25 Years of Research Excellence and Collaboration

ACTIVITY REPORT 2014
Our Vision
Together, advancing the care of our sickest patients through excellent research “Nurturing the care of our sickest patients, one person, one idea, one study at a time”

Our Mission
We are a diverse group of researchers and practitioners committed to improving the lives and care of critically ill patients by conducting relevant research in response to healthcare needs

Our Values
All of our initiatives are underpinned by common values of EXCELLENCE, PATIENT-CENTERED FOCUS, INTEGRITY, INNOVATION and COLLABORATION
Table of Contents

25 years in the making! ................................................... 4
Past chairs’ reflections .................................................. 6
At a glance ................................................................... 10
Report from the chair ................................................... 11
What is the CCCTG? ..................................................... 14
Our structure and governance .......................................... 15
Our membership ........................................................... 16
Treasurer’s report .......................................................... 17
Funding history 1989-2014 .............................................. 18
CCCTG’s curriculum ...................................................... 18
Research outputs in 2014 ................................................ 19
Endorsement and review process ..................................... 21
Scientific meetings .......................................................... 22
Newly endorsed projects ................................................ 23
Career development & mentorship ................................... 24
Knowledge translation ..................................................... 26
CCCTG translational biology group (CCCTBG) ............... 27
CCCTG research coordinators group (CCCRCG) ............. 28
This year research highlights ............................................ 30
Our funding partners ....................................................... 37
Our major collaborators .................................................. 38

25 YEARS OF RESEARCH EXCELLENCE AND COLLABORATION

It’s amazing what a few visionary and dedicated souls can accomplish
I am honoured to have been asked to provide reflections on the origins and progress of the Canadian Critical Care Trials Group (CCCTG) at this juncture in its development. It’s noted that this report coincides with the 25th anniversary of the group. Its genesis actually began two years earlier in the bar of the Emerald Lake Lodge during the annual Banff Critical Care Conference. Like so many others I was in the process of moving research endeavours from the basic science laboratory to the clinical sphere. Most of my generation had virtually no training in epidemiology and its application to clinical research. Intensive Care Units across the country were struggling to do clinical trials with minimal funding and were continually unable to achieve a sample size sufficient to warrant statistical relevance. We were, as Ernest Hemingway put it “Islands in The Stream”, awash with financial woes and failing trials. In addition we faced the realization that within critical care we all came from different specialty backgrounds and a tradition of competition and unfortunately a sense of mistrust not only between specialties but also between institutions.

I would like to tell you that those thoughts were at the root of the idea to form the CCCTG. However, it sprang from the observation of my wonderful colleague Murray Girotti that we had to find an excuse to come back to the beauty of Emerald Lake. That’s when I responded that we really needed a national group to undertake trials in critical care. All the obstacles noted above then came crashing down on us. We were however emboldened by the rejuvenated Canadian Critical Care Society (CCCS), which over the previous 3-4 years had restructured itself to reflect the views of all specialties engaged in critical care. With the latter’s full support there were at least two formative meetings prior to the first “serious” trials group meeting at none other than Emerald Lake, Alberta. We established the format that the group still employs for discussion of protocols - an open discussion and opinion before any prospective trial could move into the detailed planning stages. I Chaired that first meeting and by noon of the first day was greatly concerned that the experiment would suffer an early demise. The old pitfalls of ego and competition amongst individuals and institutions reared its head and impaired our ability to “hear” and understand each other. We broke early and instructed those at odds with each other to meet separately for the afternoon and then report back for a late afternoon discussion to determine if we had the will to move forward. I remember walking the grounds of the lodge that afternoon and watching the formation of a few groups intently discussing what had happened. I’m sure there was much discussion of which I was and am still unaware but suffice it to say they all returned that afternoon in a constructive and collegial atmosphere and the CCCTG has never looked back.
The years that followed until I left the group for overseas were wonderful and I value the friendships and the lessons those folks all taught me. They overcame all the obstacles noted above. It was several years before peer reviewed funding was obtained. It is important to remember that the group funded itself at first. There was an annual “dues” paid to fund our meagre infrastructure and local funds were scraped together to fund the first trial in order to obtain preliminary data to support our first Medical Research Council grant. All members funded their expenses to the bi-annual meeting and the group grew. The lessons of that first meeting stayed with us. At Lake Louise AB, we always skied in the afternoon. Those who were locked in debate at the conclusion of the morning session would ski with their antagonist or meet for après-ski in order to reach a compromise before the evening session began. A “private chat” removed from the pressures of presenting in front of the group worked wonders.

Looking back, I admire the dedication and sacrifice of every one of the group. The difficulties they faced were not unique but we were one of the first to overcome them to form an investigative powerhouse. Think of where we came from to now have 200 peer reviewed publications and 84 million dollars of funding!!! I am delighted to have read in Paul Hebert’s report that the participatory approach inaugurated at Emerald Lake persists. It’s amazing what a few visionary and dedicated souls can accomplish.

My congratulations to all.

THOMAS TODD
While scientific productivity demands metrics, intangible ingredients of success that fuel a research group such as ours are seldom captured by bibliographic analyses and impact measures. **When** we came together has been outlined by our first visionary Chair, Tom Todd, who assembled people from coast to coast in new academic territory. We always kept patients, their conditions and their complications at the center of our projects - this is **why** we came together. I was deeply honoured to be the second CCCTG Chair for 8 years. They were the most meaningful and memorable of my career, helping our nascent consortium write the next chapter.

A clear purpose, strong methods and shared values helped us to harmonize. However, **what** we worked on was witnessed or experienced in the Intensive Care Unit (ICU) every day in our practice. We began by thinking about old problems in new ways. We avoided letting the rigour of our work outshine its relevance. The sense of discovery was palpable from the beginning. The early days were exhilarating - we were making history, and we knew it!

**How** we work has always been the spice. We try to avoid recipes, overselling a point of view, group-think, and premature closure on debates. Truly synergistic science requires honouring different perspectives and empathetic listening. We developed a tacit agreement that everyone checked their egos at the door. A culture of egalitarianism quickly emerged, and remains. At protocol presentation meetings, constructive critique has always been expected. Through to the present day, although feisty discussions are not unusual, and provocative questions arise, everyone’s input is respectfully delivered.

Attention to **where** we work has been important. Our conference rooms are set up to encourage ideas from the group. We have consciously avoided classroom set-ups in favour of either several round tables or a perimeter of tables along 3 sides of a room. Essential to our success has been scheduled time to relax together outside the seminar setting. Science is discussed during a stroll, on the slopes, or over supper. We convene as friends and collaborators over coffee or a cocktail. We understand that scientists are social creatures.

**With whom** we work matters. In Canada, voices of junior colleagues are valued as much as mid-career and senior colleagues. Ideas are welcome from all corners – coinvestigators, collaborators, veterans and visitors. Concepts are developed and refined by community mentoring, which augments the individual mentoring that is so special in this country. This modus operandi has led to an uncommon depth of respected ICU scientists of all ages across the country who are now leading investigator-initiated research.
We have had many transition points in our 25 year history. Early on, we branched out to embrace study designs beyond randomized trials. In collaboration with Research Coordinators, we conducted “research on how we do research”, creating metrics for recruitment efficiency, clarifying models of informed consent, developing enrolment concepts, and establishing safety oversight principles. We pioneered research programs, attentively fostered pediatric research, and collaborated with the eclectic Translational Biology Group. We have tried to be nimble to adapt to the challenging granting climate, creating economies of scale and hybrid funding models. We are rich with many resources, but money is not one of them. We have engaged in international collaboration for 2 decades. However, over his 8 year tenure, our third Chair, John Marshall, took this to a new level with passion, perseverance and poise.

We are humbly and yet proudly Canadian, while excited about the future. The proverbial whole is so much greater than the sum of the parts. In the years ahead, renewed and new dedicated partnerships will be needed to accelerate improvements in the process and outcomes of critical illness, starting in our own backyard and “going global”. Our current Chair, Paul Hébert, is our energetic and fearless leader who can always be counted on to help us creatively “think outside the box”. The Canadian Critical Care Trials Group is up for it!

We always kept patients, their conditions and their complications at the center of our projects - this is why we came together.

DEBORAH COOK
As Tom Todd reflects, there is a kind of magic in the Canadian Rocky Mountains. They inspire a sense of peace and of awe, but they have also inspired cooperation, trust, and collegiality – three elements that are fundamental to great clinical science. Their constancy has been the backdrop against which the CCCTG has grown over the past quarter century, and the embodiment of a collective passion that we share.

I joined the CCCTG at one of its first organizational meetings in the basement of a Holiday Inn in Hamilton in the spring of 1989. I was a neophyte surgeon and intensivist, less than two years into an academic career. I suspect that I was not alone in feeling intimidated by the enormity of what we were trying to do, and equally uncertain about the impact that we might ultimately have. It is probably the greatest delight of my career to have been wrong on both counts!

We have created something very special. The CCCTG has brought together some very bright and hard-working people whose ideas have resonated with the world of critical care, and so whose publications have had broad impact. Yet it is not the individual skills of our members, but rather the overarching culture of collegiality and respect within which they work, that has been responsible for our success. Early on we turned to card-carrying clinical epidemiologists such as Gordon Guyatt and Russell Hull for advice. But we very quickly developed our own internal expertise. For example, our first research endeavor – chosen because it was clearly the dominant issue vexing intensivists – was a study to determine whether cytoprotection with sucralfate was superior to acid suppression with H2 blockers in preventing stress ulceration while preventing ventilator-associated pneumonia. We were fortunate to engage a young critical care trainee named Deborah Cook who had focused on this question as part of her Master’s degree in Clinical Epidemiology. Deborah realized that before we could answer the question, we needed to know how common the problem was, and who was at risk; this was our first paper in the *New England Journal of Medicine* (NEJM), and the resulting Randomized Clinical Trial (RCT) was our third. Our second was led by a young research fellow named Paul Hébert who as a result of spending some research time in Vancouver had become enthusiastic about the concept of supranormal oxygen delivery in critical illness. He came to the CCCTG with a proposal to undertake a trial comparing transfusion to a target threshold of 100 to transfusion to a more normal value of 120. Through an enormously exciting series of discussions, we all agreed that there was an even better question waiting to be asked – could we transfuse at a lower threshold. The result was the TRICC trial, and the launch of the remarkably successful career of our current chair.
There are many other examples. The core foundation of the CCCTG’s success has been its capacity for community mentoring, a process that has transformed good ideas into great ideas, and so built our impressive curriculum vitae. We have been mentors to each other. I suspect that there are very few CCCTG members who would disagree with the statement that engagement in the group has been the single most important element of their education and maturation as clinical researchers: that certainly is the case for me.

For all that we have accomplished within Canada, I see our influence on international critical care as our greatest legacy - not just the many practice-changing studies that we have published, but the fact that we have inspired others to create sister groups. Our colleagues in Australia and New Zealand were next, and using a model very similar to ours, they have gone on to conduct the largest critical care trials ever undertaken. They may even best us when it comes to camaraderie and good fun, but this is controversial, and we certainly won’t cede defeat just yet. Similar groups have emerged in Ireland, Scandinavia, Germany, the UK, the United States, and France. China has established a critical care trials group that published its first paper last year, while a Brazilian group structured on the CCCTG model has just completed the largest trial ever undertaken in critical care, recruiting more than 20,000 patients to a cluster RCT to evaluate the utility of an ICU checklist. Groups have formed in Asia and sub-Saharan Africa, and I am writing this from Chile, where the third meeting of the Latin American Critical Care Trials Investigators Network (LACCTIN) meeting is taking place. We have given birth to a global phenomenon. We are fundamentally changing critical care clinical research. These groups, with the CCCTG very much at the helm, are exploring new models of collaboration, accomplishment, and global mentorship through the International Forum for Acute Care Trialists (InFACT).

It is no coincidence that InFACT held its first dedicated meeting this past January at Lake Louise, and plans to return there following the CCCTG meeting in 2016. The Rockies are inspirational. We can be very proud!

JOHN MARSHALL
At a Glance

CCCTG ACTIVITY REPORT 2014

19 NEW PROJECTS
MORE THAN 75
ACTIVE RESEARCH STUDIES

32 NEW ARTICLES
A TOTAL OF 210 PUBLICATIONS
INCLUDING 15 IN THE NEW ENGLAND JOURNAL OF MEDICINE

OVER 160 ACTIVE MEMBERS ACROSS THE COUNTRY

16 Funding and Collaborating Partners

OVER $84M IN TOTAL RESEARCH FUNDING
This year was our 25th - Amazing!

This year again we had a lot of fun which started with a great party in Lake Louise to celebrate our 25th anniversary! And to top this, we continued to build on our success and further our mission to improve the lives and care of critically ill patients by conducting practice-changing research. Our 25th year was marked by incredible achievements. We secured core funding through a grant from the Canadian Institutes of Health Research (CIHR), we passed the milestone of more than $80M total funding for CCCTG investigator-initiated research, including $49.7M from CIHR, and added to our curriculum growing to more than 200 publications.

This was also the first full year of our Strategic Plan 2013-2018 launched in December 2013. The plan is ambitious and compels us to strengthen our existing activities and to pursue new directions in areas such as quality of care, formalized partnerships with institutions, and engagement of patients, citizens and decision-makers in our research. There were four key objectives for 2014: 1) to obtain core funding, 2) to develop means to and begin engaging more with patients, families and other key stakeholders, 3) to establish overarching themes for our research and refine our scientific meetings, and 4) to develop a core information system and means to work with method centres. We were quite successful with the first three objectives!

CORE FUNDING
Our most important achievement in 2014 was to obtain funding through the Community Development Program grant from CIHR. With the funding that we will receive over the next 5 years, we plan to expand our core infrastructure to enhance the care delivered to children and adults to achieve better outcomes. We will accomplish this through engagement and partnerships; by providing resources, including common databases to our researchers; by enhancing our training and mentorship; and by broadening our research focus to include quality of care. We also secured smaller planning grants that helps us fund some key activities described below.

ENGAGEMENT
Aligned with our commitment to improve our engagement with stakeholders, we held our first stakeholder outreach event in conjunction with the Spring 2014 Scientific Meeting held in Montréal QC. The event was held at the Musée Pointe-à-Callières and reunited CCCTG members, patients and family members and representatives from local research and healthcare centers, universities, funding organizations and government. We also revamped our website and finalized a communication plan that aims at raising awareness and educating about the work of ICU physicians and health professionals, about critical care research and the CCCTG.

DR. PAUL HÉBERT
CCCTG CHAIR
RESEARCH
For the benefit of external stakeholders and funders in terms of their understanding of the range and depth of our research, we identified thematic areas to strengthen and better profile our research. We also included a new domain into our research – Quality of Care. Quality of Care research and evaluation is likely to expand in the coming years and policy makers will need guidance for quality measures and systems. We have therefore embarked on and are leading an initiative which aims to develop this agenda. As a first step and with the support of a $25,000 Planning Grant from CIHR, we convened a Focus Group Meeting held October 29, 2014 in Toronto ON. The CCCTG Focus Group meeting brought together a complimentary cross-section of researchers, ICU clinicians and health professionals, health care organizations and patient representatives, and governments. Together we developed a conceptual framework and defined key elements for the elaboration of a National Strategy on Quality of Care Research and Evaluation for which a manuscript is currently being drafted.

During 2014 we have also seen significant success with research project funding. Of note, the international SuDDICU (Selective Decontamination of the Digestive Tract in the ICU) collaborative lead by Brian Cuthberston on CCCTG’s side was successful with $4.9M in grants from the Australian National Health and Medical Research Council and the Health Research Council of New Zealand; Tom Stelfox received a grant from Alberta Innovates Health Solutions ($749K) for Reassessing Practices in the Daily Care of Critically Ill Patients; TVN granted $ 589K for Reengineering the Discharge of Elderly Patients from Intensive Care (Pls – Bagshaw, Dodek, Foster, Stelfox, Lamontagne, Turgeon); a grant of $617K from CIHR was awarded to Anne-Marie-Guerguerian for her project on Quantifying brain injury on computed tomography in hospitalized children; STRIPES (Kusum Menon) was granted $597K from CIHR; François Lauzier’s project Clinical outcomes and predictors of pituitary disorders in Traumatic Brain Injury was awarded $278K from CIHR and Ron Wald $220K from CIHR (Standard vs Accelerated Initiation of Renal Replacement Therapy in Acute Kidney Injury). Adding to our list of programs, 19 new research projects were endorsed by the CCCTG in 2014.

The growing numbers of research projects and investigators seeking peer review and collaboration have strained the capacity to provide adequate time for constructive discussion and feedback at the CCCTG meetings. This year we have made efforts to strengthen our meetings and deal with an increasingly complex agenda, reviewed our processes for registration and clarified expectations from presenters and meeting participants.

Our most important achievement in 2014 was to obtain funding through the Community Development Program grant from CIHR.
Finally, recognizing our track record and leadership in the field and reinforcing our international footprint, the CCCTG has been invited to sit on the Steering Committee of the NIH/NHLBI newly funded PETAL Network.

We did not meet the objective to develop a core information system and means to work with method centres. We did, however, define the position for a National Research Platform Coordinator that we hope to recruit in 2015. This person will be key in helping us to develop, coordinate and manage our core documentation resources.

THE YEAR AHEAD

Beside the recruitment of the National Research Platform Coordinator, our objectives for 2015 will be to broaden the consultation, including patients and family members, to develop a coordinated Quality of Care vision for the ICU in Canada and begin the implementation of a nation-wide program of systematic data gathering and analysis about intensive care delivery; launch funding opportunities such as Fellowship and Travel Awards; and develop a strategy for patient and family member engagement.

It is an honour to serve as Chair of the CCCTG. I look forward to continue working with you as we pursue our shared vision.

Sincerely,

PAUL HÉBERT
The CCCTG (www.ccctg.ca) is a group of Canadian critical care professionals from ICUs across the country. Collectively, we plan and implement innovative investigator-initiated, patient-focused, multicentre research. The dedication, shared expertise, collaboration and spirit of collegiality that are embodied by the CCCTG have been internationally recognized and our model replicated globally. The world class high clinical impact research we conduct has helped advance health care in Canada and around the world by changing the practice and the quality of care of the critically ill. Since the CCCTG was established in 1989, our researchers have published more than 200 scientific articles including 15 in the prestigious *NEJM*.

Through more than 75 ongoing initiatives, we are evaluating how best to care for critically ill patients with severely injured vital organs (heart, brain, lung and kidneys) and how best to care for dying patients. The research conducted by the CCCTG is organized around research themes that are important to critically ill patients, their families and clinicians. These themes represent the temporal continuum of critical care – from prevention, to acute resuscitation and recovery, to delivery of supportive care or compassionate care at the end of life, continual patient and family engagement and technology assessment. We strive to ensure that our programs have both an adult and pediatric component. Over the years, we have also engaged scientists who explore the mechanism of disease and underpinnings of treatments in our translational biology research group (CCCTBG). They have helped us explain why critically ill get sick, get worse or how our treatments work.

This year, we have added a new quality of care dimension. This is one of the key foci for our future as we plan to develop both evaluative and research facets. The evaluative component will provide a means to describe, contrast and compare critical care practices in adults and children from coast to coast. This will inform decision-making and assist in the identification and evaluation of strategies to improve the care of the critically ill. It will also inform the research agenda by identifying significant variations in care.

Finally, through our Career Development & Mentorship program, we are also committed to sustain our legacy into the future by improving the training for our future colleagues, mentoring our young investigators and the next generation of leaders in critical care research, and ensuring our more experienced investigators remain competitive by providing continued support and mentorship.
The CCCTG is administered by an Executive Committee. In addition to a Chair, Past Chair, Secretaries and Treasurer, this Committee consists of two Adult Counsellors and two Pediatric Counsellors and Chairs of the CCCTG Translational Biology Group (CCCTBG) and CCCTG Research Coordinators Group (CCCRCG), and Chairs/Co-Chairs of the different Subcommittees. Other members include Ethics and International Collaborations/InFACT representatives. Ex Officio members of the Executive Committee include the CCCTG Executive Director and representatives from the Canadian Critical Care Society (CCCS) and the Canadian Intensive Care Foundation (CICF). The Executive Committee meets face-to-face in January, June and October during the thrice yearly CCCTG Meetings as well as via teleconference in April, September and December. The involvement of Committee members throughout the year is substantial. They all volunteer their time to facilitate the strategic development of the CCCTG, lead and contribute to special initiatives and interest working groups. Through the various Subcommittees they coordinate review of grants and manuscripts, plan scientific meetings, develop and manage career development activities and programs, and represent the CCCTG on external initiatives and committees. All members of the Executive Committee are gratefully acknowledged for their time, expertise and dedication to the CCCTG.

EXECUTIVE COMMITTEE

DR. PAUL HÉBERT
Chair, CCCTG

DR. JOHN MARSHALL
Past chair

DR. JAMIE HUTCHISON
Chair, CCCTBG

DENISE FOSTER
Chair, CCCRCG

NICOLE EL-HARES
Administrative Assistant

DR. NICOLAY FERRARI
Executive Director

DR. TAZ SINUFF
Co-Chair, KT Committee

DR. JOHN MUSCEDERE
Co-Chair, KT Committee

DR. DEBORAH COOK
Ethics representative

DR. MARISA TUCCI
Pediatric Counsellor

DR. RICK HALL
Adult Counsellor

DR. LAURALYN MCMINTRE
Co-Chair, Grants & Manuscript Review Committee

DR. ALEXIS TURGEON
Co-Chair, Grants & Manuscript Review Committee

DR. KAREN BURNS
InFACT Liaison

DR. FRANÇOIS LAMONTAGNE
Chair, Communication Committee

DR. ELAINE GILFOYLE
Chair, Career Development & Mentorship Committee

DR. ANDREW SEELY
Secretary

DR. MAUREEN MEADE
Treasurer

DR. KAREN CHOOING
Secretary, Pediatric Counsellor

DR. ROB FOWLER
Secretary

DR. MARGARET HERRIDGE
CICF Representative

DR. CLAUDIO MARTIN
CCCS Representative
Membership to the CCCTG is open to all ICUs health professionals - physicians and health scientists, nurses, pharmacists and physiotherapists, research coordinators and trainees who care for critically ill adults or children. From its foundation, the operational activities of the CCCTG have been supported through membership subscriptions. We currently have three membership types: intensive care physicians and healthcare professionals (Full Member/Physician), ICU Trainees and Research Coordinators. Annual membership fees for January – December 2014 ($400 for Full Members/Physicians, $200 for ICU Trainees and $50 for Research Coordinators) remained unchanged. The support received from these members is vital, both in terms of voluntary subscriptions and active participation in CCCTG research and scientific activities. Revenue from memberships is used to support the three regular meetings per year where project updates, study progress and results are discussed and critique and new project ideas are presented for endorsement.

Thank you to all our members.
In this 25th anniversary year, the success of the CCCTG can be measured in many ways, and our ability to sustain ourselves financially for more than two decades without government funding is one of these. We are extremely grateful to our membership that supported the group from the beginning through membership subscriptions. Our three yearly scientific meetings are well attended with an average between 80 and 100 participants each.

However, 2014 was marked in a special way by an important milestone, our successful application for Network funding from the Community Development Program of the Institute of CIHR. Over the next 5 years, the funding received will allow us to transition from an investigator-led project-based network to developing cohesive, nation-wide infrastructure capable of supporting and enhancing practice changing research programs in critical care across the centres and provinces participating in this work. On behalf of the CCCTG, I am also grateful for the support we received from our partners which helped us with the necessary matching funds required for the Network funding.

**CCCTG REVENUE AND EXPENSE STATEMENT**

**FINANCIAL YEAR 2014/2015**

<table>
<thead>
<tr>
<th>Revenues</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Membership Subscriptions</td>
<td>$82,350</td>
</tr>
<tr>
<td>Meeting Registrations</td>
<td>$1,250</td>
</tr>
<tr>
<td>Sponsorship &amp; Donations</td>
<td>$4,845</td>
</tr>
<tr>
<td>Balance Transfer</td>
<td>$16,416</td>
</tr>
<tr>
<td>Partners Contributions</td>
<td>$72,284</td>
</tr>
<tr>
<td>Grants</td>
<td>$158,909</td>
</tr>
<tr>
<td><strong>Total Revenues</strong></td>
<td><strong>$336,054</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Expenses</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meetings</td>
<td>$78,787</td>
</tr>
<tr>
<td>Funding Programs</td>
<td>$2,997</td>
</tr>
<tr>
<td>Salary &amp; General Administration</td>
<td>$97,035</td>
</tr>
<tr>
<td><strong>Total Expenses</strong></td>
<td><strong>$178,819</strong></td>
</tr>
</tbody>
</table>

**Total Balance** $157,235

* Fiscal year April 1, 2014 to March 31, 2015.
Unaudited balance statement; Amounts are CDN$
In 2014, the CCCTG received Network funding totalling $3,9M over 5 years

Since the CCCTG was established, 25 years ago, our researchers have secured funding of more than $84 million, including $49.7 million in CIHR project-specific funds. In 2014, the CCCTG received its first Network funding through a Community Development Program Grant of $1.5 million from the CIHR Institute of Circulatory and Respiratory Health with an additional $2.4 million matching funds from partners.

As of December 31, 2014.
Non-validated

CCCTG’s Curriculum

32 peer-reviewed articles from CCCTG-endorsed projects published in 2014

We have studied how best to support critically ill patients. Our research contributions have changed the practice of critical care around the world. Our publication record includes 15 articles in the New England Journal of Medicine.

As of December 31, 2014
**Research Outputs in 2014**

**WE ADDED TO OUR CURRICULUM TO MORE THAN 200 PUBLICATIONS**

<table>
<thead>
<tr>
<th>First Author</th>
<th>Title</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALBERT, MARTIN</strong></td>
<td>Candida in the Respiratory Tract Secretions of Critically Ill Patients and The Efficacy of Antifungal Treatment: a randomized placebo controlled trial (CANTREAT Study)</td>
<td>Intensive Care Med. 40: 1313–1322</td>
</tr>
<tr>
<td><strong>ARCHAMBAULT, PATRICK</strong></td>
<td>Development and validation of questionnaires exploring health care professionals’ intention to use wiki-based reminders to promote best practices in trauma</td>
<td>JMIR Res Protoc, 3(3):e50</td>
</tr>
<tr>
<td><strong>BURNS, KAREN</strong></td>
<td>Automated weaning and SBT systems versus non-automated weaning strategies for weaning time in invasively ventilated critically ill adults</td>
<td>Cochrane Database of Systematic Reviews, Sept 9;9:CD008638</td>
</tr>
<tr>
<td><strong>BURNS, KAREN</strong></td>
<td>Evaluation of an internal review process for grants and manuscripts in the Canadian Critical Care Trials Group</td>
<td>Can Respir J; 21(5):283-6</td>
</tr>
<tr>
<td><strong>BURNS, KAREN</strong></td>
<td>SmartCare™ versus non-automated mechanical ventilation strategies on discontinuation time for adults in the postoperative period</td>
<td>Cochrane Database of Systematic Reviews 2014. Issue 2. Art. No.: CD008639</td>
</tr>
<tr>
<td><strong>CAHILL, NAOMI</strong></td>
<td>Improving the provision of enteral nutrition in the intensive care unit: a description of a multifaceted intervention tailored to overcome local barriers</td>
<td>Nutr Clin Pract;29(1):110-7</td>
</tr>
<tr>
<td><strong>CAHILL, NAOMI</strong></td>
<td>Implementing a multifaceted tailored intervention to improve nutrition adequacy in critically ill patients: results of a multicenter feasibility study</td>
<td>Crit Care;18(3):R96</td>
</tr>
<tr>
<td><strong>CANTER, RUTH</strong></td>
<td>Selective Decontamination of the Digestive tract in critically ill patients treated in Intensive Care Unit (SuDIDICU) Investigators. Observational study of current use of selective decontamination of the digestive tract in UK critical care units</td>
<td>Br J Anaesth;113(4):610-7</td>
</tr>
<tr>
<td><strong>COOK, DEBORAH</strong></td>
<td>Barriers and facilitators of thromboprophylaxis for medical-surgical intensive care unit patients: a multicenter survey</td>
<td>J Crit Care;29(3):471</td>
</tr>
<tr>
<td><strong>CROWTHER, MARK</strong></td>
<td>Heparin-induced thrombocytopenia in the critically ill: interpreting the 4Ts test in a randomized trial</td>
<td>J Crit Care;29(3):470.e7-15</td>
</tr>
<tr>
<td><strong>DEMARET, PIERRE</strong></td>
<td>Red blood cell transfusion in critically ill children (CME)</td>
<td>Transfusion;54(2):365-75</td>
</tr>
<tr>
<td><strong>DHANANI, SONNY</strong></td>
<td>Vital signs after cardiac arrest following withdrawal of life-sustaining therapy: a multicenter prospective observational study</td>
<td>Crit Care Med;42(11):2358-69</td>
</tr>
<tr>
<td><strong>DUNCAN, EILIDH</strong></td>
<td>For the SuDIDICU International Study Group. The views of health care professionals about selective decontamination of the digestive tract: An international, theoretically informed interview study</td>
<td>J Crit Care;29(4):634-10</td>
</tr>
<tr>
<td>First Author</td>
<td>Title</td>
<td>Reference</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>DUPONT-THIBODEAU, GENEVIEVE</td>
<td>Survey on stated transfusion practices in PICUs</td>
<td>Pediatr Crit Care Med;15(5):409-16</td>
</tr>
<tr>
<td>FOWLER, ROBERT</td>
<td>Economic evaluation of the prophylaxis for thromboembolism in critical care trial (E-PROTECT): study protocol for a randomized controlled trial</td>
<td>Trials;15(1):502</td>
</tr>
<tr>
<td>FOWLER, ROBERT</td>
<td>Cost-effectiveness of Dalteparin vs Unfractionated Heparin for the Prevention of Venous Thromboembolism in Critically Ill Patients</td>
<td>JAMA 312(20):2135-45</td>
</tr>
<tr>
<td>FRANCIS, JILLIAN</td>
<td>Selective decontamination of the digestive tract in critically ill patients treated in intensive care units: a mixed-methods feasibility study (the SUDICU study)</td>
<td>Health Technol Assess;18(2):1-170</td>
</tr>
<tr>
<td>FRANCIS, JILLIAN</td>
<td>Comparison of four methods for assessing the importance of attitudinal beliefs: An international Delphi study in intensive care settings</td>
<td>Br J Health Psychol;19(2):274-91</td>
</tr>
<tr>
<td>HEYLAND, DAREN</td>
<td>Glutamine and Antioxidants in the Critically Ill Patient: A Post Hoc Analysis of a Large-Scale Randomized Trial</td>
<td>J PEN J Parenter Enteral Nutr;May 5 (Epub ahead of print)</td>
</tr>
<tr>
<td>HOSEIN, SHAUN</td>
<td>A meta-analysis to derive literature-based benchmarks for readmission and hospital mortality after patient discharge from intensive care</td>
<td>Crit Care;18(6):2558</td>
</tr>
<tr>
<td>KARAM, OLIVER</td>
<td>International survey on plasma transfusion practices in critically ill children</td>
<td>Transfusion;54(4):1125-32</td>
</tr>
<tr>
<td>LAUZIER, FRANCOIS</td>
<td>Thromboprophylaxis patterns and determinants in critically ill patients: a multicenter audit</td>
<td>Crit Care;18(2):R82</td>
</tr>
<tr>
<td>MARSHALL, ANDREA</td>
<td>Implementing selective digestive tract decontamination in the intensive care unit: A qualitative analysis of nurse-identified considerations</td>
<td>Heart Lung;43(1):13-8</td>
</tr>
<tr>
<td>MEHTA, SANGEETA</td>
<td>A ventilator strategy combining low tidal volume ventilation, recruitment maneuvers, and high positive end-expiratory pressure does not increase sedative, opioid, or neuromuscular blocker use in adults with acute respiratory distress syndrome and may improve patient comfort</td>
<td>Ann Intensive Care;4:33</td>
</tr>
<tr>
<td>SEELY, ANDREW</td>
<td>Do heart and respiratory rate variability improve prediction of extubation outcomes in critically ill patients?</td>
<td>Crit Care;18(6):620</td>
</tr>
<tr>
<td>STEINBERG, MARILYN</td>
<td>A National Survey of Critical Care Physicians’ Knowledge, Attitudes, and Perceptions of Antimicrobial Stewardship Programs</td>
<td>J Intensive Care Med;Jul 8 (Epub ahead of print)</td>
</tr>
<tr>
<td>WALD, RONALD</td>
<td>Changing Incidence and Outcomes Following Dialysis-requiring Acute Kidney Injury Among Critically Ill Adults: A Population-Based Cohort Study</td>
<td>Am J Kidney Dis, Dec 17 (Epub ahead of print)</td>
</tr>
</tbody>
</table>
Endorsement and Review Process

The CCCTG itself does not conduct studies; rather it provides endorsement for studies proposed to be conducted in its name. As such, the process by which studies are critically reviewed and endorsed is paramount for the group’s success.

The requirements for endorsement are set out in guidelines which include that: All new projects/programs of research, including new studies within existing programs, must be presented at one of the three annual CCCTG meetings for approval in order to obtain the support and endorsement of the group; all projects/programs of research must be presented by an active member of the CCCTG; members presenting a new project/program of research for the first time must be mentored by a senior member of the CCCTG; projects and programs of research must be presented to the group prior to their initiation. In addition, new protocols should be discussed during their development phase at CCCTG meetings for intellectual content and methodology. Once endorsed, CCCTG projects and programs of research are expected to be discussed at a CCCTG meeting at least once per year and/or during CCCTG business meetings as required.

All grant proposals and manuscripts arising from CCCTG studies must be submitted to the CCCTG Grants & Manuscripts Review Committee for an internal review prior to being submitted to the funding agency for publication. The format is open such that authors know who is reviewing their document and reviewers know the identity of the authors. The review undertaken by members of the CCCTG is voluntary and unstructured, and aims at improving proposals and manuscripts.

CCCTG’s review process was formally evaluated and results published in the Canadian Respiratory Journal in 2014 (Burns et al. 2014). Confirming the overall perception, the evaluation report a highly favourable evaluation of our internal review process for grants and manuscripts.

We thank all who have contributed with a significant amount of time and expertise to ensure the maintenance of CCCTG’s highest scientific standards for all of the 33 grant proposals and more than 20 manuscripts received in the past year.
The CCCTG was established during what would be considered to be the first CCCTG meeting in the fall of 1989 in Emerald Lake, AB. Draft protocols were presented and discussed during the meeting with the goal of deciding on a first collective research activity. Since that very first meeting, the CCCTG has been holding three yearly meetings – Winter, Spring and Fall - using that very same collegial and respectful spirit of collaboration and trust. The programmes of the scientific meetings are under the responsibility of the Scientific Committee and are developed based on an open call for presentation requests to CCCTG’s members.

For the last two decades, the Winter meeting runs end of January, always in Lake Louise, Alberta. The Fall (end of October - beginning of November) meetings are also organized in the same city, Toronto (Ontario), since we have been organizing them in parallel to the Canadian Critical Care Forum. On the other hand, we travel across the country in June for the Spring meetings. In 2014, the meetings were held as follow:

- **WINTER MEETING**
  January 27-30, 2014 at the Post Hotel in Lake Louise, Alberta.

- **SPRING MEETING**
  June 16-19, 2014 at the Centre de recherche du Centre hospitalier de l’Université de Montréal (CRCHUM) in Montréal, Québec.

- **FALL MEETING**
  October 27-28, 2014 at the University Club of Toronto, Toronto, Ontario.

This year, due to the increasing number of requests for presentation, we reviewed our meeting structure, standardized presentations formats and time allotted to each. About **80 to 100** critical care researchers, fellows and research coordinators attended each of these three meetings. In total there were more than **90 presentations** and we were able to devote over **44 hours** to discuss, provide assistance and critique ongoing projects as well as new projects.

Essential to the CCCTG endorsement process of new projects/programs, new projects/programs proposals must be presented at one of the meetings for approval and endorsement. Approval and endorsement is undertaken by members of the CCCTG in attendance. In 2014, a total of **19 new projects or new projects within existing programs** received approval and endorsement.
Newly Endorsed Projects

19 NEW PROJECTS OR NEW PROJECTS
WITHIN EXISTING PROGRAMS
WERE ENDORSED BY THE CCCTG IN 2014

<table>
<thead>
<tr>
<th>Principal Investigator</th>
<th>Mentor(s)</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHRISTIAN, MICHAEL</td>
<td>MARSHALL, JOHN</td>
<td>The GRASP-1 Study – Global Resource Allocation Survey Project - I</td>
</tr>
<tr>
<td>COOK, DEBORAH &amp; ALHAZZANI, WALEED</td>
<td></td>
<td>REVISE: Re-Evaluating Inhibition of Stress Erosions</td>
</tr>
<tr>
<td>D’ARAGON, FREDERICK</td>
<td>MEADE, MAUREEN</td>
<td>A program of research in the medical management of deceased organ donors (DONATE)</td>
</tr>
<tr>
<td>DUFFET, MARK</td>
<td>COOK, DEBORAH</td>
<td>Barriers and facilitators of randomized controlled trials in pediatric critical care</td>
</tr>
<tr>
<td>DU PONT-THIBODEAU, GENEVIE</td>
<td>LACROIX, JACQUES</td>
<td>Erythropoietin and neurologic outcome of children undergoing congenital cardiac surgery</td>
</tr>
<tr>
<td>FOSTER, JENNIFER</td>
<td></td>
<td>Melatonin in Critically Ill Children</td>
</tr>
<tr>
<td>FOX-ROBICHAUD, ALISON</td>
<td>COOK, DEBORAH</td>
<td>Patient and Family-Centred Critical Care</td>
</tr>
<tr>
<td>GUERGUERIAN, ANNE-MARIE</td>
<td>HUTCHISON, JAMIE</td>
<td>Pediatric Traumatic Brain Injury CT Tool</td>
</tr>
<tr>
<td>GARCIA GUERRA, GONZALO</td>
<td>JOFFE, ARI</td>
<td>Comfort measures and sedo/analgesia in PICU</td>
</tr>
<tr>
<td>HÉBERT, PAUL</td>
<td></td>
<td>Prospective Surveillance Plus (PS+) research program - Quality of care in the critically ill</td>
</tr>
<tr>
<td>HÉBERT, PAUL</td>
<td></td>
<td>The MINT Study - Myocardial Ischemia and Transfusion</td>
</tr>
<tr>
<td>LAMONTAGNE, FRANÇOIS</td>
<td></td>
<td>The OVATION in Trauma Study</td>
</tr>
<tr>
<td>MAROIS, GRÉGOIRE</td>
<td>SKROBIK, YOANNA</td>
<td>Early mobilization of mechanically ventilated patients: development of a tool to evaluate the safety of weight-bearing mobilization</td>
</tr>
<tr>
<td>MEHTA, SANGEETA</td>
<td></td>
<td>Sedation management in patients with Traumatic Brain Injury: a survey of Canadian clinicians</td>
</tr>
<tr>
<td>MURTHY, SRINIVAS</td>
<td>MARSHALL, JOHN</td>
<td>Period Incidence Study of Severe Respiratory Infections in Critical Care</td>
</tr>
<tr>
<td>MURTHY, SRINIVAS</td>
<td>MARSHALL, JOHN</td>
<td>The impact of cytomegalovirus on critically ill children</td>
</tr>
<tr>
<td>PARKER, MELISSA</td>
<td></td>
<td>Exception to consent in pediatric resuscitation research: Exploring the experiences of substitute decision makers</td>
</tr>
<tr>
<td>SEELEY, ANDREW</td>
<td></td>
<td>The WAVE Study - Weaning and Variability Evaluation</td>
</tr>
<tr>
<td>TINMOUTH, ALAN</td>
<td>MCINTYRE, LAURALYN</td>
<td>Frozen plasma transfusions prior to invasive procedures</td>
</tr>
</tbody>
</table>
The purpose of the Career Development & Mentorship Committee is to nurture and support aspiring investigators and future leaders in critical care research. To achieve its objective, it develops educational and mentoring activities directed at trainees, faculty and research coordinators in critical care, and coordinates all educational activities held in association with meetings of the Trials Group.

In 2014 we maintained key training programs such as the CCCRCG Research Grant Competition and mentoring workshops geared toward research coordinators (CCCRCG Workshop) and medical trainees (Residents Research Day). In addition, we were pleased to launch the Deborah J. Cook Mentorship Award to recognize the important contributions of mentors for the career development of trainees, young investigators, research coordinators and other healthcare professionals. Finally, we are looking forward to the coming year as we will be adding new funding programs such as Travel Awards designed to facilitate attendance to the CCCRCG Workshop and Residents Research Day, and Fellowship Awards to support trainees in furthering their research education.

Funding Programs

THE CCCRCG RESEARCH GRANT COMPETITION
The CCCRCG Research Grant has been established to provide funds to support the research activities of research coordinators who are members of the CCCTG. As funding permits, the CCCTG expects to fund two grants of up to $2,500 each for a research study that directly relates to the practice of critical care. In 2014, one grant was funded through the CCCRCG Research Grant Competition.

Principal Investigator: Leena Rizvi (St-Michael’s Hospital)
Project Title: Variation in Ethics Approval and Contract Execution Processes and Regulatory Timelines in an International Observation Study of Mechanical Ventilation Discontinuation Practices: A Nested Study
Grant amount: $2,498

THE DEBORAH J. COOK MENTORSHIP AWARD
Launched in 2014, the CCCTG Deborah J. Cook Mentorship Awards highlights the importance of mentorship in developing Canada’s next generation of critical care researchers. The Deborah J. Cook Mentorship Awards honour persons who have made exceptional contributions to the promotion of critical care research among Canadian fellows, graduate and post-graduate students, young investigators, research coordinators and allied health care providers. All award recipients share their passion for research and their scientific know-how with today’s youth who will be tomorrow’s innovators!

2014 Award Recipient
Maureen Meade
(McMaster University Health Sciences Center)
Award amount
$500
Workshops

THE CCCRCG WORKSHOP
This one day workshop takes place on an annual basis and provides critical care research coordinators with the opportunity to participate in educational sessions specific to the work that they do. The workshop is scheduled to occur in conjunction with the CCCTG Fall Meeting.

This year, the meeting was held on October 29th, 2014 at the Sheraton Centre Hotel in Toronto ON and was attended by 27 research coordinators. Workshop programme included Keynote Speakers Deborah Cook and John Marshall, and presentations from Ryan Zarychanski, Kusum Menon, Jamie Hutchison, Orla Smith and France Clarke. The most recent recipients of the CCCRCG Grant, Leena Rizvi and Katie Griffin, also presented their study.

Evaluations received following the Workshop stated that the agenda not only fulfilled educational needs, but also provided a valuable opportunity for networking with research coordinators from across the country.

THE RESIDENTS RESEARCH DAY
The CCCTG hosts an annual Residents Research Day to promote research education for critical care trainees across Canada. The day consists of talks geared to trainees from CCCTG members on research-related topics such as career planning, grant and manuscript writing, research ethics boards, etc. In addition, fellows have the opportunity to present their research projects for feedback from the CCCTG membership on issues such as methodology, statistics or patient recruitment. Typically the Resident Research Day occurs in conjunction with the CCCTG Spring Meeting.

This year’s Residents Research Day was held on June 16th, 2014 at the Embassy Suite Hotel in Montréal QC and was attended by record number of fellows - 21. Programme included 11 presentations from fellows as well as mentors talks from Paul Hébert, Ellen McDonald, Rick Hall, Deborah Cook and John Marshall. On behalf of the CCCTG, we are also grateful for the financial support we received from the Pediatric Critical Care Medicine Department at the Montreal Children's Hospital and the Soins intensifs pédiatriques of the CHU Sainte-Justine.

The core foundation of the CCCTG's success has been its capacity for community mentoring.
The Knowledge Translation (KT) Committee is a joint committee of the CCCTG and the CCCS. The KT Committee reports both to the CCCTG and the CCCS and its chair(s) are members of both the CCCTG executive and the board of the CCCS.

In 2014, the KT Committee has been involved in several initiatives. These have been predominantly for the development of guidelines in a variety of topic areas. The development of the Guidelines for the treatment of Calcium Channel Blocker Poisoning is being led by Maude St-Onge. The guidelines have been completed and the manuscript is being prepared. They are being reviewed by the sponsoring organizations and have been reviewed by the CCCTG. It is expected that they will be published in 2015. Dan Howes is also leading the development of the Guidelines for Therapeutic Hypothermia after Cardiac Arrest. These guidelines have also been completed and the manuscript is under review. They are currently being reviewed by the sponsoring organizations and have been reviewed by the CCCTG. It is expected that they will be published in 2015.

aC3KTion Net is the Canadian Critical Care Knowledge Translation Network (www.acktionnet.ca), a CIHR funded Initiative which seeks to improve the implementation of evidence informed best practices in critical care. The network became operational in 2012 with the following mandate: to survey practice, identify variations in practice, conduct knowledge translation efforts for selected initiatives and then monitor the results of its efforts.

In 2014, the network made significant progress of collecting baseline critical care practice data across the country. Data has been obtained from ICUs in British Columbia, Alberta, Manitoba, Ontario, Quebec and Newfoundland. The data collection phase is almost complete and the analysis will be starting shortly. The next steps will depend on findings from the data collected.
The CCCTG Translational Biology Group (CCCTBG) (www.ccctbg.ca) was founded by Dr. Brent Winston in 2003 to provide a forum for the development of research projects that benefit from the diverse knowledge, expertise, and advice of its members. The group consists of critical care physicians, PhD scientists, their research coordinators and trainees. We conduct laboratory-based and clinical research focused on molecular mechanisms of critical illness and organ injury and the discovery of novel biomarkers and treatments. Through the CCCTBG, regional biobanks from critically ill adults and children with sepsis, lung and brain injury have been established. Our biobanks now contain more than one million biological samples from more than 2500 critically ill patients linked to prospectively collected clinical data. Our databases include patient demographics, acute clinical, physiologic, imaging and outcomes data. We use animal and cellular models of critical illness and injury, and genomic, proteomic and metabolomic platforms.

The CCCTBG also provides a national venue for continuing education about translational biology research methodologies and their applications. We have developed the Dr. Michael Ward lectureship at the St. Michael’s Hospital Foundation. Donations to this fund will allow us to support a lecture by a famous scientist at the annual Critical Care Canada Forum. Donations can be made by contacting the St-Michael’s Hospital Foundation (foundation@smh.ca, Michael Ward Lectureship in the subject line; or (416) 864 5000 x 5044, administrator Leslie Rowan).

As for the CCCTG, the CCCTBG is administered by an Executive Committee comprised of the Chair, Past-Chair, Secretary, Treasurer and Member-at-Large. The operational activities of the CCCTBG have been supported by membership subscriptions separate from the CCCTG - annual membership fees for January to December 2014, $150.

The CCCTBG has been holding one and a half day-long meetings twice yearly – Winter and Spring – just before, the CCCTG meetings. In 2014, the meetings were held as follow:

■ WINTER MEETING
  January 26-27, 2014 at the Post Hotel in Lake Louise, Alberta

■ SPRING MEETING
  June 15-16, 2014 at the Centre de recherche du Centre hospitalier de l’Université de Montréal (CRCHUM) in Montréal, Québec

This year again, 35 to 40 critical care researchers, fellows and research coordinators attended each of the two meetings and engaged in meeting sessions to discuss, provide assistance and critique ongoing projects as well as new projects.
The CCCRCG is a sub-group of the CCCTG and was established in June 2004. Membership is comprised of research coordinators from across Canada, working primarily in critical care research with adult and pediatric populations. The main objective of the CCCRCG is to create networking opportunities and foster local and national collaboration between critical care research coordinators, provide peer support, develop opportunities for professional growth and lead research initiatives of interest to the CCCRCG membership.

After serving 6 years, I am stepping down as Chair of the CCCRCG. Orla Smith and Nicole Zytaruk now serve as interim Co-Chairs. The infrastructure funding received by the CCCTG will allow creation of a National Platform Coordinator position. Once the responsibilities of this position are defined a new CCCRCG Chair will be sought. The CCCRCG executive facilitates an annual workshop and also coordinates a grant competition that is open to research coordinators who are members of the CCCTG.

The first CCCRCG Grant competition was announced in 2010 with the first awards being provided in 2011. Funding available for each grant was limited to a maximum of $2,500 with up to 2 grants being funded each year. Over the course of the 4 competitions a total of 14 applications were received and 7 grants awarded. The following outlines the previous successful recipients.
2011

**Principal Investigator:** Orla Smith (St-Michael’s Hospital)
**Project Title:** Multi-centre Survey of Nurse Attitudes to the Conduct of Critical Care Research

**Principal Investigator:** Roxanne Ward (Children’s Hospital of Eastern Ontario)
**Project Title:** Examining Methods and Practices of Source Data Verification in Canadian Critical Care Randomized Controlled Trials

2012

**Principal Investigators:** Nicole Zytaruk and Ellen McDonald (St. Joseph’s Healthcare)
**Project Title:** MOTIVATE, What are the motivational determinants (key motivators and stressors) for Research Coordinator’s when making choices to pursue or change their career in this clinical health profession?

**Principal Investigator:** Marilyn Steinberg (Mount Sinai Hospital)
**Project Title:** A National Survey of Critical Care Physicians’ Knowledge, Attitudes and Perceptions of Antimicrobial Stewardship Programs.

2013

**Principal Investigator:** Nicole O’Callaghan (Kingston General Hospital)
**Project Title:** The TiM Study: A Time in Motion study to assess the time burden/feasibility of utilizing a newly defined core data set with associated data dictionary.

**Principal Investigators:** Aarthi Kamath, Sue Ferri, Kate Byrne (Hospital for Sick Children)
**Project Title:** Understanding resource allocation requirements related to site performance and case report form (CRF) complexity: A retrospective review of data accuracy in the EPOCH study.

---

**THE CCCRCG EXECUTIVE COMMITTEE**

DENISE FOSTER, Chair

LUCY CLAYTON, Francophone Representative

ORLA SMITH

LISA JULIEN

JUDY VAN HUYSE, Pediatric Representative

NICOLE MARTEN

NICOLE ZYTARUK

ANDREA MATTE
Harm Prevention

THE AGE OF BLOOD EVALUATION STUDY (The ABLE Study)

Principal Investigator: Jacques Lacroix

It is work led by CCCTG members that transformed transfusion practice! The ground breaking trial entitled Transfusion Requirements in Critical Care (The TRICC Study) led by Paul Hébert was published in the NEJM and cited more than 3000 times. This study has affected how clinicians approach blood transfusion in the critically ill and in other acute care settings worldwide. It provided the first evidence that giving less blood was associated with comparable rates of death and organ failure and fewer complications. A related trial involving critically ill children (The TRICC-PICU Study) co-lead by Jacques Lacroix and Paul Hébert with findings similar to those of the TRICC study was also published in NEJM in 2007.

This seminal work has generated a significant research agenda including studies focused on the use of alternatives to transfusion, blood conservation, resuscitation fluids, cardiac resuscitation and trauma. In 2014, Jacques Lacroix and Paul Hébert completed a large international trial (The ABLE Study) in critically ill patients to determine the effect of red blood cell storage on the clinical outcomes of transfusion. In total, 2430 critically ill patients were randomly assigned to fresh red blood cell units stored less than 8 days or standard issue red cells stored for more than 20 days on average. The trial hypothesis was whether fresh blood would decrease 90 day all cause mortality. The study concluded that transfusing blood stored on average for 6 days did not decrease the 90-day mortality of critically ill adults as compared to blood stored for an average of 22 days.
Important inferences for the critical care and blood banking communities may be derived from this trial. First, from a clinical and policy perspective, the ever increasing pressure on blood banks by clinicians requesting fresh red cells would seem unjustified in critically ill adults. Second, if true, from a basic science perspective changes noted to red-cells or the storage medium documented in many laboratory studies may have limited clinical consequences. The ABLE Study was published in *NEJM* on March 17th 2015.

**Marisa Tucci** is currently leading a parallel international study in children (The ABC-PICU Study). This study plans to assess the effect of the age of blood during transfusion on the gravity of organ failure in 1538 critically ill children admitted to pediatric intensive care units.

**THE PROPHYLAXIS FOR THROMBOEMBOLISM IN CRITICAL CARE TRIAL (The PROTECT Trial)**

**Principal Investigator:** Deborah Cook

A clot (thrombus) that is formed in a vein (a type of blood vessel) can be in the leg, arm, gastrointestinal tract or elsewhere. This venous thrombus can break loose and then be carried by the blood stream to plug another vessel (venous thromboembolism). If the travelling clot plugs an artery (another type of blood vessel) in the lung, it can have serious adverse effects and can cause death. Venous thromboembolism is a very common and potentially fatal problem in critically ill patients, and is a preventable cause of death in the intensive care unit (ICU). Prevention of venous thromboembolism is a key component of care of critically ill patients to try to reduce the chance of clot formation, reduce the chance of embolization and reduce the risk of death. The anticoagulant drug heparin is an effective and a safe prevention strategy, used around the world.

Researchers from the CCCTG, led by Deborah Cook and others, in addition to colleagues from the Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZICS CTG) compared the two most common prevention strategies in critically ill medical-surgical patients - the newer and more expensive low-molecular-weight-heparin (LMWH) dalteparin versus the standard unfractionated heparin (UFH).

The results of the PROTECT Trial were published in the *NEJM* in 2011. PROTECT showed that while there was no difference between the two drugs in mortality nor leg clots, patients who received LWMH had the same bleeding rates but reduced rates of clots in the lung and reduced risk of a potentially fatal drug allergy called heparin-induced thrombocytopenia (HIT) (a reduced number of platelets in the blood that increases the clotting risk).
In 2014, Robert Fowler of the CCCTG and colleagues from ANZICS CTG, in an article in the Journal of the American Medical Association, now demonstrated the economic consequences of these two prevention strategies (Fowler et al. 2014). The lower rates of pulmonary embolism and heparin-induced thrombocytopenia and corresponding lower overall use of resources with LMWH means that from a health care payer perspective, venous thromboembolism prophylaxis with LMWH was more effective and had similar or lower costs than the use of UFH. For example, if an ICU with 1000 medical-surgical admissions per year uses UFH instead of LMWH, the increase in cost may be between $1,000,000 and $1,500,000 per year with similar or worse clinical outcomes. In other word, this careful economic analysis showed better health outcomes and overall, lower health care costs when using LMWH for the prevention of venous thromboembolism in the ICU.

In addition, Mark Crowther led a study that evaluated whether a published clinical prediction rule (the “4Ts score”) reliably rules out HIT. This study was conducted in “low-risk” patients from PROTECT and concluded that real-time 4Ts scoring by research coordinators at the time of testing for HIT was not consistent with 4Ts scores obtained by central adjudicators. The results of this comprehensive HIT testing published in 2014 in the Journal of Critical Care highlighted the need for further research to improve the assessment of PTP scoring of HIT for critically ill patients (Crowther et al. 2014).

End of Life Care

DEATH DETERMINATION PRACTICES IN INTENSIVE CARE UNITS
(The DDePICt Research Program)

Principal Investigator: Sonny Dhanani

The dying process is a natural part of life, and while difficult and sad, can also present opportunities for new beginnings through organ and tissue donation. When possible, the opportunity to donate organs after death should be integrated into good end of life care. A growing number of donations in Canada are resulting from “donation after circulatory death” (DCD), a type of donation that does not require donors to meet stringent brain death testing criteria. Physicians and the public are supportive of DCD, but ethical and logistical concerns continue to hinder its uptake. Some of these concerns include: the inability to predict which donors will successfully proceed to donation after withdrawal of life support therapy, lack of consensus on the definition of circulatory death and how to diagnose it, and disagreement about how long to wait after a person has died before organ procurement begins. In addition, some critics of DCD cite the
possibility of autoresuscitation, or spontaneous resumption of circulation without intervention, as a reason to delay the time to organ procurement after cardiac death. Each delay increases the amount of time that organs remain without oxygen and risks the potential for organ damage. A systematic review of scientific literature completed by the study team in 2010 found no reports of autoresuscitation after a withdrawal of life sustaining therapy, but concluded that evidence was not sufficient to draw a final conclusion.

The DePPICt research program lead by Sonny Dhanani from the CCCTG aims to provide much needed information about the physiology of death after withdrawal of life sustaining therapy in the ICU, helping to inform DCD practice and thereby ultimately increasing organ donation rates in Canada.

In 2014, the DePPICt study team published the results of the pilot study in Critical Care Medicine (Dhanani et al. 2014). The pilot study recruited 41 out of a goal of 45 patients, had a consent rate of 87%, and recorded 73% protocol compliance. The landmark pilot study was able to show feasibility of examining the natural history of the dying process following withdrawal of life sustaining therapies in Canadian ICUs by recording and analyzing the vital signs of dying patients.

In 2014, the DePPICt team received funding as part of the Canadian National Transplant Research Program for a larger study. Death Prediction and Physiology after Removal of Therapy (DePPaRT) will aim to recruit 500 patients at 14 sites across Canada, and several sites internationally, including in the Czech Republic and the United Kingdom. The DePPaRT study will document the physiology of the dying and will also aim to develop a tool that will allow doctors to predict how long it will take patients to die after the removal of life sustaining therapy. A qualitative component of the study will investigate the decision-making surrounding organ donation and how family members felt when their loved ones became organ donors or were unable to proceed to donation. Results from both the quantitative and qualitative aspects of this study will be invaluable in influencing DCD policies across Canada. By answering questions about DCD, this study will help to ensure an increase in organ donation.
Technology Evaluation

EVALUATION OF ALTERED HEART RATE AND RESPIRATORY RATE VARIABILITY TO PREDICT EXTUBATION (The WAVE Study)

Principal Investigator: Andrew Seely

Extubation, defined as the removal of the endotracheal tube used in mechanically ventilated patients, is one of the most critical steps in the care of Intensive Care Unit (ICU). Expeditious yet safe extubation is critical, as prolonged mechanical ventilation harms patients and failed extubation (requiring re-intubation within 48 hours) is associated with increased morbidity, mortality and elevated costs.

Spontaneous breathing trials (SBTs) are the current standard of care to assist in the determination of timing of extubation. During SBTs, patients are subjected to trials of reduced ventilatory support, taking on a greater workload of breathing and simulating breathing after extubation. Absence of rapid shallow breathing or other evidence of increased stress during an SBT are the current standard indicators that it is safe to extubate. Despite this practice, numerous literature reports document an average failed extubation rate of 15%.

In 2009, researchers from the CCCTG, led by Andrew Seely, and others from 12 hospitals across Canada and the United States, initiated the Weaning and Variability Evaluation (WAVE) study, a large prospective, blinded observational multicenter cohort study to improve safety when liberating patients from mechanical ventilation by evaluating novel means to predict extubation failure, utilizing continuous variability monitoring. In particular, WAVE researchers investigated the added value of using heart and respiratory rate variability (HRV and RRV) during SBTs to predict extubation failure. Variability analysis documents the degree and patterns of change of physiologic parameters over intervals-in-time. Loss of variability is generally indicative of reduced adaptability, increased stress and illness severity.

721 ICU patients were enrolled and high quality continuous heart rate and respiratory rate data from 434 patients were used to train and validate a predictive model, and estimate the probability of extubation failure (WAVE score), based on a small subset of variability measures. The WAVE score was able to predict extubation failures better than simple vitals, clinical impression and commonly used indices, such as the rapid shallow breathing index (RSBI), in particular in patients perceived as high-risk. Altered HRV and RRV (during the SBT prior to extubation) were shown to be significantly associated with extubation failure.

The results of the WAVE study were published in Critical Care in April 2014 (Seely et al. 2014).
Enhancing Recovery

SEDATION LIGHTENING – EVALUATION OF A PROTOCOL
(The SLEAP Trial)
Principal Investigator: Sangeeta Mehta

All critically ill, mechanically ventilated patients in the Intensive Care Unit (ICU) receive medications to relieve pain and anxiety. However, accumulation of these medications can be associated with serious complications, most notably longer time on the breathing machine and in the ICU. Two strategies have been shown to dramatically improve patient outcomes: nurse-directed protocols for giving sedation, and daily interruption of sedation. However, these strategies were not widely adopted, because of clinicians’ concerns about patient discomfort and agitation, and additional workload imposed by these strategies. Further, it was unclear which strategy was better for patients. Given that patient outcome could potentially be improved with either of these strategies, the fundamental question that arose was whether patients managed with a combination of two strategies which both reduce drug accumulation (protocolized sedation and daily interruption) would have an even better outcome than patients managed with only one of them (protocolized sedation).

Led by Sangeeta Mehta, researchers from the CCCTG compared protocolized sedation alone, or protocolized sedation and daily interruption, in critically ill mechanically ventilated patients. The SLEAP Trial was published in the Journal of the American Medical Association (JAMA) in 2012. The SLEAP trial showed that there was no difference between the two groups in the time spent on the breathing machine, nor in the ICU. Unexpectedly, the daily interruption group received higher doses of sedatives, and the nurses taking care of these patients reported a higher workload. By demonstrating that daily sedation interruption is not advantageous if a protocol which targets minimal sedation is used in all patients, the SLEAP Trial informed sedation practice around the world.

In early 2015, the SLEAP Collaborators published two additional articles showing results from the SLEAP Trial. In an article in Critical Care Medicine, Sangeeta Mehta and her coauthors described the incidence, risk factors and outcomes of delirium in mechanically ventilated adults. Among critically ill patients enrolled in the SLEAP trial, delirium was common, occurring in 54% of patients, with the same frequency in both groups. Delirium was associated with longer time on the breathing machine (by 6 days) and in the ICU (by 4 days). The application of physical restraints while in the ICU was most strongly associated with delirium; patient age, severity of illness, and prior alcohol or tobacco use were not associated with delirium.

70% of patients had delusional memories 28 days after discharge, and these were not related to the sedation strategy they were managed with.
In an article published in *Journal of Critical Care* in April 2015, Louise Rose and the SLEAP Collaborators described the results of a survey of nurse and physician perspectives on the sedation protocol and daily sedation interruption strategies used in the SLEAP Trial. While most respondents (81%) liked both sedation strategies, more physicians than nurses liked DI (100% vs 61%). Nurses and physicians had different preferences and rationales for liking or disliking each strategy. Compared with physicians, fewer nurses liked using daily sedation interruption, citing patient discomfort and safety concerns.

In 2012, Louise Rose presented data on sleep and psychological illness of SLEAP patients after ICU discharge, at the Society of Critical Care Medicine conference in Houston, Texas. Of 63 patients evaluated at 6 months, 14% had an anxiety disorder, 7% had a mood disorder, and 13% had symptoms of post-traumatic stress disorder. On average, patients had moderate sleep impairment.

In 2013, Lisa Burry presented data on the recall of ICU stay in SLEAP patients at the European Society of Intensive Care Medicine Congress in Paris, France. On days 3, 28 and 90 after ICU discharge, 28%, 26%, and 36% of patients, respectively, reported no recall of being in the ICU. 70% of patients had delusional memories 28 days after discharge, and these were not related to the sedation strategy they were managed with.

In 2014, Louise Rose presented data on factors associated with physical restraint use in patients enrolled in the SLEAP trial, at the European Society of Intensive Care Medicine Congress in Barcelona, Spain. 76% of patients had physical restraints applied, for a median of 4 days; and restraint use was similar in the two groups. Restrained patients received higher daily doses of sedatives, pain medications, and antipsychotic drugs. More restrained patients had unintentional device removal (26% vs 3%). We did not identify any patient characteristics or treatment factors that predicted restraint application.

The SLEAP Trial has provided the Critical Care Community with a wealth of information about sedation management and critically ill patients.
Our Funding Partners

Institute of Circulatory and Respiratory Health of the Canadian Institutes of Health Research
www.cihr.ca

Centre de recherche du Centre hospitalier de l’Université de Montréal
crchum.chumontreal.qc.ca

Critical Care Strategic Clinical Network, Alberta Health Services
http://www.albertahealthservices.ca/9437.asp

The Ottawa Hospital
www.ottawahospital.on.ca

The Hospital for Sick Children (SickKids)
www.sickkids.ca

Centre hospitalier universitaire Sainte-Justine
www.chusj.org

Regroupement de Soins Critiques Respiratoires, Réseau en santé respiratoire du FRQS
rsr.chus.qc.ca

International Forum for Acute Care Trialists
www.infactglobal.org

McMaster University
www.mcmaster.ca

Canadian National Transplant Research Program
www.cntrp.ca
Our Major Collaborators

Canadian Critical Care Society
www.canadiancriticalcare.org

aC3KTion Net
www.acktionnet.ca

The ANZICS Clinical Trials Group (CTG)

International Severe Acute Respiratory and Emerging Infection Consortium
isaric.tghn.org

Acute Respiratory Distress Syndrome (ARDS) Network
www.ardsnet.org

U.S. Critical Illness and Injury Trials (USCIIT) Group
www.usciitg.org
CANADIAN CRITICAL CARE TRIALS GROUP

900 St-Denis Street, Room R04-470
Montréal, Québec, H2X 0A9

T 514 890-8000 EXT 30833

E paul.hebert.chum@ssss.gouv.qc.ca
nicolay.ferrari.chum@ssss.gouv.qc.ca