



COVID-19 Network of Clinical Trials Networks



Canadian Critical Care
Trials Group

YEAR ONE OVERVIEW

MARCH 2022

The Network of COVID-19 Clinical Trials Networks is supported by the **Canadian Institutes of Health Research (CIHR)**, hosted at the **Sunnybrook Research Institute** and led by the **Canadian Critical Care Trials Group (CCCTG)**.



Contact

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COVID-19 AND BEYOND

Creating a Durable Infrastructure for Canadian Acute Care
Clinical Trials and Emergency Research Response

Led by the **Canadian Critical Care Trials Group (CCCTG)**, the **COVID-19 Network of Clinical Trials Networks (Network of Networks)** is a pan-Canadian partnership of over **400** inter-professional members - patient partners, clinical and translational scientists, health care professionals, research coordinators and trainees - at healthcare centres across Canada. As a national collaborative, we are already **solidifying a dynamic, responsive, nimble and durable clinical trials network in acute care.**

The CCCTG has **mentored and served as a template for many research networks** both in Canada and internationally. In January 2021, with support from CIHR, the CCCTG established the Network of Networks. It is building on 30 years of collaborations and a history of **championing scalable, context-responsive research approaches.**

The Network of Networks is:

- Supporting capacity at new sites, and in community hospitals, to participate in clinical trials and reach Canadians where they receive their care
- Building a tool to track enrollment and capacity at sites
- Developing infrastructure to automate data collection at hospital sites and linking it to trial data and population health data
- Establishing a Canadian framework for adaptive platform trials
- Encompassing a continuum of pre- to post- hospital research relevance and impact beyond the ICU, including rehabilitation and recovery
- Enhancing national partnerships and creating a framework for Indigenous engagement, and
- Creating tools to evaluate and enhance diversity in critical care research.

We are pleased to share the progress of the first full year of Network activities, and the foundation that is being created for lasting capacity-building and collaboration to embed research into clinical care and support a learning health system.

>1 dozen

Engaged
Networks

>4000

Canadians
in Trials

>40,000

Patients in
Partner Trials

>95,000

Canadians in
Studies

>100

Publications
Guiding Practice

GOVERNANCE



Rob Fowler, Chair
Sunnybrook Research Institute



Kusum Menon, Vice-Chair
Children's Hospital of
Eastern Ontario



Brenda Lucas
Executive Director
CCCTG & the Network of
Clinical Trials Networks

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Ryan Zarychanski
CancerCare Manitoba
University of Manitoba

GOVERNANCE

WORKING GROUPS

Community Acute & Critical Care

Platform Trials Committee

Equity, Diversity, Inclusion & Indigeneity

Pre-hospital & Emergency

Health Data Integration

Regulatory, Legal & Ethics Framework

Hospital Sites, Metrics, Tracking

Rehabilitation & Recovery

Hospital-based Research

Research Coordinators

International Partners

Training & Mentoring

Knowledge Translation & Rapid Mobilization

Translational Biology

Patient & Family Partnerships

ACROSS THE NETWORKS

HIGHLIGHTING OUTCOMES FROM COLLABORATIVE RESEARCH

NETWORKS, TRIALS & STUDIES



GUIDING CLINICAL PRACTICE

SOLIDARITY, CATCO



Remdesivir has a modest but significant effect on outcomes important to patients and health systems, such as the need for mechanical ventilation.

Canadian Medical Association Journal 2022; early-released January 19, 2022.
doi:10.1503/cmaj.211698

Repurposed medication did not reduce mortality, initiation of ventilation or hospitalization duration.

New England Journal of Medicine 2021; 384:497-511. doi:10.1056/NEJMoa2023184

Networks: WHO Solidarity Consortium, CATCO, CCCTG, AMMI



ATTACC

Therapeutic-dose anticoagulation with heparin increased the probability of survival until hospital discharge with reduced use of ICU-level organ support in noncritically ill patients hospitalized with COVID-19.

New England Journal of Medicine 2021; 385:790-802.
doi:10.1056/NEJMoa2105911

In contrast to the benefit that was found in noncritically ill patients, a parallel analysis from the same multiplatform trial showed that empirical therapeutic-dose anticoagulation was not beneficial in critically ill patients.

New England Journal of Medicine 2021; 385:777-789.
doi:10.1056/NEJMoa2103417

Networks: CanVEctor; National Institutes of Health, REMAP-CAP, ACTIV-4a, and ATTACC Investigators



REMAP-CAP



Among critically ill patients with COVID-19, lopinavir-ritonavir, hydroxychloroquine, or combination therapy worsened outcomes and the interleukin-6 receptor antagonists tocilizumab and sarilumab improved outcomes including survival. Use of hydrocortisone in patients with severe COVID-19 did not show a conclusive benefit and convalescent plasma in critically ill adults with COVID-19 had a low likelihood of increasing organ support-free days.

Intensive Care Medicine 2021 Aug;47(8):867-886.
doi:10.1007/s00134-021-06448-5

New England Journal of Medicine 2021 Apr 22;384(16):1491-1502. doi:10.1056/NEJMoa2100433

Journal of the American Medical Association 2020 Oct 6;324(13):1317-1329. doi:10.1001/jama.2020.17022

Journal of the American Medical Association 2021 Nov 2;326(17):1690-1702. doi:10.1001/jama.2021.18178

Networks: REMAP-CAP investigators



GUIDING PLANNING AND POLICY

RESTRICTED FAMILY VISITATION POLICIES DURING COVID

Visitation policies varied between centres during the COVID-19 pandemic with some allowing visitation in end-of-life cases and with COVID-19 patients while others did not allow any visitors. The use of videoconference technology and changes to communication structure were important strategies to facilitate effective communication within the ICU. Further studies are underway to understand the impacts of these policies on patient- and family-centred care.



Annals of the American Thoracic Society 2021; online ahead of print. doi:10.1513/AnnalsATS.202107-877OC

Canadian Journal of Anesthesia 2021;68, 1474–1484. doi:10.1007/s12630-021-02049-4



ISARIC



Canadian data contributions to the ISARIC global federation of clinical research networks

Infection 2021;49, 889–905. doi:10.1007/s15010-021-01599-5

European Respiratory Journal Open Research 2021;8. doi:10.1183/23120541.00552-2021

The Lancet Infectious Diseases 2021;21, e363. doi:10.1016/S1473-3099(21)00565-X

Networks: ISARIC Clinical Characterization Group

SPRINT-SARI CANADA



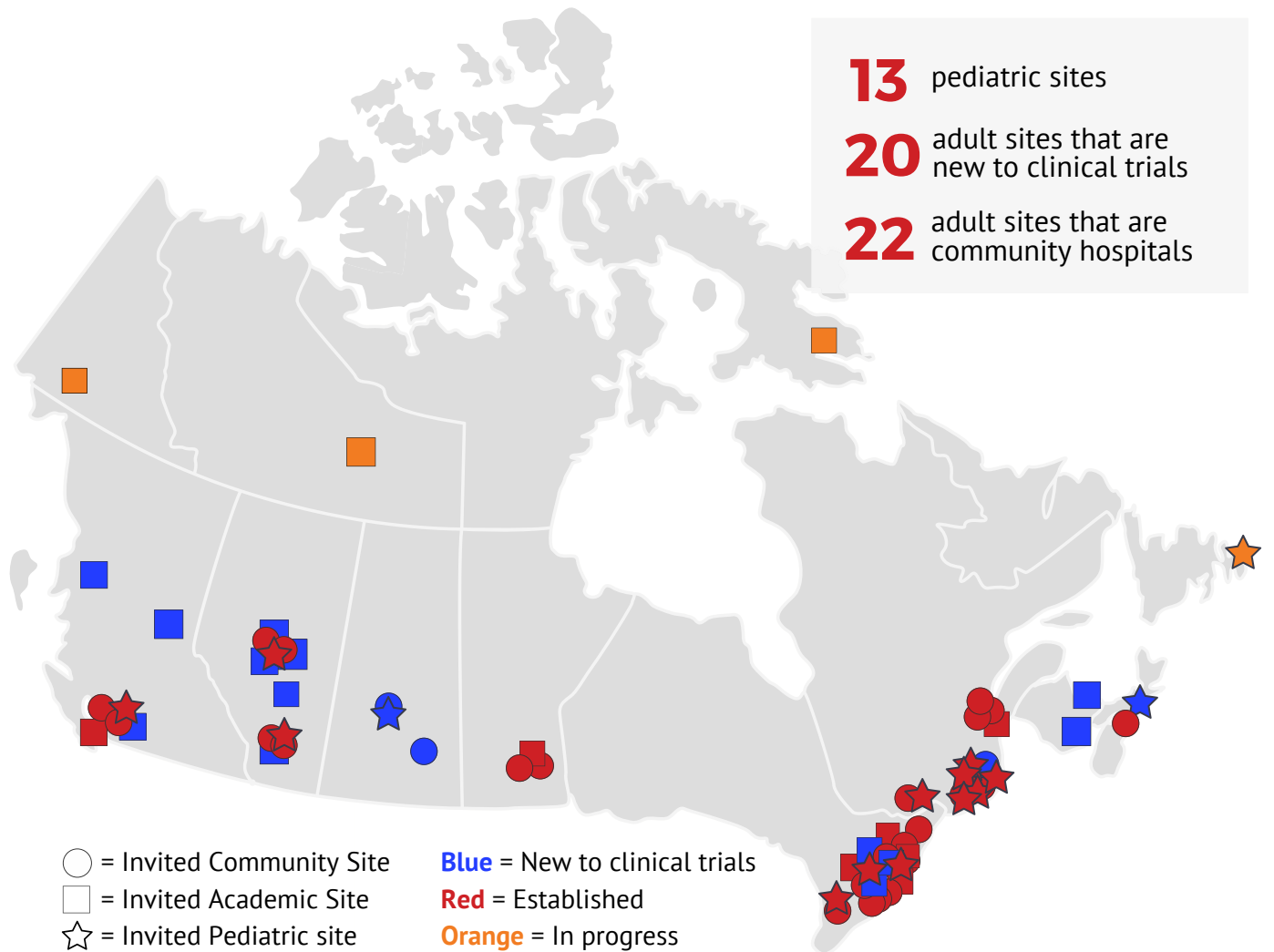
Reported clinical characteristics and outcomes of 811 patients admitted to hospital during the first wave of the COVID-19 pandemic in Canada. These data are crucial to understand the impact of COVID-19 on our hospitals, identify areas for improvements in clinical management, and allow for ongoing comparisons of outcomes for patients with COVID-19.

CMAJ Open. 2021 Mar 8;9(1):E181-E188. doi:10.9778/cmajo.20200250



Networks: SPRINT-SARI Canada Investigators and the CCCTG

CAPACITY BUILDING



The Network of Networks is supporting new and established sites, **building the needed capacity at hospitals to participate in multi-centre clinical trials.** Sites will be provided both direct and indirect support to create or augment research programs.

Research Coordinators (RCs) play a critical role in a site’s ability to participate in clinical research. Among the **66** invited hospital sites, initial responses indicated **12** sites that have no RC capacity, and many others have only partial support or uncertain funding to support this vital role.

By inviting and selecting sites based on their potential to increase capacity to both engage in research and enroll patients into clinical trials, we will:

- Provide **>\$2M total direct financial support** as partial salary for Research Coordinator positions to at least **50 sites** (community and academic, adult and pediatric)
- Provide **critical non-financial support**, particularly for new RCs
- As a national team, create a **dedicated RC Navigator role** to provide direct training and assistance for new sites
- Increase linkages, development and support among trialists at **community sites**

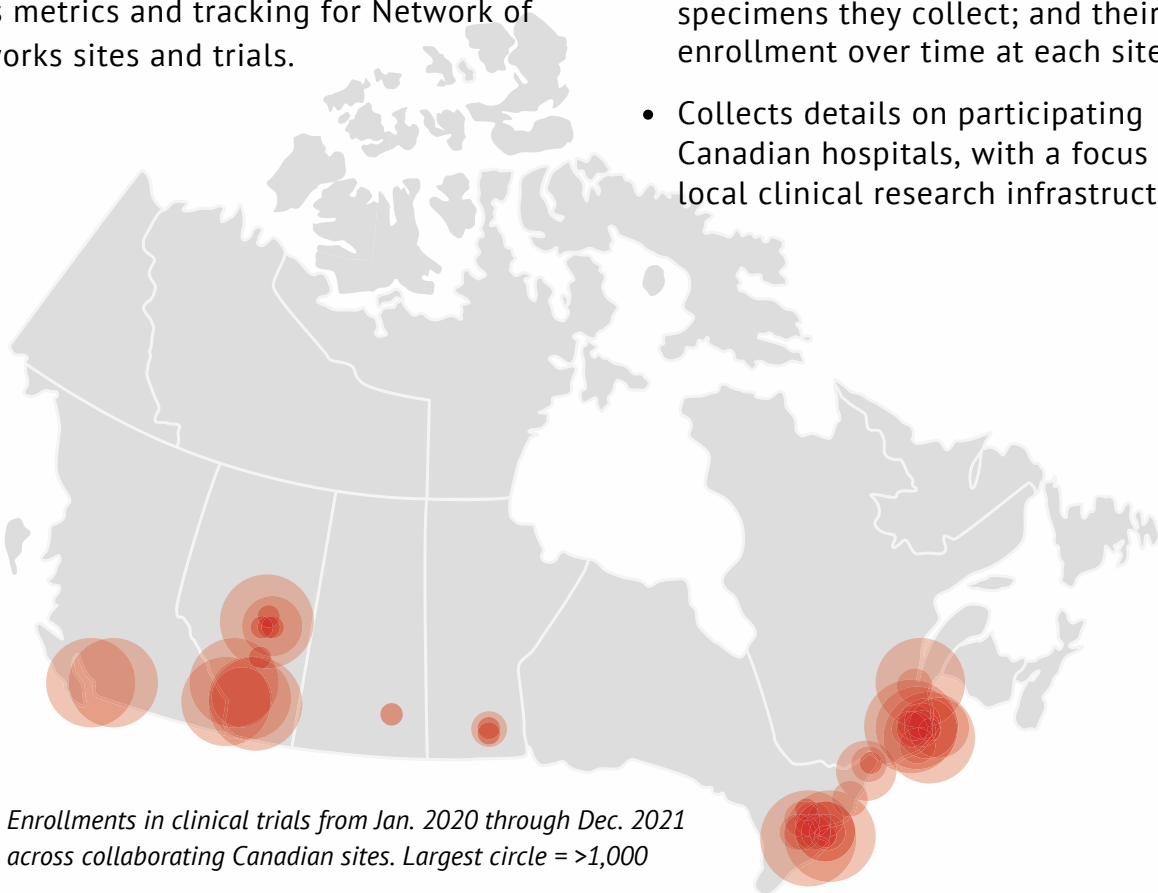


HOSPITAL SITES, METRICS, TRACKING

The Network of Networks has partnered with the **Canadian Clinical Research Network**, an initiative created by l'Université de Sherbrooke and also supported by Sepsis Canada. This network leads metrics and tracking for Network of Networks sites and trials.

The Canadian Clinical Research Network:

- Describes studies conducted across Canadian hospitals: their patient populations, interventions, comparators and outcomes; the data and biological specimens they collect; and their enrollment over time at each site
- Collects details on participating Canadian hospitals, with a focus on the local clinical research infrastructure



Enrollments in clinical trials from Jan. 2020 through Dec. 2021 across collaborating Canadian sites. Largest circle = >1,000



LEADERSHIP

François Lamontagne
Université de Sherbrooke

Michelle Kho
McMaster University

Marie-Hélène Masse
Université de Sherbrooke

Marilyn Swinton
McMaster University

Katie O'Hearn
Children's Hospital of Eastern Ontario



Irene Watpool
The Ottawa Hospital

Aleksandra Leligowicz
University Health Network

Sheila Sprague
McMaster University

Denis Boutin
Patient Partner





EQUITY, DIVERSITY, INCLUSION AND INDIGENEITY

The Network of Networks seeks to **advance equity-focused health care through equity-focused research**. Specifically, we are:

- Integrating EDII-related considerations into research design and practices
- Promoting equitable and inclusive participation in the research system, including on research teams; and
- Collecting data and conducting analyses needed to include EDII considerations in decision-making

We commit to increasing the representation and role of Indigenous peoples in Network activities in order to improve the care of critically ill Indigenous peoples in Canada.



LEADERSHIP

Sangeeta Mehta
Mount Sinai Hospital

Kirsten Fiest
University of Calgary



REHABILITATION AND RECOVERY



LEADERSHIP

Angela Cheung
University Health Network

Michelle Kho
McMaster University

OUTCOMES OF CRITICALLY ILL COVID-19 SURVIVORS AND CAREGIVERS

Outcomes of critically ill COVID-19 survivors and caregivers: a case study-centred narrative review

Canadian Journal of Anesthesia 2022 Jan 31; online ahead of print. doi:10.1007/s12630-022-02194-4

The Network of Networks is improving care for patients with COVID-19 and addressing **rehabilitation and recovery for survivors of COVID-19**. This working group connects with other networks and trials to meet this objective, including:

- The **REVIVE** trial, which is examining the association of frailty, rehabilitation, and extubation with short term outcomes
- The **Canadian COVID-19 Prospective Cohort Study (CANCOV)** collaboration and multi-centre prospective observational study, looking at long-term outcomes for ambulatory and hospitalized patients.





TRAINING AND MENTORING



The Network of Networks is providing training and mentoring opportunities that foster the conduct of rigorous, relevant, ethical, and efficient COVID-19 research to three key stakeholder groups from academic and community institutions:

- Early-career, mid-career and senior investigators
- Research coordinators, new and established
- Citizens, including patients and family members across Canada



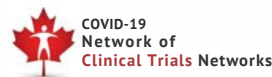
LEADERSHIP

Dominique Piquette
University of Toronto

Krista Wollny
University of Calgary

LifTING RESEARCH TRAINING PLATFORM

Under the leadership of Dominique Piquette, Patricia Fontela and Denise Jaworsky, the Network of Networks and Sepsis Canada will pilot the **Life Threatening Illness National Group (LifTING) Research Training Platform: Spanning Boundaries Between Research and Care**. The platform was awarded \$2.4M in funding from the CIHR Health Research Training Platform Pilot opportunity.



COMMUNITY AND EMERGENCY CARE



COMMUNITY ACUTE AND CRITICAL CARE

The Network of Networks is supporting community-based ICUs to participate in clinical trials with additional capacity building, including:

- **Coordinating links between study investigators and community ICUs**, and supporting physicians at community hospitals who want to undertake research
- Supporting the Network in the creation of a **Research Coordinator Navigator** role to assist the development of community-based research programs

This work will increase:

- The number of community hospitals actively participating in clinical trials
- The number of trials occurring in community hospitals, and
- The geographic diversity of community hospitals participating in clinical trials



Jennifer Tsang
Niagara Health

Alexandra Binnie
William Osler
Health System



PRE-HOSPITAL AND EMERGENCY

The **Canadian COVID-19 Emergency Department Rapid Response Network (CCEDRRN)** is a national collaboration with Public Health partners to harmonize data collection related to COVID-19 in more than 51 Emergency Departments across 8 provinces.



Patrick Archambault
CSSS Alphonse-Desjardins
CHAU Hôtel-Dieu de Lévis

*Working group Co-lead
May Solis, pictured
with her late father,
who is the reason
behind her leadership
in Patient & Family
Partnerships*



PATIENT & FAMILY PARTNERSHIPS

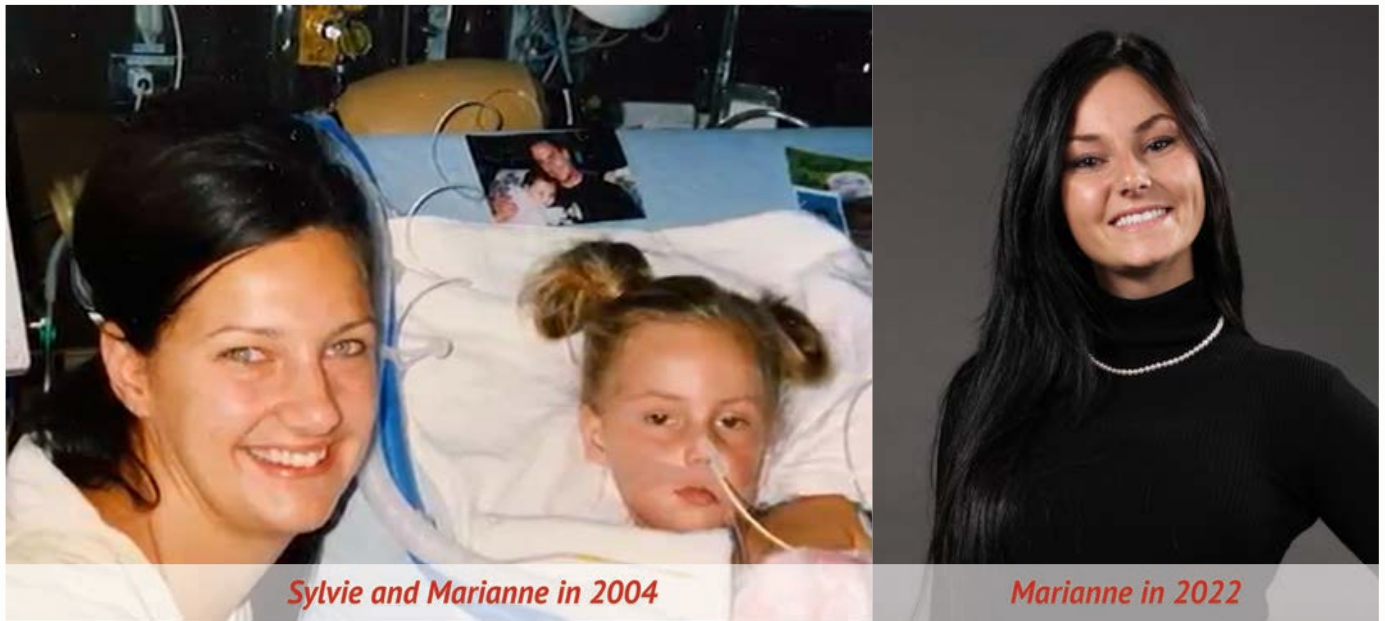
Fostering partnership between patients and family and researchers and other health care professionals is at the core of the Network of Networks' activities.

Building and strengthening its links with patients, families and caregivers, the Network of Networks Patient and Family Partnerships Working Group is curating and developing resources for the research community, patients and family members to facilitate and improve engagement.



In partnership with the Alberta SPOR SUPPORT Unit, the Patient and Family Partnerships Working Group has developed and delivered patient engagement training modules for the Network of Networks and CCCTG members.

Two sessions were offered in the fall of 2021: The first was delivered to a broad audience and covered Patient Oriented Research. The second session engaged patients, other non-researchers (including health care professionals and system decision-makers) in situating their interests and roles within a well-rounded understanding of research processes.



SYLVIE'S STORY

My name is Sylvie Debigaré and I am a school psychologist in Québec, but first and foremost I am mom to my two amazing children. Back in 2004 my mommy role was put through the hardest situation any parent can go through. My 3-year-old daughter became so ill she had to be placed in an induced coma and mechanically ventilated to save her life. This month-long episode has impacted our family profoundly.

We are extremely lucky and grateful that Marianne pulled through intact without lasting deficits except for the family PTSD associated with this ordeal. Part of the healing process has rested on the continued connection that I kept with some of the PICU doctors at Ste-Justine's hospital that saved Marianne. It ultimately led to my participation in the creation of the Patient and Family Partnerships Committee of the CCCTG that I have been co-chairing and chairing since 2015.

I strongly believe that the collaboration between Patients and Family and researchers contributes to more holistic and inclusive approach and outcomes. The CCCTG's actions towards inclusion of Patients and Families can surely be considered a success. I personally feel privileged and proud to have contributed to this from the beginning.

The knowledge that your partnership and engagement will help improve the quality of care and quality of life of ICU patients and their families - in the immediate or long term - is a powerful incentive.

Sylvie Debigaré
Chair, CCCTG Patient & Family Partnerships Committee
Trois-Rivières, Québec



RESEARCH COORDINATORS

The Network of Networks is developing resources to **streamline study startup, management and recruitment**, and creating training and professional supports that will **facilitate research coordination** across the country.

We have established a National Research Coordinator role, convened a team of research coordinator mentors, and hosted a mentorship training session. In 2022, we will:

- Build a small national team to work with the national coordinator
- Launch a mentorship program
- Finalize, implement and disseminate resources, tools and supports across sites, including creation of a new template library
- Host the first Network of Networks Research Coordinators workshop



HOSPITAL-BASED RESEARCH

The Network of Networks is growing the network of clinicians and researchers who participate in outpatient and hospital-based non-critical care research on COVID, sepsis and other significant infectious diseases in Canada.

Specifically, the group is engaging medical subspecialists in hospital-based research, especially in the domains of general internal medicine, infectious diseases and microbiology, respiratory and cardiology. They are **linking research taking place in the community, on the medical wards and on clinical teaching units, with research taking place in the critical care setting.**





DATA STRATEGY

Establishing and Piloting a National Infrastructure for Automated Data Collection at Source and Integration of Data

The **Data Strategy Working Group** was established to engage experts from across Canada in developing a strategy to leverage new technologies that improve data collection and analytics for clinical trials in a real-world context.

The Network of Networks is facilitating implementation and testing of a data infrastructure to support clinical trials by identifying prospective pilot sites and building local awareness in collaboration with individuals, teams and departments within each member's organization or jurisdiction.

The Data Strategy Working Group is building an Application Programming Interface (API) that will allow for data mapping from sites to a target electronic Case Report Form, with a goal of minimizing manual data collection. The Data Strategy is expected to be launched and piloted in 2022. The first trials piloted will be **REMAP-CAP** and **CATCO**, spanning multiple jurisdictions.

This Working Group is Co-Chaired in collaboration with **Health Data Research Network Canada (HDRN)** to maintain alignment across the respective multi-jurisdictional CIHR-funded networks.

LEADERSHIP

Nicole Yada
Health Data Research Network Canada

Michaël Chassé
Centre Hospitalier de l'Université de Montréal

Réseau de recherche sur les données de santé du Canada
Health Data Research Network Canada

CRCHUM
CENTRE DE RECHERCHE
Centre hospitalier
de l'Université de Montréal

NATIONAL PEDIATRIC CRITICAL CARE DATA STRATEGY



With support from a CIHR Community Development Grant, CCCTG held a competition for a project that would benchmark services across ICUs. Funding was awarded in 2020 to Patricia Fontela and Srinivas Murthy to undertake a **National Pediatric Critical Care Data Strategy**. Building on established data collection strategies at individual PICUs, the project will develop a framework for a national registry of patients admitted to Canadian PICUs.



KNOWLEDGE TRANSLATION

The Network of Networks is leveraging its members' extensive knowledge translation and mobilization roles within national and international agencies to build our knowledge translation community, strengthen established national and international partnerships, and enhance engagement of patients and family caregivers. Through an integrated knowledge mobilization network approach, knowledge users are involved throughout the Network's activities.

ENHANCED PATIENT ENGAGEMENT: IC4U

IC4U is a platform and online community for patients and caregivers to partner with researchers and health care providers on ICU research studies. IC4U will invite diverse communities and historically under-represented groups to participate, directing research focus to issues that are relevant to a greater diversity of Canadians.





Dayre McNally
University of Ottawa

Bram Rochweg
McMaster University



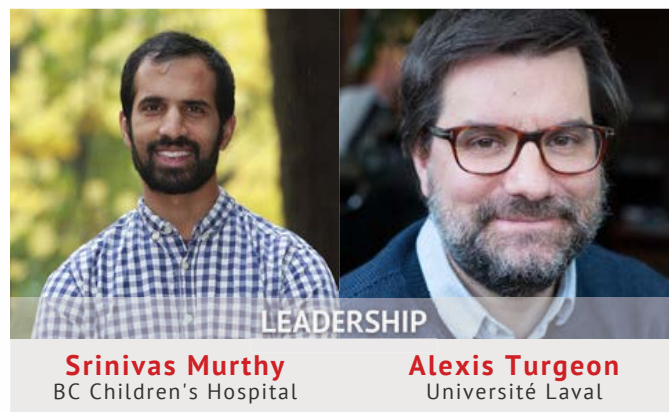
WHO GUIDELINE

A living WHO guideline on drugs for COVID-19
 BMJ. 2020 Sep 4;370:m3379.
[doi: 10.1136/bmj.m3379](https://doi.org/10.1136/bmj.m3379)


REGULATORY, LEGAL AND ETHICS

To be able to respond quickly and efficiently to health emergencies, the Network of Networks is developing **legal and regulatory tools for expediting investigator-led clinical trials research**. We will support efforts to streamline current process, and to create **unique, timesaving processes** where needed that can be invoked in response to a declared health emergency.



Srinivas Murthy
BC Children's Hospital

Alexis Turgeon
Université Laval





PLATFORM TRIALS



Adaptive trials allow investigators to study multiple therapies within a single clinical trial and allow for planned changes to the study protocol to occur at pre-specified times during the life cycle of a trial. Adaptive platform trials (APTs) enable different interventions or treatments to be studied in a perpetual way, without the need to stop or create a brand new study protocol. Modifications can be made based on interim data collected that indicates that a particular intervention is working or does not warrant further study, based on criteria that are defined in advance. APTs also help to get answers in relatively short periods of time, facilitating international collaboration.

Several APTs are established internationally, and Canada has been a leading jurisdiction in two of them: CATCO and REMAP-CAP.

The Network is helping to build a platform trial infrastructure, including the creation of a Director of Platform Trials role. The **Canadian Adaptive Platform Trial (Can-ADAPT)** platform will provide opportunities for research teams to study priority interventions into a platform structure highlighted by common case report forms, outcome definitions, informed consent processes, contracts, and an analytic structure. It will be piloted in 2022 with two initial trials.

Creating the templates and processes for APTs will not only make the approach more efficient and cost-effective, it will enable researchers to utilize this novel research design more easily, facilitating adoption by a broader and more diverse community of investigators.





Photos provided by Sunnybrook Health Sciences Centre



LOOKING AHEAD

During the COVID-19 pandemic, we incorporated COVID-19 pandemic-relevant treatment arms and enrolled COVID-19 infected patients in Canada and – with international partners – around the world through adaptive platform clinical trials.

CCCTG, the Network of Networks and our partners have made globally significant research contributions. But the speed and agility of our research response, and the reach of our engagement of Canadian patients must be better when we face the next health emergency. **We will create the tools and capacity that Canada needs to be a leader in embedding research into critical care** to improve treatment every day, and to quickly and effectively respond to future emergencies.



CAPACITY

Train future researchers and build robust research programs at community hospitals



INFRASTRUCTURE

Create a Canadian adaptive platform trial infrastructure

Establish tools for automated data collection, integration with health administrative data and tracking of enrollment across the country



COMMUNITY

Continue to enhance knowledge translation, facilitate collaboration with other networks and organizations

Rigorously evaluate – and increase – diversity among researchers and patients who participate in clinical trials, and create meaningful partnerships with Indigenous Peoples