

The Canadian Cardiac Chronicle

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“Genius is 1% inspiration and 99% perspiration”

- **Thomas Edison**

With the summer officially drawing to an end, schools get ready for a new term and we prepare our environment for the eventual cooler nights and shorter days. For those in North America, and especially western Canada, this has been a scorcher that replaced our usual cold ‘dome’ of January with a ‘heat’ dome of July. Has the heat melted our neurons or ensured that we remain focused on always looking forward? While the quote above is intended to convey the value and importance of hard work, it has taken on a different meaning this summer.

As teams at the CVC and across the myriad of collaborators, sites, people and places continue the active work of research, we have learned that perspiration leads to advances in science. The hard work done by many has led to innovations in care delivery, new medications for our sickest patients and new understandings of the construction and analysis of the data that underpins so much of what we do. The data is often seen ‘sweating it out’ with computational analysis to understand complex systems requiring incredible firepower, but none

greater than the biostatistical brains that create, troubleshoot and empower the data to come to life. This data is not possible without the patients who provide the sweat equity and the clinical and research teams at sites who work with the complexity that is science. Thus, the circle of asking yet un-answered questions, putting in the hard work of understanding the importance and feasibility of the answers if generated, setting a course and then asking new questions after the data is generated.

Science is always changing – sometimes incrementally, and often with a leap. When deciding on a program of research, it is built upon a solid foundation and inevitably changes the environment around it as it goes, therefore leading to disruption. The disruption that occurs is often good- that is not all change is bad- but frequently it requires an open mind and more often time. The change we are seeing for patient visits, clinical research, hybrid work environments and clinical trial design offers a unique opportunity to provide positive momentum towards a common goal.

An example of changes afoot is the pragmatic approaches underway with current and upcoming trials, including the EMPACT-MI trial, which is testing empagliflozin (vs. placebo) in patients with acute coronary syndrome. The mechanisms utilized to identify patients, maintain engagement throughout the trial (and afterwards) and minimize the site burden while maintaining trial and data integrity are evolving. This change has accelerated in the last year and will continue as we move from the era of mega- to giga- trials, and from population to precision health.

So, as the summer winds down, look for inspiration, dig in with perspiration and bring back some ‘genius’ ideas to change the environment for the better.

A handwritten signature in black ink, appearing to read 'Justin Ezekowitz', written in a cursive style.

Dr. Justin Ezekowitz
CVC Co-Director

CLINICAL TRIALS

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AEGIS-II

Thank you to all of our sites for their efforts and attention to detail leading up to the analysis of the data that occurred just prior to the summer. The Canadian data clean metrics have been excellent thanks to your hard work.

All of our sites have now been re-activated for enrollment following the COVID-19 hold, and our CVC CRAs are beginning to conduct on-site monitoring visits again!

As we are now moving towards the end of the enrollment phase, and after many months of decreased randomizations due to COVID-19 restrictions, we are all eager to get back to enrolling patients in a safe and healthy environment. While doing so please remember that successful study recruitment and retention begins with enrolling the right participants! It is more important than ever that the participants you enroll are able to follow the protocol and visit schedule as closely as possible. Missing data will have a negative impact on the final study analysis.

We hope that everyone has been able to enjoy some well deserved time off during the summer months, and are able to focus that renewed energy on enrollment going into the fall. We are challenging each site to enroll at least one patient in September!

If a patient has missed a visit, is contemplating IP discontinuation or consent withdrawal, please contact the CVC

immediately to ensure that the appropriate processes are followed. Principal investigator involvement in each of these situations is very important and should be documented in your source.

Lost to Follow Up patients should be extremely rare, and the expectation is that if a patient cannot be reached at any protocol-specified visit timepoint, you must continue to attempt to locate the patient through to the end of the study and database lock.

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 lyndsey.garritty@ualberta.ca.



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STREAM-2

This trial is 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. Our local site led by Drs. Welsh and Bainey has excelled in enrollment these last couple of months. Amazing job! Let's keep the momentum going this fall!

A special thanks for working quickly to implement the recent amendment locally. As global enrollment steadily climbs, the study team continues to monitor data entry carefully. Thank you to our local site for continuing to enter data in a timely

manner and resolve queries as they arise.

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



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EMPACT-MI

Startup is almost complete in Canada with 20 sites activated for enrollment! Globally, over 220 sites have been activated and recruitment is progressing nicely in this pragmatic trial led in Canada by Dr. Jay Udell (Women's College Hospital), Dr. Shaun Goodman (CVC Faculty) and Dr. Shelley Zieroth (St. Boniface Hospital).

Enrollment is going strong in Canada with over 50 patients randomized. Congratulations go out to our top 3 enrolling sites, **Dr. Burstein and Anita Andoh; Dr. Udell and Michelle Filice; Dr. Daneault and Julie Caron.**

We look forward to activating our remaining sites in the coming weeks, so they too can begin enrolling and contributing to this important trial.

Reminders:

- Training Documentation – This is to be maintained for ALL study staff listed on the delegation log in the event of an audit. There should be documentation of training on GCP, HC Div 5, Protocol (IM modules relevant to the person's role) and other training as needed (such as review of the IB and Events Review Charter for sub-Is).
- Rave data entry – Enter visits within **3-5 business days** so that Data Management can review all data for any errors or omissions. Log into Rave frequently to check for any

open queries so they can be resolved asap.

- Local Labs – Enter the Lab Ranges in Rave once you have randomized your first patient. This will allow the lab to be available when entering lab values for all of your patients. Refer to the eCRF instructions found in the Rave EDC.
- Always Serious AEs – Refer to this list (found in the Rave EDC, under "Rave Modules") to determine if an AE must be reported as an SAE.
- Drug Supply – Keep an eye on your number of kits listed as "available" and be sure to let the CVC know if you have a potential bolus of patients so that you have enough drug on site to randomize them all (and avoid a Failed Randomization). The CVC can increase your resupply of drug to a higher level, if needed.

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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HEART-FID

The enrollment countdown is on! We have seen an uptick in Canada's enrollment over the last several months and we commend you for working to enroll new participants over these last months of recruitment. We appreciate your extra efforts! Remember enrollment is competitive and will close as soon as 3,014 participants are enrolled.

Data

After we reach our enrollment goal, we will be shifting our focus from screening and enrollment to data cleanliness. As always, our sites continue to do an excellent job with getting data entered and resolving queries.

Protocol Amendment

Most sites are activated under the latest protocol amendment. One of the activation requirements was that each principal investigator and main study coordinator complete training. Even though your site has been activated, please remember to finish training all of your study team on the Amendment and have your team document their training on a protocol training log. A reminder that writing 'self-review' on the

training log will not be accepted. The principal investigator or main study coordinator need to sign off as trainer. Please send a copy of your completed training log to the CVC.

Sub-Study

With the new protocol amendment providing the option of on-site visits, Canada has started enrolling into the sub-study. We are excited to report that a number of our sub-study sites have enrolled! We are looking forward to our remaining sub-study sites contributing to enrollment soon as well. Also, a reminder that there is a new sub-study page in the eCRF to complete for all sub-study participants.

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



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SODIUM-HF

Thank you to all of our SODIUM-HF sites for their dedication and creativity in following their patients during the pandemic. Every patient counts so we appreciate you keeping your patients engaged!

A special thank you to select sites who have completed all study procedures and are now closed. We anticipate many more sites will reach this exciting milestone in the coming months.

For sites participating in the long-term follow up sub-study, nearly three-quarters of eligible patients have been approached thus far – keep up the excellent work!

Reminder:

- 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. Thank you for your continued diligence in this regard.

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

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



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SONOSTEMI-LYSIS

The **SONO**thrombolysis in patients with an **ST**-segment Elevation Myocardial Infarction with fibrino**LYSIS** (SONOSTEMI-LYSIS) Trial is a single-centre project taking place at the University of Alberta Hospital / Mazankowski Alberta Heart Institute. Congratulations to Dr. Kevin Bainey and his team for a successful start to recruitment earlier this year!

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 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 the Clinical Trial Project Lead, Karin Kushniruk, at 1-800-707- 9098, ext. 7 or karin.kushniruk@ualberta.ca.

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MOIST

Congratulations to Dr. James White and his team at the University of Calgary on joining the **M**ulti-**O**rgan **I**maging with **S**erial **T**esting in COVID-19 infected patients (MOIST) study!

Recruitment in Edmonton is nearly complete and we wish to thank Dr. Ian Paterson and his team for their stellar efforts. We look forward to meeting our final recruitment goal in the very near future.

Patients with COVID-19 infection are at significant risk of deterioration from pulmonary AND extra-pulmonary causes and the long-term consequences of these abnormalities are unknown. Systemic inflammation is considered to be a central feature of disease pathogenesis, however, the respective extent and time-course of multi-organ involvement (heart, lungs,

brain and liver) has not yet been evaluated to date. Furthermore, their respective and combined impact on patient morbidity and mortality has not been assessed.

Using novel MRI pulse sequences, the MOIST study aims to assess the presence, extent and time course of inflammation in the heart, lungs, brain and liver of participants with new or recent COVID-19 infection.

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

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FEAST-HF

We have now recruited about half of our total recruitment goal so a huge thank you to our sites for continued enrollment over the summer. Great work!

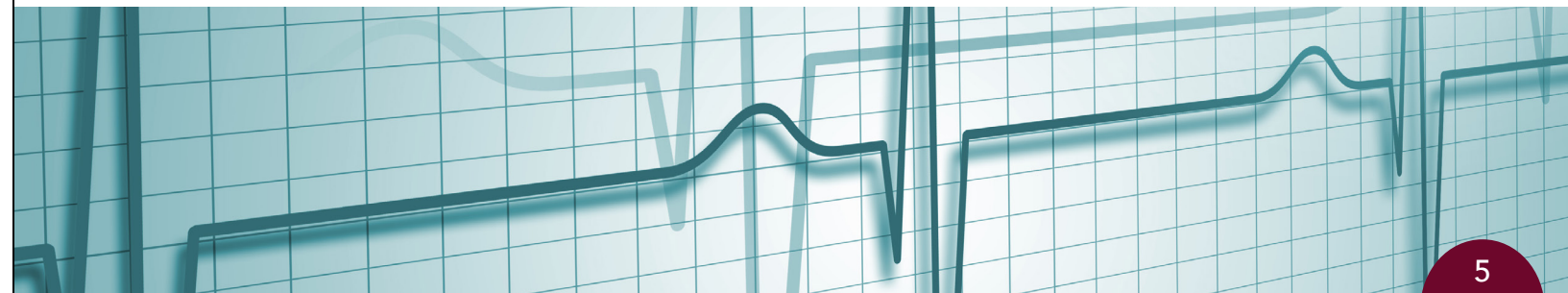
Got Fiber?

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.

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NEWS & UPDATES

New Staff



Farhat Ahmed recently joined the CVC as a Regulatory Specialist. She comes to us from her role as a Clinical Research Coordinator in the Stroke Research Program at the University of Alberta, with experience in various areas of medicine as well as regulatory processes. She holds a Bachelor of Medicine and Bachelor of Surgery degree and has worked on different clinical trials in the US in the areas of endocrinology, pulmonology, and oncology. As a research coordinator, she initiated various research studies including Mediject, Charm, Timeless, and Arcadia, which allowed her to deep dive into the regulatory process of studies and to excel in her current position as a regulatory specialist. In her free time, Farhat enjoys spending time with her family, painting, and reading. She can be reached at fzahmed@ualberta.ca.



Guillermo Hasbun recently joined the CVC as an ECG Reader. He graduated this spring with a Bachelor of Science with specialization in integrative physiology with distinction from the University of Alberta. During his studies, Guillermo obtained experience in clinical research by performing an undergraduate research project on the severity of neuromuscular disorders and their relation to adherence to positive pressure ventilation treatment with the Department of Pediatrics. Additionally, he obtained a certificate in ECG Assessment from St. George's, University of London. Guillermo can be reached at hasbun@ualberta.ca.



Utkarsha Kothavade recently joined the CVC as an ECG reader. She is a medical graduate and received a Doctor of Medicine degree in 2019. Utkarsha has experience in reading and interpreting ECGs through clinical rotations at various hospitals and clinics in both the US and Canada. In addition to clinical experience, she also had the opportunity to work as a research assistant on the Care of Elderly project with the Department of Family Medicine at the University of Alberta under Dr. Lesley Charles. Outside of work Utkarsha enjoys gardening and hiking. She can be reached at utkarsha@ualberta.ca.

On May 19, 2021 we held the second of three virtual CVC Colloquium sessions for 2021. In this session we focused on *Mentoring and Diversity in Clinical Research*.

It was a pleasure to welcome Dr. Roxanna Mehran, Professor of Cardiovascular Clinical Research and Outcomes, Professor of Medicine (Cardiology), and Population Health Science and Policy, and Director of Interventional Cardiovascular Research and Clinical Trials with the Icahn School of Medicine at Mount Sinai in New York, NY. In a very open, animated, and genuine talk she provided many insights on both mentoring and diversity. She shared that strong mentorship has been linked to:

- Enhanced science identity, sense of belonging and self-efficacy
- High career satisfaction
- Research productivity
- Persistence

She evolved the discussion, highlighting the uneven mentoring landscape, which includes more obstacles for minorities to obtain funding, and inequities and limitations for women with the same knowledge/experience as their male counterparts. As one of the founding directors of [Women as One](#), Dr. Mehran shared the efforts her and others are putting forth to promote equity in medicine and encourage others to do the same.

Following Dr. Mehran's presentation we broke out into three regional workshops led and supported by Drs. Shelley Zieroth and Shuangbo Liu (Manitoba), Warren Cantor and Alexandra Bastiany (Ontario) and Shaun Goodman and Abhinav Sharma (Ontario/Quebec). In these breakouts we discussed:

- Identifying and training new researchers and coordinators
- The building blocks for establishing new research sites
- Attracting the next generation
- Growing interest and involvement in clinical trials among women and underrepresented individuals
- How to mentor and support others without a research infrastructure, as well as the potential benefits of being involved in clinical research

This was an excellent opportunity to hear and learn from many of our investigators and study coordinators across Canada. The key takeaways from this session included the importance of mentoring the next generation, ensuring opportunities exist and there is support for new researchers to build and establish research/infrastructure within their practice, a willingness to incorporate new ideas, and support for inclusivity and equality. We want to thank everyone for the positive response and taking the time to join us for this session.

We are excited about the upcoming **Colloquium Session #3 on September 23, 2021 from 3:30 – 5:30 pm ET (4:30 AT, 2:30 CT, 1:30 MT, 12:30 PT)** where we will be focusing on **Operationalizing Clinical Research**. We look forward to having you join our next session detailed below and encourage you to share this with other colleagues who are interested or participating in clinical research. Once you register via the link below, a calendar invitation will be sent out shortly after with the details to join us on September 23, 2021.

If you have any questions regarding the CVC Clinical Trials Colloquium please reach out to Tracy Temple at tracy.temple@ualberta.ca or by phone at 780-952-2140.

CVC 2021 VIRTUAL COLLOQUIUM SERIES

Rapid Fire Session Presenters

Patrick Clifford, BA, BEd, MSW
Southlake Regional Health Centre

Michael Heffernan, MD, PhD
Oakville Trafalgar Memorial Hospital

Lyndsey Garritty, BA
Canadian VIGOUR Centre

Courtney Gubbels, BA
Canadian VIGOUR Centre

Karin Kushniruk, RN, PhD
Canadian VIGOUR Centre

Noreen Lounsbury, RN, BN, CCRN
Victoria Heart Institute Foundation

Jodi Parrotta, MA
Canadian VIGOUR Centre

Marlon Rajakaruna, MBA, LLB
Kingjigallo Legal

Session 3
Sept 23, 2021
3:30 - 5:30 pm ET

Operationalizing Clinical Research

3:30 - 3:40 pm	Welcome and Opening Remarks	Shaun Goodman Tracy Temple
3:40 - 4:00 pm	Key Insights for Working With Your Hospital Administration	Patrick Clifford
4:00 - 4:20 pm	Tips to Becoming a Successful Recruiter and Top Performing Site	Noreen Lounsbury
4:20 - 4:40 pm	An Investigator/Site Perspective on Surviving a Regulatory Inspection	Michael Heffernan
4:40 - 5:00 pm	Key Tips you Should Know When Negotiating Your Study Budgets	CVC Operations Team
5:00 - 5:20 pm	Top Things to be Aware of When Negotiating Your Clinical Trial Agreements	Marlon Rajakaruna

REGISTER HERE



2020 CVC Annual Report: Bridging the Gap

“We build too many walls and not enough bridges.”

- Isaac Newton

Although the pandemic walled us in physically, the CVC continued to build virtual bridges to improve our understanding of cardiovascular disease over the past year. Accordingly, the theme of our 2020 CVC annual report is ‘Bridging the Gap’ and it collates some of the key advances engineered in part by our excellent team. Our commitment to bridging gaps

through discovery and translational cardiovascular science in fulfillment of our social contract remains paramount.

We would like to thank and acknowledge our collaborators for your continued support and contributions to the work we all do together. We appreciate the interest and support of the many people who make it possible for us to succeed.

[View the 2020 CVC Annual Report here.](#)

FEATURED PUBLICATIONS

Vericiguat in Patients with AF and HFrEF



Dr. Paul W. Armstrong and his coauthors recently published their article, [Vericiguat in Patients with Atrial Fibrillation and Heart Failure with Reduced Ejection Fraction: Insights from the VICTORIA trial](#), in the *European Journal of Heart Failure*. We asked Dr. Armstrong a few questions to better understand the key findings of this study:

What were the important study findings? What are the key takeaways from this research?

Nearly half of this high-risk population of VICTORIA patients with heart failure with reduced ejection fraction (HFrEF) and recent heart failure (HF) decompensation had

atrial fibrillation (AF). Only patients with intermittent AF (but no AF on enrollment ECG) had worse outcomes as compared with those without AF.

Post-randomization, new-onset AF occurred relatively commonly (in 1 out of 10 patients) during a short follow-up of less than 1 year, was distributed evenly by treatment groups, and was associated with an excess in risk of both the primary and secondary outcomes.

The beneficial effect of vericiguat was unaffected by any type of AF at baseline.

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

AF is very common in HF. Vericiguat works equally well even if it is present. New onset AF occurs in 1 of every 10 patients with high-risk HF and is associated with increased cardiovascular disease and HF hospitalizations, but its incidence was unaffected by vericiguat Rx.

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

Who is at risk to new onset AF in HF, why does it occur, and what can we do to prevent its consequences?

Long-Term Risk of Death and Recurrent Cardiovascular Events Following ACS

Drs. Robert Welsh, Ana Savu, Kevin Baine, Padma Kaul, and former CVC trainee, Dr. Pishoy Gouda, recently published the article [Long-Term Risk of Death and Recurrent Cardiovascular Events Following Acute Coronary Syndromes](#) in *PLoS One*.

Although advances in the treatment of acute coronary syndromes (ACS) over the past several decades have resulted in significant improvements in clinical outcomes, a substantial proportion of individuals will experience a subsequent cardiovascular (CV) event. This study sought to determine the impact of common comorbidities on residual CV risk in a

large, inclusive population of patients following an ACS.

The authors demonstrated that, in a large contemporary and generalizable population, there is a significant risk of recurrent CV events following an index ACS presentation. The incremental presence of commonly observed comorbidities is associated with worse long-term outcomes. These individuals have the highest residual risk for a subsequent event and represent the greatest opportunity for novel interventions to demonstrate a meaningful clinical benefit and cost-effectiveness.



BRIDGING THE GAP



Drug Adherence and Long-Term Outcomes in Non-Revascularized Acute MI Patients

Drs. Shaun Goodman, Padma Kaul, Ana Savu, Sean van Diepen, Kevin Baine, Robert Welsh, and Sunjida Islam, along with their fellow coauthors (Drs. Razi Khan and Akshay Bagai), recently published the article [Drug Adherence and Long-Term Outcomes in Non-Revascularized Patients Following Acute Myocardial Infarction](#) in the *American Journal of Cardiology*.

The use of optimal medical therapy (OMT) at discharge and subsequent adherence to guideline-based medications is a strong predictor of mortality after myocardial infarction (MI). Suboptimal adherence to guideline-based medications has been associated with adverse outcomes and may have even greater importance in patients who are not revascularized post-MI. This study aimed to compare the prognosis between those non-revascularized MI patients who did and did not undergo angiography, as well as to examine the association of OMT adherence on 2-year outcomes.

The authors found that patients managed non-invasively after MI presented with more co-morbidities and had worse

long-term outcomes when compared to those who underwent angiography. Further, while high adherence to OMT in MI patients managed non-invasively was associated with a ~50% reduction in long-term mortality, this was observed in less than 1/3 of patients. The study findings highlight the importance of adherence to secondary prevention medications and suggest potential opportunities to optimize care of patients undergoing non-invasive management for MI.



Visit the [publication archive](#) on our website for a comprehensive list of the CVC's publications.

About the Chronicle

Chronicle Editorial Board

Paul W. Armstrong	Courtney Gubbels	Ellen Pyear
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