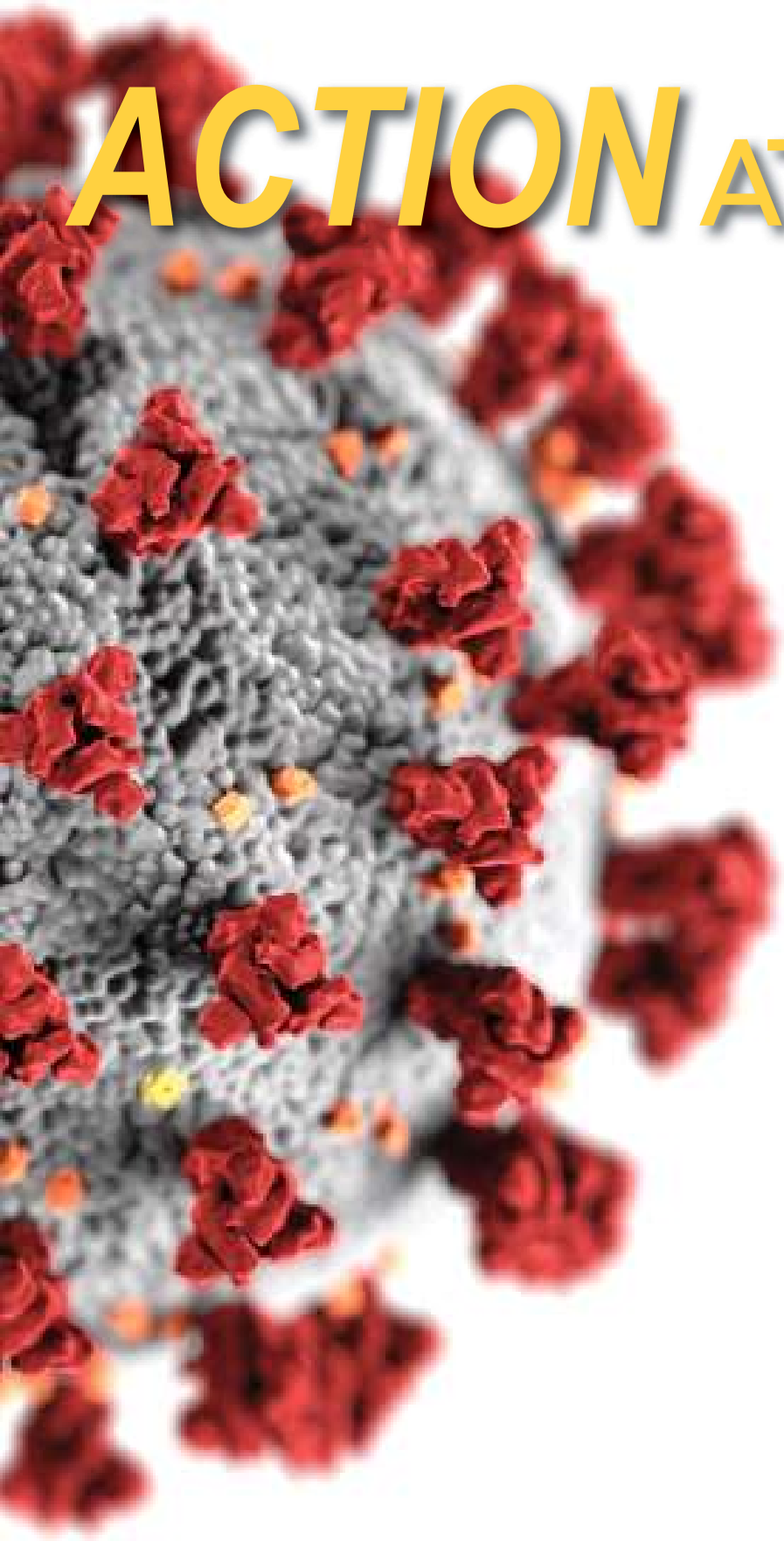
ACTION AT GRH



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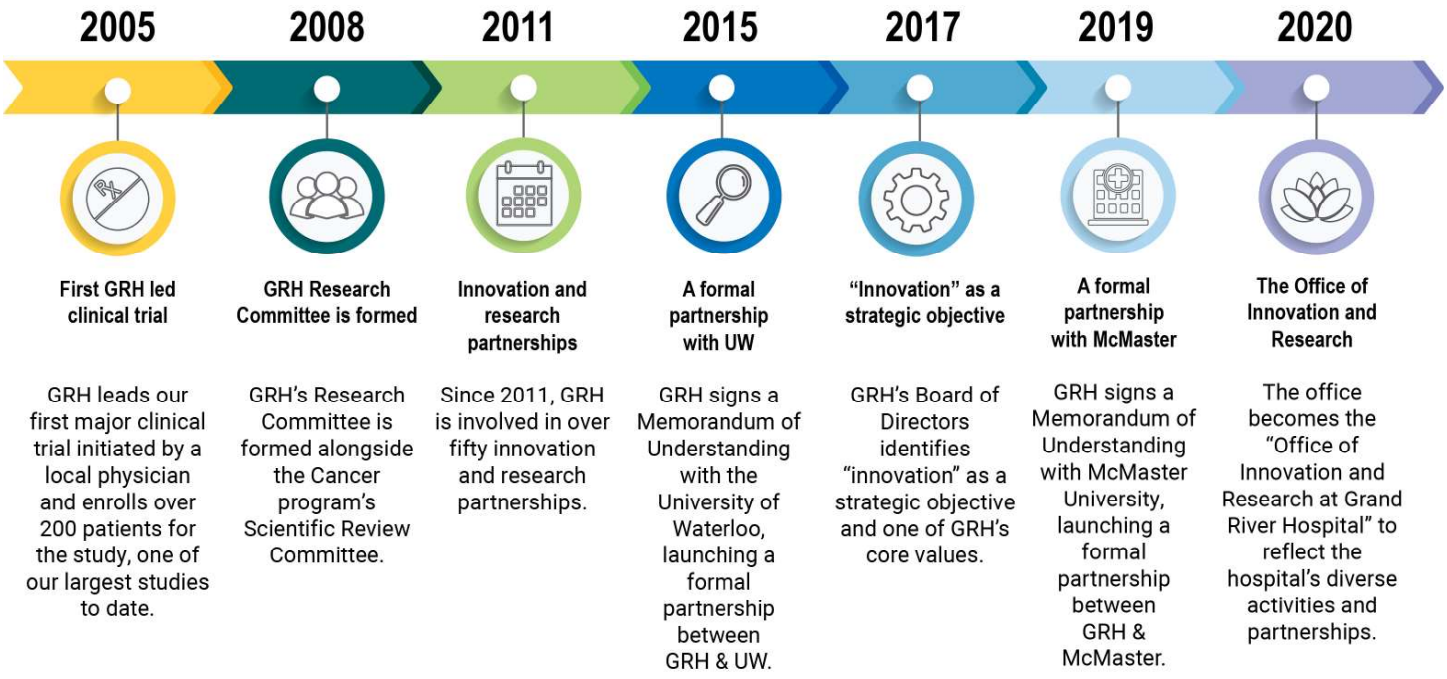
BRINGING TOGETHER INNOVATION AND EXCEPTIONAL CARE

Summer 2020

The Office of Innovation and Research (OIR) at Grand River Hospital brings clinicians and research and industry partners together to explore new ways of improving patient care.

We coordinate all innovation and research activities at Grand River Hospital, one of the largest and busiest community hospitals in Ontario, with 665 beds, over 3700 staff, approximately 700 physicians, dentists, midwives and nurse practitioners, and 1,000 volunteers. OIR supports and participates in multi-disciplinary clinician-based applied research in each of GRH's 15 clinical programs and service areas. Through partnerships with institutions across the Waterloo-Wellington region, such as the University of Waterloo and McMaster University Michael G. DeGroote School of Medicine, OIR provides researchers and clinicians with the opportunity to work together on groundbreaking studies that advance exceptional care at GRH.



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OIR-GRH

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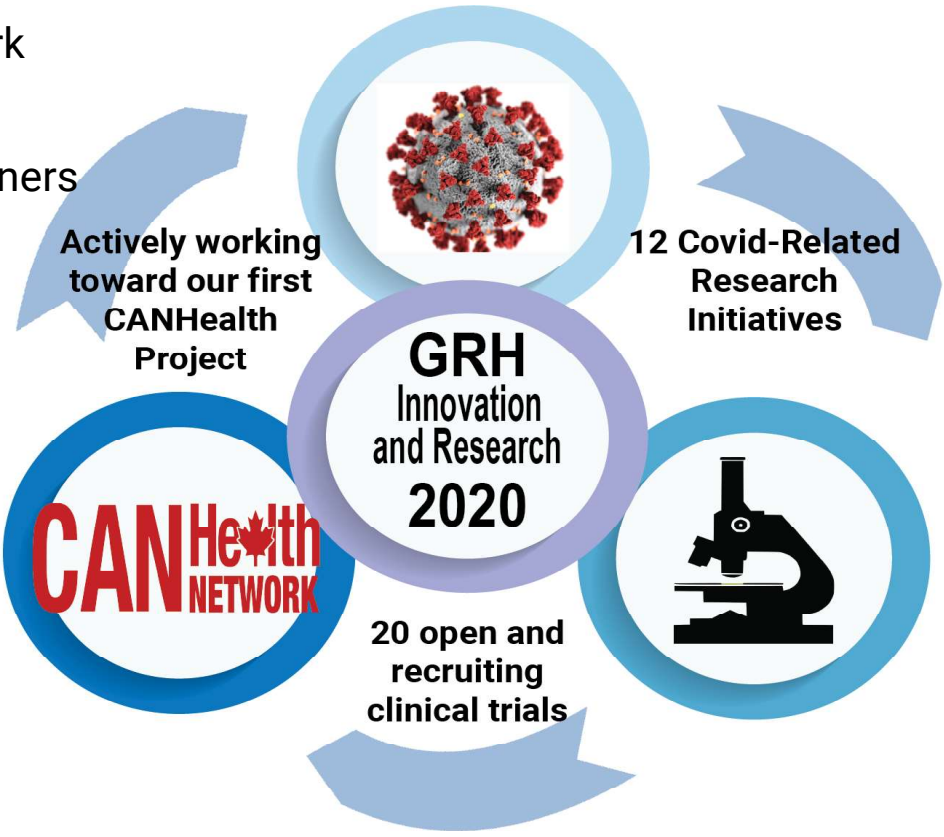
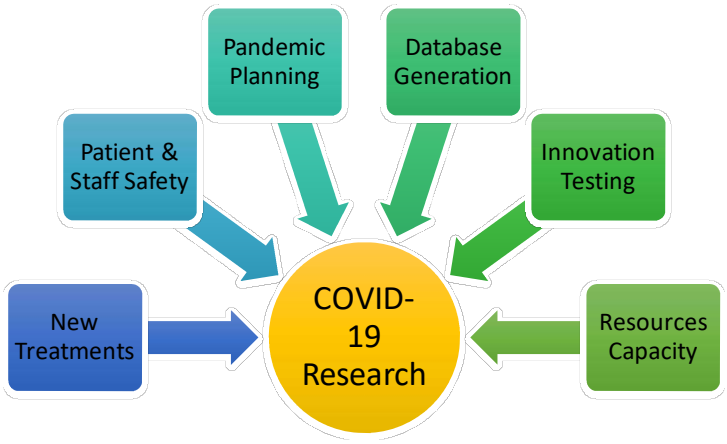


As the COVID-19 Pandemic reached our community in the spring of 2020, Grand River Hospital (GRH) saw and took the opportunity for increased research clinical trials and innovative activities to support healthcare efforts in the treatment of COVID-19 as well as to monitor its impact on our healthcare resources. This edition of "ACTION at GRH" focuses on some of the most impactful innovative initiatives that we undertook to support the fight against COVID-19.



One of these initiatives is highlighted in our feature story, 'Monitoring COVID-19 impact from a collaborative local and global perspective.' The joint efforts between GRH, St. Mary's General Hospital (SMGH) and McMaster University saw the creation of the **Co**ronavirus (COVID-19) **Reg**istry (COREG).

This case registry aims to collect and organize data on the microbiology and characteristics of COVID-19 in order to analyze trends that could reveal critical information for the treatment and trajectory of the disease. The data collected in COREG will also be used to support further research in the management of severe acute respiratory infections.

During this pandemic that has gripped the entire world, there is much pride in witnessing such research projects being completed right here at home. Our ability to promptly partner with local universities and innovators has made it possible for GRH to lead impactful new initiatives in the fight against COVID-19 in various areas affected by this virus.

When it is easy to feel separated from our community, it is all the more important to maintain a sense of togetherness. In the Waterloo-Wellington region, GRH will continue to provide improved innovative care to the community as we all navigate this new normal together.

Carla

Carla Girolametto
Director,
Innovation, Research, and Clinical Trials

Letter from the Director

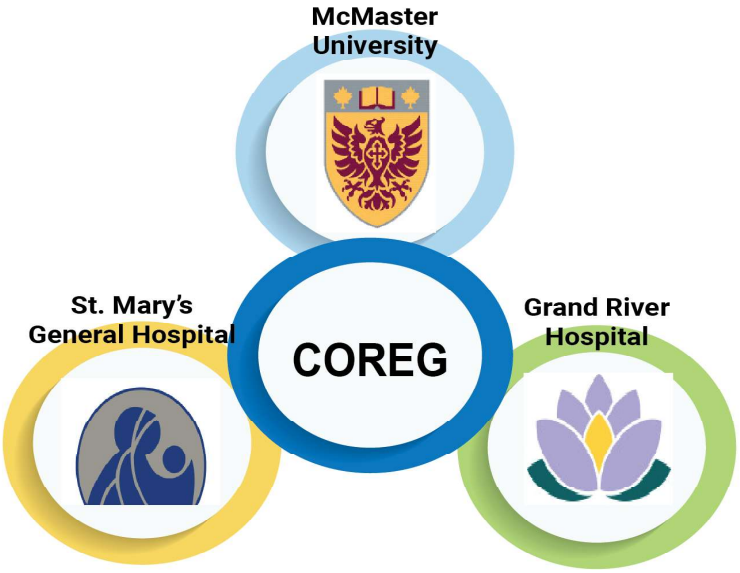
Monitoring COVID-19 impact from a collaborative local and global perspective

One of the many things local healthcare clinicians have identified about the fight against COVID-19 is the need to unify efforts and collaborate with each other to learn more about the virus and its effects on people. This is crucial to monitor the current treatment of COVID-19 patients as well as to prepare for future pandemic events.

True to this principle, Grand River Hospital (GRH) and St. Mary's General Hospital (SMGH) in collaboration with McMaster University are working together on a case registry of patients who have been admitted to GRH or SMGH with either suspected or confirmed cases of the novel coronavirus disease (COVID-19).

COREG

The **Co**ronavirus (COVID-19) **Reg**istry (COREG) - (pronounced as 'courage'), will enable both local and global research efforts to monitor the clinical and epidemiological data gathered from COVID-19 cases while creating a robust data repository that can be used for future pandemic preparedness planning. As a case registry, COREG documents and charts information related to the course of the COVID-19 disease, the disease spread, and possible outcomes in a comparative format. The goal of COREG is to collect and organize the data of COVID-19 patients in a way that can inform local pandemic evaluation and



Spotlight on COREG

Dr. Rebecca Kruisselbrink

decisions, including: clinical course, incidence, complications, and vulnerability.

The registry is led by Dr. Rebecca Kruisselbrink, Chief of Academic Affairs at both GRH and SMGH, and Andrew Costa, PhD, an Assistant Professor in the Department of Clinical Epidemiology and Biostatistics at McMaster University and the Research Lead for the Michael G. DeGroote School of Medicine, Waterloo Regional Campus. Under the lead of Drs. Kruisselbrink and Costa, the registry is updated and reviewed by trained research staff and fourteen McMaster medical students.

The registry is being supported from in-kind resources, partnering institutions and volunteer time by investigators, medical students and local physician residents.

The analytics from COREG will target several areas of focus, including characteristics and microbiology of the COVID-19 disease; treatments, time trends and symptomatic disease course of patients, including length of hospital admission, critical care bed usage, and ventilatory support, if needed; and the comparative outcomes of patients.

While COREG has its roots in Kitchener-Waterloo, the collaborative nature of GRH, SMGH and McMaster University has already allowed the registry to grow into a large COVID-19 research platform. Data from hospitals in Kitchener-Waterloo, Hamilton and Niagara are now included in the registry and the research team hopes to further extend the data collection to other hospitals still. In Kitchener-Waterloo alone, COREG has over six-hundred records.

“It’s a home-grown success at the national level. COREG will house the vast amount of information that is constantly evolving regarding COVID-19 disease,” says Dr. Costa. “Once this information is available to us, the case registry will allow us to organize this data in a way that highlights patterns and helps us better learn how to manage and treat this disease.”

SPRINT-SARI

Dr. Andrew Costa

On a more global scale, both GRH and SMGH are also participating in the **S**hort **P**e**R**iod **I**ncide**N**ce s**T**udy of **S**evere **A**cute **R**espiratory **I**nfection (SPRINT-SARI) Registry. Along with other sites across the globe, GRH and SMGH are providing clinical data from local cases contributing to more information regarding the management and epidemiology of severe acute respiratory infection (SARI).

Data will be collected from each patient during the period of hospital admission to discharge, up to 60 days. Similar to the information collected for the COREG registry, data collected for the SPRINT-SARI registry will include demographics and co-morbidities, as well as the administration of antibiotics and/or major therapies, including ventilation, and patient outcomes. To better prepare for future outbreaks, the study team will repeat data collection on an annual basis.

SPRINT-SARI primarily aims to foster and strengthen a global research response in the cases of current and future pandemic and epidemics with the ability to reactivate the study as needed should a future outbreak occur. The study team also hopes to better understand the microbiology of SARI, including the severity and potential treatments of the infection. Finally, Ethics, Administrative, Regulatory and Logistic (EARL) barriers will be analyzed on a global scale as this research takes place.

ICOVID-ICU

While studies have been conducted in China on the efficacy of inflammatory biomarkers as predictors of hospital mortality for COVID-19 patients, the ICOVID-ICU Study is currently the only study in North America to undertake research on **I**nflammatory biomarkers as independent prognosticators in the disease course for **COVID**-19 diagnosed patients admitted to **ICU**.

The primary aim of ICOVID-ICU is to better inform and prepare clinicians for the management and treatment of COVID-19 patients. COVID-19 disease affects patients across many

"The COVID-19 pandemic is of a magnitude not rivaled in recent outbreaks and without patient data collection, clinicians worldwide lack the necessary resources and information to rapidly and effectively respond to this disease."

Dr. Rebecca Kruisselbrink, Chief of Academic Affairs, Grand River Hospital

different demographics and evidence is lacking to determine biomarkers that could reveal which patients require different courses of treatment in the hopes of producing better outcomes.

In an effort to streamline the data collection for ICOVID-ICU, data collected from COREG will be used. Data collection and recruitment of patients will be on a rolling basis, as it is anticipated that data will be collected until the incidence of COVID-19 disease declines to the point that social isolation as a public health safety measure is no longer implemented.

The age of COVID-19 patients and admission and discharge dates from the hospital will be key information to analyze. In particular, age is a strong predictor linked to the prognosis of patients who have tested positive. The study will also analyze comorbidities and population demographics. The study team hopes that inflammatory biomarkers can inform and assist clinicians in predicting the severity and course of COVID-19 disease among patients.

Recent graduate from McMaster University's Michael G. DeGroote School of Medicine, Dr. Tyler Pitre will act as Co-Investigator for ICOVID-ICU. Dr. Pitre also contributed to COREG as Operations Lead, as he designed the data collecting process, trained the McMaster medical students, supervised the collection of data and performed independent audits on the data to increase data quality for COREG.

Dr. Tyler Pitre

"This registry has the potential to impact not only the local community but on a global scale as these biomarkers have not yet been researched in North America."

Dr. Tyler Pitre

Canadian COVID-19 therapies

Grand River Hospital (GRH) has joined as a participating site in the SOLIDARITY megatrial (a large-scale randomised controlled clinical trial recruiting thousands of patients from large numbers of trial sites).

Launched globally by the World Health Organization (WHO), the goal of this megatrial is to increase the rate in which evidence-based data on the efficacy of various drugs used to treat COVID-19 patients becomes available.

Over 39 countries will be participating in the study, which was renamed for Canada as "CATCO": Multi-Center, Adaptive, Randomized, Open-label, Controlled Clinical Trial of the Safety and Efficacy of Investigational Therapeutics for the **Ca**nadian **T**reatments of **CO**VID-19 in Hospitalized Patients.

In Canada, the trial will be led by sponsor Sunnybrook Research Institute and include up to seventy participating sites across the country. Dr. Stephen Giilck, Internal Medicine physician at GRH, will serve as the Local Responsible Investigator.

The trial will include at least 400 and up to thousands of participants in Canada, all adults that have been hospitalized with confirmed cases of COVID-19 disease.

All Canadian participants currently recruited will be randomly allocated to receive one of two interventions: Remdesivir + Standard of care or Standard of Care alone.

The administration of the treatment will occur daily until discharge. A telephone follow-up with each participant will occur three times over the course of 60 days to evaluate clinical status.

Outcome data that is collected from participants will include the type of intervention used and duration of treatment as well as other clinical outcomes.

The WHO believes in the power of a megatrial over multiple individual trials to provide widespread evidence as to effective therapies to treat COVID-19 disease.

"The CATCO trial allows Grand River Hospital to participate in groundbreaking global research that could provide fast relief and further guidance to fight COVID-19," says Dr. Giilck.

A megatrial is a large scale study recruiting thousands of patients from many clinical sites around the world.

Convalescent plasma used to fight COVID-19

Grand River Hospital (GRH) in partnership with 50 other academic and community hospitals across Canada and New York will be participating in a study of the effects of convalescent plasma as a treatment method for COVID-19. The study is being led by Principal Investigator Dr. Donald Arnold of McMaster University Medical Centre. Dr. Colin Yee, a benign hematologist, will be the local responsible investigator of the study for GRH and St. Mary's General Hospital (SMGH).

While there is currently no cure for COVID-19, an acute respiratory illness, the use of convalescent plasma has seen prior success when used as therapy for previous viral infections, including SARS. The CONCOR-1 study will compare patient outcomes of those that receive standard of care for the treatment of COVID-19 illness and those that receive the plasma which has been donated by patients previously diagnosed with COVID-19 and who have recovered from the illness.

The study is run in partnership with Canadian Blood Services (CBS) where the donated plasma is stored and distributed to the various research sites when a potential participant consents to participate in the trial. To donate plasma, donors must meet all CBS donation criteria as well as have recovered from COVID-19 illness. Other specific eligibility criteria also have to be met at the time of the donation. In order to participate in the study to receive the convalescent plasma, prospective participants must be admitted to the hospital and receiving supplemental oxygen with a confirmed case of COVID-19 illness as well as comply with other study criteria.

All participants will be randomly assigned to one of two groups: some patients will continue to receive standard of care while others will receive the Convalescent Plasma. After receiving their one-time treatment in hospital, the study team at GRH and SMGH will follow up with each patient via telephone 30 and 90 days and 1-year after their participation in the study.

The first collection of CCP and donor enrollment began in April 2020. The trial midpoint is estimated to occur in September 2020 with the hopes of having approximately 600 patients enrolled across all participating sites. Enrollment is estimated to be completed at 1200 patients in January 2021.

The study team hopes that donations from recovered patients provide quick and convenient access to this potential treatment and that COVID-19 Convalescent Plasma will prove a safe, suitable therapy for COVID-19 illness.

"It is hoped the study results will contribute to research on both the local and global levels into possible treatment plans for COVID-19," says Dr. Yee.

Treating Community-Acquired Pneumonia

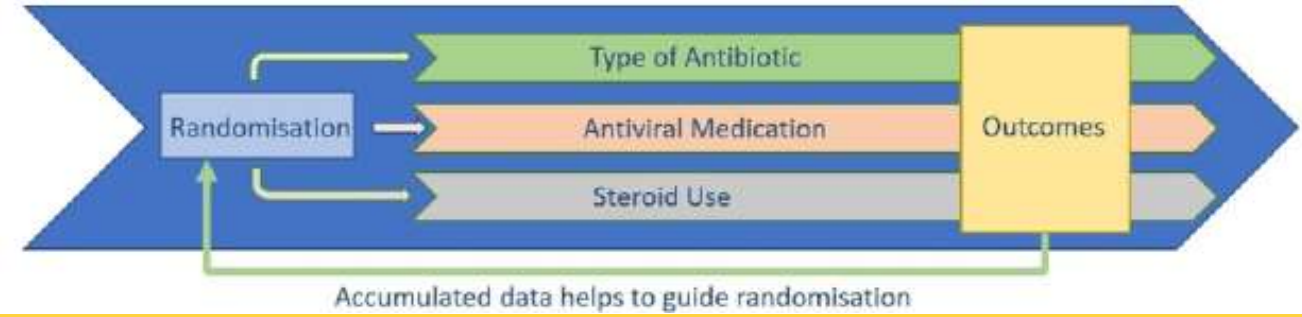
Grand River Hospital (GRH) will participate in a multinational clinical trial with the goal to determine various effective treatments and therapies that can be used to treat severe Community-Acquired Pneumonia (CAP) patients. The **R**andomized, **E**mbedded, **M**ultifactorial **A**daptive **P**latform trial for **C**ommunity-**A**cquired **P**neumonia (REMAP-CAP) will include patients admitted to the ICU with CAP in over 200 sites across 14 countries.

Dr. Theresa Liu, of the Department of Infectious Diseases at GRH, will serve as the Local Responsible Investigator. "REMAP-CAP's adaptive trial design will allow us to evaluate the strengths and weaknesses of many different interventions at once, in order to optimize the treatment plans for critically-ill patients with severe community-acquired pneumonia and respiratory failure, including in patients with COVID-19 infection," says Dr. Liu.

Currently, many different types of interventions are used to treat CAP patients in the ICU but concrete evidence as to the most effective therapies is not yet available. The treatments that GRH will test within the study include antivirals, immune modulation, antibiotics, steroids and therapeutic anticoagulation. The primary aim of REMAP-CAP is to find the strongest treatment per intervention type, including support for failing organ systems; antibiotics; immunomodulation strategy and overall improvement in patient outcomes. Each study participant will be followed up by telephone once at three months and once at six months post discharge to evaluate recovery.

The adaptive nature of the trial is a unique feature. Random treatment allocation will allow the efficacy of various treatment options to be assigned without bias. Therapies will be preferentially distributed as the data collected during the trial reveals patterns of higher success among treatments. As ongoing study data is collected and analyzed, the randomization pattern adjusts to enroll more patients within the study arms that are seeing success. As new treatment options become available, the study continues to evolve to include those treatments as study interventions.

The study team will also examine the impact the various therapies have on length of stay in the ICU and in the hospital as well as other clinical outcomes and quality of life.



"Through my involvement with REMAP-CAP as well as with our other COVID-19 trials, I've learned a lot about the impressive amount of coordination and logistics involved in clinical trials."

Dr. Theresa Liu, Department of Infectious Diseases, Grand River Hospital

CAN Health NETWORK

Empowering Canadian innovators to lead the global MedTech industry

As previously announced, Grand River Hospital (GRH) is proud to have been chosen as one of the Ontario edges in the CAN Health network. This partnership of leading Canadian medical and technology institutions will take a nationwide approach to introduce technology into the healthcare system.

As one of the edges, GRH will provide opportunities where the most promising Canadian health-tech companies will have access to real healthcare environments. Here, their solutions will receive the support they need for widespread adoption, helping companies scale first locally, then nationally and finally internationally. The CAN Health Network will enable promising companies to work directly with healthcare organizations to understand their needs and commercialize health technologies to meet those needs and scale up their companies. Through this, small and medium-sized enterprises and leading start-ups will be able to work with early adopter institutions to collaboratively innovate, research, develop, and refine Canadian medical technologies to make them market-ready.

Let's learn more about the Grand River Hospital – CAN Health partnership.

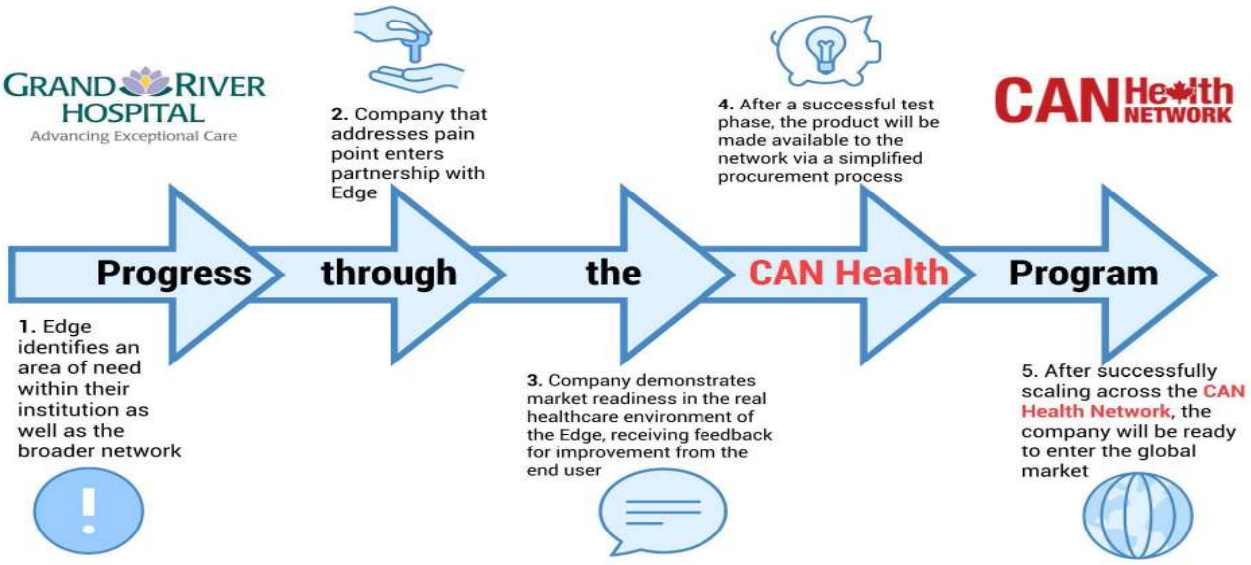
What will the Edge do?

- Within the Ontario Region, Grand River Hospital is an Edge, or demonstration site;
- Edges help bridge the gap between market needs and the key challenges and issues that healthcare organizations face;
- As an Edge, the innovation program will become more sustainable while contributing to economic growth of the local community and supporting innovators to grow and stay locally.

How will the partnership between Grand River Hospital and Innovators work?

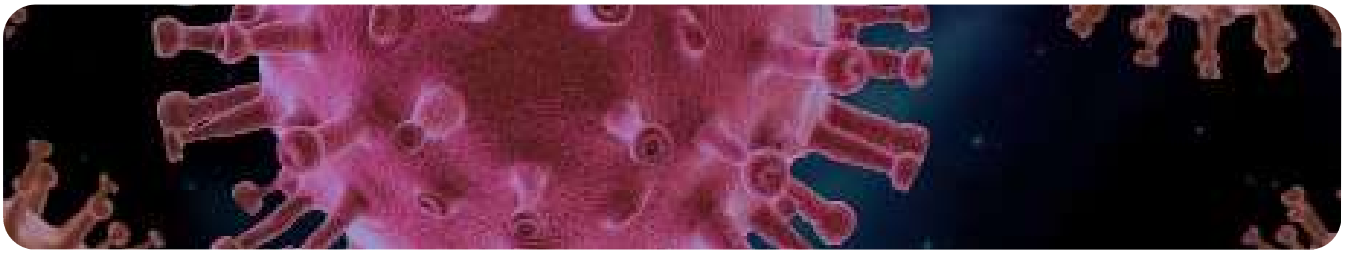
- The partnership is a collaborative relationship between the Edge, Grand River Hospital, and the company;
- The company is able to test their product in real healthcare environments and receive invaluable feedback from the end user on how to improve the technology;
- Edges enter into the partnership with the intent to procure if the test phase is successful.

How will the partnership between Grand River Hospital and Innovators work?



Grand River Hospital is actively working to confirm our first CAN Health Project! Stay tuned for future news on this exciting initiative!

Other COVID-19 research partnerships



COVID-19 Biobank

The biobank of COVID-19 plasma officially launched in May with Dr. Kevin Stinson of St. Mary's General Hospital (SMGH) as the local responsible investigator.

Currently, four studies have been brought forth by collaborators that will utilize samples from the biobank:

1) Analysis of antibody development and antibody profiles during COVID-19 infection with the **University of Waterloo**

2) Analysis of cytokine profiles during COVID-19 infection and correlation to a cytokine storm humanized mouse model with the **University of Guelph**

3) Analysis of immune cell subsets, with a focus on T-cell memory and non-neutralizing antibodies with **McMaster University**

4) Antibody sequencing for development of an anti-SARS-CoV-2 antibody bank, and subsequent analysis by mouse infection models for therapeutic agents with the **University of Guelph** and **Rapid Novor Inc.**

COVID-19: Optimizing Operations of Cancer Centres during the Pandemic

In collaboration with Prof. Houra Mahmoudzadeh from the department of Management Sciences at the **University of Waterloo**, GRH's own Dr. Ernest Osei serves as the local responsible investigator of this study.

The study aims to provide insights into cancer centre operations during a pandemic outbreak.

Using historical data on scheduling, clinical care paths (RT planning and treatment process), clinical protocols, and pandemic progression, resource optimization for different scenarios of the disease outbreak among current and future cancer patients will be simulated.

The output of this research would shed light on what policies can cancer centres generally employ to increase the resilience of the system against resource uncertainties and provide general insights into how to manage future pandemics.

Innovation driven by partnership

All 15 of GRH's clinical programs and services participate in innovation and research activities. Since 2003, GRH has conducted over 80 clinical trials and over 190 research studies. Since 2011, GRH has participated in over 50 innovation and research partnerships. Innovation in health care is a major growth area for GRH covering a broad range including medtech, processes and systems, artificial intelligence, nanotechnology, and quantum physics. Community partnerships help improve the ways GRH delivers safe patient care.

The Office of Innovation and Research is proud to partner with the following organizations to advance exceptional innovation and research and inform our continued efforts to improve how we deliver health care and the health of our community at Grand River Hospital.

McMaster University

University of Waterloo

University of Guelph

Ontario Veterinary College

CAN Health Network

Clinical Trials Ontario

ocreb

Canadian Cancer Clinical Trials Network

N2 Network of Networks / Réseau des réseaux

Tri-Hospital Research Ethics Board (THREB)

Cambridge Memorial Hospital

Grand River Hospital — Advancing Exceptional Care

St. Mary's General Hospital

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