

The Canadian Cardiac Chronicle

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“It’s essential to keep moving, learning, and evolving for as long as you’re here and this world keeps spinning.”

– Rasheed Ogunlaru

The end of summer and beginning of autumn marks a return to school for many of us, as students, teachers, or both. At the Canadian VIGOUR Centre (CVC), we’ve been “back to school” planning our next Colloquium Series and anticipating learning from our site coordinators, investigators, and patients how to do the best job possible in carrying out clinical research.

Our two-decade-plus track-record of excellence in clinical trial participation is in large part due to the coast-to-coast, high-performing site network (all of you!) across Canada. However, even prior to the pandemic, it has become increasingly challenging to maintain robust site engagement given the time, complexity, and costs associated with performing clinical research. For the last 8 years, the CVC has undertaken a Clinical Trials Colloquium — an opportunity to meet with our sites, patient representatives, collaborators, and sponsors, to connect, collaborate and find solutions to key issues affecting clinical research in Canada. The Colloquium meeting was first established in 2014, annually bringing together 10-15 Canadian investigative site principal investigators and study coordinators, aiming to: (1) identify major impediments to timely and efficient participation in clinical trials; (2) understand how best to add value to the clinical trial experience; and (3) establish a network of high performing sites across the country. While the pandemic prevented us from meeting in-person for the 8th Annual Colloquium in 2021, we pivoted and created a new opportunity to reach out more broadly, through a virtual platform, and extend the invitation to our entire network.

The virtual Colloquium Series has been planned and led by the CVC (spearheaded by our Associate Director of Clinical Trials Tracy Temple, RN) together with the CVC Site Engagement Working Group (established in 2020), including the Co-Chairs Drs. Shelley Zieroth (U. of Manitoba) and Warren Cantor (U. of Toronto).

The 1st virtual CVC Colloquium in 2021 included 64 Canadian investigators and study coordinators. The keynote speaker was Dr. Adrian Hernandez (Executive Director, DCRI, Duke Univ-

ersity, Durham, North Carolina, USA), who presented “Clinical Trials During a Pandemic: What we’ve learned and where we are headed”. Following a Q&A session, we undertook a provincial/regional breakout session related to clinical trial research during a pandemic, focusing on challenges from an institutional perspective; screening, recruitment, and follow-up of patients; and approaches to monitoring visits. The 3 regional groups shared their experiences and pragmatic approaches, including discussions regarding remote/electronic consent, drug dispensing, and contract/budget negotiations/execution.

The 2nd virtual Colloquium included 79 Canadian investigators, study coordinators, and sponsor representatives. The keynote speaker was Dr. Roxana Mehran (Professor in CV Clinical Research and Outcomes, and Director of Interventional CV Research and Clinical Trials, Icahn School of Medicine, Mount Sinai Hospital, New York, USA, and Founding Director & Board Member of Women as One), and she presented on “Diversity & Mentoring in Clinical Research”. Following a Q&A session, we undertook 3 provincial breakout sessions related to how we can collectively identify/encourage/ train new researchers/coordinators (including women and under-represented individuals), and mentor/support those without a research infrastructure to become involved in clinical research.

Our 3rd virtual Colloquium included 87 participants, focused on “Operationalizing Clinical Research”, and provided pragmatic approaches from experts from across the country, including Noreen Lounsbury, RN, BN (Victoria Heart Institute Foundation) and Kim Robbins, RN (York PCI Research) on “Tips to Becoming a Successful Recruiter and Top Performing Site”, Michael Heffernan, MD, PhD (Oakville Trafalgar Memorial Hospital) on “An Investigator/Site Perspective on Surviving a Regulatory Inspection”, and Jodi Parotta, MA, Courtney Gubbels, BA, Lyndsey Garritty, BA, and Karin Kushniruk, RN, PhD (CVC) on “Key Tips you Should Know When Negotiating Your Study Budgets”.

The feedback from prior Colloquiums has been very positive with many identifying this is a unique opportunity to share best strategies for enhancing clinical research locally and across the country. Building on the success of the 2021 virtual

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series, this fall we have organized two webinars (October 4: “Regulatory Inspections and Audits” and November 23: “Research ‘Potpourri’”) with investigative sites, sponsors, operational experts and invited speakers with a third webinar (“Research Budgeting, Costs, Legal/Contracts, and Efficient Start-Up”) planned for the first quarter of 2023. The virtual platform will again allow us the opportunity to broadly extend the invitation to the entire CVC network and we encourage you to [register](#) and join us for this chance to exchange

experiences and practical solutions to the challenges we all face in doing clinical research.



Dr. Shaun Goodman
CVC Co-Director

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CLINICAL TRIALS

HEART-FID

Our trial investigating the efficacy and safety of Injectafer® as treatment for heart failure with iron deficiency is nearing conclusion. In just a few short months, our last visits with participants will be completed. As we approach this final milestone, we want to take a minute to thank all of you who have worked tirelessly on this trial and continue to do so. Without people like you, a large trial spanning many years would not be possible. Thank you!

Final Visit Tips

- Start planning today! Call your participants and schedule a date and time to complete the final visit.

- All final visits are expected to be completed in person as per the protocol.
- Keep participants on study drug! We are so close to the end. Those participants that temporarily discontinued study drug can be brought back on study drug if the participant is willing and if it is safe to do so.
- Remember to complete all protocol specified 6MWTs.
- Reminder to re-consent all participants that are on study drug with the 2022 ICF Addendum if not already completed. Note: the 2022 ICF Addendum does not need to be entered into the eCRF as it was not released with a protocol amendment.
- Ensure the PI has access to the eCRF and has completed

the required training so eCRF pages can be reviewed and signed off in a timely manner.

- Once a participant has completed their final visit, no additional data will be collected for events that occur after that visit.

Data Cleaning

We are currently in our 15/15/15 data campaign. Our focus is no open queries greater than 15 days, no overdue visits greater than 15 days, and no missing forms greater than 15 days. As we near the end of the trial, it becomes even more important to keep your data as clean as possible. Please ensure you are spending time every day to check for queries. Please enter your data as soon as possible after a visit has been conducted. The cleaner the data is now, the easier it will be at the end of the study to lock the database.

SONOSTEMI-LYSIS

The **SONO**thrombolysis in patients with an **ST**-segment **E**levation **M**yocardial **I**nfarction with fibrino**L**ysis (SONOSTEMI-LYSIS) trial is a single-centre project taking place at the University of Alberta Hospital/Mazankowski Alberta Heart Institute.

While prompt reperfusion therapy has been shown to reduce mortality, infarct size and improve left ventricular function in patients with STEMI, reperfusion itself may result in adverse events such as reperfusion injury. In patients with STEMI receiving fibrinolysis therapy, this study will explore whether the addition of sonothrombolysis (i.e., high mechanical index

Data Tip: PIs should review each hospitalization for potential SAEs and endpoints.

Invoices

As we approach the end of study, it is a good time to review your site's budget and ensure all invoices have been sent to CVC for review. Don't delay!

If you are interested in further information regarding this trial, please contact Clinical Trials Project Lead, Courtney Gubbels at 1-800-707-9098 (ext. 2) or courtney.gubbels@ualberta.ca.



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impulses during diagnostic ultrasound) to standard care results in enhanced myocardial perfusion, improved left ventricular function, and better clinical outcomes.

If you are interested in further information about the SONOSTEMI-LYSIS study, please contact Clinical Trials Project Lead, Karin Kushniruk at 1-800-707- 9098 (ext. 7) or karin.kushniruk@ualberta.ca.

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EMPACT-MI

Happy autumn everyone! I hope everyone had a relaxing summer break. We are down to the final season before the enrollment target of 6,500 patients is expected to be met at the end of 2022. Canadian sites have randomized over 280 participants into the trial thus far! However, there has been a noticeable decline in enrollment over the summer globally, as well as in Canada. We are hoping to see Canada finish off enrollment on a high note and look forward to sites enrolling robustly in these final few months!

Congratulations to **Dr. Cantor and Kim Robbins, Dr. Ball and Jeff Dunlop, Dr. Gosselin and Valerie Dargis, Dr. Daneault and Julie Caron, Dr. Burstein and Areti Apatsidou, and Dr. Fordyce, Syndey Thorsteinsson and Naomi Uchida**, who each enrolled a patient in September!

Protocol Version 2 was sent to sites this summer. We have only a handful of sites left to activate under the amendment. The CVC will give your site the green light to implement the amendment once all requirements are met.

Though enrollment is expected to close in December, the study will continue until the required number of endpoints are

collected. Sites are reminded to ask patients at each visit (phone; clinic) about any hospitalizations, and report the SAE in the database within 24 hours of knowledge. To this end, sites are encouraged to review the EMR for any hospitalizations or encounters ahead of patient visits, so that none are missed being reported by the patient.

Thanks to all the study coordinators for keeping their data as current and clean as possible by entering data within 2 business days after a visit has occurred, and answering queries within 5 business days. Keep up the great work!

For questions about EMPACT-MI, please contact Jodi Parrotta, Clinical Trials Project Lead/QA-Regulatory Compliance Lead at 1-800-707-9098 (ext. 3) or Jodi.Parrotta@ualberta.ca.



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AEGIS-II is a large, international, multicentre Phase 3 trial of infusing an intravenous formulation of apolipoprotein A-I (CSL112) to reduce cardiovascular events in acute coronary syndrome patients. CSL112, an intravenous formulation of apoA-I, enhances cholesterol efflux capacity, and therefore has the potential to reduce plaque burden, stabilize plaque lesions at risk of rupture and decrease the high rate of early recurrent events.

The countdown is on! The enrollment phase of AEGIS-II will soon be coming to a close, and with that we want to encourage all of our sites to make AEGIS-II a priority for the remainder of 2022. We need your help to secure a strong finish in Canada, and we want every site to embrace the opportunity to contribute as meaningfully as possible to this important study.

Recruitment of the right patients is the main focus at this time, and with that in mind, the CVC would like to share a few helpful tips as you screen and approach potential patients:

- Golden Rule: Respect!
- Listen and be engaged with the patient

- Utilize the study materials (participant brochure, visual aid, and factsheet) to help the patient understand the history, purpose, and safety background of the investigational product
- Ensure the patient and their support system are fully aware of the commitment involved with participating
- Continuity of care and ongoing communication: keep patients informed of new trial information or disease education
- Provide options for flexible visit times and conduct the visits efficiently to ensure the patient's time is valued
- **Always remember to thank the patient for what they are doing - without them we would not have a trial!**

If you are interested in further information regarding this trial, please contact Clinical Trials Project Lead, Lyndsey Garritty at 1-800-707-9098 (ext. 4) or lyndsey.garritty@ualberta.ca.



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Our trial designed to determine efficacy and safety of early fibrinolytic treatment, with half-dose tenecteplase and additional antiplatelet and antithrombin therapy, in subjects with acute ST-elevation myocardial infarction, completed enrollment this September! We want to thank our amazing Canadian team for their dedication to this trial. Also, a big congratulations to them on their amazing recruitment rate—they are the top enrolling site for the study! A remarkable achievement.

Now that enrollment has been reached, we turn our focus to wrapping things up. Please continue to complete all follow-up visits and enter your data as quickly as possible. Please continue to ensure that you send in all ECGs to the CVC ECG Core Lab.

Make sure to review your study files to confirm they are current and complete, as study files will be reviewed at your close-out visit. We look forward to sharing the results of the trial in the coming months!

If you are interested in further information regarding this trial, please contact Clinical Trials Project Lead Courtney Gubbels at 1-800-707-9098 (ext. 2) or courtney.gubbels@ualberta.ca.



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SODIUM-HF is a multicenter, randomized, open-label Study of Dietary Intervention Under 100 MMOL in Heart Failure.

We are in the home stretch! Just a handful of visits to go before all patients reach their 24-month milestone. As we complete these final visits, please make every effort to keep searching for any LTFU patients – every patient counts.

Keep up the excellent work and let's finish strong!

For general study updates and news, visit sodiumhftrial.com or follow us on Twitter [@sodiumhf](https://twitter.com/sodiumhf).

If you have questions about the SODIUM-HF trial, please contact Clinical Trials Project Lead, Karin Kushniruk at 1-800-707- 9098 (ext. 7) or karin.kushniruk@ualberta.ca.



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The CVC is pleased to announce a collaborative partnership with the Duke Clinical Research Institute and Bayer on the upcoming Phase 3 OCEANIC-AF trial, which will enroll patients with Atrial Fibrillation (AF).

This trial will investigate the safety and efficacy of asundexian, an investigational oral Factor XIa (FXIa) inhibitor. The CVC will provide strategic leadership for the OCEANIC-AF trial, with faculty member **Dr. Roopinder Sandhu** serving as Canada's National Lead, and co-director **Dr. Shaun Goodman** as a member of the Executive Committee. Our clinical operations team will also play an important role in supporting

site engagement efforts across Canada along with the Bayer Canada team.

We look forward to sharing additional details over the coming months. For questions, please contact CVC Clinical Trials Project Lead, Melisa Spaling at 780-492-4011 (ext. 6) or mspaling@ualberta.ca.



NEWS & UPDATES

CVC Staff Updates



Audrey Kyle recently joined the CVC as an Administrative Coordinator. She completed a Bachelor of Business Administration in 2008. Prior to her current role at the CVC, Audrey worked in a variety of industries, including health care, real estate, and construction. She will be working closely with the business operations team on HR, IT, and other business-related issues. Audrey loves to organize and create new processes, and will bring a different perspective and a positive energy to the team. In her free time, Audrey enjoys creating arts and crafts with her two young daughters as well as spending time with friends and family. Audrey can be reached at akyle2@ualberta.ca.



Kalli Renner has recently returned from maternity leave. She has resumed her position as Senior Regulatory Specialist at the CVC and is working on the AEGIS-II and EMPACT-MI trials. Kalli has been with the CVC since 2013 and we are happy to have her return to the team! Kalli can be reached at kalli@ualberta.ca.



CVC 2022 VIRTUAL COLLOQUIUM SERIES

Regulatory Inspections and Audits: Best Practices and Lessons Learned | **Tuesday October 4, 2022**
9am PT / 10am MT / 11am CT / 12pm ET / 1pm AT

Session Presenters

- Dr. Shy Amlani, Rosa Marticorena and Galo Ginocchio**
Brampton Civic Hospital
- Kim Robbins**
York PCI Group, Inc.
- Dr. Michael Heffernan**
Oakville Cardiovascular Research

We are looking forward to the upcoming virtual colloquium session on **Tuesday October 4, 2022 (9am PT/10am MT/11am CT/12pm AT)**. The topic for this one hour session is **Regulatory Inspections and Audits: Best Practices and Lessons Learned**. If you are interested in attending, and have not yet registered, you can do so at the [link provided](#). We look forward to having you join us for this session and encourage you to share this invitation with other colleagues and those interested in getting more involved in clinical research.

We would also like to remind everyone to save the date for our next session on **November 23, 2022**. Stay tuned for details on the topic and session presenters!

If you have any questions regarding the CVC Clinical Trials Colloquium, please do not hesitate to reach out to Tracy Temple at tracy.temple@ualberta.ca.

Peripheral Artery Disease: Q&A with Dr. Sean McMurtry



September was Peripheral Artery Disease (PAD) Awareness Month. We spoke with CVC Associate Faculty Member **Dr. Sean McMurtry** to learn more about the risk factors, symptoms, treatment, and public health impact of PAD.

Compared with other cardiovascular diseases there is generally less public awareness of PAD. Can you briefly describe what PAD is?

While the term peripheral artery disease (PAD) sometimes is used in a general way to denote the set of artery diseases that affect arteries other than the coronary artery tree, most people use the term to mean atherosclerotic lower extremity PAD. Atherosclerotic lower extremity PAD is atherosclerotic plaques

that occur in the leg arteries, and are similar to those that cause coronary artery disease. These plaques are caused by the same risk factors, including smoking, high cholesterol, diabetes, and high blood pressure. While often the plaques do not block the arteries enough to cause symptoms, many people with PAD have claudication, or pain in the legs when they walk, pain at rest, or skin breakdown with ulcers or gangrene. In addition to having problems with leg pain or even leg wounds, people with PAD are at high risk for heart attacks and strokes since they usually have atherosclerotic plaques in other places, too.

What are the top 3 unmet needs for patients with PAD?

Recognition: Often people with PAD do not know they have it. They may have no symptoms yet, or they may have minor or unusual symptoms. This is important, since they may be at high risk for heart attacks or strokes without knowing it, or have elevated risk for developing leg wounds that can lead to amputation. PAD is diagnosed with a test called the ankle brachial index (ABI), and patients with leg pain with walking or leg wounds may need an ABI to know whether they have PAD or not.

Adequacy of medical treatment: Studies in Canada and elsewhere have consistently shown that the medical treatment of people with PAD has gaps, and people are living with preventable risk for worsening PAD as well as heart attacks and strokes. All caregivers that look after people with PAD should collaborate to improve medical treatment for these high risk people so they have longer and healthier lives.

Adoption of new treatments: While most caregivers know that people with PAD should quit smoking, and have their chole-

sterol, high blood pressure, or diabetes treated, and also know that people with symptomatic PAD should be on an aspirin, there are new treatments that can save lives and save limbs when added on to the other treatments. For example, people with PAD and diabetes do better when they also take an SGLT-2 inhibitor like empagliflozin or dapagliflozin. Similarly, most people with symptomatic PAD likely do better when they take a medication called rivaroxaban in addition to aspirin. Making sure that the best new treatments are used can help people with PAD have longer and healthier lives.

What is the current public health impact of PAD in Canada?

The incidence of PAD in Canada is approximately 200 per 100,000 for males and 170 per 100,000 for females. This translates into tens of thousands of new cases of PAD every year in Canada. These people are at relatively high risk for dying (4-5% per year) or having a major cardiovascular event (4-5% per year). This means there are thousands of Canadians who are hospitalized or die from PAD-associated problems each year.

You were a Primary Panel author for the [Canadian Cardiovascular Society's 2022 Guidelines for PAD](#). What are some of the key recommendations from this publication?

There are many important recommendations, but from my perspective the highlights include that:

1. We recommend using an ABI and/or a TBI study to confirm the diagnosis of PAD in patients with symptoms of PAD;
2. We recommend smoking cessation to prevent PAD, and to prevent major adverse cardiovascular events (MACE) and major adverse limb events (MALE) in patients with PAD;
3. We recommend that patients with PAD and type 2 diabetes should be offered a SGLT-2 inhibitor compared with usual diabetic control because of the reduction in MACE without any risk of increased amputation; and
4. We recommend treatment with rivaroxaban 2.5 mg twice daily in combination with aspirin (80-100 mg daily) for management of patients with symptomatic lower extremity PAD who are at high risk for ischemic events (high-risk comorbidities such as polyvascular disease, diabetes, history of heart failure, or renal insufficiency) and/or high-risk limb presentation post peripheral revascularization, limb amputation, rest pain, ischemic ulcers) and at low bleeding risk.

The first of these highlights the importance of recognition, and the second highlights the importance of smoking cessation as the cornerstone of management. The third and fourth are the recommendations that are about adding new medical therapies that are proven to save lives and limbs.



Epidemiology of WHF in a Population-Based Cohort from Alberta

Drs. Nariman Sepehrvand, Douglas Dover, Padma Kaul, Finlay McAlister, Paul W. Armstrong and Justin Ezekowitz, and Sunjita Islam recently published their manuscript [Epidemiology of Worsening Heart Failure in a Population-Based Cohort from Alberta, Canada: Evaluating Eligibility for Treatment with Vericiguat](#) in the *Journal of Cardiac Failure*.

Heart failure (HF) is a major public health concern with high health care burden and high rates of morbidity and mortality owing to frequent worsening HF (WHF) events despite current standard of care therapies.

The Vericiguat Global Study in Subjects with Heart Failure with Reduced Ejection (VICTORIA) trial showed the efficacy and safety of vericiguat, an oral soluble guanylate cyclase stimulator, in patients with chronic HF with reduced ejection fraction (HFrEF) and WHF.

The authors designed this study to examine a broader population-based sample of patients with HFrEF, representing both hospitalized patients and outpatients, to describe the epidemiology of WHF and, secondarily, to explore the proportion of patients potentially eligible for vericiguat.

This research concludes that a relatively large proportion of patients with HFrEF in this population-based cohort study experienced WHF and met trial eligibility criteria for vericiguat therapy. There was a gap in the use of guideline-directed medical therapy (GDMT) among patients both with and without a WHF event, and patients with WHF had generally worse outcomes compared with those without WHF. The authors believe that improving outcomes for this high-risk population of HFrEF patients and WHF requires alternate strategies to ameliorate the adoption of current and future GDMT in the care of these patients.



Dr. Roopinder Sandhu and coauthors (including **Drs. Douglas Dover, Finlay McAlister, Shaun Goodman, Justin Ezekowitz, and Padma Kaul** from the CVC) recently published their article, [Trends in Uptake and Adherence to Oral Anticoagulation for Patients with Incident Atrial Fibrillation at High Stroke Risk Across Health Care Settings](#), in the *Journal of the American Heart Association*. Dr. Sandhu shares some insights on this research below.

What are the key findings from this research?

We report the following key findings in the population-based study of incident nonvalvular atrial fibrillation (NVAF) at increased risk of stroke (i) oral anticoagulation (OAC) therapy

for stroke prevention has increased over time for all healthcare settings (emergency department (ED), hospital, outpatient) and is driven by higher use of direct oral anticoagulants (DOACs), (ii) among patients who are initiated on OAC therapy, three-quarters were found to have high adherence (defined as a proportion of days covered > 80%) and this has increased over time and across healthcare settings, (iii) compared to the hospital setting, patients with NVAF first diagnosed in the outpatient setting are more likely to have OAC uptake and have high adherence to DOACs, (iv) warfarin control was sub-optimal and declined in the ED, and (v) variable or persistently low adherence was associated with a poor prognosis, particularly for warfarin.

What are the real-world implications of these research findings?

In this study we found although OAC uptake increase over time, overall, a third of eligible patients are not being prescribed OAC therapy. As providers, particularly in the ED, we need to emphasize the importance of OAC adherence in addition to identifying where an opportunity may exist for DOAC over warfarin prescription.

What should be the focus of future research on this topic?

Future research should focus on strategies aimed at improving OAC uptake and adherence across all healthcare settings where AF diagnosis occurs.



Visit the [Publications Archive](#) for a comprehensive list of CVC publications.

About the Chronicle

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