2021-22 ANNUAL REPORT

Cystic Fibrosis Canada Accelerating Clinical Trials (CF CanACT)

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Cystic Fibrosis Canada | Fibrose kystique Canada

CF CanACT | FK ÉCLAIR

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Dr. John Wallenburg

BUILDING A CANADIAN NETWORK

In October 2016, at a plenary session at the North American Cystic Fibrosis Conference on international clinical research, Canada was conspicuously absent. At the time, the Therapeutic Development Network (TDN) in the USA was 19 years old and linked 82 clinical research centres. The European Cystic Fibrosis Society Clinical Trial Network (ECFS-CTN) was eight years old and comprised of 40 centres from 15 countries, and a clinical research network in the UK (CF Clinical Trials Accelerator Platform or CTAP) had just been launched. Canada needed to step up and ensure that our contributions reflected the enthusiasm and passion of our community.

Clinical trials are critical to regulatory approval of new therapies; without the data to support the safety and efficacy of new drugs they cannot be released to the public. And without participants, clinical trials fail. On the one hand we were lucky. Cystic fibrosis is a rare disease, but it had garnered a great deal of industry interest and a rich pipeline of drugs was under development. On the other hand, data showed that as a rare disease, there simply weren't enough people living with cystic fibrosis participating in trials to bring all those drugs to market.

Fast forward to 2022, and Cystic Fibrosis Canada's Accelerating Clinical Trials (CF CanACT) network, launched in 2018, is comprised of 10 clinical research sites that stretch from Vancouver to Halifax, plus three satellite sites in Quebec. Since its inception, a total of 277 participants from across the country have participated in 47 industry sponsored clinical trials that the network as a whole has supported. In addition, the network put in place the infrastructure to allow Investigator initiated trials to start quickly, and with minimal resources.

As an example, a heroic effort by Alam, a research manager at BC Children's Hospital (BCCH), resulted in all 10 network sites implementing a single research registry agreement template. This template will serve to significantly speed investigator trials in the future.

The network has benefited richly from its more mature cousins, their experience and generosity propelled CF CanACT to the forefront of international trial participation. Over the next five years, CF CanACT will continue to mature; as we continue our work to prepare for a new generation of trials. Trials that feature novel, genetic approaches to therapy, new primary outcome measures, and, importantly, ever more rare mutations. Trial designs may need to adapt to tiny sub-populations of what is already a rare disease. Whatever the future holds, we know that the coming trials will excite our community, and that with the support of our international partners, CF CanACT will rise to the challenge.

John Wallenburg PhD
Chief Scientific Officer
Cystic Fibrosis Canada

Dr. Felix Ratjen

MEET A PRINCIPAL INVESTIGATOR – DR. FELIX RATJEN

From his first encounter with a cystic fibrosis (CF) study, Dr. Felix Ratjen was fascinated. As a medical student, initially aiming to enter the field of psychoanalysis, Dr. Ratjen's plans took a turn when he assisted in a randomized controlled trial studying lung functions in people with CF. This was his first introduction to CF research and the positivity and optimism of the people living with this chronic disease captivated his attention and inspired him to further explore the field of CF.

From New York, to Boston, to Essen in Germany, to Toronto, Dr. Ratjen has since become an internationally renowned investigator in the field of CF, leading ground-breaking research to expand the scope of knowledge on the disease and the clinical care of individuals living with CF. For decades, Dr. Ratjen has been extensively involved in conducting clinical trials in CF.

"I REALLY ENJOY THE COMBINATION OF CLINICAL CARE FOR PATIENTS AND RESEARCH IN CLINICAL TRIALS. NOT ONLY CAN I PROVIDE MEANINGFUL CLINICAL CARE, BUT I ALSO CONTRIBUTE TO MOVING FORWARD THE FIELD OF CF FOR THE IMPROVED QUALITY OF CARE OF FUTURE PATIENTS," said Dr. Ratjen.

Dr. Ratjen was instrumental in setting up the Cystic Fibrosis Canada Accelerating Clinical Trials (CF CanACT) network in 2018 and has since been a very active member, in addition to his involvement in other international and national networks. In collaborating amongst different centres, he contributes immensely towards amplifying Canada's voice in the field of CF on the international stand. "It gives patients in Canada the opportunity to be working with those medicines that will have a positive impact on their outcome," said Dr. Ratjen.

Within Canada, CF CanACT advances the discoveries of knowledge on cystic fibrosis by allowing for easy collaboration and communication between centres across Canada. Dr. Ratjen recognizes the benefits of such national clinical trial networks, as he himself has seen the benefits of such efforts through his expertise and decades of work in the field. **"A lot of research questions can only be answered in multi-centre studies, so we need to collaborate amongst different centres. It is something we do well in CF internationally."**

Dr. Ratjen is hopeful that the next generation of CF researchers will continue the momentum of those who have come before them and that people living with cystic fibrosis will continue to participate in clinical trials. "**We must adequately train the next generation of researchers to grab the baton of CF research and run with it.** Additionally, with newly emerging, highly effective therapies today, there is rising concern for the declining interest in study participation within CF patients. We must hope that patients will see the greater good of their participation and continue to involve themselves in clinical trials, even with less personal benefit."

Dr. Ratjen believes that research is a driver of improving clinical care and that one of the reasons cystic fibrosis research has been so successful is because of the strong partnership between people living with CF, caregivers and health providers. "We all hold the same understanding, that research is the way we move forward. Seeing improved outcomes is so rewarding for everyone involved, and it is crucial to focus on it for the future."

2021-2022 CF CANACT HIGHLIGHTS

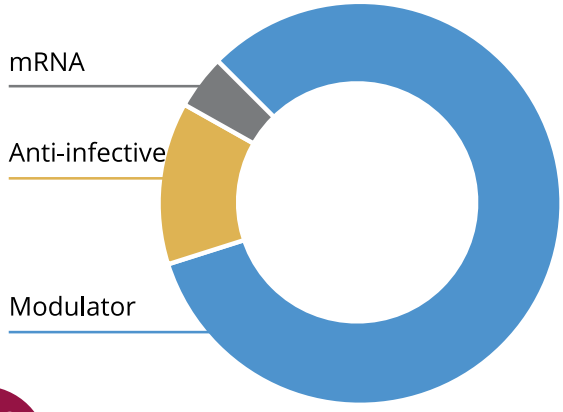
10.6% of patients at CF CanACT sites are enrolled in a **clinical trial**

2 protocol reviews feasibility studies

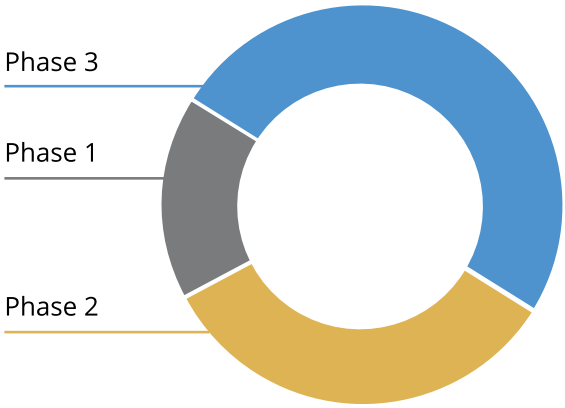
215 patients enrolled in **23** interventional clinical trials

468 patients enrolled in **3** observational clinical trials

Types of treatments in trials



Phases of trials



COVID-19 Antibody Response in CF (CAR-CF)

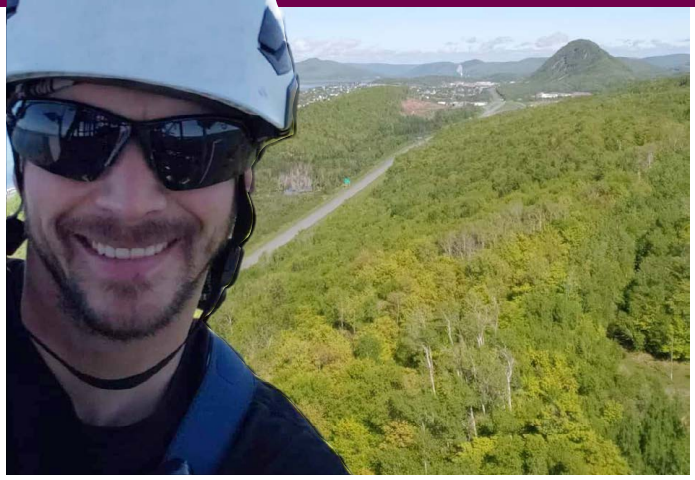
IN CANADA as of AUGUST 2022:

12 sites

442 patients consented

394 patients enrolled for their first blood draw in the CAR-CF program

MY WHOLE LIFE CHANGED



Despite his cystic fibrosis (CF), Roger is often seen 100 feet up in the air working as a telecommunications mechanic and living an active outdoor life in New Brunswick. But for three months, Roger also participated in an early clinical study of a drug by AbbVie, what he calls a life changing experience. It was a cutting-edge modulator drug thought to correct the basic defect in CF which would be a game changer in cystic fibrosis clinical research if it worked. He was directly contacted by the research coordinator of the trial at the Halifax CF CanACT site, who had previously ensured his eligibility. With a leap of faith, Roger decided to explore the unknown.

"My initial thoughts were the same that goes through everyone's head. 'I'm about to become a guinea pig and things may go horribly wrong.' But you must hope that things go amazingly right." Roger's display of strength and bravery was well-placed, as when Roger started the trial, he recalls "my whole life changed."

The participant's comfort and reassurance are a priority for each CF CanACT trial. For Roger, the research coordinator provided an abundance of information on both the investigational drug and the study, along with the support of the research coordinator and study physician at his disposal. His full understanding of the drug and the effects he would likely experience allowed him to progress through the study feeling prepared.

After having preliminary blood tests, Roger proceeded to take the drug as instructed by the clinic, who made the process as straight-forward as possible. Any accommodations required for Roger to travel from New Brunswick to participate in the trial in Halifax were supported by the clinic to make the process as smooth as possible.

During regular check-in visits at the clinic, he never felt as if he were just another subject in a study; **he was a critical member of the team who contributed something invaluable to the trial.**

"MY EXPERIENCE WAS HUGELY IMPACTFUL FOR ME," SAID ROGER. "MY LIFE IS TYPICAL OF SOMEONE WITH CF. ALTHOUGH EVERY FEW YEARS, A NEW TREATMENT COMES OUT THAT HELPS WITH THE SYMPTOMS, YOU COME TO TERMS WITH THE FEELING THAT YOUR HEALTH IS ON A SLOW DOWNWARD TRAJECTORY. WHEN I STARTED THE TRIAL, MY WHOLE LIFE CHANGED, SUDDENLY I WAS SYMPTOM-FREE. FOR THE FIRST TIME IN MY LIFE, I BELIEVED I COULD BEAT THIS DISEASE."

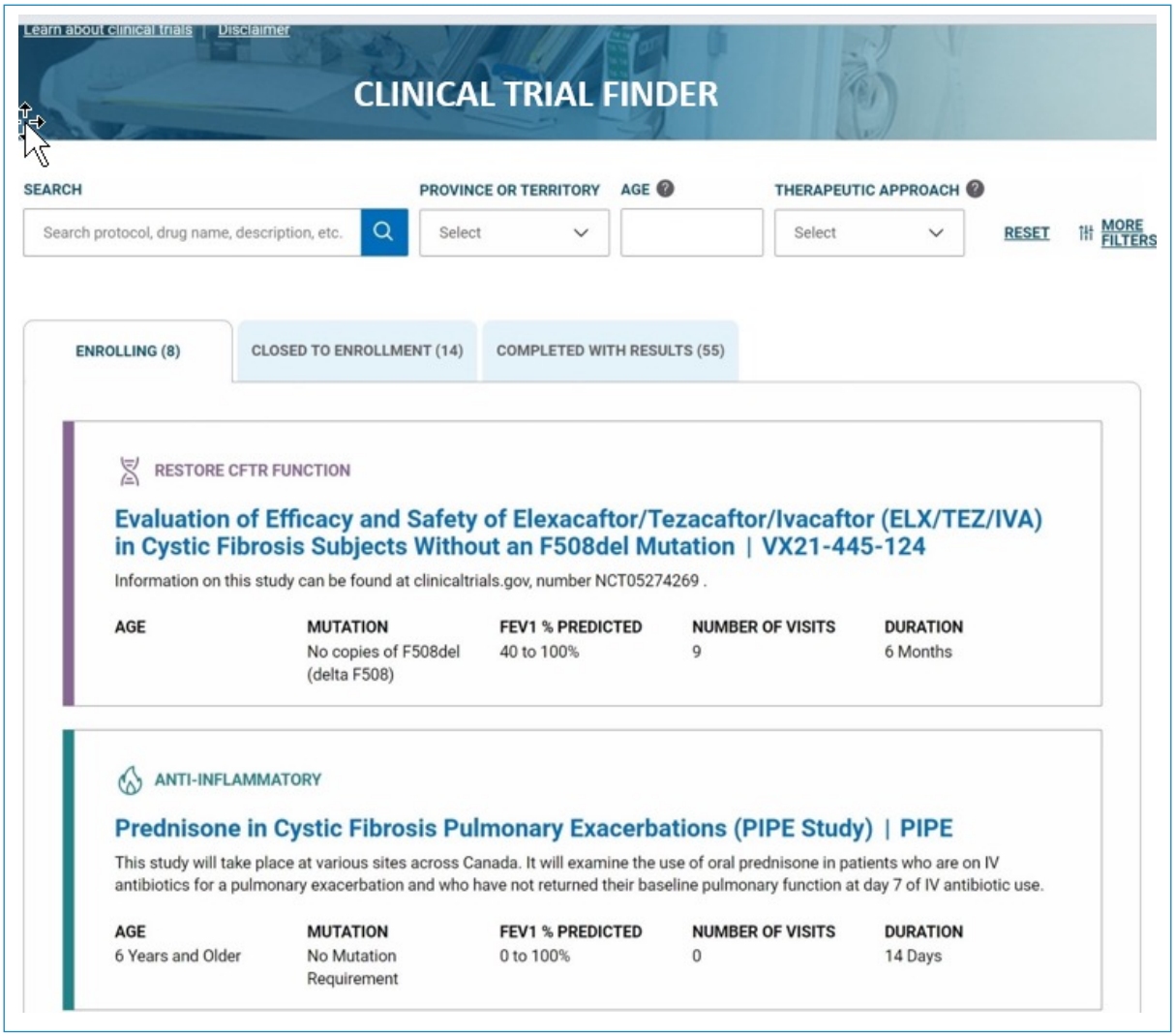
Roger says his participation in the clinical trial means more to him than most people realize. "The only reason I am alive is because organizations like Cystic Fibrosis Canada are pushing research forward, leading to a longer lifespan and increased quality of life for people living with cystic fibrosis. This trial could mean no symptoms for future generations of people living with CF."

"Absolutely," Roger responds in an instant when asked if he would participate in another trial in the future. "I only have medication because someone before me participated in a trial. I feel like it is my duty to keep up the momentum and do my part in the fight against cystic fibrosis." Roger would like any individuals considering participating in a trial to know he had a great experience. "Give it a try, you never know what might happen.".

MAKING IT EASIER TO FIND CLINICAL TRIALS IN CANADA

In 2022, Cystic Fibrosis Canada launched a new Clinical Trial Finder tool to make it easier for people to search for clinical trials that are currently enrolling across Canada, find information on previous trials and their results. We worked with our partners at the Cystic Fibrosis Foundation and their Therapeutics Development Network (TDN) to bring this tool to our community so that people with CF and their caregivers can more easily find trials that they are eligible for and interested in. Using the new search tools a person can find information about the type of study, trial duration, study eligible population, treatment, site locations and contact information.

The clinical trial finder is located on Cystic Fibrosis Canada's website and is updated automatically after a new trial has been sanctioned. To be deemed a 'CF CanACT-sanctioned study," study protocols must be jointly reviewed by the CF CanACT executive committee and the CF CanACT Protocol Review Committee (PRC). Reviews are conducted alongside an adult person with CF or a CF parent for pediatric studies. Critical protocol evaluation ensures feasibility, appropriate study design, and that study goals address the priorities of CF CanACT and the CF community. These clinical trials have the power to impact the future of cystic fibrosis care.



Alam

MEET ALAM - A RESEARCH MANAGER AT BC CHILDREN'S HOSPITAL CF CANACT SITE

"Every day brings exciting new opportunities, new challenges, new studies and new participants from different backgrounds," describes Alam. At the BC Children's Hospital (BCCH) Cystic Fibrosis Canada Accelerating Clinical Trials (CF CanACT) the voices of people with cystic fibrosis (CF) are incorporated right from the beginning of the study design process. **"There should be collaborative involvement of participants right from the start of designing the trials,"** says Alam. Direct involvement of people with CF allows for the alignment of the clinical and participant priorities, while also incorporating outcomes that are relevant to all people living with CF.

The direct involvement of people with CF in clinical trials means extensive time is taken with participants and their families to ensure they understand the risk and benefits of the trial. No matter the age of the child, (some are as young as one year of age) the clinic verifies that the family fully understand what is involved in participating in the clinical trial before proceeding with it. At BC Children's Hospital, the participating child is given an assent form written at a language level that they can easily understand.

The uncertainty that accompanies a clinical trial can be unnerving for the participant. "As a research coordinator, we do our best to go above and beyond, to make it easier and more enjoyable for the child while performing the tests associated with the trial. **Every study visit is tailored to each individual participant, and we get to know them and their families very well.** Every member of the research team, including physicians, nurses, and research coordinators, to connect with the participant and make it an enjoyable experience."

Consent in a research study is an ongoing conversation with the participant and their caregiver. Over time, individuals might feel differently about participating and can withdraw or cancel at any point. However, researchers and physicians are always available to discuss participation and alternative options."

Alam hopes CF CanACT will further improve the equitability and accessibility of clinical trial participation to all people living with CF.

> "THERE ARE MANY BARRIERS TOWARDS PATIENT PARTICIPATION, INCLUDING LANGUAGE BARRIERS OR GEOGRAPHIC BARRIERS SUCH AS THOSE ENCOUNTERED BY PEOPLE WITH CF LIVING IN RURAL AREAS WITHOUT A CLINICAL TRIALS CENTER NEARBY. PARTICIPATING PROVIDES BETTER OUTCOMES; THE MORE ALL-ENCOMPASSING THE PARTICIPATION IS WITH PEOPLE WITH CF, THE MORE WE WILL COME TO UNDERSTAND THE LANDSCAPE OF CF."

From direct interaction with people with CF to Canada-wide coordination with other CF CanACT researchers, Alam is motivated by everyone that he interacts with including his colleagues at BC Children's Hospital CF clinic. This includes the research team, students, nurses, physicians, clerks, pharmacists, physiotherapists, and other allied health workers. The dedication shown by his clinic's team members, along with the resilience of people with CF as they collaborate in the journey of cystic fibrosis is inspiring for Alam.

Through the complexities of designing, initiating, and conducting a clinical trial, the team at BC Children's Hospital strongly believes in the importance of the voices of people with CF to strive to reach new healthcare goals. "The burden of the research weighs heavily on the participant, and that is something we can never forget. That must be front and centre always."

A LIFE-CHANGING REFERRAL

Isaiah

Edmonton to Vancouver, Vancouver to Edmonton. In 2019, Isaiah, who lives with cystc fibrosis (CF), was at the airport every two months travelling from home in Edmonton to participate in an antibiotic study at the BC Children's Hospital in Vancouver, a distance of 1,200 kms. He was referred to the study by his clinic team in Edmonton and was then contacted by Alam, the research coordinator from the BC Children's Hospital CF CanACT site. Even prior to agreeing to participate, Isaiah recalls having numerous email exchanges with Alam where they got to know each other, and Isaiah was able to learn about the clinic, the team, and the study that he would participate in.

Isaiah didn't know what to expect going into a clinical trial, but the research team provided him with all the information he needed to ease his uncertainty. The team walked through information about the drug, including any side effects, instructions on its use, and more. "Everything was laid out in front of me in case I needed it through the process," he says.

Isaiah was required to fly to Vancouver bimonthly for his clinic visits as part of the trial. He coordinated the flights based on his convenience and schedule, and was reimbursed for his travel expenses, including the flight tickets, hotels, and food during his stay. His regular clinical care continued in Edmonton; yet the additional visits in BC for the trial was a responsibility that he was willing to take on. "The clinic made it so accessible and easy for me to be a part of the trial," said Isaiah. **"With their help, I was able to contribute to the advancement of CF medications and research. I felt honoured to participate, as I was advocating for CF patients like myself through this study."**

Isaiah's experience as part of the trial was simple, comfortable, and more relaxed than he had envisioned. His role consisted of a simple scale-based questionnaire about his health, along with blood work and pulmonary function tests (PFT). The clinic involved him as much as possible in the trial process. **"They did more than give me instructions on the drug and brush me off. They wanted to know how I felt on top of it all, which made me feel very respected in the clinic",** Isaiah shares. Isaiah was reassured by the clinic team with understanding, creating a safe, and enjoyable process for Isaiah.

"It was exciting to be a part of. With a less prevalent disease like CF, it feels as though there is less pressure to advance the technology, medication, and knowledge related to it. However, my participation in the clinical trials helped me learn that there was progression and movement forward in the fight against CF." His experience has given him a new appreciation for the work being done to improve the lives of Canadians living with CF. "The whole experience has made me realize the immense, ongoing team effort in the fight against CF in Canada. Knowing that there are a lot of people involved in CF research is very encouraging. It was amazing to feel like I was a part of something greater for the CF community. I am not surrounded by my compatriots also battling CF."

> "I'M VERY PROUD TO HAVE CONTRIBUTED TO A CLINICAL TRIAL", SAID ISAIAH. "TO ME, IT MEANS THAT I HAVE CONTRIBUTED SOMETHING GREAT TO THE CF COMMUNITY, AND I WOULD 100% PARTICIPATE IN ANOTHER CLINICAL TRIAL GIVEN THE CHANCE".

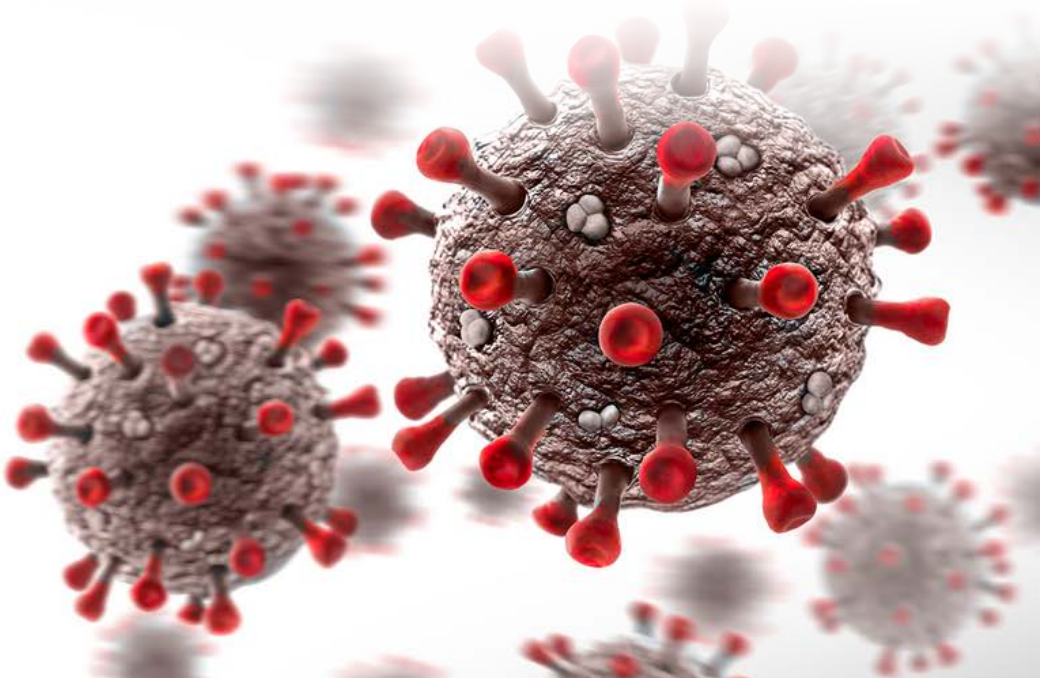
COVID-19: AN UPDATE

The COVID-19 pandemic called for many adjustments, changes, and adaptations to best accommodate for the wellbeing of the global community. For CF CanACT, there were many challenges that arose with the pandemic, and inevitably many mitigation strategies implemented by Cystic Fibrosis Canada in collaboration with other national cystic fibrosis organizations. In 2020 and 2021, CF CanACT adapted to continue the quality research performed while keeping the health and well-being of individual patients and the CF community at the forefront:

Changes in Clinical Trial Practices

Trial Initiation	Trial Enrollment	Trial Practices
One Year Ago		
Restricted clinic capacity hindered or halted the initiation of new studies.	**Regional lockdowns** and **limited in-person consultations** made it difficult to recruit new participants.	CF CanACT practices **changed in new ways** according to the prevalence of the COVID-19 virus.
Today		
Clinics work **at full capacity** and **open for new trials;** however, new trials take time to attract. (reflected in the Metrics, 2021)	**25% of trials are still virtual** as flight delays can impact patients visits. Sites are recruiting new participants.	**Tightened infection control policies are** in effect, although there are discrepancies in regulatory practices at sites across Canada.

1. Certain components of clinical trials were completed at home, including drug deliveries and sputum collections.
2. Regular CF care visits and clinical trials were shifted to online platforms, allowing individuals to continue their regular care and participate in trials despite lockdowns and social distancing.
3. Additional infection-control measure, such as pulmonary function tests, were set in place to address infection control policies.



1 St. Pauls Hospital, Vancouver

- 75% in person and 25% virtual patient visits
- Flight delays with remote participants

BC Children's Hospital, Vancouver

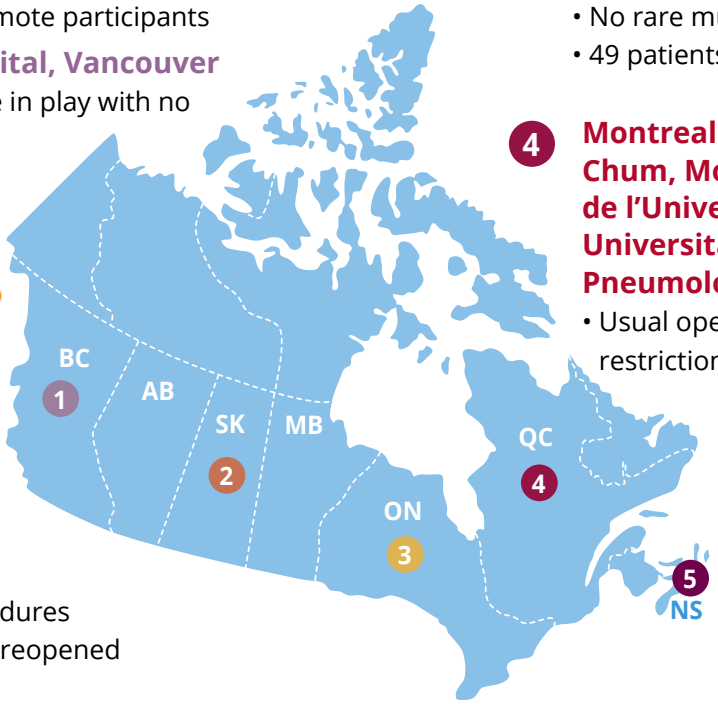
- Usual operations are in play with no restrictions

3 The Hospital for Sick Children (SickKids), Toronto

- Mask mandates to prevent spread of COVID and other viruses

St. Michael's Hospital, Toronto

- Maintain usual precautionary procedures
- Contracts office has reopened



2 Royal University Hospital, Saskatoon

- Usual operations are in play
- No rare mutation trials
- 49 patients enrolled in CAR-CF

4 Montreal Children's Hospital and Chum, Montreal Centre hospitalier de l'Université Laval and Institut Universitaire de Cardiologie et de Pneumologie de Québec, Quebec City

- Usual operations are in play with no restrictions.

5 Queen Elizabeth II, Halifax

- Usual operations are in play with no restrictions.

COVID-19 ANTIBODY RESPONSE IN CF (CAR-CF)

As of September 30, 2022, in Canada, there were **12 sites up** and running with **442 patients consented** and 394 patients enrolled and having their first blood draw. The first results can be expected to be reported in 2024.

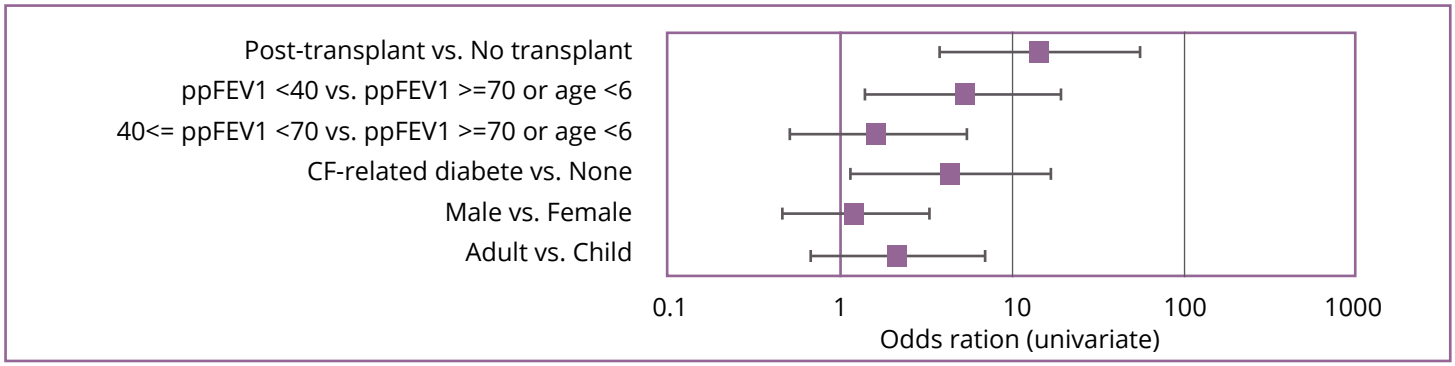
Covid-19 Antibody Response in CF (Car-CF) is an investigator-initiated trial examining whether people with CF have had COVID-19. Blood samples are drawn at enrollment, 6 months, 12 months and 24 months to look for antibodies to COVID-19.

In Canada, the trial is supported by CF CanACT and is led by Ranjani Somayaji who is working with our European and American partners in the CTN and the CFF-TDN.

Canadian CF COVID Update

As of September 2022, there have been 172 reported cases of COVID among the Canadian cystic fibrosis population. Of these 26 (15%) required hospitalization and there were 5 deaths (3%).

Odds ratio of factors associated with hospitalization in the Canadian CF population

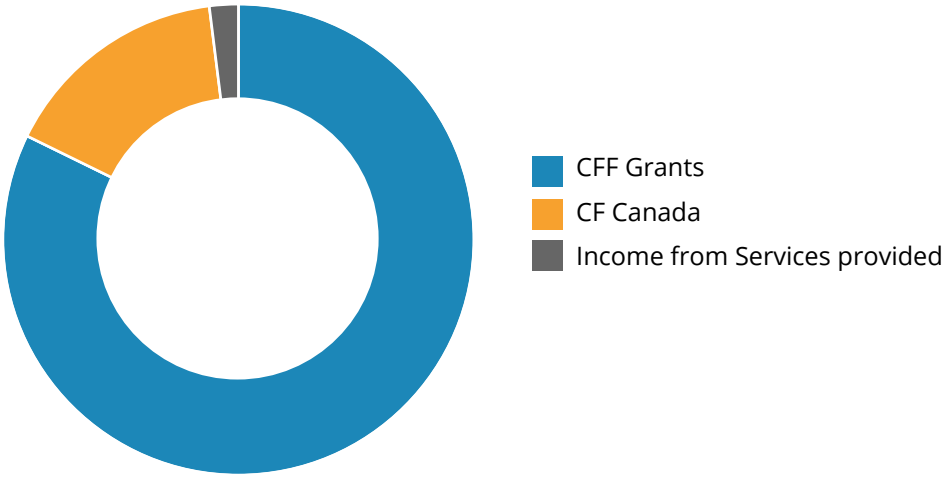


FUNDING

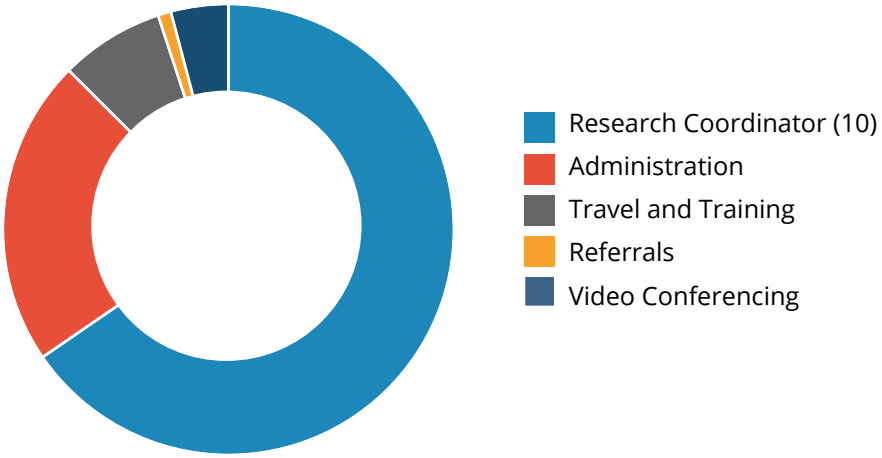
CF CanACT is partially funded by grants from the Cystic Fibrosis Foundation in the US and Cystic Fibrosis Canada. Additional income is generated by charging fees for scientific services to pharmaceutical companies such as for performing protocol reviews or feasibility studies across CF CanACT sites.

It is important for the network to be financially independent of pharmaceutical companies to ensure there is no conflict of interest when providing scientific advice on clinical trials.

Income 2021-2022



Expenditures 2021-2022*



*There was less travel during 2021-2022 due to COVID-19 but virtual conferencing fees increased. Cystic Fibrosis Canada continued partial support for research coordinator time at the original six sites.

PRINCIPAL INVESTIGATORS AND LEAD RESEARCH COORDINATORS

VANCOUVER ADULTS, ST PAUL'S HOSPITAL
Principal Investigator: Dr. Brad Quon
Research Coordinator: Taryn Leach

VANCOUVER PAEDIATRICS, BC CHILDREN'S HOSPITAL
Principal Investigator: Dr. Mark Chilvers and Dr Jonathan Rayment
Research Coordinator: Alam Lakhani

CALGARY ADULTS, UNIVERSITY OF CALGARY, FOOTHILL'S HOSPITAL SITE
Principal Investigator: Dr. Mike Parkins
Research Coordinator: Clare Smith

SASKATOON ADULTS AND PEDIATRICS, ROYAL UNIVERSITY HOSPITAL
Principal Investigator: Dr. Julian Tam and Dr. Martha McKinney
Research Coordinator: Dawn Johnson

TORONTO ADULTS, ST. MICHAEL'S HOSPITAL
Principal Investigator: Dr. Elizabeth Tullis
Research Coordinator: Arunan Selvarajah

TORONTO PAEDIATRICS, SICKKIDS HOSPITAL
Principal Investigator: Dr. Felix Ratjen
Research Coordinator: Stephanie Jeanneret-Manning

MONTREAL MCGILL SITE ADULTS AND PEDIATRICS, MONTREAL CHILDREN'S HOSPITAL
Principal Investigator: Dr. Larry Lands
Research Coordinator: Tracey Mercier

MONTREAL ADULTS, CENTRE HOSPITALIER UNIVERSITAIRE DE MONTREAL (CHUM)
Principal Investigator: Dr. François Tremblay
Research Coordinator: Nadia Beaudoin

QUEBEC CITY ADULTS, INSTITUT UNIVERSITAIRE DE CARDIOLOGIE ET DE PNEUMOLOGIE DE QUÉBEC PAEDIATRICS, CENTRE MÈRE-ENFANT DU CHU DE QUÉBEC
Principal Investigators: Dr. Lara Bilodeau and Dr. Patrick Daigneault
Research Coordinator: Andrée-Anne Therrien

HALIFAX -ADULTS QUEEN ELIZABETH II HOSPITAL
Principal Investigator: Dr. Nancy Morrison
Research Coordinator: Andrea Dale

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