The Canadian Cardiac
Chronicle

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"**It is not the strongest of the species that survives, nor the most intelligent that survives. It is the one that is most adaptable to change**". Anon.

The quote, often misattributed to Charles Darwin, is relevant for this spring. As many in Canada brave -15ºC and may not feel very 'spring-like', others are basking in +15ºC and ready to be in outdoor mode. However, this spring is very different (other than neither the Oilers nor the Leafs are playing in the Stanley Cup) and it may not feel that we have quite got the same spring in our step (pun-intended). A pandemic is upon us – a serious, challenging, life-threatening and global health and economic event that has transformed life as we know it, will do for some time and will leave an indelible mark on us all.

In the face of the challenge the pandemic gives us, we must adapt. What is very clear in disaster management for dealing with the pandemic, is that as a community, we can do so, and as an individual within the community, we must do so. We're already seeing examples of how individuals are pulling together to be creative and talents are shining through within teams whether they are in healthcare or not. This unique opportunity gives everyone a time to rise to the occasion (albeit it humbly in a truly Canadian way) and rapidly care for those that need it as well as your families and friends.

Patients with cardiovascular disease that you work with every day in research or practice are at particularly high risk for complications of COVID-19 and as such, may not fare well. Likewise, many healthcare workers will be pulled into care for patients or have exposure to COVID-19, become ill, and will face difficult choices. The mental health issues that will stem from this will need attention, and a critical reminder to pay close attention to mental health issues of yourself, your family and friends and those in your community. None of this is easy.

So, what examples can we draw from on how to proceed? You and your research teams are already prepared as you are used to working together and solving problems. As an example, in this Chronicle you will see details about the CVC Colloquium, held in Banff, Alberta in March 2020. This is a striking example of collaboration, creative thinking, and ensuring we ask and start to answer the right questions. A second example is VICTORIA. This global trial, led by the CVC in collaboration with academic partners (DCRI, Stanford) and industrial partners (Bayer, Merck) was presented by Dr. Armstrong and published on March 28, 2020 after a 5-year collaborative effort. The trial enrolled a complex, high-risk population and had 5050 participants from 42 countries and should be looked at as an incredible achievement. Recruiting ahead of schedule, with >40,000 patient visits, 125,000 blood samples collected and ~8000 endpoints collected, it will serve as a foundation for years of work to understand heart failure and generate additional hypotheses worthy of testing. This cannot be accomplished without team work.

We're looking to you to remain healthy, collaborative, creative and ensure our future together remains bright. Please reach out to any of us as needed – our CVC team may be working remotely but are fully engaged on all fronts.

Justin Ezekowitz
CVC Co-Director

CVC Clinical Trials Colloquium

On March 1st, 2020, the Canadian VIGOUR Centre welcomed 19 sites from 8 different provinces to participate in the 7th Annual **CVC Clinical Trials Colloquium** in Banff, AB.

A sincere thank you to our sponsors Amgen, AstraZeneca, BMS-Pfizer Alliance, Boehringer-Ingelheim, CSL Behring, and Novartis for their support towards making this event possible!

Building upon objectives and key feedback from previous colloquia, the focus of this year's gathering was to enhance clinical research in Canada, including primary objectives to:

1. enhance best practices in conducting clinical trials, through an open forum of discussions, breakouts and sharing;
2. build and maintain strong and engaged research teams who can continue to enhance research locally and nationally as well as adapt to a changing clinical research environment;
3. enhance patient identification and recruitment, and explore strategies that facilitate patient engagement in clinical trials conduct;
4. share knowledge and lessons learned from Regulatory Inspections and Audits; and
5. explore pragmatism, innovation and technology in trials as well as the changing landscape of clinical trial design.

Led by **Dr. Shaun Goodman**, CVC Co-Director and consultant **Ms. Lisa Berdan**, we began the day by exploring how to build and maintain strong and engaged research teams. This session involved some enlightening breakout discussions during which we discovered how sites seek out and select trials for participation, what helps keep sites motivated and interested in long-term trials, and the optimization of site operations, including how Sponsors/AROs/CROs can help reduce inefficiencies and support the overall research process.

In what was perhaps one of the most impactful sessions of the day, we were thrilled to welcome research patient advocate, **Jillianne Code, PhD**. Through her experience as a professor, researcher, heart failure patient and heart transplant recipient, Dr. Code shared her story and how her experience has informed her advocacy work towards patient engagement. From this unique patient advocate perspective, the participants worked to design an optimal 'road map' to better engage patients in research, from the time of entry into the healthcare system throughout trial participation and communication of study results.

We then turned our focus to regulatory inspections and audits, including best practices and lessons Learned. Led by **Tracy Temple**, CVC Associate Director of Clinical Trials, we heard from several sites first-hand accounts of their inspection and audit experiences with Health Canada, FDA, study sponsors, and others. The positive post-Colloquium feedback from the participants further highlighted the unique lessons and 'cross-pollination' of ideas afforded by this sharing session.

We closed our day with a session titled The Wave of the Future in Clinical Trials, which included a look at pragmatic design and operations, electronic health records, and the use of technology in research. **Dr. Justin Ezekowitz**, CVC Co-Director and **Craig Reist**, Director of Megatrials at the Duke Clinical Research Institute invited us to explore how we can potentially make trials more simple and how we might utilize technology to support a pragmatic approach.

With an aim towards supporting innovation in research and remaining adaptable to the changing research landscape, we brainstormed on how to foster pragmatism within key clinical trial elements and processes.

We wish to extend our appreciation to all investigators, coordinators, and sponsors who participated in this year's

CVC Clinical Trials Colloquium

Colloquium. Your valuable experiences and contributions from a variety of research settings across Canada are what make this such a unique and engaging event.

As we can gather only a modest number of sites to the Colloquium each year, we look forward to inviting others to join in the future. Our goal is to continue to provide a forum in which we all can share with each other how best to optimize clinical trial conduct and performance.

If you are interested in hearing more about this year's meeting or would like to inquire about participation in a future Colloquium, please contact Tracy Temple at **tracy.temple@ualberta.ca** or 780-492-1876.

Check out the highlights from the event here:

@CVC_UAlberta

#CVCBanff

SODIUM-HF

Thank you to all site personnel and teams for your flexibility, diligence and support of SODIUM study participants during these unprecedented times!

The CVC SODIUM Operations team remains operational and available to work with you should have you have any questions or concerns. We wish to remind you of the following:

- Please continue to notify CVC of any changes to your institution's policies and standards for screening and follow up of research participants.
- Please continue to conduct remote or phone follow up visits with study participants.
- Please continue to collect 3-day Food Records from study participants and submit them to **sodcore@ualberta.ca** after review / clarification by the dietitian.
- Please continue to query patients (or review medical records) for Clinical Outcomes and, if possible, submit source documentation to the above email.
- Please continue to enter data in a timely manner (five days of visit completion), with available source. Please refer to the document previously distributed with respect to guidelines on remote data capture.
- Health Canada and other regulatory agencies advise keeping a log of all study visits completed remotely / over the phone. Such documentation can be submitted to your ethics board when normal operations resume, as per the reporting policies of your ethics board.

Updates

We cannot have any LTFU patients in this trial! Every patient counts so the expectation is for sites to search for all potentially LTFU patients until database lock. Your diligence in patient follow up is even more important at this time and until normal operations resume.

Contract amendments are being distributed by Research Services Office at the University of Alberta to applicable sites, per previous communication. Contact Melisa with any questions.

For general study updates and news, follow us on Twitter **@sodiumhf**.

If you are interested in receiving more information about the SODIUM-HF trial, please contact the Clinical Trials Project Lead, Melisa Spaling, via email at **mspaling@ualberta.ca** or 1-800-707- 9098, ext. 1. You may also contact the SODIUM-HF trial Regulatory Specialist, Kate Dawson, via email at **kedawson@ualberta.ca** or 1-800-707- 9098, ext. 8.

SODIUM-HF

Funded by the Canadian Institute of Health Research (CIHR) and University Hospital Foundation, SODIUM-HF is a multicenter, randomized, open-label Study Of DIetary Intervention Under 100 MMOL in Heart Failure.

ClinicalTrials.gov Identifier: NCT02012179

HEART-FID

Enrollment for 2020 started very well. Thanks to all our sites for your diligent work on screening and enrolling into our important heart failure trial. A special thanks to Canada's top recruiting sites!

- **Dr. Shekhar Pandey** and **Ian Bonvanie** (Cambridge Cardiac Care Centre, Cambridge, ON)
- **Dr. Elizabeth Swiggum** and **Sarah Nelson** (Victoria Heart Institute, Victoria, BC)
- **Dr. Dante Manyari** and **Tracy Cleveland** (Surrey Memorial Hospital – Cardiology Clinical Trials, Surrey, BC)
- **Dr. Miroslaw Rajda** and **Suzanne Greeley** (Queen Elizabeth II Health Sciences Centre, Halifax, NS)
- **Dr. Justin Ezekowitz** and **Quentin Kushnerik** (University of Alberta Hospital, Edmonton, AB)
- **Dr. Eileen O'Meara** and **Carolina Barrera-Ruiz** (Montreal Heart Institute, Montreal, QC)

COVID-19

Like everyone, our trial is adjusting to the COVID-19 pandemic. Please follow study provided guidance on moving on-site visits out of window or conducting phone visits instead of on-site visits. Please remember to notify your REB, as per their requirements, about protocol deviations due to the pandemic.

Data Cut

The trial had a data cut in early April and we want to thank every site for working so diligently on having data entered and clean. Amazing job from our sites!

Sub-Study

Currently the sub-study is on hold. Sites participating should still proceed with REB approvals and contract amendments during this time. Once ready to restart, training will be the last step remaining for site activation.

New Central Lab Portal

Each Principal Investigator and main blinded Study Coordinator will receive access to the new lab portal. Please watch for an email explaining how to gain access to the system. If other staff at your site require access, please let us know. At this time, only blinded team members will be provided access. The upgrade from faxed lab results to labs appearing on the online portal will take place over the next 1 to 2 months.

If you are interested in further information regarding this trial, please contact Clinical Trial Project Lead Courtney Gubbels at 1-800-707-9098 ext 2 or via email at **courtney.gubbels@ualberta.ca** or Regulatory Specialist Kate Dawson, 780-492-3789 or via email at **kedawson@ualberta.ca.**

Sponsored by American Regent, HEART-FID is 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

ClinicalTrials.gov Identifier: NCT03037931

STREAM-2

Our local team continues to impress with an outstanding enrollment total for March! We wish to commend the team on their efforts and encourage them to keep the pace going.

Global enrollment continues to climb as more sites join this 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.

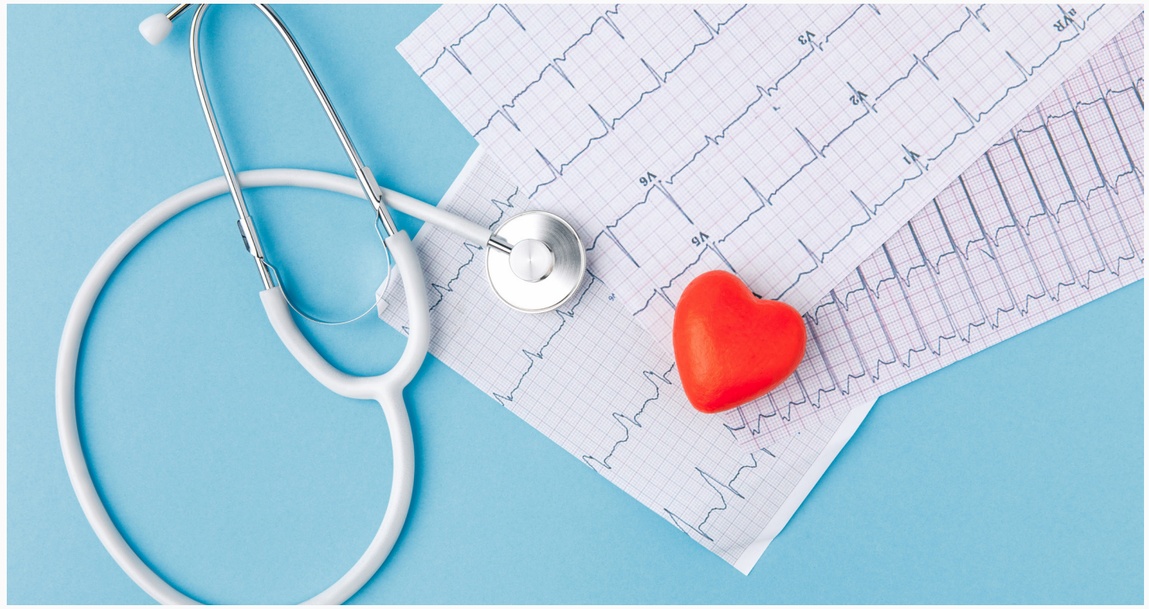
As this trial goes hand in hand with standard of care at hospitals, the global pandemic has had minimal effect on the recruitment for this trial. Follow up does not require on-site participant visits therefore protocol deviations are kept to a minimum. We are eager to see continued enrollment over the coming months to move one-step closer to answering this important research question.

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

Sponsored by Leuven Research & Development (LRD) at University of Leuven, Belgium, STREAM-2 is a Phase 4 trial on STrategic Reperfusion in elderly patients Early After Myocardial Infarction

ClinicalTrials.gov Identifier: NCT02777580

AEGIS-II



The AEGIS-II CVC Team would like to extend a huge **thank you** to all of our sites for your efforts thus far to support the integrity of the study during the COVID-19 pandemic.

Your ability to continue with timely data entry, patient follow-up visits, patient infusions where possible, and communicating with us regarding your specific working situations has been extremely important. The last few weeks have been challenging for everyone, and your dedication is greatly appreciated!

The sponsor has provided guidance and options for temporarily implementing alternative methods of performing study procedures in order to ensure the safety of patients and study personnel. These temporary measures will be in place until further notice. Please continue to record all deviations from the protocol and submit these to CVC at the start of each month.

Please ensure that, at minimum, patient visits are being completed via phone or video chat and that these visits are done within the protocol specified time windows wherever possible. A reminder that eCRF data entry should be complete within two days of each visit, or within 24 hours of knowledge for all Endpoints and Serious Adverse Events.

If a patient has missed a visit or a patient is contemplating consent withdrawal, please contact CVC immediately.

Remote monitoring phone calls will continue with some modifications that will be communicated to each site soon.

The AEGIS-II CVC Team is working remotely and fully functional so please do not hesitate to reach out to us with questions or concerns at any time.

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.

If you are interested in further information regarding this trial, please contact Clinical Trial Project Lead, Lyndsey Garritty at 1-800-707-9098, ext 4 or via email at **lyndsey.garritty@ualberta.ca** or Senior Regulatory Specialist Kalli Renner, 1-800-707-9098 ext 6 or via email at **kalli@ualberta.ca**.

Sponsored by CSL Behring LLC, this is a Phase 3, Multicentre, Double-blind, Randomized, Placebo-controlled, Parallel-group Study to Investigate the Efficacy and Safety of CSL112 in Subjects with Acute Coronary Syndrome.

ClinicalTrials.gov Identifier: NCT03473223

MAP-AHF

The MRI Assessment of Pulmonary Edema in Acute Heart Failure study is a single-centre project taking place at the University of Alberta Hospital / Mazankowski Alberta Heart Institute in collaboration with the Peter S. Allen MR Research Centre.

Congratulations to **Dr. Richard Thompson, Dr. Ian Paterson and their team** on their first enrollment! Study recruitment is currently on hold due to the COVID-19 pandemic but we look forward to seeing this resume in the future.

Cardiogenic pulmonary edema is a cardinal sign of Acute Heart Failure and is a cause of the primary HF symptom – shortness of breath – which is most commonly treated with diuretic therapy. While increased lung water is typically reported descriptively (i.e., auscultation and/or chest x-ray), these measures are not sufficiently sensitive to exclude pulmonary congestion.

Further research is needed to a) determine changes is Lung Water Density (i.e., quantification of pulmonary edema on MRI) over the course of hospitalization and standard treatment of Acute Heart Failure, and b) explore whether Lung Water Density is predictive of long term outcomes in the Acute HF population.

If you are interested in further information about the MAP-AHF study, please contact the Clinical Trial Project Lead, Karin Kushniruk, at 1-800-707- 9098, ext. 7 or **karin.kushniruk@ualberta.ca**.

Sponsored by: Canadian Institutes of Health Research MAP-AHF will examine the changes in lung water density over the course of treatment in patients hospitalized for acute heart failure, and will explore whether changes in lung water levels can predict long term outcomes.

ClinicalTrials.gov Identifier: NCT03999138

FEAST-HF

We would like to welcome **Dr. Robert Miller and Study Coordinator Ms. Sneha Patel** at the University of Calgary to the study. They have been quite busy recruiting patients and we look forward to seeing this collaboration move us towards our enrollment goal more quickly!

We also wish to thank both of our sites for their dedication and creativity during these challenging times - we look forward to seeing recruitment resume after the COVID-19 pandemic.

Got Fiber?

Recent attention has been focused on the role of the gut microbiome in human disease, including its significant role in the pathogenesis of Heart Failure. Several small studies have shown an interplay between the microbiome and Heart Failure, and that the gut microbiome can be modulated by dietary interventions, such as the addition of dietary fiber.

This trial will explore if modification of the microbiome can mitigate the symptoms of patients with Heart Failure and whether new avenues for treatment and future research for patients with Heart Failure will be revealed.

If you are interested in further information about the FEAST-HF trial, please contact the Clinical Trial Project Lead, Karin Kushniruk, at 1-800-707- 9098, ext. 7 or **karin.kushniruk@ualberta.ca**.

Sponsored by University Hospital Foundation, FEAST-HF trial will explore the potential beneficial effects of dietary fiber supplementation, compared with placebo, in patients with Heart Failure

ClinicalTrials.gov Identifier: NCT03409926

VICTORIA

VICTORIA was a large randomized placebo-controlled, double-blind, event-driven, multi-center pivotal phase III clinical outcome trial of efficacy and safety of a novel oral sGC simulator vericiguat in patients with heart failure with reduced ejection fraction (HFrEF). A total of 5,050 patients were enrolled in the study at more than 600 centers in 42 countries. Patients were followed for a median of 10.8 months.

This study focused on patients with HFrEF who were at high risk of death or hospitalization from heart failure. The study was led collaboratively by the Canadian VIGOUR Centre and Duke Clinical Research Institute, and co-sponsored by Merck & Co, Inc. and Bayer AG.

The results showed that vericiguat added to guideline based heart failure therapies met the composite primary efficacy endpoint by reducing heart failure hospitalizations or cardiovascular death. The once daily oral treatment was also found to be well tolerated and safe with few side effects. In patients with worsening heart failure with reduced ejection fraction, vericiguat achieved a clinically meaningful absolute primary event reduction of 4.2 per 100 patient years or a number needed to treat of 24 for one year to prevent one primary event.

"*We were very gratified by these results because we now have a new therapy for heart failure in this high risk population with an unmet need who are already receiving guideline based therapy. Because this guanylate cyclase stimulator agent approaches and targets a new pathway in heart disease, we think it may open up a new horizon for other cardiac issues that deserves to be explored,*" said Dr. Paul Armstrong, study chair and founding director of CVC.

The VICTORIA trial was presented as a Late-Breaking Clinical Trial on March 28, 2020 at the virtual American College of Cardiology's 69th Annual Scientific Session Together With World Congress of Cardiology (ACC.20/WCC). The results were also published simultaneously in the New England Journal of Medicine (NEJM).

In addition to the publication in NEJM, a partnered context paper was also published in Circulation. This companion manuscript to the VICTORIA Primary Results compares the results from the VICTORIA trial against the Efficacy and Safety of LCZ696 Compared to Enalapril on Morbidity and Mortality in patients With Chronic Heart Failure with Reduced Ejection Fraction (PARADIGM-HF) and the Effect of Dapagliflozin on the Incidence of Worsening Heart Failure or Cardiovascular Death in Patients With Chronic Heart Failure (DAPA-HF) trials.

The authors who compared the trial in the Circulation manuscript conclude that, while comparative efficacy of different therapies is best assessed with head-to-head randomized trials, such data are often unavailable. An alternative and informed approach includes consideration of the estimated relative and absolute risk reductions. A simple cross-trial comparison of hazard ratios is suboptimal and may be misleading given that the combined comparator arms for the primary outcome in VICTORIA was 38.5%; more than double that observed in recent HF trials. Hence a more holistic approach to assess the totality of evidence is the best option to assess the merits of a particular therapy in a given clinical situation.

As a result of the team efforts of so many including the participating sites, the patients who volunteered, the study committees and the study leadership at the CVC, our academic partners at DCRI as well the two sponsors, we hope to see a new therapy approved for clinical use that will help patients with heart failure. Importantly, because of its novel mechanism of action, we anticipate it will likely also lead to exploration of new cardiovascular indications.

Achieving this goal, analyzing the data, presenting it publicly, publishing it in high-quality peer reviewed journals and describing the results to the lay public is part of the CVC's continuing responsibility and commitment to enhance cardiovascular health for current and future generations.

Visit thecvc.ca/victoria to view the ACC presentation, press releases, media, and more.

Quality

COVID-19 and Clinical Trials

In March 2020, Health Canada published a notification on their website regarding COVID-19 and clinical trials, entitled "**Management of clinical trials during the COVID-19 pandemic: Notice to clinical trial sponsors**".

Highlights for sponsors include:

- There needs to be a system in place to identify and document/report all Protocol Deviations (PDs); the sponsor should define the PDs that are to be reported
- If halting enrollment, sponsors are required to notify HC via a CTA-N (notification).
- Sponsors may consider shipment of clinical trial investigational products (IP) from Canadian sites directly to patients, with certain considerations.

Please read the full notice here: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/announcements/management-clinical-trials-during-covid-19-pandemic.html

GCP E6(R2)

In 2018, Health Canada formally adopted ICH GCP E6(R2), and in April 2019, Health Canada implemented these new guidelines. This means that sponsors and HC inspectors would expect to see documentation of training on the updated GCP guidelines for site study staff.

ICH GCP E6 was updated from R1 to R2 "to encourage implementation of improved and more efficient approaches to clinical trial design, conduct, oversight, recording, and reporting while continuing to ensure human subject protection and reliability of trial results.

New terms such as "Certified copy," "Monitoring Plan" and "Validation of computerized systems" have been added to the guidelines. Additional recommendations have also been included, specifically pertaining to PI responsibilities (Delegation of Duties and Maintenance of Records); Sponsor responsibilities (Quality Management and Risk-based Monitoring); and Essential Documents. If you haven't already done so, training on these updated guidelines should be done now to align with Health Canada's implementation of E6(R2).

For sites affiliated with the CITI program, both the CITI GCP – Canada course (since 04Apr2018), and the CITI Canada GCP Refresher course (since 25Jan2017) have included version 2 of the guidelines [E6(R2)]. If you have completed GCP training as of these dates using one of these courses, then you are up to date. As usual, please ensure that CVC receives a copy of any updated GCP training so we can update your site's training file for your respective trial(s).

For questions about Quality, please contact Jodi Parrotta, Clinical Trials Project Lead/QA-Regulatory Compliance Lead/Clinical Research Associate at 1-800-707-9098, ext. 3 or via email at **Jodi.Parrotta@ualberta.ca**.

Monitoring Tips

As we navigate these uncharted waters together, it's difficult to know where best to direct our limited resources and energy to uphold our responsibilities, while keeping the safety of ourselves, our families and our patients/research participants at the forefront.

Over the coming weeks and months, we will be called upon to continually adapt and find creative ways to accomplish everything we need to in both our personal and professional lives.

The CVC has been in close contact with our Sponsor partners and our DCRI colleagues, as well as consulting other outside sources of information in an ongoing effort to provide our Canadian sites with the most up-to-date guidance on how to keep our work moving forward. Preserving participant safety is, of course, everyone's primary goal. Secondary to that is for each site to do whatever they can, to the best of their ability, to preserve the integrity of the study. How each site will accomplish that depends on a multitude of factors that are continually changing. Some sites are still able to see participants for in-person visits while other sites are doing all visits by phone. Some sites have all research staff working only from home while others continue to have limited hours in the office. Many sites have some capability to do remote monitoring.

The key for all sites will be to maintain contact with study participants, perform whatever procedures/visits possible, either in person or by phone and **document, document, document**! If you cannot reach a participant by phone, rather than a missed visit, many studies have a provision that you can at least report information obtained by contacting alternative contacts, reviewing medical records and/or contacting the primary care physician. Sites will need to clearly document what *was* done, what *wasn't* done

and why these changes were made. If you altered the ways you do things due to restrictions imposed due to the pandemic, it is critical you document all relevant details of that in your research source.

Both the HC (see link in Quality) and FDA guidance on conducting clinical trials during COVID-19 recommend that when on-site monitoring visits cannot take place, the Sponsor and sites consider utilizing remote or central monitoring as a replacement.

At the CVC, we have been organizing our in-house and on-site teams to do remote monitoring visits that will be efficient, useful and value-added, but also mindful of the work this creates for already stretched-thin research site staff.

If you have any questions regarding remote visits or documentation during this time, please reach out to your CVC Project Lead or Corrina Boyd, CVC Monitoring Lead at **corrina.boyd@ualberta.ca.**

CVC News

Tinuola Omidiya recently started working as a Clinical Research Associate with the Canadian VIGOUR Centre. Tinuola has over ten years of experience as a CRA and a registered nurse. Before her current role at CVC, she worked at IQVIA Biotech and Parexel as a Clinical Research Associate. Tinuola has a Bachelor degree in Nursing from University of Texas and MBA from University of North Alabama. She is a dedicated and patient focused Registered Professional Nurse with proven strengths in acute patient care, staff development, clinical research, and family advocacy. Tinu is based in Alberta and will be monitoring sites in western Canada.

Feature Publications

Dr. Sean van Diepen

Drs. Sean van Diepen, Justin Ezekowitz, Finlay McAlister and **Padma Kaul, along with their fellow coauthors,** recently published their article "Incremental costs of high intensive care utilisation in patients hospitalised with heart failure" in the European Heart Journal: Acute Cardiovascular Care.

The estimated annual cost of heart failure hospitalisations is US$34b in the USA and CAN$482m in Canada. Intensive care unit admissions account for up to 13% of all hospital costs and are over three times more expensive than hospital ward beds, therefore reducing potentially unnecessary low-risk HF ICU admissions may be a potential source of healthcare savings.

Registries have reported large inter-hospital differences in intensive care unit admission rates for patients with acute heart failure, but little is known about the potential economic impact of over-admission of low-risk patients with heart failure to higher cost intensive care units.

In a Canadian national population health database the authors described the variability in intensive care unit admission practices, the provision of critical care therapies, and estimated the potential national cost savings if all hospitals adopted low intensive care unit admission practices for patients admitted with heart failure. The authors found that the overall inter-hospital intensive care unit admission rate for patients with heart failure was 0.3 to 51% including a mean of 5.4% in low, 14.5% in medium and 30% in high utilisation hospitals. Intensive care unit therapies in low, medium and high intensive care unit utilisation hospitals were 54.5%, 45.1% and 24.1%, respectively and adjusted in-hospital mortality was not significantly different by intensive care utilization. The proportion of hospital costs incurred by intensive care unit care was 7.8% in low, 19.8% in medium and 28.2% in high admission hospitals. The potential cost savings of altering intensive care unit utilisation practices for patients with heart failure was CAN$234.8m over the study period and CAN$26.1m per year.

In a national cohort of patients hospitalised with heart failure, the authors observed that low intensive care unit utilisation centres had lower hospital costs with no differences in mortality rates. These data suggest that future efforts to standardise ICU admission practices by limiting the use of higher cost intensive care beds to higher acuity patients with HF could substantially reduce costs to the healthcare system.

Feature Publications

Dr. Nariman Sepehrvand

Drs. Nariman Sepehrvand, Wendim Alemayehu, Finlay McAlister, and **Justin Ezekowitz** recently published their article "External validation of the H2F-PEF model in diagnosing patients with heart failure and preserved ejection fraction" in Circulation.

Patients with heart failure (HF) and preserved ejection fraction (HFpEF) often have a more complicated diagnostic pathway compared to those with reduced ejection fraction. Several diagnostic criteria and algorithms have been proposed to aid clinicians with the diagnosis of HFpEF but lacked sensitivity and had reasonable performance metrics. A recent diagnostic model (H2FPEF) may have the potential to overcome the hurdle of HFpEF diagnosis.

The authors used data collected from the Alberta HEART (Alberta Heart Failure Etiology and Analysis Research Team) cohort, and evaluated the performance of the H2FPEF model across the spectrum of cardiovascular disease. A H2FPEF score of > 2 had a sensitivity of 89-90% to detect HFpEF and a H2FPEF score < 6 had a specificity of 82% to rule out HFpEF in the Alberta HEART population.

They found that the range of scores in the H2FPEF model provides the opportunity to apply separate cut-off points to rule-in or rule-out the diagnosis of HFpEF; however, the H2FPEF performed only slightly better than chance in patients presenting with dyspnea, limiting its potential utility as a screening or diagnostic tool for front-line clinicians.

The authors conclude that further validation and refinement of the H2FPEF model is likely needed, such as the inclusion of natriuretic peptides, phenotypic cluster analysis, and testing in different patient populations with different prevalences of HFpEF. In the interim, applying this diagnostic model should be done with caution.

Visit the **publication archive** on our website for a comprehensive list of the CVC's publications.

About the Chronicle

This newsletter is published periodically as a service to Canadian investigational sites. The purpose is to provide information of interest to individuals involved in cardiovascular clinical trials managed by the Canadian VIGOUR Centre, University of Alberta in Edmonton, Alberta, Canada.

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Canadian Institute of Health Research
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Merck
University Hospital Foundation

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Bridging Hearts and Minds

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