CHARTING A COURSE TO OUR FUTURE

2012 ANNUAL REPORT

CANADIAN VIGOUR CENTRE

Bridging Hearts and Minds to Enhance Cardiovascular Care

MESSAGE FROM THE DIRECTOR 4
VISION, MISSION, CORE VALUES 6

2012 HIGHLIGHTS
INSIGHT: STREAM 10
IMPACT: FEATURED PUBLICATIONS 17
INNOVATION: INTRODUCING NEW FACULTY 25
INSPIRATION: THE NEXT GENERATION OF HEALTH RESEARCHERS 29

THE YEAR IN REVIEW
THOUGHT LEADERSHIP
FACULTY 32
PEER REVIEWED PUBLICATIONS 34
BEYOND 2000 40
THE CANADIAN CARDIAC CHRONICLE 41
SERVICES AND ACTIVITIES 42
CLINICAL TRIALS 44
SITE NETWORK AND PROFILE 45
ACTIVE CLINICAL TRIALS 46
ECG CORE LABORATORY 50
BIOSTATISTICAL ANALYSIS 51
POPULATION AND HEALTH ECONOMIC OUTCOMES 52
CLINICAL TRIAL PORTFOLIO 54

CVC OPERATIONS
SOURCES OF REVENUES
CLINICAL TRIALS 56
GRAND FUNDED PROJECTS 57
MANAGEMENT TEAM 58
WORLDWIDE COLLABORATORS 59

ACKNOWLEDGEMENTS 62

MESSAGE FROM THE DIRECTOR

There is genuine value in the production of an annual report. This is a good thing to remember, given the substantial time and effort required to produce it. Surveying a year of work on behalf of my band of brotherly and sisterly colleagues, this annual report gives me pause to reflect on what a great team of people we have that are committed to our common cause of enhancing cardiovascular health for current and future generations.

The theme of this year's report "Charting a Course for the Future" is well aligned with our recent faculty and leadership advance. This annual strategic planning session helps us focus on future research and operational priorities. This year we employed the compass as a model to assist in setting our direction. Notice this compass shown opposite our vision and mission on page 7 has an outer ring framed by four phrases we believe capture the context of our work:

1. Leading hearts and minds which echoes CVC's tag line
2. Continuously innovating or exploring new paths to enhance the care of our patients but also finding new and better way of doing things
3. Ensuring our work has impact on cardiovascular health and on health policy and
4. Career development of our most valuable resource, our people.

Central to the compass and our entire organization is our purpose, to enhance cardiovascular health for current and future generations. Within the compass are four essential quadrants, the CVC vision and core values which were the product of a prior advance, and the two new quadrants are occupied by our promise which is how we propose others would see us and what commitments we aim to keep in fulfilling our purpose, and finally,what operational priorities we propose to live by to stay on course as we move forward.

Consistent with these strategic research priorities, the 2012 annual report reflects several key highlights of the past year:

- The culmination of over five years of collaborative work with many global partners was the unveiling of the STREAM trial. It has generated worldwide attention and widespread uptake by demonstrating the tremendous advantage of early pre- hospital treatment of heart attack patients. The results, which spill over into the first quarter of 2013, demonstrate a remarkably low mortality of these high risk patients and highlight that there are two legitimate options for best care thereby providing excellent options to such patients worldwide and irrespective of where they live.
- Our work continues to be well recognized in the peer-reviewed literature. Amongst the several publications of our faculty listed herein, seven have been chosen that are particularly noteworthy. They signify our commitment to the cycle of quality by exemplifying the compelling linkages between discovery science, novel clinical investigation and clinical trials. By taking creative approaches to enhancing cardiovascular care to the Alberta community, we have made a genuinely positive impact on mortality and hospital readmission rates in heart failure. We found an innovative statistical method to better understand the results of our research and that of others: this not only makes the work more efficient but also provides better insight into what it really means. We have identified a new approach to improve understanding of our patients symptoms and analytical models that enhance our ability to to predict the likelihood our patients will experience future events.
- I am delighted to formally announce the addition of Shaun Goodman, Professor of Medicine at the University of Toronto and Adjunct Professor of Medicine at the University of Alberta to our faculty. Shaun brings a wealth of expertise and experience and provides vital east-west collaborative link to our future. Readers of this report will appreciate excerpts from a recent interview that describes his philosophy and desire to participate in CVC's future academic and research initiatives
- Mentoring continues to be a fundamental part of our mission, and this year we highlight an interview from Neda Dianata Maleki, a physician-trainee, who worked with us for a year on the STREAM project. Her insights and experiences are shared within this report. We continue to learn from our trainees and welcome others from within our own ranks and around the world to join us in pursuing our mission.

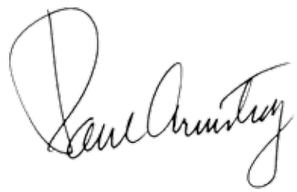
As we mark year 15 of CVC's existence as a centre within the Faculty of Medicine and Dentistry, we are pleased to have a continuing and vigorous pipeline of ongoing cardiovascular projects. We are grateful for funding provided by our industrial partners as well as the Canadian Institutes of Health Research, the Heart and Stroke Foundation, Alberta Innovates-Health Solutions, the University of Alberta, and the Mazankowski Alberta Heart Institute and University Hospital Foundation.

The quality and quantity of our work is a tribute to an outstanding faculty, whose unique synergies catalyze our efforts and attract an energetic group of trainees that together comprise our promise for tomorrow. Operationalizing all of these ideas into reality takes a great team whose talents, commitment and personalities decorate this report.

To be a good sailor and know where you are going, you need both a chart and a compass. To read a compass you need to understand where you are and to what extent the magnetic forces of the earth deflect your compass away from a true northerly direction. So here in Edmonton our co-ordinates are 53°31'20" N & 113°31'14"W : however if you were to arrange to point your compass due north you need to know that it is actually pointing 15°1' east of true north because of the magnetism of the earth's core. From this metaphor emerged the theme "Recalibrating Our Compass" that we share here in this annual report, as it reflects our steadfast commitment and determined direction to lead novel cardiovascular research.

I heartily commend this year's report to you so you may better understand who we are and what we do. In so doing I trust that the CVC spirit of crafting innovative solutions, inspiring the next generation of health professionals, seeking insight into the unmet needs of our patients and generating results that have impact on health policy is clearly evident.

With kind regards,



Paul. W. Armstrong, MD

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.

INTERGRITY

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.

“We shall not cease from exploration, and at the end of all our exploring will be to arrive where we started and know the place for the first time.”

— T. S. Eliot

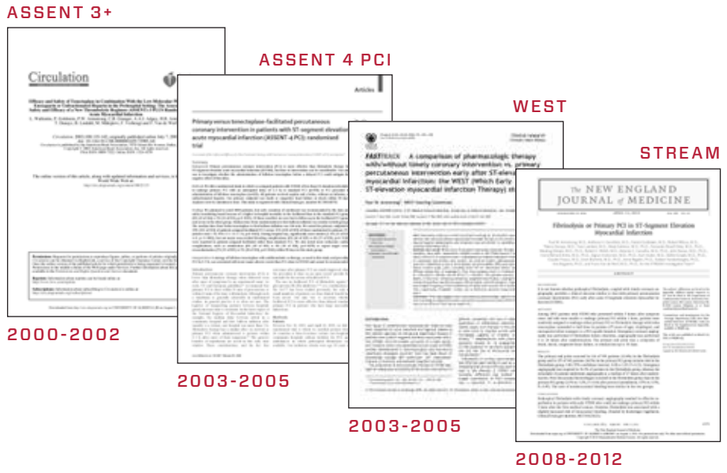
2012 HIGHLIGHTS

Paul Armstrong (left) is joined by Robert Harrison, who had a major heart attack two years ago and took part in the study.

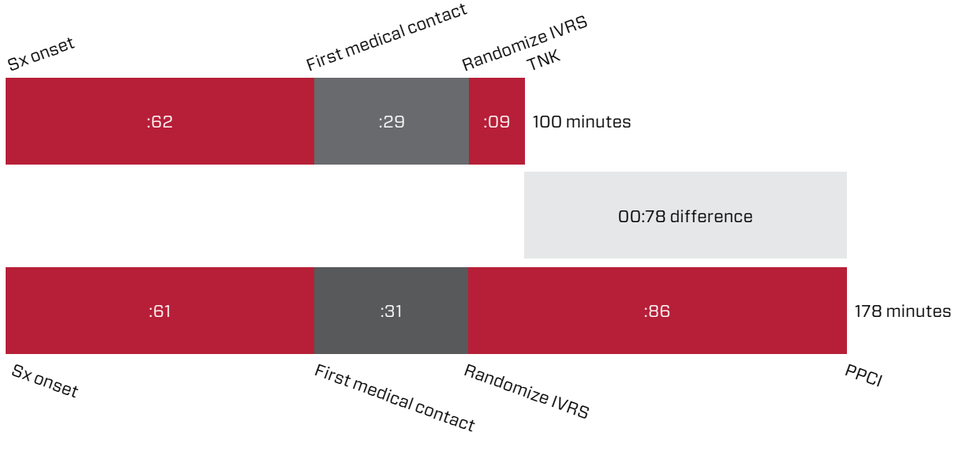
INSIGHT

EVOLUTION OF STEMI CARE

STREAM (Strategic Reperfusion Early after Myocardial Infarction) represents the recent culmination of over five years of collaborative work relating to the recent successful late breaking trial ACC presentation by Frans Van der Werf (March 10, 2013) and publication of the STREAM Trial, N Engl J Med 2013; 368:1379-1387 DOI: 10.1056/NEJMoa1301092.



MEDIAN TIMES TO TREATMENT (MIN)



n=1892

N Engl J Med online March 2013

STREAM

STREAM is a milestone on a much longer journey in the care of patients with ST elevation myocardial infarction. Few individuals will have worked during the pre-reperfusion era, when in-hospital mortality from STEMI was 30% and cardiogenic shock, heart failure were common place. The remarkable 30 day mortality rate of 4.5% achieved in STREAM, is a tribute, not only to better understanding of MI pathophysiology, the development of novel molecular therapies and advances in PCI, but also the effectiveness of a cadre of multidisciplinary healthcare professionals working in teams, essential to ensuring maximal efficacy of our greatly advanced but time dependent therapies.

In this regard, we all owe a debt to our French colleagues who developed the SAMU system of emergency care and contributed the majority of patients to STREAM.

After exploring this first-hand early in 2000, Dr. Armstrong and his colleague and CVC faculty member Robert Welsh, MD undertook to lead the Edmonton initiative within the local health community. Together, they adopted the approach first used in the ASSENT 3+ trial and then in another transforming Canadian trial of 300 patients called WEST, which provided a key stepping stone to STREAM.

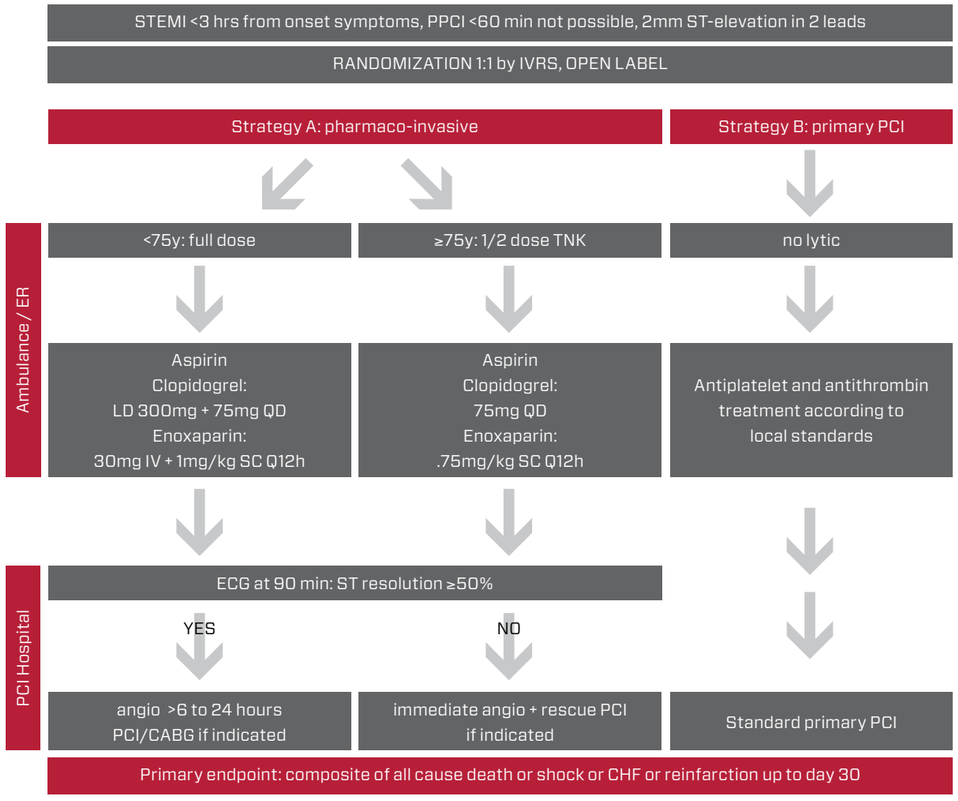
In STREAM we achieved unprecedented short times to reperfusion namely 100 minutes from first medical contact to initiation of fibrinolysis in the field and 178 minutes to first coronary intervention in one half of the patients randomized to primary PCI. The results demonstrated remarkable similarity in efficacy with a trend towards less shock and heart failure in the early lytic treated group (approximately 1/3 of whom underwent rescue PCI; the remainder undergoing catheterization and as appropriate, coronary intervention within the first 24 hours). When we observed excess intracranial hemorrhage in the over 75 year group after approximately 21% of the enrolment, we reduced the dose of TNK by half with greatly improved safety and sustained efficacy.

We have much more to learn from STREAM, but, we must await the one year results of mortality to further establish the relative efficacy of both therapies. STREAM however was unquestionably a successful trial. It demonstrates that we have two viable therapeutic options for reperfusion in STEMI. Since one size does not fit all in the real world of STEMI care, reasoned clinical judgment is required to assess which strategy is most appropriate in each circumstance.

We salute our patients who willingly volunteered to participate in helping us define a most meaningful result.

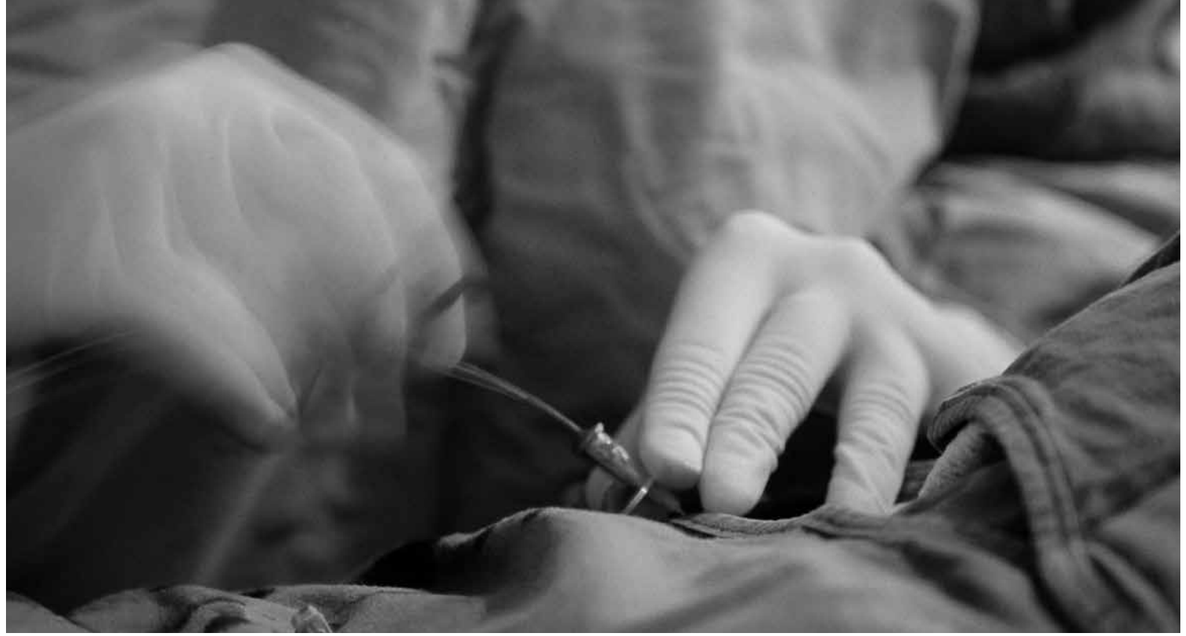
We are grateful to our many colleagues globally, our sponsor Boehringer-Ingelheim, and the leadership team in Leuven Belgium who supported this important trial. Finally, and most importantly we salute our patients who willingly volunteered to participate in helping us define a most meaningful result.

STUDY PROTOCOL



Armstrong PW et al NEJM 2013

This trial (which began in 2008 and enrolled the last patient in July 2012), compared pre-hospital fibrinolysis followed by coronary angiography within 6-24 hours to primary percutaneous coronary intervention (PCI) in patients presenting with an acute ST-segment elevation myocardial infarction (STEMI) within 3 hours of symptom onset and who had at least 2mm STelevation in 2 contiguous leads. To be eligible these patients could not have accessibility to PCI within 1 hour. The primary end point of this trial was a 30 day composite of death, cardiogenic shock, congestive heart failure or reinfarction.



STREAM IN THE NEWS

Fibrinolysis or Primary PCI in ST-Segment Elevation Myocardial Infarction
Paul W. Armstrong, M.D., Anthony H. Gershlick, M.D., Patrick Goldstein, M.D., Robert Wilcox, M.D., Thierry Danays, M.D., Yves Lambert, M.D., Vitaly Sulimov, M.D., Ph.D., Fernando Rosell Ortiz, M.D., Ph.D., Miodrag Ostojic, M.D., Ph.D., Robert C. Welsh, M.D., Antonio C. Carvalho, M.D., Ph.D., John Nanas, M.D., Ph.D., Hans- Richard Arntz, M.D., Ph.D., Sigrun Halvorsen, M.D., Ph.D., Kurt Huber, M.D., Stefan Grajek, M.D., Ph.D., Claudio Fresco, M.D., Erich Bluhmki, M.D., Ph.D., Anne Regelin, Ph.D., Katleen Vandenberghe, Ph.D., Kris Bogaerts, Ph.D., and Frans Van de Werf, M.D., Ph.D. for the STREAM Investigative Team
N Engl J Med 2013; 368:1379-1387April 11, 2013DOI: 10.1056/NEJMoa1301092

Edmonton study could set world standard for treating heart attack patients
http://www.edmontonjournal.com/search
Edmonton+study+could+world+standard+treating+heart+attack+patients/8076145/story.html

Research suggest drugs may be as effective as angioplasty
http://edmonton.ctvnews.ca/video?playlistId=1.1190270

New hope for heart attack victims
http://www.fortmcmurraytoday.com/2013/03/10/new-hope-for-heart-attack-victims
http://www.torontosun.com/2013/03/10/new-hope-for-heart-attack-victims

New study could change how heart attack patients are treated world-wide
http://www.globaltvedmonton.com/
new+study+could+change+how+heart+attack+patients+are+treated+world+wide/6442826269/story.html

Research excellence results in better care for heart patients
http://news.ualberta.ca/newsarticles/2013/march/research-excellence-results-in-better-care-for-heart-patients

Acute coronary syndromes. STREAMlining care for patients with STEMI
Bagai A and Granger CB. Nat Rev Cardiol. 2013 Jun;10(6):304-6
http://www.ncbi.nlm.nih.gov/pubmed/23609173#

IMPACT

The following are selected highlights from a more extensive list of peer-reviewed publications that appear elsewhere in this annual report. They were selected because of their novelty, diversity and interest. In several instances they have been accompanied by editorials, an important signal by the journal in which they are published that they deserve special recognition and expert opinion drawing attention to the significance of the findings.

FEATURED PUBLICATIONS

The Core ECG Laboratory at CVC provides useful insight into our conduct of clinical trials and care of patients. In this study arising from the PLATO (A Platelet Inhibition and Patient Outcomes) trial, a study of over 6000 patients, we demonstrated that the extent of deviation of the ST-segment on the baseline ECG was independently associated with one year vascular death and recurrent myocardial infarction. Because no difference was evident in the resolution of baseline ST-segments after percutaneous coronary intervention, these data suggest that the active treatment i.e. ticagrelor, as compared with clopidogrel, probably prevented recurrent vascular events rather than their affecting reperfusion. In addition because ticagrelor seem to provide the greatest benefit amongst those who had the greatest resolution of their abnormal ST segments, this highlights a category of patient that may derive particular benefit from more powerful platelet inhibition.

ST-Elevation Acute Coronary Syndromes in the Platelet Inhibition and Patient Outcomes (PLATO) Trial

Insights From the ECG Substudy

Paul W. Armstrong, MD; Hany Siha, MD; Yuling Fu, MD; Cynthia M. Westerhout, PhD; Ph. Gabriel Steg, MD; Stefan K. James, MD, PhD; Robert F. Storey; MD, DM; Jay Horrow, MD; Hugo Katus, MD; Peter Clemmensen, MD, PhD; Robert A. Harrington, MD; Lars Wallentin, MD, PhD

Background—Ticagrelor, when compared with clopidogrel, reduced the 12-month risk of vascular death/myocardial infarction and stroke in patients with ST-elevation acute coronary syndromes intended to undergo primary percutaneous coronary intervention in the PLATelet inhibition and patient Outcomes (PLATO) trial. This prespecified ECG substudy explored whether ticagrelor's association with vascular death and myocardial infarction within 1 year would be amplified by (1) the extent of baseline ST shift and (2) subsequently associated with fewer residual ST changes at hospital discharge.

Methods and Results—ECGs were evaluated centrally in a core laboratory in 3122 ticagrelor- and 3084 clopidogrel-assigned patients having at least 1 mm ST-elevation in 2 contiguous leads as identified by site investigators on the qualifying ECG. Patients with greater ST-segment shift at baseline had higher rates of vascular death/myocardial infarction within 1 year. Among those who also had an ECG at hospital discharge (n=4798), patients with ≥50% ∑ST-deviation (∑ST-dev) resolution had higher event-free survival than those with incomplete resolution (6.4% versus 8.8%, adjusted hazard ratio 0.69 (0.54–0.88), P=0.003). The extent of ∑ST-dev resolution was similar irrespective of treatment assignment. The benefit of ticagrelor versus clopidogrel on clinical events was consistent irrespective of the extent of baseline ∑ST-dev (P(interaction)=0.728). When stratified according to conventional times from symptom onset, ie, <3 hours, 3 to 6 hours, >6 hours, the extent of baseline ∑ST-dev declined progressively over time. As time from symptom onset increased beyond 3 hours, the benefit of ticagrelor appeared to be more pronounced; however, the interaction between time and treatment was not significant (P=0.175).

Conclusions—Ticagrelor did not modify ∑ST-dev resolution at discharge nor was its benefit affected by the extent of baseline ∑ST-dev. These hypothesis-generating observations suggest that the main effects of ticagrelor may not relate to the rapidity or the completeness of acute reperfusion, but rather the prevention of recurrent vascular events by more powerful platelet inhibition or other mechanisms.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00391872.

(*Circulation*. 2012;125:514-521.)

Key Words: myocardial infarction ■ electrocardiography ■ angioplasty ■ thrombosis ■ platelets

The PLATelet inhibition and patient Outcomes (PLATO) study demonstrated that, in comparison with clopidogrel, the reversibly binding oral $P2Y_{12}$ receptor antagonist ticagrelor reduced the 12-month risk of death resulting from vascular causes, myocardial infarction (MI), or stroke in a spectrum of both non–ST-elevation acute coronary syndromes (non-ST-E ACS) as well as ST-E ACS patients intended to undergo primary percutaneous coronary intervention (PCI).[1] A prespecified analysis of the ST-elevation (ST-E) PLATO cohort patients subsequently confirmed that the effects of ticagrelor were consistent with the results in the overall trial; it was noted, however, that this ST-E cohort was somewhat heterogeneous, and that the majority of clinical benefit was obtained during the long term.[2,3]

Editorial see p 471
Clinical Perspective on p 521

Given that the window of randomization for ST-E patients in PLATO was temporally broad, ie, within 24 hours of

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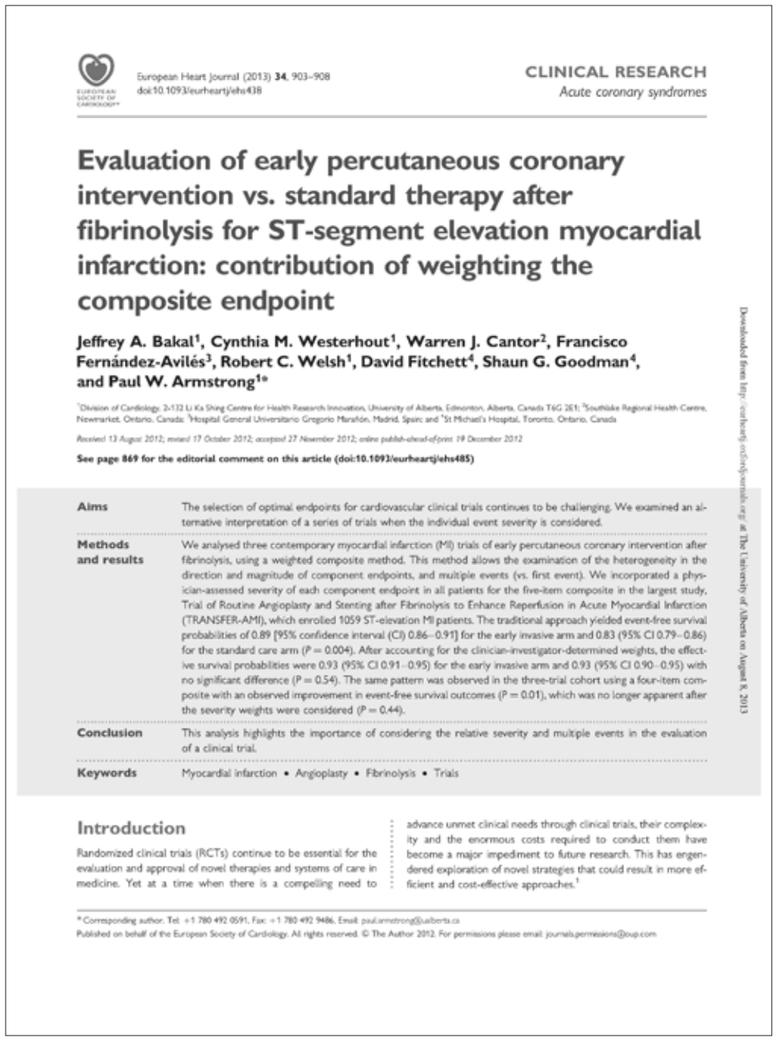
From the University of Alberta, Edmonton, Canada (P.W.A., H.S., Y.F., C.M.W.); INSERM U-698, Assistance Publique-Hôpitaux de Paris, and Université Paris-Diderot, Paris, France (G.S.); Uppsala University Hospital, Uppsala, Sweden (S.K.H.); University of Sheffield, Sheffield, United Kingdom (R.F.S.); AstraZeneca, Wilmington, MA (J.H.); University of Heidelberg, Heidelberg, Germany (H.K.); Copenhagen University Hospital, Copenhagen, Denmark (P.C.); Duke Clinical Research Institute, Durham, NC (R.A.H.); Uppsala Clinical Research Center, Uppsala, Sweden (L.W.)
The online-only Data Supplement is available with this article at http://circ.ahajournals.org/lookup/suppl/doi:10.1161/CIRCULATIONAHA.111.047530/-/DC1
Correspondence to Paul W. Armstrong, MD, 2-51 Medical Sciences Building, University of Alberta, Edmonton, AB T6G 2H7, Canada. E-mail paul.armstrong@ualberta.ca

Circulation is available at http://circ.ahajournals.org **DOI: 10.1161/CIRCULATIONAHA.111.047530**

FEATURED PUBLICATIONS

For a long time our approach to assessing outcomes in clinical trials has involved measuring different outcomes such as mortality, heart attack, heart failure and shock and then adding them up and reporting the total event rate without reference to the relative importance. In this study by Bakal and coworkers which involved a collaboration of our newest faculty member Shaun Goodman, the importance of considering the relative severity of different endpoints and how this in turn led to a new perspective on the outcome of a clinical trial.. This research adds genuine value to the way future trials should be analysed and thereby provides more meaningful and cost efficient results.



European Heart Journal (2013) **34**, 903–908
doi:10.1093/eurheartj/ehs438

CLINICAL RESEARCH
Acute coronary syndromes

Evaluation of early percutaneous coronary intervention vs. standard therapy after fibrinolysis for ST-segment elevation myocardial infarction: contribution of weighting the composite endpoint

Jeffrey A. Bakal[1], Cynthia M. Westerhout[1], Warren J. Cantor[2], Francisco Fernández-Avilés[3], Robert C. Welsh[1], David Fitchett[4], Shaun G. Goodman[4], and Paul W. Armstrong[1]*

[1]Division of Cardiology, 2-132 Li Ka Shing Centre for Health Research Innovation, University of Alberta, Edmonton, Alberta, Canada T6G 2E1; [2]Southlake Regional Health Centre, Newmarket, Ontario, Canada; [3]Hospital General Universitario Gregorio Marañón, Madrid, Spain; and [4]St Michael's Hospital, Toronto, Ontario, Canada

Received 13 August 2012; *revised* 17 October 2012; *accepted* 27 November 2012; *online publish-ahead-of-print* 19 December 2012

See page 869 for the editorial comment on this article (doi:10.1093/eurheartj/ehs485)

Aims The selection of optimal endpoints for cardiovascular clinical trials continues to be challenging. We examined an alternative interpretation of a series of trials when the individual event severity is considered.

Methods and results We analysed three contemporary myocardial infarction (MI) trials of early percutaneous coronary intervention after fibrinolysis, using a weighted composite method. This method allows the examination of the heterogeneity in the direction and magnitude of component endpoints, and multiple events (vs. first event). We incorporated a physician-assessed severity of each component endpoint in all patients for the five-item composite in the largest study, Trial of Routine Angioplasty and Stenting after Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction (TRANSFER-AMI), which enrolled 1059 ST-elevation MI patients. The traditional approach yielded event-free survival probabilities of 0.89 [95% confidence interval (CI) 0.86–0.91] for the early invasive arm and 0.83 (95% CI 0.79–0.86) for the standard care arm ($P = 0.004$). After accounting for the clinician-investigator-determined weights, the effective survival probabilities were 0.93 (95% CI 0.91–0.95) for the early invasive arm and 0.93 (95% CI 0.90–0.95) with no significant difference ($P = 0.54$). The same pattern was observed in the three-trial cohort using a four-item composite with an observed improvement in event-free survival outcomes ($P = 0.01$), which was no longer apparent after the severity weights were considered ($P = 0.44$).

Conclusion This analysis highlights the importance of considering the relative severity and multiple events in the evaluation of a clinical trial.

Keywords Myocardial infarction • Angioplasty • Fibrinolysis • Trials

Introduction

Randomized clinical trials (RCTs) continue to be essential for the evaluation and approval of novel therapies and systems of care in medicine. Yet at a time when there is a compelling need to advance unmet clinical needs through clinical trials, their complexity and the enormous costs required to conduct them have become a major impediment to future research. This has engendered exploration of novel strategies that could result in more efficient and cost-effective approaches.[1]

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FEATURED PUBLICATIONS

For a long time, the assessment of heart failure in clinical trials has been challenging. This has been especially true as it relates to objectively evaluating the cardinal symptom of heart failure, namely shortness of breath or dyspnea. In this study, Ezekowitz was able to capitalize on a clinical trial of acute heart failure by undertaking a careful substudy in over 400 patients from 37 participating institutions in Canada and the United States. By carefully monitoring characterizing changes in shortness of breath with spirometry (an established measurement of lung and airway function used in patients with respiratory disease), he was able to establish the clinical utility of this method thereby setting an important new platform for future studies of acute heart failure.

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Heart Failure

Assessment of Dyspnea in Acute Decompensated Heart Failure

Insights from ASCEND-HF (Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure) on the Contributions of Peak Expiratory Flow

Justin A. Ezekowitz, MBBCH, MSC,* Adrian F. Hernandez, MD,‡ Christopher M. O'Connor, MD,‡ Randall C. Starling, MD,§ Guy Proulx, MD,† Mason H. Weiss, MD,‖ Jeffrey A. Bakal, PHD,* Robert M. Califf, MD,‡ John J. V. McMurray, MD,¶ Paul W. Armstrong, MD*

Edmonton, Alberta, and Quebec City, Quebec, Canada; Durham, North Carolina; Cleveland, Ohio; Inglewood, California; and Glasgow, United Kingdom

Objectives This study hypothesized that peak expiratory flow rate (PEFR) would increase with acute heart failure (AHF) treatment over the first 24 h, related to a Dyspnea Index (DI) change and treatment effect.

Background Dyspnea is a key symptom and clinical trial endpoint in AHF, yet objective assessment is lacking.

Methods In a clinical trial substudy, 421 patients (37 sites) underwent PEFR testing at baseline, 1, 6, and 24 h after randomization to nesiritide or placebo. DI (by Likert scale) was collected at hours 6 and 24.

Results Patients were median age 70 years, and 34% were female; no significant differences between nesiritide or placebo patients existed. Median baseline PEFR was 225 l/min (interquartile range [IQR]: 160 to 300 l/min) and increased to 230 l/min (2.2% increase; IQR: 170 to 315 l/min) by hour 1, 250 l/min (11.1% increase; IQR: 180 to 340 l/min) by hour 6, and 273 l/min (21.3% increase; IQR: 200 to 360 l/min) by 24 h (all $p < 0.001$). The 24-h PEFR change related to moderate or marked dyspnea improvement by DI (adjusted odds ratio: 1.04 for each 10 l/min improvement [95% confidence interval (CI): 1.07 to 1.10]; $p < 0.01$). A model incorporating time and treatment over 24 h showed greater PEFR improvement after nesiritide compared with placebo ($p = 0.048$).

Conclusions PEFR increases over the first 24 h in AHF and could serve as an AHF endpoint. Nesiritide had a greater effect than placebo on PEFR, and this predicted patients with moderate/marked improvement in dyspnea, thereby providing an objective metric for assessing AHF. (Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure [ASCEND-HF]; NCT00475852) (J Am Coll Cardiol 2012;59:1441–8) © 2012 by the American College of Cardiology Foundation

Shortness of breath is 1 of the principal presenting symptoms of patients with acute decompensated heart failure (AHF) (1), and relief of this dyspnea is a commonly employed endpoint for clinical care and randomized clinical trials of AHF therapy (2). Yet assessment of dyspnea is subjective, difficult to validate, and the relationship to objective measures is unknown (1,3,4). Despite this shortcoming, 3 major clinical trials in AHF (supported by the European Medicines Agency and U.S. Food and Drug Administration) have used dyspnea as a primary endpoint, given the importance assigned to this symptom (5–7).

See page 1449

From the *University of Alberta, Edmonton, Alberta, Canada; †Laval University, Quebec City, Quebec, Canada; ‡Duke Clinical Research Institute, Durham, North Carolina; §Cleveland Clinic, Cleveland, Ohio; ‖Centinela Freeman Regional Medical Center, Inglewood, California; and the ¶University of Glasgow, Glasgow, United Kingdom. Funding was provided by Janssen Inc. to support this substudy, and by Johnson and Johnson for the overall ASCEND-HF trial. Drs. Ezekowitz, McMurray, and Armstrong have received research grants from Scios Inc., Ortho-Biotech, Johnson & Johnson, and Janssen Ortho Inc. in conjunction with Duke Clinical Research Institute. Dr. Hernandez has received research support from Johnson & Johnson, Proventys, and Amylin, as well as honoraria from Amgen and Corthera. Dr. O'Connor has received research funding from JNJ. Dr. Califf has received research grants from Johnson & Johnson; and consulting fees from Johnson & Johnson. All other authors have stated that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received August 11, 2011; revised manuscript received November 26, 2011, accepted November 29, 2011.

FEATURED PUBLICATIONS

Kaul and colleagues have provided interesting new insights into the differences between men and women presenting with heart attack. It appears as though the baseline electrocardiogram gives a better indication of the evolving nature of heart attack in women than men. Given that symptom of heart attack in women tend to be less straight forward than those of men, this new data provides physicians with a new marker to better predict clinical outcomes of death, shock and heart failure which may assist in the choice and timeliness of lifesaving reperfusion therapy.

Relative Prognostic Value of Baseline Q Wave and Time from Symptom Onset Among Men and Women With ST-Elevation Myocardial Infarction Undergoing Percutaneous Coronary Intervention

Padma Kaul, PhD[a,*], Yuling Fu, MD[a], Cynthia M. Westerhout, PhD[a], Christopher B. Granger, MD[b], and Paul W. Armstrong, MD[a]

Q waves have been shown to be a stronger prognostic marker than time from symptom onset to percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction. We examined whether the relative importance of these 2 measurements is modulated by patient gender. Q waves in the area of ST-segment elevation on baseline electrocardiogram were evaluated at a central core laboratory in 4,530 patients with ST-segment elevation myocardial infarction (3,468 men and 1,062 women) without previous infarction and who underwent PCI in the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX-AMI) trial. Women were older and had higher rates of diabetes, hypertension, Killip class >1, and lower creatinine clearance compared to men. Time from symptom onset to PCI >3 hours was associated with a trend toward worse 90-day mortality (adjusted hazard ratio 1.5, 95% confidence interval 0.9 to 2.2) in men but not in women (0.8, 0.5 to 1.4). In contrast, presence of Q waves on baseline electrocardiogram was associated with significantly higher 90-day mortality in men (adjusted hazard ratio 1.7, 95% confidence interval 1.0 to 2.7) and women (2.3, 1.2 to 4.2). In conclusion, in this gender-specific analysis, baseline Q wave was found be a better marker of risk of 90-day mortality than time from symptom onset to PCI, overall, and especially in women. (Am J Cardiol 2012;110:1555–1560)

Assessing time of symptom onset may be more complicated for women with ST-segment elevation myocardial infarction (STEMI) given their higher likelihood of developing atypical and prodromal symptoms.[1,2] Therefore, a more objective measurement of the evolution of the infarct would be particularly useful in assessing risk and informing treatment decisions in these patients. One such measurement is the presence of Q wave on baseline electrocardiogram (ECG).[3–6] We extended our previous analysis in the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX-AMI) trial to examine the relative prognostic significance of time from symptom onset to percutaneous coronary intervention (PCI) and presence of Q waves on baseline ECG on 90-day outcomes of death and the composite of death/congestive heart failure (CHF)/cardiogenic shock.

Methods

The APEX-AMI trial was a multicenter, randomized, double-blinded, placebo-controlled trial of intravenous pexelizumab administered immediately before primary PCI for patients with electrocardiographically high-risk STEMI.[7] Study end points were 90-day mortality and the composite of death, centrally adjudicated CHF, or cardiogenic shock at 90 days. Because no significant difference was observed in the primary end point between the treatment and placebo arms, the 2 arms were pooled for the present analysis.

In total 5,745 patients were enrolled in the APEX-AMI trial according to the following specific entry criteria described previously: briefly, patients were ≥18 years old, with symptom onset <6 hours, and had an ECG indicative of acute STEMI that fulfilled any of the following 3 criteria: ≥2-mm STE in 2 anterior or lateral leads, or ≥2-mm STE in 2 inferior leads coupled with ST-segment depression in 2 contiguous anterior leads for a total ST-segment deviation of ≥8 mm, or new left bundle branch block with ≥1-mm concordant STE. For the present analysis, patients with previous MI were excluded to remove any potential confounding of Q-wave ascertainment during the acute index event.

All baseline ECGs were evaluated centrally at electrocardiographic core laboratories (Canadian VIGOUR Centre, Edmonton, Alberta, Canada; Duke Clinical Research Institute, Durham, North Carolina) without knowledge of treatment assignment and outcomes. Q wave or Q-wave equivalent was determined on baseline ECG using the Selvester QRS screening criteria: Q wave ≥30 ms in lead aVF (inferior), ≥40 ms in leads I and aVL (lateral), ≥40 ms in ≥2 of leads V_4, V_5, and/or V6 (apical), or any Q wave in lead V_2 (anterior).[8] Further, Q-wave equivalents were defined as

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FEATURED PUBLICATIONS

Finlay McAlister led this key strategic effort examining the impact of the Alberta Cardiac Access (ACA) initiative which was implemented in early 2008. This program, aimed at enhancing access to specialized heart failure clinics after a heart failure initiative using de-identified yet sophisticated linking of data sets from a variety of sources within Alberta over a 10 year period ending in December 2009 and encompassing over 45,000 hospitalizations for heart failure. Importantly, they found that access to heart failure management programs substantially improved during this interval. Moreover this access was associated with improvements in 30-day post-discharge mortality and readmission rates that had been climbing during the decade prior to the initiation of the program. Finally and especially germane in the health care resource constrained environment where we function, they identified that the benefits accruing to the patients had no negative impact on health care resource use.

Changes in Heart Failure Outcomes After a Province-Wide Change in Health Service Provision

A Natural Experiment in Alberta, Canada

Finlay A. McAlister, MD, MSc; Jeffrey A. Bakal, PhD; Padma Kaul, PhD; Hude Quan, PhD; Robyn Blackadar, MBA; David Johnstone, MD; Justin Ezekowitz, MB, BCh, MSc

Background—The Alberta Cardiac Access (ACA) initiative was implemented in the spring of 2008 to increase access to specialized heart failure (HF) clinics after hospital discharge.
Methods and Results—We identified all adults hospitalized with a most responsible diagnosis of HF between April 1999 and December 2009. We randomly selected 1 episode of care per patient and evaluated outcomes using interrupted time series: the a priori specified primary outcome was all-cause readmission or death in the first 30 days postdischarge. Between 1999 and 2009, median length of stay increased from 8 days to 10 days (P<0.001), and 30-day mortality increased from 9.1% to 11.5% (P<0.001) in the 37 891 HF hospitalizations we examined. However, these temporal changes were attributable to the increasing comorbidity burden over time: the adjusted Risk Ratio for 30-day mortality in 2009 versus 1999 was 0.99, 95% confidence interval, 0.86 to 1.15. After adjusting for secular trends, the ACA initiative was associated with changes in 30-day postdischarge mortality or readmission rates (which were increasing 0.3% per month [0.2%–0.3%] pre-ACA and decreased 1.4% per month [0.3%–2.5%] in the 18 months post-ACA; P=0.008). After roll out of the ACA initiative, patients discharged from vanguard regions (those that had specialized HF clinics) exhibited lower 30-day postdischarge death/readmission rates than those discharged from other areas of the province (18.6% versus 22.2%, adjusted odds ratio 0.83, 95% confidence interval, 0.75–0.93).
Conclusions—An initiative which increased specialized HF clinic access was associated with a statistically significant improvement in 30-day postdischarge mortality/readmission rates. (***Circ Heart Fail***. **2013;6:76-82.**)

Key Words: disease management epidemiology ■ heart failure ■ outcomes

Despite many advances in diagnosis and therapy during the past 2 decades, heart failure (HF) remains the most common cause of hospitalizations and readmissions in North America and Europe.[1–3] Although traditional strategies of knowledge dissemination have minimal effects on physician-prescribing habits in HF,[4] involvement of specially trained multidisciplinary teams or specialists in the care of patients with HF has been shown to improve the use of proven efficacious therapies and clinical outcomes.[5,6] However, there is still debate about whether wider implementation of specialized HF management programs will yield similar benefits as in randomized trials or whether there will be unanticipated consequences (such as increased hospitalizations or health resource use in other areas because of closer patient follow-up). Unfortunately, only a minority of patients, even in publicly funded health care systems with universal access like Canada, have access to these resources.

Clinical Perspective on p 82

Between April and May 2008, the Alberta provincial government initiated the Alberta Cardiac Access (ACA; see www.cardiacaccess.ab.ca for full details) initiative to improve access to cardiac care. One area of focus was to enhance access to specialized HF clinics for patients recently discharged after a HF hospitalization. The ACA initiative funded (1) training preceptorships for family physicians, pharmacists, and nurses in HF, (2) the expansion of capacity within the 6 specialized HF clinics, already existing pre-2008, and (3) the establishment of 5 new HF clinics in different regions of the province. Each of the specialized HF clinics implemented or expanded as a result of the ACA initiative were designed as high-intensity clinics that scored maximum points on the HF Disease Management Scoring Instrument[7] including: targeted both patients and caregivers, provision of education,

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The online-only Data Supplement is available at http://circheartfailure.ahajournals.org/lookup/suppl/doi:10.1161/CIRCHEARTFAILURE.112.971119/-/DC1.
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FEATURED PUBLICATIONS

Welsh reported on this study he led, in collaboration with colleagues from the Duke Clinical Research Institute and elsewhere, examining a novel platelet inhibitor called elinogrel. Whereas these P2Y12 agents have been available in oral form, few have been formulated for intravenous use and clinically evaluated. Given the limitations of current oral agents, this study demonstrated that elinogrel had an acceptable safety and tolerability profile as compared with conventional clopidogrel in patients undergoing percutaneous coronary intervention. This new work supports further development of this agent for the treatment of patients with ischemic heart disease.

Original Article

A Randomized, Double-Blind, Active-Controlled Phase 2 Trial to Evaluate a Novel Selective and Reversible Intravenous and Oral $P2Y_{12}$ Inhibitor Elinogrel Versus Clopidogrel in Patients Undergoing Nonurgent Percutaneous Coronary Intervention

The INNOVATE-PCI Trial

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Background—We evaluated the safety, efficacy, and tolerability of elinogrel, a competitive, reversible intravenous and oral $P2Y_{12}$ inhibitor that does not require metabolic activation, in patients undergoing nonurgent percutaneous coronary intervention.
Methods and Results—In a randomized, double-blind, dose-ranging phase 2b trial, 652 patients received either 300 or 600 mg of clopidogrel pre-percutaneous coronary intervention followed by 75 mg daily or 80 or 120 mg of IV elinogrel followed by 50, 100, or 150 mg oral elinogrel twice daily. Numerous exploratory safety and efficacy end points were assessed and, as such, had no prespecified primary end point, and the study was not powered to conclusively evaluate its objectives. Thrombolysis in myocardial infarction combined bleeding was increased with elinogrel (hazard ratio, 1.98; 95% confidence interval, 1.10 to 3.57), related largely to increased bleeding requiring medical attention (elinogrel 47/408 [11.5%] versus clopidogrel 13/208 [6.3%]) and occurring primarily at the percutaneous coronary intervention access site. Efficacy end points and postprocedure cardiac enzyme were similar, but there was a nonsignificant higher frequency of periprocedural myocardial infarctions in the elinogrel arms (OR, 1.59; 95% confidence interval, 0.79 to 3.48). There was an increased incidence of dyspnea (elinogrel 50/408 [12.3%] versus clopidogrel 8/208 [3.8%]) and transaminase elevation (alanine transferase/aspartate transferase >3× the upper limit of normal; elinogrel 18/408 [4.4%] versus clopidogrel 2/208 [1.0%]) in the elinogrel arms, but there were no cases of heart block, bradycardia, hypotension, or liver failure.
Conclusions—In patients undergoing nonurgent percutaneous coronary intervention and in comparison with clopidogrel, intravenous and oral elinogrel therapy did not significantly increase thrombolysis in myocardial infarction major or minor bleeding, although bleeding requiring medical attention was more common. The significance of these findings will need to be more definitively determined in future Phase 3 studies.
Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00751231.
(*Circ Cardiovasc Interv*. 2012;5:336-346.)

Key Words: chronic ischemic heart disease ■ catheter-based coronary interventions ■ cardiovascular pharmacology ■ antiplatelets ■ platelet function inhibitors

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Antiplatelet therapy is a fundamental aspect of the management of ischemic heart disease. The addition of a thienopyridine to aspirin is recommended by practice guidelines to reduce the risk of short- and long-term ischemic events in patients with acute coronary syndrome and those undergoing percutaneous coronary intervention (PCI)[1–4]; however, despite the administration of dual antiplatelet therapy, adverse clinical events continue to accrue in high-risk patients.[5–7] The limitations

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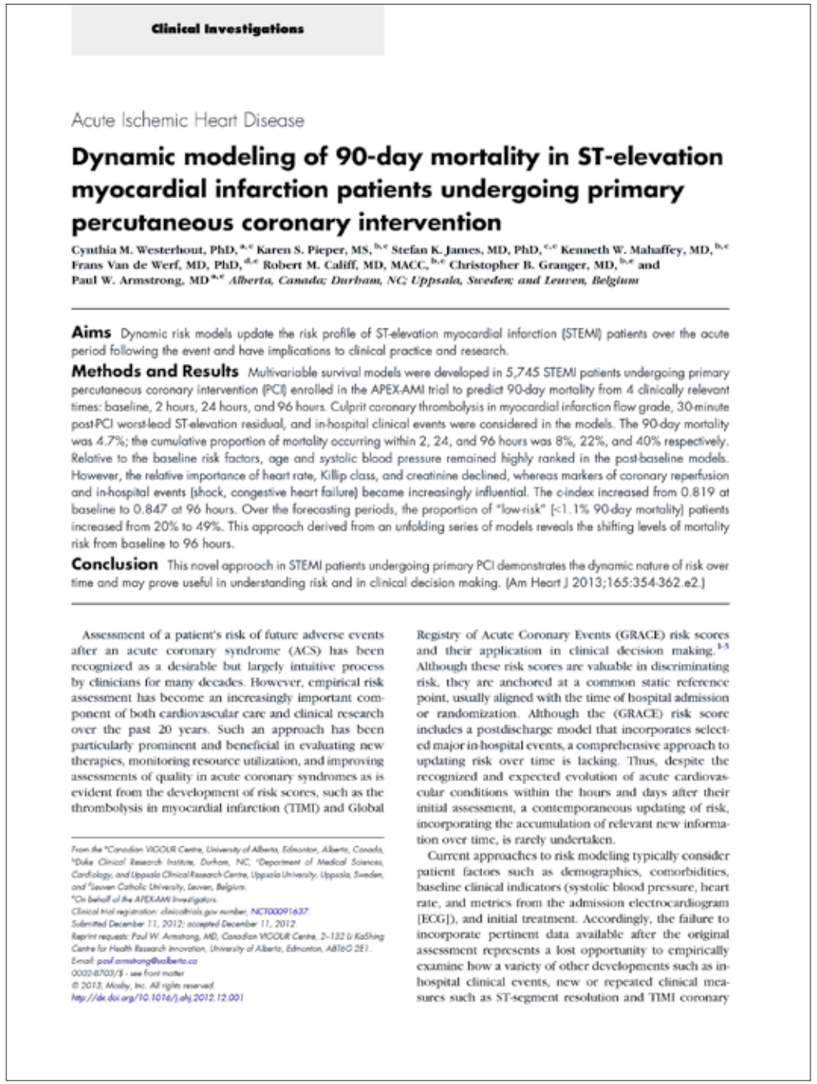
FEATURED PUBLICATIONS

Working with data acquired in over 5000 patients in the APEX-AMI trial, Westerhout and colleagues crafted a new approach to accessing risk in patients with ST- elevation myocardial infarction. Using multi-variable survival models and data acquired from 4 key time points (i.e. baseline, 2 hours, 24 hours and 96 hours after admission to hospital), she characterized the dynamic nature of risk over time thereby demonstrating not only the evolving nature of risk but assisting clinicians to be able to make more sensible clinical decisions .



Clinical Investigations

Acute Ischemic Heart Disease

Dynamic modeling of 90-day mortality in ST-elevation myocardial infarction patients undergoing primary percutaneous coronary intervention

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Aims Dynamic risk models update the risk profile of ST-elevation myocardial infarction [STEMI] patients over the acute period following the event and have implications to clinical practice and research.

Methods and Results Multivariable survival models were developed in 5,745 STEMI patients undergoing primary percutaneous coronary intervention (PCI) enrolled in the APEX-AMI trial to predict 90-day mortality from 4 clinically relevant times: baseline, 2 hours, 24 hours, and 96 hours. Culprit coronary thrombolysis in myocardial infarction flow grade, 30-minute post-PCI worst-lead ST-elevation residual, and in-hospital clinical events were considered in the models. The 90-day mortality was 4.7%; the cumulative proportion of mortality occurring within 2, 24, and 96 hours was 8%, 22%, and 40% respectively. Relative to the baseline risk factors, age and systolic blood pressure remained highly ranked in the post-baseline models. However, the relative importance of heart rate, Killip class, and creatinine declined, whereas markers of coronary reperfusion and in-hospital events (shock, congestive heart failure) became increasingly influential. The c-index increased from 0.819 at baseline to 0.847 at 96 hours. Over the forecasting periods, the proportion of "low-risk" [<1.1% 90-day mortality] patients increased from 20% to 49%. This approach derived from an unfolding series of models reveals the shifting levels of mortality risk from baseline to 96 hours.

Conclusion This novel approach in STEMI patients undergoing primary PCI demonstrates the dynamic nature of risk over time and may prove useful in understanding risk and in clinical decision making. (Am Heart J 2013;165:354-362.e2.)

Assessment of a patient's risk of future adverse events after an acute coronary syndrome (ACS) has been recognized as a desirable but largely intuitive process by clinicians for many decades. However, empirical risk assessment has become an increasingly important component of both cardiovascular care and clinical research over the past 20 years. Such an approach has been particularly prominent and beneficial in evaluating new therapies, monitoring resource utilization, and improving assessments of quality in acute coronary syndromes as is evident from the development of risk scores, such as the thrombolysis in myocardial infarction (TIMI) and Global Registry of Acute Coronary Events (GRACE) risk scores and their application in clinical decision making.[1-5] Although these risk scores are valuable in discriminating risk, they are anchored at a common static reference point, usually aligned with the time of hospital admission or randomization. Although the (GRACE) risk score includes a postdischarge model that incorporates selected major in-hospital events, a comprehensive approach to updating risk over time is lacking. Thus, despite the recognized and expected evolution of acute cardiovascular conditions within the hours and days after their initial assessment, a contemporaneous updating of risk, incorporating the accumulation of relevant new information over time, is rarely undertaken.

Current approaches to risk modeling typically consider patient factors such as demographics, comorbidities, baseline clinical indicators (systolic blood pressure, heart rate, and metrics from the admission electrocardiogram [ECG]), and initial treatment. Accordingly, the failure to incorporate pertinent data available after the original assessment represents a lost opportunity to empirically examine how a variety of other developments such as in-hospital clinical events, new or repeated clinical measures such as ST-segment resolution and TIMI coronary

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INTRODUCING NEW FACULTY

The Canadian VIGOUR Centre is proud to introduce to its faculty Shaun Goodman, MD. Based out of St. Michael's Hospital in Toronto, Ontario, Dr. Goodman has been a key partner and operational leader on several clinical trials managed by the CVC. In joining our faculty in 2012, he is the key to developing and implementing a brand new cross-Canada program for mentoring cardiovascular researchers. Dr. Goodman is committed to the knowledge transfer derived from clinical trials that lead to enhancements in quality of life and improved standards of care in cardiovascular disease. He has a pivotal role in fostering and inspiring the next generation of health researchers in Canada. Below, Dr. Goodman shares some responses to a recent interview, describing his interest, association and ongoing plans with the Canadian VIGOUR Centre.

Would you describe how you became involved with CVC or its faculty? I feel very privileged. I remember vividly the moment I met Dr. Armstrong. I was a first year cardiology resident on my very first day, and the small group of cardiology residents arrived at 0800 on Canada Day, July 1st many years ago! Now Dr. Armstrong wasn't even on-call, and pretty much everyone else in the country was taking the holiday off! However, as the great role model he is, he made it clear that he intended to invest his full time and expertise in us—the "next generation"—and we, in turn, had an obligation to learn and work hard to provide the best care possible to our patients. I worked extremely hard that year, but everywhere I turned, I saw Dr. Armstrong working even harder (and longer hours) than me (talk about leading by example!) I also started one of my first research projects with him that year and 23 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.

Dr. Paul Armstrong has been an outstanding mentor, colleague, and friend to me and I've 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 the University of Alberta and established the CVC. We've worked together on a number of ECG Core Laboratory-based studies led by the CVC, and in addition, Dr. Armstrong connected me with Dr. Rob Welsh, Padma Kaul, and Cynthia Westerhout many years ago and we've enjoyed working together on a variety of national and international collaborations. So when Dr. Armstrong offered the chance to become more formally and extensively involved in the CVC's many activities, I welcomed the opportunity to work even more closely with the CVC team.

What areas of clinical research interest you most? I have, and continue to be, extremely interested in the diagnosis, risk stratification, treatment, and prognosis of acute coronary syndromes. Beyond the acute, in-hospital management, I've also explored a number of strategies aimed at the secondary prevention of cardiovascular disease. In the last few years, in part because of my interest in antithrombotic drugs, I've also been engaged in research related to stroke prevention in atrial fibrillation. In the past few years, I've helped lead some studies in Canada that have looked at combinations and

permutations of “clot busting” and “anti-clotting” types of treatments.

I’m hoping that I can bring some experience in facilitating clinical trial-based research across Canada and internationally, including the provision of some leadership in important projects led by the CVC and in collaboration with our Duke Clinical Research Institute colleagues. One example is the ongoing EXSCEL trial of a novel, once-weekly therapy for patients with type 2 diabetes mellitus. I’m also excited about the recently initiated ODYSSEY Outcomes trial of a new twice-monthly cholesterol-lowering drug for patients recovering from a recent acute coronary syndrome that may provide additional benefit beyond the gold-standard statin treatment we currently employ. In addition to representing the CVC and serving as the National Leader, Dr. Armstrong enabled my joining the global Executive Steering Committee of the ODYSSEY trial.

I’ve recently taken on a more formal mentoring role at the University of Toronto as the Heart & Stroke Foundation of Ontario “Polo” Chair and I’m hopeful we can expand further upon the “V” for virtual in the acronym for VIGOUR (Virtual CoordInating Centre for Global COllaborative CardiovascUlar Research) and capitalize on the enthusiasm and skill sets these fine young researchers possess. Indeed, I hope we can strengthen the cross-country relationships the CVC has fostered for many years and develop some new ones by engaging the “next generation”.

What do you consider to be your most important contributions to improving patient care? Beyond our involvement in clinical research studies, we have a responsibility to translate evidence-based strategies into routine clinical practice. I’ve learned it isn’t “enough” to perform a trial and then present and publish the results—we need to get whatever new information is important out to our peers in a manner that “fits” with their reality. This is especially critical if the research results involve a change from what we were taught in medical school or learned during our post-graduate training. In addition, there are often differences between patients and how they are cared for as part of a research project when compared to the “real” world. We therefore need to work with our peers across the country (and the rest of the world) to integrate whatever we’ve learned in an unbiased manner and in a way that is applicable and generalizable to the front-line health care providers. So some of my most important contributions to improving patient care have included some of the knowledge-translation programs I’ve been involved with the past few years where we get health care providers to measure and take stock of what they are doing, offer up some practical tips as to how implement new knowledge, and provide constructive feedback. We can do fantastic research but unless it gets translated into clinical practice, we’re not much further ahead in improving patient care.

Beyond our involvement in clinical research studies, we have a responsibility to translate evidence-based strategies into routine clinical practice.

“An ARO (Academic Research Organization) in my view possesses scholarly values of inquiry and truth, shares knowledge in an ethical framework, is dedicated to enhancing public health, and values discovery, novel approaches and methodologies over profit. It strives to achieve the operational efficiency of a contract research organization and is directly linked to patient care and the bedside. It is almost always embedded in a University, functions on a not-for-profit basis, is committed to the education of the next generation of professionals and fulfills its contract with society by emphasizing the public good.”

— Paul W. Armstrong, MD

THE NEXT GENERATION OF HEALTH RESEARCHERS

Neda Dianati Maleki joined the CVC in March 2012 on a part time basis, as she continues her medical studies as a graduate student at the University of Alberta, and has worked with the CVC primarily in the capacity of the ECG Core Laboratory on the STREAM clinical trial and the PROACT projects. We are delighted that the manuscript (of which she is lead author) has recently been accepted by the AHA for the STREAM trial. Neda has taken a lead role in the interpretation of ECG's on these projects, and in collaboration with the ECG Core Laboratory team, under the guidance of Dr. Armstrong, has made significant findings that have been recognized throughout the international research community. Neda shares her experiences and insights as a mentee with the CVC.

Why did you choose to work at CVC? As a medical graduate and a graduate student in clinical epidemiology, I was seeking an opportunity to develop my research skills through hands-on experience and to contribute in clinical research in the field of Cardiology under the guidance of experienced academics. I was also trying to build a strong resume to pursue my clinical career goals. I found CVC the best match to my needs.

CVC has a dynamic and vibrant academic environment. At CVC, experts from different disciplines are brought together to combine their unique perspectives and generate new research ideas. From my perspective, as a graduate student, this creates an ideal environment that facilitates interactions between trainees and worldclass physician-scientists. As a student, you will gain experience in conducting clinical research at different levels. There is a strong spirit of cooperation at CVC and help and guidance is always provided to you. I personally have had one of the most valuable learning opportunities in CVC.

What did you learn during your time with CVC? Do you have any experiences based on your collaboration with CVC you would like to share? At CVC I was exposed to the excitement and enthusiasm of a research career. I had the chance to expand my knowledge and research skills into a range of fields including pathophysiology of cardiovascular diseases, the latest treatment strategies for STEMI, designing and conducting clinical trials, etc. Moreover, I was able to improve my understanding of the principles of biostatistics and to apply my theoretical knowledge, gained through graduate courses at U of A, in various projects. The experience provided me with excellent preparation for my application to residency programs in internal medicine.

What was most satisfying about your CVC mentorship experience? I enjoyed multidisciplinary research training at CVC under the supervision of dedicated mentors. Above all I had the pleasure and the honor to meet and work with Professor Paul W. Armstrong; an outstanding mentor to whom I owe a profound debt of gratitude for the guidance and insights he offered to me, and an inspiring speaker who influenced my thinking, he helped me to develop my critical thinking skills. I am, and will always be, deeply grateful for this invaluable experience at CVC.

Would you tell us about some significant advances that have resulted from your time at CVC? As a result of all the support, encouragement and advice I received from Dr. Armstrong, I was able to submit a successful application to a graduate medical training program in internal medicine and I will start my residency program in July 2013. Once again I am very thankful to him and I wish to continue my collaboration with CVC in future. I would like to acknowledge all the great people at CVC from with whom I have worked and thank them for the opportunity to learn together as we work collaboratively in advancing cardiovascular research to better the quality of life, and outcomes for those suffering from cardiovascular disease.

THE YEAR IN REVIEW

“We can chart our future clearly and wisely only when we know the path which has led to the present.”

— Adlai E. Stevenson

FACULTY

Our CVC Faculty are internationally recognized as Thought Leaders in their respective areas of interest. They represent a unique and dynamic integration of clinical research. The approach begins by addressing unmet clinical needs through conducting rigorous clinical investigation and clinical trials of novel diagnostic and therapeutic interventions in selected areas of cardiovascular medicine. It extends from that pivot to the knowledge gained through detailed registries of all patients in areas of particular interest and relevance to public health, namely Acute Coronary Syndromes and Heart Failure. Our group has been especially keen to explore better ways of analyzing the responses of patients to interventions by modeling their outcomes over time, taking account of the relative value patients put on differing outcomes and their implications for quality of life and health care costs. Finally we are well positioned to study health care outcomes at a population level for all Albertans to assess how well new advances are being applied and whether they are making a meaningful difference.

JUSTIN EZEKOWITZ, MB, BCH, MSc

- Associate Professor, Division of Cardiology, University of Alberta
- Director, Heart Function Clinic, Mazankowski Alberta Heart Institute
- Alberta Innovates - Health Solutions Population Health Investigator

Dr. Ezekowitz' research interests include:

- Testing the impact of drugs and processes of care for acute heart failure patients;
- Novel interventions for patients with chronic systolic and diastolic heart failure;
- The impact of comorbidities such as atrial fibrillation, anemia and hip fractures;
- Knowledge gaps for drugs and devices in heart failure.

SHAUN GOODMAN, MD, MSc

- 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; and,
- Primary and secondary prevention of cardiovascular disease.

PADMA KAUL, PhD

- Director, Outcomes Research, CVC
- Associate Professor, Department of Medicine, University of Alberta
- Adjunct Assistant Research Professor, Duke University Medical Center
- Adjunct Associate Professor, School of Public Health, University of Alberta
- Alberta Innovates – Health Solutions Population Health Investigator

Dr. Kaul's research interests include:

- International differences in practice patterns and outcomes;
- Sex differences in treatment and outcomes of cardiovascular disease;
- Issues related to access and delivery of care at a population level; and
- Health economics.

FINLAY A. MCALISTER, MD, MSc

- Professor of Medicine, University of Alberta
- Director, Patient Health Outcomes Research and Clinical Effectiveness Institute, University of Alberta
- Senior Health Scholar, Alberta Innovates - Health Solutions (2010 - 2017)
- Capital Health Chair in Cardiovascular Health Outcomes
- Chair, Outcomes Research Task Force, Canadian Hypertension Education Program
- Past-President, Canadian Society of Internal Medicine

Dr. McAlister's research interests include:

- Outcomes research in hypertension, heart failure, perioperative care, and coronary artery disease
- Clinical epidemiology methodology with a focus on evidence-based medicine and implementation of evidence at the bedside
- Methodology of trials and systematic reviews

ROBERT WELSH, MD

- Professor, Division of Cardiology, University of Alberta
- Interventional Cardiologist, Mazankowski Alberta Heart Institute
- Director, Adult Cardiac Catheterization and Interventional Cardiology program
- Co-Director, University of Alberta Chest Pain Program
- Co-chair of Vital Heart Response
- Co-chair of the Mazankowski TAVI program

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)

2012 PEER-REVIEWED PUBLICATIONS

	Title	Authors	Journal
	ACS: Non ST Elevation		
1	Treatment and outcomes of patients with suspected acute coronary syndromes in relation to initial diagnostic impressions (insights from the Canadian Global Registry of Acute Coronary Events [GRACE] and Canadian Registry of Acute Coronary Events [CANRACE]).	Bajaj RR, Goodman SG, Yan RT, Bagnall AJ, Gyenes G, Welsh RC, Eagle KA, Brieger D, Ramanathan K, Grondin FR, Yan AT; Canadian GRACE and CANRACE Investigators.	*Am J Cardiol. 2013 Jan 15;111(2):202-7*
2	Temporal patterns of lipid testing and statin therapy in acute coronary syndrome patients (from the Canadian GRACE Experience).	Elbarouni B, Banihashemi SB, Yan RT, Welsh RC, Kornder JM, Wong GC, Anderson FA, Spencer FA, Grondin FR, Goodman SG, Yan AT; Canadian Global Registry of Acute Coronary Events (GRACE/GRACE(2)) and Canadian Registry of Acute Coronary Events (CANRACE) Investigators.	*Am J Cardiol. 2012 May 15;109(10):1418-24.*
3	Recent temporal trends and geographic distribution of cardiac procedures in Alberta.	McMurtry MS, Southern DA, Lewin AM, Galbraith PD, Kaul P, Ghali WA, Knudtson ML, Graham MM.	*Can J Cardiol. 2013 Apr;29(4):460-5.*
4	Platelet function during extended prasugrel and clopidogrel therapy for patients with ACS treated without revascularization: the TRILOGY ACS platelet function substudy.	Gurbel PA, Erlinge D, Ohman EM, Neely B, Neely M, Goodman SG, Huber K, Chan MY, Cornel JH, Brown E, Zhou C, Jakubowski JA, White HD, Fox KA, Prabhakaran D, Armstrong PW, Tantry US, Roe MT; TRILOGY ACS Platelet Function Substudy Investigators.	*JAMA. 2012 Nov 7;308(17):1785-94.*
5	Prior smoking status, clinical outcomes, and the comparison of ticagrelor with clopidogrel in acute coronary syndromes-insights from the PLATelet inhibition and patient Outcomes (PLATO) trial.	Cornel JH, Becker RC, Goodman SG, Husted S, Katus H, Santoso A, Steg G, Storey RF, Vintila M, Sun JL, Horrow J, Wallentin L, Harrington R, James S.	*Am Heart J. 2012 Sep;164(3):334-342.e1.*
6	Association of global weather changes with acute coronary syndromes: gaining insights from clinical trials data.	Bakal JA, Ezekowitz JA, Westerhout CM, Boersma E, Armstrong PW.	*Int J Biometeorol. 2013 May;57(3):401-8.*
7	Road mapping ATLAS ACS 2: are we there yet?	Armstrong PW, Harrington RA.	*Eur Heart J. 2012 Oct;33(20):2510-2.*
8	Thrombin-receptor antagonist vorapaxar in acute coronary syndromes.	Tricoci P, Huang Z, Held C, Moliterno DJ, Armstrong PW, Van de Werf F, White HD, Aylward PE, Wallentin L, Chen E, Lokhnygina Y, Pei J, Leonardi S, Rorick TL, Kilian AM, Jennings LH, Ambrosio G, Bode C, Cequier A, Cornel JH, Diaz R, Erkan A, et al.	*N Engl J Med. 2012 Jan 5;366(1):20-33.*
9	Comparison of the prognosis of spontaneous and percutaneous coronary intervention-related myocardial infarction.	Leonardi S, Thomas L, Neely ML, Tricoci P, Lopes RD, White HD, Armstrong PW, Giugliano RP, Antman EM, Califf RM, Newby LK, Mahaffey KW.	*J Am Coll Cardiol. 2012 Dec 4;60(22):2296-304.*
10	Regional patterns of use of a medical management strategy for patients with non-ST-segment elevation acute coronary syndromes: insights from the EARLY ACS Trial.	Roe MT, White JA, Kaul P, Tricoci P, Lokhnygina Y, Miller CD, van't Hof AW, Montalescot G, James SK, Saucedo J, Ohman EM, Pollack CV Jr, Hochman JS, Armstrong PW, Giugliano RP, Harrington RA, Van de Werf F, Califf RM, Newby LK.	*Circ Cardiovasc Qual Outcomes. 2012 Mar 1;5(2):205-13.*
11	Trends in clinical trials of non-ST-segment elevation acute coronary syndromes over 15years.	Chan MY, Sun JL, Newby LK, Lokhnygina Y, White HD, Moliterno DJ, ThÃ©roux P, Ohman EM, Simoons ML, Mahaffey KW, Pieper KS, Giugliano RP, Armstrong PW, Califf RM, Van de Werf F, Harrington RA.	*Int J Cardiol. 2013 Jul 31;167(2):548-54.*
12	Age, treatment, and outcomes in high-risk non-ST-segment elevation acute coronary syndrome patients: Insights from the EARLY ACS trial.	Lopes RD, White JA, Tricoci P, White HD, Armstrong PW, Braunwald E, Giugliano RP, Harrington RA, Lewis BS, Brogan GX Jr, Gibson CM, Califf RM, Newby LK.	*Int J Cardiol. 2012 Jul 12.*
	ACS: ST Elevation MI		
13	Troponin I in acute decompensated heart failure: insights from the ASCEND-HF study.	Felker GM, Hasselblad V, Tang WH, Hernandez AF, Armstrong PW, Fonarow GC, Voors AA, Metra M, McMurray JJ, Butler J, Heizer GM, Dickstein K, Massie BM, Atar D, Troughton RW, Anker SD, Califf RM, Starling RC, O'Connor CM.	*Eur J Heart Fail. 2012 Nov;14(11):1257-64.*
14	Reperfusion strategies and outcomes of ST-segment elevation myocardial infarction patients in Canada: observations from the Global Registry of Acute Coronary Events (GRACE) and the Canadian Registry of Acute Coronary Events (CANRACE).	Czarnecki A, Welsh RC, Yan RT, DeYoung JP, Gallo R, Rose B, Grondin FR, Kornder JM, Wong GC, Fox KA, Gore JM, Goodman SG, Yan AT; Global Registry of Acute Coronary Events (GRACE/GRACE2); Canadian Registry of Coronary Events (CANRACE) Investigators.	*Can J Cardiol. 2012 Jan-Feb;28(1):40-7.*
15	International variation in and factors associated with hospital readmission after myocardial infarction.	Kociol RD, Lopes RD, Clare R, Thomas L, Mehta RH, Kaul P, Pieper KS, Hochman JS, Weaver WD, Armstrong PW, Granger CB, Patel MR.	*JAMA. 2012 Jan 4;307(1):66-74.*
16	Aborted myocardial infarction after primary percutaneous coronary intervention: magnetic resonance imaging insights from the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX-AMI) trial.	Patel MR, Westerhout CM, Granger CB, Brener SJ, Fu Y, Siha H, Kim RJ, Armstrong PW.	*Am Heart J. 2013 Feb;165(2):226-33.*
17	Third universal definition of myocardial infarction.	Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD; Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction, Katus HA, Lindahl B, Morrow DA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, et al.	*Circulation. 2012 Oct 16;126(16):2020-35.*

2012 PEER-REVIEWED PUBLICATIONS

	Title	Authors	Journal
18	Serious infection after acute myocardial infarction: incidence, clinical features, and outcomes.	Truffa AA, Granger CB, White KR, Newby LK, Mehta RH, Hochman JS, Patel MR, Pieper KS, Al-Khalidi HR, Armstrong PW, Lopes RD.	*JACC Cardiovasc Interv. 2012 Jul;5(7):769-76.*
19	Impact of weighted composite compared to traditional composite endpoints for the design of randomized controlled trials.	Bakal JA, Westerhout CM, Armstrong PW.	*Stat Methods Med Res. 2012 Jan 24.*
20	Computer-assisted paramedic electrocardiogram interpretation with remote physician over-read: the future of prehospital STEMI care?	Welsh RC.	*Can J Cardiol. 2012 Jul-Aug;28(4):408-10.*
21	Contemporary pharmacological reperfusion in ST elevation myocardial infarction.	Welsh RC, Armstrong PW.	*Curr Opin Cardiol. 2012 Jul;27(4):340-6.*
22	Anticoagulation after subcutaneous enoxaparin is time sensitive in STEMI patients treated with tenecteplase.	Welsh RC, Westerhout CM, Buller CE, O'Neill B, Gordon P, Armstrong PW.	*J Thromb Thrombolysis. 2012 Jul;34(1):126-31.*
23	Relative prognostic value of baseline Q wave and time from symptom onset among men and women with ST-elevation myocardial infarction undergoing percutaneous coronary intervention.	Kaul P, Fu Y, Westerhout CM, Granger CB, Armstrong PW.	*Am J Cardiol. 2012 Dec 1;110(11):1555-60.*
24	Baseline NT-proBNP and biomarkers of inflammation and necrosis in patients with ST-segment elevation myocardial infarction: insights from the APEX-AMI trial.	van Diepen S, Roe MT, Lopes RD, Stebbins A, James S, Newby LK, Moliterno DJ, Neumann FJ, Ezekowitz JA, Mahaffey KW, Hochman JS, Hamm CW, Armstrong PW, Theroux P, Granger CB.	*J Thromb Thrombolysis. 2012 Jul;34(1):106-13.*
25	Baseline Q waves as a prognostic modulator in patients with ST-segment elevation: insights from the PLATO trial.	Siha H, Das D, Fu Y, Zheng Y, Westerhout CM, Storey RF, James S, Wallentin L, Armstrong PW.	*CMAJ. 2012 Jul 10;184(10):1135-42.*
26	Pexelizumab fails to inhibit assembly of the terminal complement complex in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. Insight from a substudy of the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX-AMI) trial.	Martel C, Granger CB, Ghitescu M, Stebbins A, Fortier A, Armstrong PW, Bonnefoy A, Theroux P.	*Am Heart J. 2012 Jul;164(1):43-51.*
27	Transfer times and outcomes in patients with ST-segment-elevation myocardial infarction undergoing interhospital transfer for primary percutaneous coronary intervention: APEX-AMI insights.	van Diepen S, Widimsky P, Lopes RD, White KR, Weaver WD, Van de Werf F, Ardissino D, van't Hof AW, Armstrong PW, Granger CB.	*Circ Cardiovasc Qual Outcomes. 2012 Jul 1;5(4):437-44.*

	Title	Authors	Journal
28	Prediction of enzymatic infarct size in ST-segment elevation myocardial infarction.	Mills JS, Mahaffey KW, Lokhnygina Y, Nicolau JC, Ruzyllo W, Adams PX, Todaro TG, Armstrong PW, Granger CB; CARDINAL investigators.	*Coron Artery Dis. 2012 Mar;23(2):118-25.*
29	Comparison of incidence of bleeding and mortality of men versus women with ST-elevation myocardial infarction treated with fibrinolysis.	Mehta RH, Stebbins AS, Lopes RD, Califf RM, Pieper KS, Armstrong PW, Van de Werf F, Hochman JS, White HD, Topol EJ, Alexander JH, Granger CB.	*Am J Cardiol. 2012 Feb 1;109(3):320-6.*
30	ST-elevation acute coronary syndromes in the Platelet Inhibition and Patient Outcomes (PLATO) trial: insights from the ECG substudy.	Armstrong PW, Siha H, Fu Y, Westerhout CM, Steg PG, James SK, Storey RF, Horrow J, Katus H, Clemmensen P, Harrington RA, Wallentin L.	*Circulation. 2012 Jan 24;125(3):514-21.*
31	Pattern of liver enzyme elevations in acute ST-elevation myocardial infarction.	Lofthus DM, Stevens SR, Armstrong PW, Granger CB, Mahaffey KW.	*Coron Artery Dis. 2012 Jan;23(1):22-30.*
32	Evaluation of early percutaneous coronary intervention vs. standard therapy after fibrinolysis for ST-segment elevation myocardial infarction: contribution of weighting the composite endpoint.	Bakal JA, Westerhout CM, Cantor WJ, FernÃindez-AvilÃ©s F, Welsh RC, Fitchett D, Goodman SG, Armstrong PW.	*Eur Heart J. 2013 Mar;34(12):903-8.*
	Heart Failure		
33	Translational platelet research in patients with coronary artery disease: what are the major knowledge gaps?	Gurbel PA, Roe MT, Jakubowski JA, Shah S, Erlinge D, Goodman SG, Huber K, Chan MY, Cornel JH, Tantry US, Ohman EM.	*Thromb Haemost. 2012 Jul;108(1):12-20.*
34	Neither diabetes nor glucose-lowering drugs are associated with mortality after noncardiac surgery in patients with coronary artery disease or heart failure.	Hanninen M, McAlister FA, Bakal JA, van Diepen S, Ezekowitz JA.	*Can J Cardiol. 2013 Apr;29(4):423-8.*
35	Changes in heart failure outcomes after a province-wide change in health service provision a natural experiment in Alberta, Canada.	McAlister FA, Bakal JA, Kaul P, Quan H, Blackadar R, Johnstone D, Ezekowitz J.	*Circ Heart Fail. 2013 Jan;6(1):76-82.*
36	Predicting the risk of unplanned readmission or death within 30 days of discharge after a heart failure hospitalization.	Au AG, McAlister FA, Bakal JA, Ezekowitz J, Kaul P, van Walraven C.	*Am Heart J. 2012 Sep;164(3):365-72.*
37	Testosterone supplementation in heart failure: a meta-analysis.	Toma M, McAlister FA, Coglianese EE, Vidi V, Vasaiwala S, Bakal JA, Armstrong PW, Ezekowitz JA.	*Circ Heart Fail. 2012 May 1;5(3):315-21.*
38	Renal dysfunction in patients with heart failure with preserved versus reduced ejection fraction: impact of the new Chronic Kidney Disease-Epidemiology Collaboration Group formula.	McAlister FA, Ezekowitz J, Tarantini L, Squire I, Komajda M, Bayes-Genis A, Gotsman I, Whalley G, Earle N, Poppe KK, Doughty RN; Meta-analysis Global Group in Chronic Heart Failure (MAGGIC) Investigators.	*Circ Heart Fail. 2012 May 1;5(3):309-14.*

2012 PEER-REVIEWED PUBLICATIONS

	Title	Authors	Journal
39	ICDs, guidelines, and national registries: opportunities to enhance quality of patient care.	Singh JP, Ellenbogen KA, Desai NR, McAlister FA.	*Pacing Clin Electrophysiol. 2012 Mar;35(3):253-8.*
40	Acute heart failure: perspectives from a randomized trial and a simultaneous registry.	Ezekowitz JA, Hu J, Delgado D, Hernandez AF, Kaul P, Leader R, Proulx G, Virani S, White M, Zieroth S, O'Connor C, Westerhout CM, Armstrong PW.	*Circ Heart Fail. 2012 Nov;5(6):735-41.*
41	Association of proton pump inhibitor use on cardiovascular outcomes with clopidogrel and ticagrelor: insights from the platelet inhibition and patient outcomes trial.	Goodman SG, Clare R, Pieper KS, Nicolau JC, Storey RF, Cantor WJ, Mahaffey KW, Angiolillo DJ, Husted S, Cannon CP, James SK, Kilhamn J, Steg PG, Harrington RA, Wallentin L; Platelet Inhibition and Patient Outcomes Trial Investigators.	*Circulation. 2012 Feb 28;125(8):978-86.*
42	Predictors of early dyspnoea relief in acute heart failure and the association with 30-day outcomes: findings from ASCEND-HF.	Mentz RJ, Hernandez AF, Stebbins A, Ezekowitz JA, Felker GM, Heizer GM, Atar D, Teerlink JR, Califf RM, Massie BM, Hasselblad V, Starling RC, O'Connor CM, Ponikowski P.	*Eur J Heart Fail. 2013 Apr;15(4):456-64.*
43	The 2012 Canadian Cardiovascular Society heart failure management guidelines update: focus on acute and chronic heart failure.	McKelvie RS, Moe GW, Ezekowitz JA, Heckman GA, Costigan J, Ducharme A, Estrella-Holder E, Giannetti N, Grzeslo A, Harkness K, Howlett JG, Kouz S, Leblanc K, Mann E, Nigam A, O'Meara E, Rajda M, Steinhart B, Swiggum E, Le VV, Zieroth S, Arnold JM, et al.	*Can J Cardiol. 2013 Feb;29(2):168-81.*
44	Heart failure: can we define, assess, and treat diastolic heart failure?	Ezekowitz JA.	*Eur J Heart Fail. 2012 Jul;14(7):713-5.*
45	Assessment of dyspnea in acute decompensated heart failure: insights from ASCEND-HF (Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure) on the contributions of peak expiratory flow.	Ezekowitz JA, Hernandez AF, O'Connor CM, Starling RC, Proulx G, Weiss MH, Bakal JA, Califf RM, McMurray JJ, Armstrong PW.	*J Am Coll Cardiol. 2012 Apr 17;59(16):1441-8.*
46	Update on aldosterone antagonists use in heart failure with reduced left ventricular ejection fraction. Heart Failure Society of America Guidelines Committee.	Butler J, Ezekowitz JA, Collins SP, Givertz MM, Teerlink JR, Walsh MN, Albert NM, Westlake Canary CA, Carson PE, Colvin-Adams M, Fang JC, Hernandez AF, Hershberger RE, Katz SD, Rogers JG, Spertus JA, Stevenson WG, Sweitzer NK, Tang WH, Stough WG, Starling RC.	*J Card Fail. 2012 Apr;18(4):265-81.*

	Title	Authors	Journal
47	Heart failure is a clinically and densitometrically independent risk factor for osteoporotic fractures: population-based cohort study of 45,509 subjects.	Majumdar SR, Ezekowitz JA, Lix LM, Leslie WD.	*J Clin Endocrinol Metab. 2012 Apr;97(4):1179-86.*
48	Indications for cardiac resynchronization therapy: 2011 update from the Heart Failure Society of America Guideline Committee.	Stevenson WG, Hernandez AF, Carson PE, Fang JC, Katz SD, Spertus JA, Sweitzer NK, Tang WH, Albert NM, Butler J, Westlake Canary CA, Collins SP, Colvin-Adams M, Ezekowitz JA, Givertz MM, Hershberger RE, Rogers JG, Teerlink JR, Walsh MN, Stough WG, Starling RC; Heart Failure Society of America Guideline Committee.	*J Card Fail. 2012 Feb;18(2):94-106.*
	General Cardiovascular Disease		
49	A randomized, double-blind, active-controlled phase 2 trial to evaluate a novel selective and reversible intravenous and oral P2Y12 inhibitor elinogrel versus clopidogrel in patients undergoing nonurgent percutaneous coronary intervention: the INNOVATE-PCI trial.	Welsh RC, Rao SV, Zeymer U, Thompson VP, Huber K, Kochman J, McClure MW, Gretler DD, Bhatt DL, Gibson CM, Angiolillo DJ, Gurbel PA, Berdan LG, Paynter G, Leonardi S, Madan M, French WJ, Harrington RA; INNOVATE-PCI Investigators.	*Circ Cardiovasc Interv. 2012 Jun;5(3):336-46.*
50	Pharmacokinetic and pharmacodynamic effects of elinogrel: results of the platelet function substudy from the intravenous and oral administration of elinogrel to evaluate tolerability and efficacy in nonurgent percutaneous coronary intervention patients (INNOVATE-PCI) trial.	Angiolillo DJ, Welsh RC, Trenk D, Neumann FJ, Conley PB, McClure MW, Stephens G, Kochman J, Jennings LK, Gurbel PA, WÃjcik J, Dabrowski M, Saucedo JF, Stumpf J, Buerke M, Broderick S, Harrington RA, Rao SV.	*Circ Cardiovasc Interv. 2012 Jun;5(3):347-56.*
51	Thrombin-receptor antagonist vorapaxar in acute coronary syndromes.	Tricoci P, Huang Z, Held C, Moliterno DJ, Armstrong PW, Van de Werf F, White HD, Aylward PE, Wallentin L, Chen E, Lokhnygina Y, Pei J, Leonardi S, Rorick TL, Kilian AM, Jennings LH, Ambrosio G, Bode C, Cequier A, Cornel JH, Diaz R, Erkan A, et al.	*N Engl J Med. 2012 Jan 5;366(1):20-33.*
52	Efficacy and safety of apixaban compared with warfarin according to patient risk of stroke and of bleeding in atrial fibrillation: a secondary analysis of a randomised controlled trial.	Lopes RD, Al-Khatib SM, Wallentin L, Yang H, Ansell J, Bahit MC, De Caterina R, Dorian P, Easton JD, Erol C, Ezekowitz JA, Gersh BJ, Granger CB, Hohnloser SH, Horowitz J, Hylek EM, McMurray JJ, Mohan P, Vinereanu D, Alexander JH.	*Lancet. 2012 Nov 17;380(9855):1749-58.*

BEYOND 2000

In October 2012, CVC hosted our 18th annual ground breaking symposium New Concepts in Acute Coronary Syndromes: Beyond 2000 held in conjunction with the Canadian Cardiovascular Society and Congress and supported by unrestricted educational grants from Astra Zeneca and Eli Lilly. As has been our tradition with this symposium, we were pleased to have partnered with the Mazankowski Alberta Heart Institute, and University of Alberta in undertaking this venture which probes new avenues in acute coronary syndromes and also address the role of novel technologies amidst the brave new information age in which we work. Since all of us who practice cardiovascular medicine in Canada are tasked with ensuring that we make sensible choices and take into account the best allocation of limited resources while at the same time delivering high quality cardiovascular care, the symposium addressed all of these matters head on.

Our international symposium concluded with a future look at the opportunities in clinical research elaborated by Eric Peterson, the newly appointed Chief Executive Officer of the Duke Clinical Research Institute (DCRI). The DCRI remains an important continuing collaborative partner in our education and research initiatives. To ensure the high quality presentations and video dialogues with key speakers is preserved from this legacy event; we have established a web site: www.Beyond2000.org that is now available for your viewing under the "Continuing Conversation" banner. Assuredly, this was a memorable educational experience.

Sunday, October 28, 2012, 8:00 a.m. - 12:00 p.m.

PROGRAM DESCRIPTION

This program will be comprehensive and explore broad and novel concepts relating to the large cross section of patients with ACS. Specifically, it will evaluate how to incorporate new technologies and a dynamic approach to risk modeling in order to better stratify the spectrum of these disorders. Novel pathways involved in antithrombotic therapy of ACS will be addressed. The complex navigation through the antiplatelet therapy maze will be discussed. An emphasis on quality of care and its application to cardiovascular medicine, as well as the dilemma involving best allocation of resources in an economically constrained healthcare environment will be presented. Finally, the impact of recent and evolving clinical trials as it relates to the ever changing face of ACS will be undertaken.

LEARNING OBJECTIVES

After attending this symposium participants will be able to:

1. Identify new technologies, including a dynamic approach to risk modeling for better stratification of ACS.
2. Evaluate novel pathways involved in coronary thrombosis and current antithrombotic therapies.
3. Describe a logical strategy for the use of anti-platelet therapy.
4. Measure and assess quality of care.
5. Evaluate the best cost-effective management in ACS therapy.
6. Describe how to incorporate recent ACS clinical trials into their practice.

This accredited symposium was co-developed and planned to ensure the evidence presented is valid, objective and balanced.

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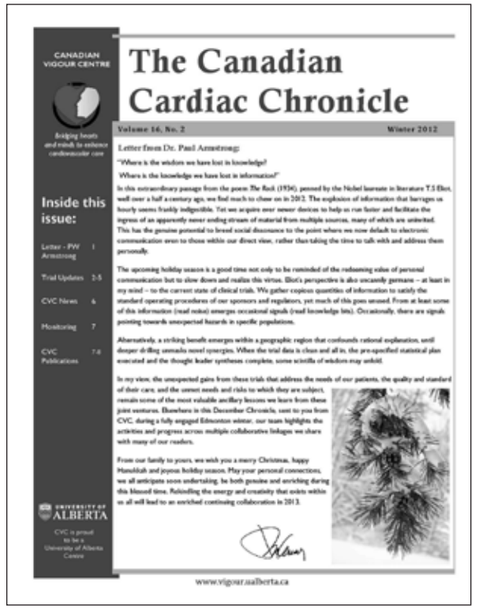
THE CANADIAN CARDIAC CHRONICLE

CVC is pleased to publish The Canadian Cardiac Chronicle, our newsletter that shares current trial information, and upcoming projects that may be of interest to our site network.

The Chronicle also lists current publications by the CVC faculty, resulting from the projects and trials data we manage. Posted on our website at www.vigour.ualberta.ca, the Chronicle is distributed to over 400 recipients, including our investigative sites, sponsors and international collaborators.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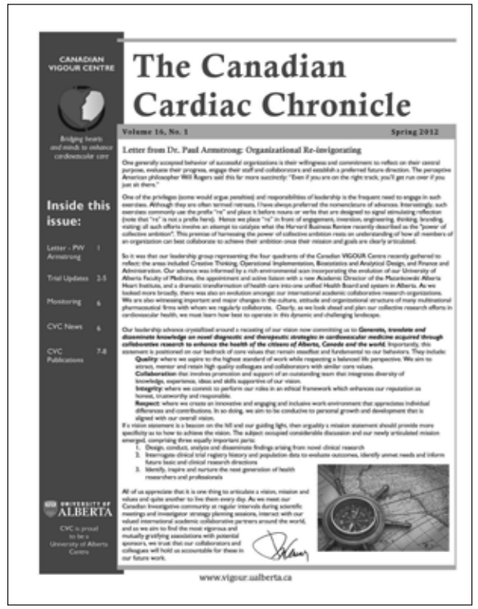
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The Canadian Cardiac Chronicle
Volume 16, No. 1 Spring 2012
Letter from Dr. Paul Armstrong: Organizational Re-invigorating
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POPULATION AND ECONOMIC HEALTH OUTCOMES RESEARCH

- Collection of resource utilization and cost data
- Development of economic models
- Cost-effectiveness analyses
- Clinical Registry development

BIOSTATISTICAL ANALYSIS

- Design of research protocols and studies
- Development of statistical analysis plans and database specifications
- Data management
- Programming expertise in SAS and R
- Generation of statistical tables, figures and listings and interpretation of findings
- Consultation and execution of advanced statistical methods
- Development and application of novel statistical methods

EGC CORE LAB

- Informing trial design
- Monitoring protocol adherence
- Guiding mechanistic insights
- Prognosis and outcomes assessment

SERVICES AND ACTIVITIES

The Canadian VIGOUR Centre is recognized as a thought leader and valuable partner in cardiovascular research across all regions of Canada and amongst key centres around the world. Its track record of conducting, delivering and publishing insightful and unbiased research and health outcomes is strongly influenced by clinical practice and health care.

THOUGHT LEADERSHIP

- Provide expert advice and promotion of cardiovascular research characterized by quality, scholarship and integrity
- Define unmet needs for patients with and those at risk of cardiovascular disease
- Align new cardiovascular research with these unmet needs
- Seek cost effective solutions and enhance return on investment in research
- Trial architecture, development, data acquisition, integration, analysis, presentation and peer-review publication
- Creation of novel substudies aimed at mechanistically informing primary clinical trial results
- Mentoring junior faculty, medical trainees, students and allied health professionals

CLINICAL TRIALS

- Investigator selection, qualification and recruitment
- Investigative site start-up and training
- Ensuring site regulatory compliance
- Project, Site and Data management
- In-house and onsite clinical monitoring (including bilingual services)

CLINICAL TRIALS

To date, the CVC has participated in 49 cardiovascular clinical trials (Phase II and Phase III) and studies, with enrollment of over 284,830 patients globally, of which over 19,018 patients were from Canada. These patient enrollment figures consistently meet or exceed anticipated and representational enrollment relative to national populations of other countries around the world. CVC's success in consistently meeting enrollment targets stems in large part from the strength of our relationships with our site network (more than 229 sites across Canada), comprised of over 425 Principal Investigators (PIs).

A barometer of our operational success and our ability to deliver on our promise of quality to each of our stakeholders is our ability to recruit sites to participate in multiple, non-competing trials. Increasingly, our site network is reflective of our involvement in cardiovascular trials involving diabetes, as the metrics on the following page indicate. In profiling our site network, we note the range in speciality of our PI's, their geographic distribution across Canada, as well as their repeated involvement and collaboration in trials managed by the CVC.

19,018

Number of Canadian patients enrolled in CVC managed studies

Dedicated to quality assurance, the CVC Clinical Trial team, works closely with our sites across Canada to ensure timely and accurate data collection, collaborative problem solving, patient safety, and audit preparedness. This requires up to date Standard Operating Procedures (SOPs) and CVC utilizes a web application platform as a collaborative tool to share key metrics with our myriad stakeholders, and to reflect our achievement of trial milestones.

In 2012, the CVC provided project management, site management and monitoring for six clinical trials, and other associated ancillary studies, and some of which are local initiatives such as PROACT, which were developed by our faculty. These trials and projects are summarized in the following pages, and reflect the purpose, scale, and timelines for each. The Clinical Trial group, led by Tracy Temple, is comprised of experienced Project Leads, administrative staff, Halina Nawrocki, our Lead CRA, along with monitoring report reviewers and six contracted monitors based regionally throughout the country.

Our Project Leads are responsible for liasing with sites in Canada, reporting internally to the Assistant Director of Clinical Trials and reporting externally to sponsors and academic partners. They answer questions related to the protocol, patient eligibility, data queries, and study drug. In their roles, they are responsible for monitoring trends and identifying issues associated with the trial, ensuring patient recruitment targets are met, ensuring data quality is maintained, and reporting trial status to key project stakeholders on a timely and consistent basis. The Clinical Trial team also works to ensure regulatory is reviewed, logged and filed appropriately, monitoring plans are adhered to, databases with both demographic and trial related documentation are maintained and are up to date.

Our work in clinical trials is both informed and enriched by connectivity to regional, provincial and national registries and population outcomes databases.

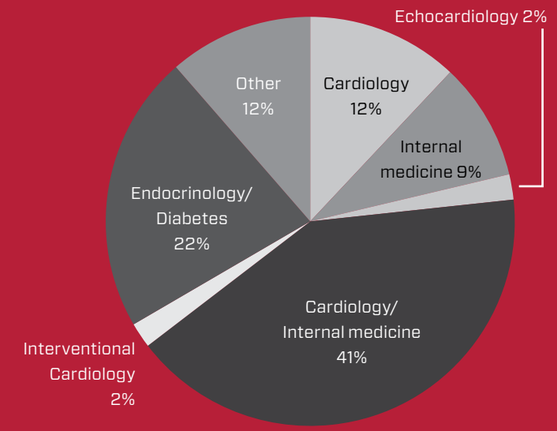
2012 SITE NETWORK AND PROFILE

100%
MONITORS COMPLETE GCP TRAINING

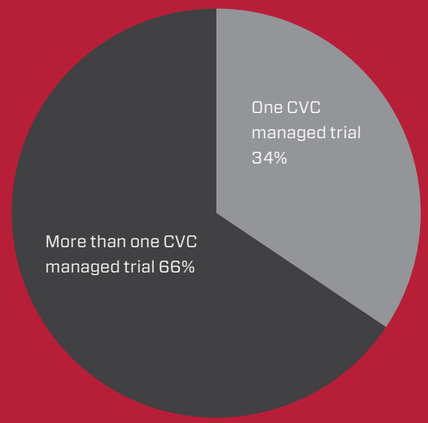
99%
ON-TIME MONITORING REPORTS TO SPONSORS

233
MONITORING VISITS TO TRIAL SITES

PI BY SPECIALTY

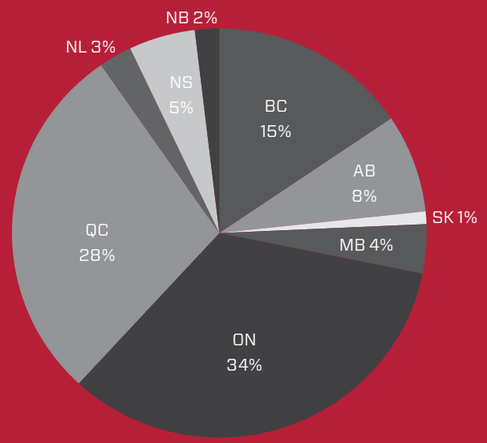


PI PARTICIPATION



PI BY REGION

Sites currently participating in a CVC trial



TECOS

Trial **E**valuating **C**ardiovascular **O**utcomes with **S**itagliptin

DESCRIPTION: Randomized, placebo controlled clinical trial to evaluate cardiovascular outcomes after treatment with sitagliptin in patients with Type 2 diabetes mellitus and inadequate glycemic control

CLINICALTRIALS.GOV: NCT00790205

SPONSOR: Merck & Co. Inc

DRUG: Sitagliptin

ANTICIPATED TIMELINE: August 2008 - June 2015

STATUS: Target enrollment reached now in patient retention and event accrual stage.

481/14,000	589/14,745	28/681
PATIENT ENROLLMENT TARGET (CANADA / GLOBAL)	PATIENT ENROLLMENT ACHIEVED (CANADA / GLOBAL)	NUMBER OF SITES PARTICIPATING (CANADA / GLOBAL)

STREAM

STrategic **R**eperfusion **E**arly **A**fter **M**yocardial Infarction

DESCRIPTION: Open label, prospective, randomized, parallel and comparative international multi-centre trial comparing the efficacy and safety of a strategy of early fibrinolytic treatment with tenecteplase and additional antiplatelet and antithrombin therapy followed by catherisation within 6-24 hours or rescue coronary intervention versus a strategy of standard primary PCI in patients with acute myocardial infarction within 3 hours of onset of symptoms.

CLINICALTRIALS.GOV: NCT00623623

SPONSOR: Boehringer Ingelheim, Hoffman LaRoche & Sanofi-aventis Canada Inc.

DRUG: Tenecteplase

ANTICIPATED TIMELINE: August 2007 - September 2013

STATUS: Database Locked, 1 year follow up and closing out sites

300/2,000	92/1,915	4/134
PATIENT ENROLLMENT TARGET (CANADA / GLOBAL)	PATIENT ENROLLMENT ACHIEVED (CANADA / GLOBAL)	NUMBER OF SITES PARTICIPATING (CANADA / GLOBAL)

IMPROVE IT

IMProved **R**eduction of **O**utcomes:**V**ytorin **E**fficacy **I**nternational **T**rial

DESCRIPTION: A multicenter, double-blind, randomized study to establish the clinical benefit and safety of Vytorin (ezetimibe/simvastatin Tablet) vs. simvastatin monotherapy in high-risk patients presenting with acute coronary syndrome

CLINICALTRIALS.GOV: NCT00202878

SPONSOR: Merck & Co. Inc.

DRUG: Vytorin

ANTICIPATED TIMELINE: March 2005 - December 2014

STATUS: Target enrollment reached now in patient retention and event accrual stage.

500/18,000	602/18,142	36/1,159
PATIENT ENROLLMENT TARGET (CANADA / GLOBAL)	PATIENT ENROLLMENT ACHIEVED (CANADA / GLOBAL)	NUMBER OF SITES PARTICIPATING (CANADA / GLOBAL)

EXSCEL

Exenatide **S**tudy of **C**ardiovascular **E**vent **L**owering

DESCRIPTION: A randomized, placebo controlled clinical trial to evaluate cardiovascular outcomes after treatment with exenatide once weekly in patients with type 2 diabetes mellitus.

CLINICALTRIALS.GOV: NCT01144338

SPONSOR: Amylin Pharmaceuticals, LLC Eli Lilly and Company

DRUG: Exenatide

ANTICIPATED TIMELINE: May 2009 - December 2017

STATUS: Actively enrolling

248/9500	120/5,565	13/436
PATIENT ENROLLMENT TARGET (CANADA / GLOBAL)	PATIENT ENROLLMENT ACHIEVED TO DATE (CANADA / GLOBAL)	NUMBER OF SITES PARTICIPATING (CANADA / GLOBAL)

ODYSSEY OUTCOMES

Trial to study the Occurrence of Cardiovascular Events in Patients Who Have Recently Experienced an Acute Coronary Syndrome

DESCRIPTION: A randomized, double blind, placebo-controlled, parallel-group study to evaluate the effect of SAR236553/REGN727 on the occurrence of cardiovascular events in patients who have already recently experienced an acute coronary syndrome.

CLINICALTRIALS.GOV: NCT01663402

SPONSOR: Sanofi-aventis Recherche & Développement

DRUG: SAR236553/REGN727

ANTICIPATED TIMELINE: June 2012 - March 2018

STATUS: Start up and actively enrolling.

357/18,000	0/4	357/18,000
PATIENT ENROLLMENT TARGET (CANADA / GLOBAL)	PATIENT ENROLLMENT ACHIEVED TO DATE (CANADA / GLOBAL)	NUMBER OF SITES PARTICIPATING (CANADA / GLOBAL)

STABILITY

The **ST**abilisation of **A**therosclerotic plaque **B**y **I**nitiaion of darap**L**ad**I**b **T**herap**Y**

DESCRIPTION: Randomized, placebo-controlled, doubleblind, parallel group, multicenter, event driven trial. A Clinical outcomes study of darapladib vs placebo in subjects with chronic coronary heart disease to compare the incidence of major adverse cardiovascular events

CLINICALTRIALS.GOV: NCT00799903

SPONSOR: GlaxoSmithKline Pharmaceuticals

DRUG: Darapladib

ANTICIPATED TIMELINE: September 2008 - December 2013

STATUS: Target enrollment reached, in patient retention stage.

775/15,500	779/15,839	34/671
PATIENT ENROLLMENT TARGET (CANADA / GLOBAL)	PATIENT ENROLLMENT ACHIEVED (CANADA / GLOBAL)	NUMBER OF SITES PARTICIPATING (CANADA / GLOBAL)

PROACT

2012 sees the continuation of a long standing transformative clinical research project known as PROACT (Providing Rapid Out of Hospital Acute Cardiovascular Treatment), which CVC initiated within the Edmonton region. This project builds on the success of our initial research in pre-hospital care for patients with ST-elevation myocardial infarction (STEMI) and the VHR (Vital Heart Response Registry) program that coordinated STEMI care in a seamless and collaborative fashion. We embarked on this faculty initiated project to extend the lessons learned to high risk non-ST elevation acute coronary syndromes which actually are more common than STEMI and possess a greater disease burden, and secondly, to acute heart failure, for which new therapy is desperately needed. In both these syndromes, like STEMI, delay from symptom onset to hospital evaluation is significant and novel diagnostic biomarkers are now available to help at an earlier point in care to help decide on more accurate diagnosis, and to contribute to better risk stratification and ultimately best appropriate triage and early care.

With the leadership of Drs Justin Ezekowitz and Robert Welsh, we continue to collaborate in this city-wide program involving the leaders from all hospitals as well as their emergency departments. One of the innovative features of this program is the installation of specialized biomarker meters that allow for measurement of cardiac troponin (a sensitive marker of myocardial injury) and brain natriuretic peptide (a sensitive marker of heart failure). Two hundred and fifty paramedics have been trained and 25 meters installed in the ambulances that facilitate the above-mentioned measurements.

CVC gratefully acknowledges seed research funding from the University Hospital Foundation and the Mazankowski Alberta Heart Institute, as well as in-kind support from Alere Inc., in the form of meters and related materials. We remain committed to ongoing collaborations with these partners within our community to advance acute cardiac care.

ECG CORE LAB

The aim of our ECG Core Laboratory is to translate research results into information useful for clinical applications. Using the ECG parameters to generate an improved understanding of the pathophysiologic processes involved in ACS enables improvements in managing cardiac patients, prediction of outcomes, and further stimulates cardiovascular scientific research.

In 2012, the ECG Core Lab at the CVC continued its tradition of conducting quality analyses using clinical research data. The Core Lab has accumulated a wealth of experience in its readers and continues to mentor and train the next generation of talented researchers. To date, ECGs from over 67,976 patients, enrolled in studies around the world, have been analyzed. This provides a rich database for additional substudies, analyses and research. The main projects for the ECG Core Lab in 2012 were STREAM, J-Point project and PROACT-3.

The ECG Core Laboratory continued with the analysis of ECGs for the STREAM trial. The examination of these ECGs includes the determination of ST deviation (area at risk), ST resolution (as marker of myocardial reperfusion) and QRS Scoring (for infarct size) in patients experiencing Acute Myocardial Infarction (AMI). The Core Lab also provides central adjudication for patients with rescue PCI to determine whether they have met the clinical indication for this procedure. The results of this process are then communicated to global investigative sites, providing timely feedback during the ongoing enrollment phase of the study.

190,694

Number of ECGs analyzed by CVC from 67,976 patients

The STREAM trial makes use of online technology for both the uploading and submission of ECGs; the investigative site is able to upload the electronic ECG photo file and once this process is complete, it is instantaneously available for download by ECG Core Lab staff at the CVC.

In 2012 the ECG Core Lab was involved in PROACT-3, the third stage of the PROACT project, which is detailed in an earlier section of this report. A key component of this project is the timely recognition of patients' needs, and how best to direct health resources for better and more efficient patient care. Our ECG Core Lab has continued their important role in analyzing the ECGs derived from this project, which will contribute to a database rich in information about outcomes of local Edmonton patients under current practices, and how we can change practice and redirect health care resources to improve patient outcomes for those suffering from acute coronary syndromes and heart failure.

The core lab has a long history of assuring the accuracy and precision of ECG analysis through inter- and intra-reader variability and reliability testing, double data entry procedures, and hard copy and electronic storage and backup procedures.

The J-Point Project, began in 2011, was designed by CVC ECG Core Lab to establish optimal measurement points on ECGs with respect to feasibility, applicability and inter-observer agreement. In addition, the prognostic relevance of this measurement would be determined by correlating the data with outcomes measures from a large sample of clinical trial data from a previously completed study. This project involved the collaboration with two other experienced, well-respected ECG Core Labs at the Duke Clinical Research Institute and the St. Louis University. The results of the first phase of the J-Point Project seeded the second ongoing phase in which we are testing the inter-reader reliability on the application of the universal definition of myocardial infarction in a broad spectrum of acute coronary syndromes (ACS) patients.

BIOSTATISTICAL ANALYSIS

The CVC Biostatistics Group works with clinician investigators to conduct innovative clinical research in cardiovascular medicine in collaboration with local, national, and international researchers. This research focuses on the assessment of patient, environmental and process-of-care factors and their association with outcomes in patients with acute coronary syndromes, acute and chronic heart failure, cardiac arrest, arrhythmias, and diabetes. Areas of interest include: international and regional differences, time to treatment, use of pharmacologic and mechanic interventions, resource allocation and utilization, and gender/sex and age differences in relation to clinical outcomes. Services provided by CVC's biostatistical team include 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.

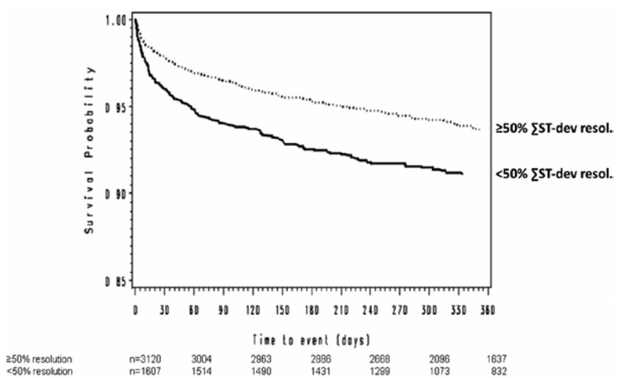
There are two main data sources on which academic research projects are based: (i) clinical trials and (ii) population-based databases and registries. The CVC houses databases from 27 clinical trials, which provide a rich cache of patient characteristics, ECGs, treatment and outcomes. The CVC also has access to population-based data for over 500,000 Albertan patients seeking cardiovascular medical care between the fiscal years 1999/2000 and 2009/2010, as well as those participating in the following registries or studies:

- Vital Heart Response Registry (over 2500 patients)
- ASCEND-HF Registry (over 690 patients)
- PROACT Retrospective Cohorts (over 550 patients)

ACADEMIC HIGHLIGHTS

In 2012, the Biostatistics Group participated in numerous studies based on clinical trial or population based data, utilizing a variety of statistical techniques. These ranged from survival analysis and metaanalysis to a novel analysis of composite endpoints in STEMI trials (i.e., weighted composite endpoint). The latter has garnered increased interest from various stakeholders and remains a key area of research.

In keeping with a key component of the CVC mandate, members of the biostatistics team contribute to mentoring the next generation of cardiovascular researchers. They work closely with medical students, residents and other junior researchers to explain the statistical techniques used and their interpretation.



This figure illustrates the survival within one year of randomization according to Sum ST-deviation resolution, a measure of micro-circulation reperfusion, in 6206 primary PCI-treated ST-elevation myocardial infarction patients enrolled in the PLatelet inhibition and patient Outcomes (PLATO) trial. Patients who achieved complete resolution (i.e., >=50% resolution (dashed line)) had significantly higher survival compared to those with incomplete resolution (i.e., <50% resolution (solid line)).

POPULATION AND ECONOMIC HEALTH OUTCOMES RESEARCH

In the last decade over half a million Albertans have been diagnosed with heart disease, which accounts for the second highest number of deaths in the province annually. Ongoing technological advances in the treatment of acute coronary syndromes and heart failure make it essential to examine whether the use of these expensive drugs and devices is equitable and to assess their impact on current and future costs of cardiac care in Alberta. The CVC Outcomes Group (led by Drs. Kaul, Ezekowitz and McAlister) has been actively involved in using health care administrative data to examine issues related to access, delivery, treatment, and outcomes of heart disease in Alberta and Canada.

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. Using administrative data received from Alberta Health, the CVC Outcomes group has developed an integrated longitudinal database linking inpatient, outpatient (including emergency department), physician office, pharmaceutical claims, registry, vital statistics and census data for all Alberta residents with heart failure, acute coronary syndromes, nonacute ischemic heart disease, cardiac arrhythmias and congenital heart disease between 1999 and 2009 in Alberta. To compare practice patterns and outcomes in Alberta with those in other Canadian provinces, we have acquired Canadian Institutes of Health Information data on all acute care hospitalizations for these five conditions for the same time period. Our extensive portfolio of research projects based on these data includes examining the following: socioeconomic and urban/rural differences in access to treatment and outcomes; outcomes among vulnerable populations such as women, the elderly, and ethnic minorities; the association of risk factors and use of evidence-based therapies on long-term outcomes; impact of alternative levels of care; resource utilization and costs of care; validity and reliability of disease coding; and novel methods to risk stratify patients.

533,188

Number of unique patients accessible to CVC for population health research

Although administrative data have the strength of being population based and are the best type of data for disease surveillance and health system evaluation, they are limited by their lack of clinical detail. Linking administrative databases to population-level clinical registries overcomes this limitation.

A major goal of the CVC Outcomes group is to identify, inspire, and train junior faculty and students in the analysis of linked administrative healthcare databases. Trainees and junior faculty continue to feature prominently in our projects Health outcomes research has been identified as an area of strong potential by the Faculty of Medicine and Dentistry: the Patient Health Outcomes Research and Clinical Effectiveness (PHORCE) Institute, directed by Dr. Finlay McAlister is a Faculty of Medicine and Dentistry initiative to engage health outcomes researchers in collaborative, interdisciplinary health research projects. As the leading cardiovascular outcomes research group, the CVC continues to interact extensively with other chronic disease groups such as Alliance for Canadian Health Outcomes Research in Diabetes (ACHORD) and the Alberta Kidney Disease Network (AKDN).

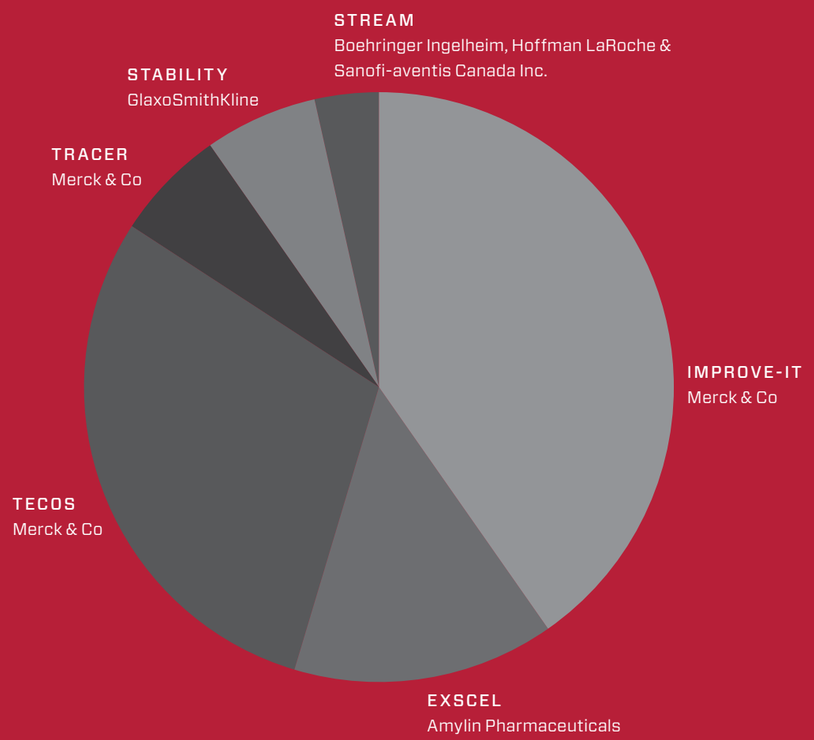
One of the major strengths of the CVC Outcomes group is its core of well-trained research personnel. The CVC Outcomes group consists of several biostatisticians and analysts who are extremely well trained in linking clinical and administrative databases, developing and validating algorithms, conducting analyses, and identifying and developing new statistical methods for administrative data.

OPERATIONS

CLINICAL TRIAL PORTFOLIO

SOURCES OF REVENUE

Revenues from industry sponsored clinical trials
January 1, 2012 - December 31, 2012



PEER REVIEWED GRANT FUNDING

Project	Sponsor(s)	Grant Holders	Term	Total Granted CAD
Providing Rapid Out of Hospital Acute Cardiovascular Treatment (PROACT)	Mazankowski Alberta Heart Institute and University Hospital Foundation	Paul Armstrong (PI), Justin Ezekowitz, Padma Kaul, Finlay McAlister, Robert Welsh	2010 - 2013	$325,000
SODIUM HF	Alberta Health Innovation Solutions University Hospital Foundation	Justin Ezekowitz	2012-2015	$50,000 $35,000
Acute Heart Failure – Emergency Management	Canadian Institutes of Health Research	Justin Ezekowitz	2009-2012	$129,000
Team Grant: Diastolic Heart Failure	Alberta Innovates-Health Solutions	Jason Dyck (PI), Todd Anderson, Justin Ezekowitz	2009-2014	$5,000,000
Cardiac Chemoreceptors in Heart Failure	Heart and Stroke Foundation	Michael Stickland (PI), Justin Ezekowitz	2009-2012	$112,700
Evaluating the impact of a Province Wide Disease Management Program on Heart Failure Outcomes in Alberta	Canadian Institutes of Health Research	Finlay A. McAlister (PI), Padma Kaul, Justin A Ezekowitz, H Quan	2010-2013	$116,765
Long-term health outcomes of mothers with gestational diabetes mellitus and their children in Alberta	Canadian Institutes of Health Research	Padma Kaul (PI)	2009-2013	$100,000

MANAGEMENT TEAM

DIANNE PAYEUR, MBA, B.Comm

Assistant Director

Dianne directs the CVC Business office and manages all aspects of finance, human resource management, strategic planning, IT infrastructure, marketing, and legal matters involving vendors and collaborative partners for CVC managed clinical trials and grants. Her oversight of CVC operations has led to several key process improvements, and has contributed to ensure CVC is an engaged and trusted partner for all service offerings.

CYNTHIA WESTERHOUT, PhD

Assistant Director, Biostatistics
Senior Research Associate

Cynthia's research interests include novel risk stratification techniques and risk adjustment procedures in acute coronary syndromes and heart failure. In addition to research and publication activities, she provides statistical oversight and consultation to the CVC Biostatistical Group, medical residents and students and serves as the biostatistics representative for CVC Faculty, management team and to the Global VIGOUR Group and other external groups.

TRACY TEMPLE, RN, BSc

Assistant Director, Clinical Trials

Tracy has a SOCRA Certified Clinical Research Professional designation, and oversees the day to day functions of our Clinical Trial team. With extensive experience in managing Phase III industry sponsored clinical trials within CVC, she works to establish and implement standard operating procedures, ongoing training initiatives, and quality controls on all of our projects. Tracy has an excellent rapport with our sites, and works closely with our collaborative partners to ensure needed consistency in Canada on global projects.

HALINA NAWROCKI, RN, CCRA

Lead Clinical Research Associate

Halina is responsible for managing the monitoring activities for all CVC clinical trials. She oversees training of CRAs, and study site personnel to ensure adherence to the protocol and investigational plan, data integrity, accurate source documentation, compliance and adherence to applicable regulatory requirements, and accurate storage and disposition of investigation product and study supplies. She is a valued representative of CVC during site audits, and an excellent ambassador for CVC within our site network.

WORLDWIDE COLLABORATORS

Professeur Philippe Gabriel Steg,
Département de Cardiologie
Hôpital Bichat, Assistance Publique - Hôpitaux de Paris

Brazilian Clinical Research Institute
São Paulo, Brazil

Duke Clinical Research Institute
Durham, USA

Estudios Clinicos Latinoamérica
Rosario, Argentina

Green Lane Coordinating Centre
Auckland, New Zealand

Flinders Medical Centre
Adelaide, Australia

Leuven Coordinating Centre
Leuven, Belgium

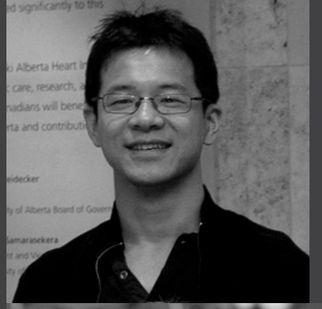
National Health and Medical Research Council
– Clinical Trials Centre
Sydney, Australia

Trials Argentine Group Organization
Buenos Aires, Argentina

Uppsala Clinical Research Centre
Uppsala, Sweden


















"Never doubt that a small group of thoughtful, concerned citizens can change the world. Indeed it is the only thing that ever has."

— Margaret Mead

ACKNOWLEDGEMENTS

CVC gratefully acknowledges and thanks:

- the CVC faculty, external advisors and collaborators for their contributions and for providing ongoing research opportunities, we look forward to providing continued services and to future collaborations;
- the CVC staff and management for their dedication, professionalism, excellent contributions and ingenuity that enhances the quality of our research work;
- our mentees for their commitment and enthusiasm as the next generation of researchers;
- the sponsors, without their financial support these trials and educational activities would not be possible;
- Dianne Payeur and Jennifer Krieger for their time and dedication required to produce this report;
- Kathy Watts and Bryan MacNeill from Watts Communications for the concept and design;
- Photographer Stephen Wreakes for many of the images enclosed in this report;
- McCallum Printing Group Inc. for their service in printing this report and our Chronicle;
- and importantly, the patients, for their willing participation in trials, they are the heroes of clinical research.