiol.* 2017;33:792-798.

"Today there is close to 2 terabytes of heath data available on the CVC servers. These vast and rich datasets have posed many computational challenges, however, wrestling these big data has shown and will reveal many interesting patterns and associations important for the advancement of health research."

- Anamaria Savu, Biostatistician

Padma Kaul, PhD
- Director, Outcomes Research

Anamaria Savu, PhD
- Biostatistician

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, alongside providing expert service in the areas of managing agreements, developing and tracking metrics, and executing invoices and site payments. Dedicated to financial stewardship, the business office prudently manages revenue and expense administration. It is also committed to the progress of information systems management, strategic planning, process improvement, and the promotion of learning and development initiatives.

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

Karen Mellor, CPA CMA CNE CISA CISSP CISM CGEIT
- Associate Director, Operations

Oksana Grant, PCP
- Finance and Operations Assistant

Ellen Pyear, MA
- Business and Communications Coordinator

"When I reflect on the experience I've had working for the CVC, I think about how supportive and genuine everybody is. The people who work for the CVC are what makes this organization stand out. You immediately get the sense that the team, no matter what level they are working on, are passionate and dedicated. I have learned so much from so many and feel fortunate to have been able to work with such talented, intelligent and grounded individuals."

- Devon Blanchette, Former Regulatory Specialist

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

- Distinguished University Professor, Division of Cardiology, University of Alberta
- Formerly Chair of the Department of Medicine, University of Alberta
- Founding Director, Canadian VIGOUR Centre
- Founding Director of TORCH (Tomorrow's Research Cardiovascular Health Professionals), a Strategic Training Program Initiative
- Founding President of the Canadian Academy of Health Sciences
- 2014 Recipient of the University 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
- Appointed Officer of the Order of Canada in 2017, in recognition 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
- Director, Heart Function Clinic, Mazankowski Alberta Heart Institute
- 2017 appointed member, Royal Society of Canada College of New Scholars, Artists and Scientists

Dr. Ezekowitz' research interests include:

- Testing the impact of drugs and processes of care for patients with acute heart failure
- Novel interventions for patients with chronic heart failure
- The impact of comorbidities such as atrial fibrillation, anemia and hip fractures in patients with heart failure
- Non-pharmacologic interventions such as diet and existing tools such as biomarkers or oxygen
- Population health outcomes and interventions
- Clinical trial design and endpoints

Shaun Goodman, MD, MSc

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

Dr. Goodman's research interests include:

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

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

Kevin Bainey, MD

- Interventional Cardiologist, Mazankowski Alberta Heart Institute
- Assistant Professor, Division of Cardiology, University of Alberta
- Director, ECG Core Lab, Canadian VIGOUR Centre
- Director, Interventional Cardiology Fellowship Program, Mazankowski Alberta Heart Institute, University of Alberta
- Director, Chest Pain Program, Mazankowski Alberta Heart Institute
- 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
- Cardiogenic shock
- Cardiac arrest care

Padma Kaul, PhD

- Professor, Division of Cardiology, University of Alberta
- Director, Outcomes Research, Canadian VIGOUR Centre
- 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
- Capital Health Chair in Cardiovascular Health Outcomes
- Senior Health Scholar, Alberta Innovates -Health Solutions (2010 - 2017)
- 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 a the bedside
- Methodology of trials and systematic reviews

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

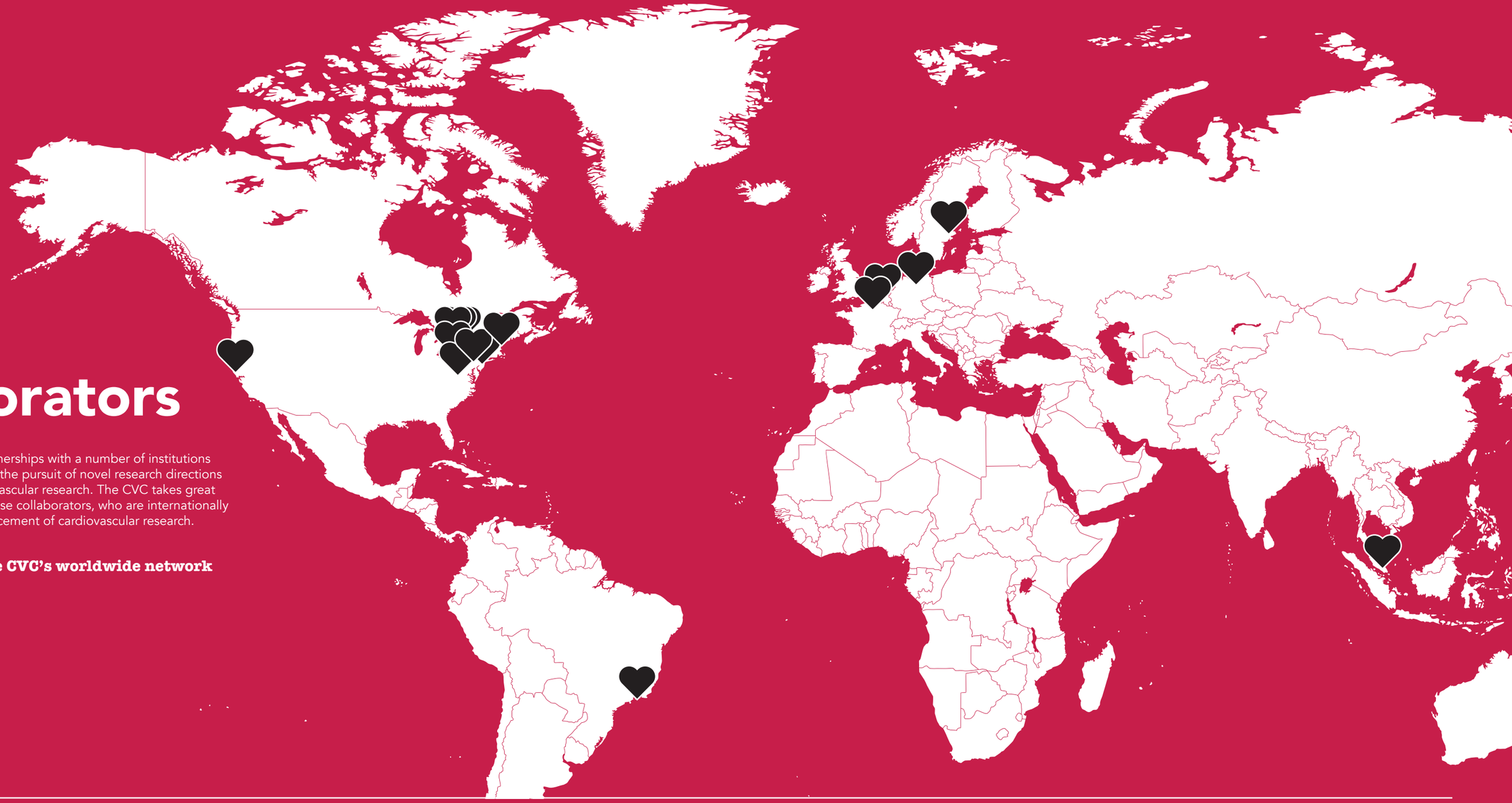
"Dr. Paul Armstrong has been a quintessential clinical and research-related mentor to me for more than 20 years. I had the good fortune to continue to collaborate with him on a number of research projects since he moved from my university-affiliated hospital in Toronto to Edmonton and the University of Alberta and established the CVC. He has served as a role model and he made it clear to me when I was a first year cardiology trainee under his guidance that he intended to invest his time and expertise in me—the "next generation"–and that I, in turn, had an obligation to learn and work hard to provide the best care possible to my patients. I worked extremely hard that year, but everywhere I turned, I saw Dr. Armstrong working even harder (and longer hours) than me–leading by example! I also started one of my first research projects with him that year and now, 28 years later, I know I wouldn't be doing what I am today without having observed and experienced his exemplary "fire in the belly" interest and commitment in both the clinical and research arenas."

- Shaun Goodman, Co-Director

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 relationship with these collaborators, who are internationally recognized leaders in the advancement of cardiovascular research.

This map illustrates the CVC's worldwide network of collaborators.



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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

ICAHN SCHOOL OF MEDICINE, MOUNT SINAI
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Leuven, Belgium

NATIONAL UNIVERSITY HEART CENTRE, NATIONAL UNIVERSITY OF SINGAPORE
Singapore

PERFUSE STUDY GROUP, HARVARD MEDICAL SCHOOL
Boston, USA

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Toronto, Canada

UPPSALA CLINICAL RESEARCH CENTRE, UPSALA UNIVERSITY
Uppsala, Sweden

Acknowledgements

The 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 that 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 Ellen Pyear, Lisa Soulard, Oksana Grant, and Karen Mellor for their time and the dedication required to produce this report;**
- **AM/FM for the concept and design;**
- **Photographer Mathew Martin for many of the images enclosed in this report.**

Canadian **VIGOUR** Centre

Bridging Hearts and Minds

2017 ANNUAL REPORT

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