



CANADIAN  
CHILDHOOD  
CANNABINOID  
CLINICAL TRIALS

## **C4T Annual Report for 2019-2020**

Message from our executives Dr. Lauren Kelly and Stephen Barbazuk.

C4T (Canadian Childhood Cannabinoid Clinical Trials) is an academic research team made up of parents, doctors, pharmacists, nurses and scientists assembled to study the use of medical cannabis for children. Our Mission is to position Canada as a global leader in the testing and implementation of paediatric cannabis therapeutics by bridging drug discovery, clinical care, the development of guidelines, and social policy recommendations.

C4T had a busy year from 2019-2020, and we would like to thank all of our 86 members and 10 partner organizations for supporting us during this exciting time. Since our research consortium launched in 2018, we have secured four research grants and awards totalling over \$1.8 million. On June 3, 2020 we held our annual C4T meeting virtually, in place of our in-person meeting planned for Vancouver. We discussed our project updates, finances and plans for the future including how the research landscape may change as a result of the COVID-19 pandemic. Below, we describe our short and long-term goals, and provide a summary of selected publications by C4T members in 2019-20.

### **What are our short-term goals?**

First, we are aiming to continue our early phase research studies and family engagement to gather evidence to inform the design of clinical trials. By the end of five years, we aim to launch phase III randomized controlled trials, comparing cannabis-based medicines to other existing therapies and standards of care. Through creating a C4T partnership agreement with legal experts representing each C4T site (institution), we will build long-term tools that will facilitate rapid implementation of new research projects.

Second, we are aiming to continue to foster collaborations and build our network of doctors, nurses, pharmacists, researchers, policy makers, youth partners and caregivers. We hope to see C4T represented across Canada and plan to build international partnerships in the United Kingdom, Israel and the United States. We will continue to engage with various stakeholders and integrate their input into our research process. We aim to have a C4T site lead at each Canadian children's hospital to increase awareness of our projects, expertise and mandates and thank our partners at MICRYN for connecting us with child health researchers across Canada to facilitate that.

We are committed to diversity and inclusion including training the C4T research team in meaningful family engagement. We seek to foster authentic partnerships embedded in our network between families, researchers and clinicians.

Third, we aim to demonstrate research process efficiency by achieving high quality results that meet our goals and timelines while staying within our project budgets.

### **What are our long-term goals?**

C4T will further Canada's position on the world stage with a reputation for putting families at the centre of medical cannabis research. We hope that in 10-20 years, C4T will be the leading national research group to conduct Phase III cannabis trials in paediatrics, through providing the knowledge base and associated infrastructure to conduct studies and by engaging in meaningful partnerships with patients and families. Our results will inform clinical and social considerations for schools and hospitals on safe and effective medical cannabis use. We plan to build and collaborate on international trials to increase the relevance of research, guidelines and policies on

a national and international level. C4T will engage with industry to design research through all phases (preclinical and clinical) in support of a Drug Identification Number with Health Canada for paediatric indications.

Our impact will include measures of capacity building (number of trainees, partnerships and C4T members), traditional and nonconventional knowledge translation products (numbers of publications, grants built off this work, contributions to patents, intellectual property, public outreach and media), development of clinical practice guidelines, and our ability to collaborate between basic scientists, policy makers and clinical researchers to study cannabis use for medical purposes in children.

We will create unique training opportunities for graduate students and clinical fellows to learn from multiple disciplines through partnered projects with mixed methods and will continuously update materials and opportunities to keep them fresh and in tune with contemporary advancements. C4T trainees will develop transferable skills in basic sciences, clinical and qualitative research areas, and will have access to a network of diverse stakeholders to collaborate with across multiple sites.

### **Summary of Select Publications by C4T members:**

#### **[“Efficacy and safety of paediatric medicinal cannabis use: A scoping review”](#)**

Colleen Pawliuk MLIS, Briana Chau BSc, S. Rod Rassekh BSc MD MHSc, Terri McKellar MLIS, Harold (Hal) Siden MD MHSc FRCPC

*Paediatrics & Child Health, 2020*

Introduction: The use of medicinal cannabis in the paediatric age group is increasing despite the lack of evidence for its efficacy or safety. Objective: To map the available evidence on the efficacy and safety of medicinal cannabis in children and adolescents. Methods: We conducted a scoping review and searched six electronic databases and grey literature. A study was eligible for inclusion when it investigated the efficacy or safety of medicinal cannabis for any condition, more than half of the participants were 0 to 18 years old, and had any study design except single case reports. Results: We included 36 studies in our final analysis, 32 of which investigated the efficacy or safety of cannabis in treatment-resistant epilepsy. The remaining 4 studies examined

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patients with cancer, dysautonomia, Epidermolysis Bullosa, and motor disorders. Conclusions: There is a lack of evidence on the efficacy and safety of medicinal cannabis in most paediatric conditions.

**“The impact of cannabis use—a tertiary care paediatric hospital’s experience and approach”**

Connie Cameron RN MN, Yaron Finkelstein MD FACMT, Karen Leslie MD MEd FRCPC

*Paediatrics & Child Health, 2020*

Conversations about cannabis and its impact on the health of children and teens are complex, given the expansion of available sources that now include illicit, medically approved, and as of October 2018, legally sourced cannabis for recreational purposes in adults. Two primary foci of this discussion are *medical* and *recreational* uses of cannabis in children and teens. These different aspects of use, though related, have important distinctions, intended outcomes and potential risks. Health care professionals working with children, teens, and their families need to be able to navigate this complex and evolving dialogue.

In this commentary, we will identify where cannabis use shows up in our institution, The Hospital for Sick Children (SickKids) in Toronto, and describe the experience of developing various interconnected approaches to the identification, assessment, and management of cannabis-related health issues to date. We will also offer some suggested directions on how Canadian health care institutions caring for children might assist patients and family caregivers as the relationship between cannabis and health continues to evolve.

**“Dosage Related Efficacy and Tolerability of Cannabidiol in Children With Treatment-Resistant Epileptic Encephalopathy: Preliminary Results of the CARE-E Study”**

Richard J. Huntsman, Richard Tang-Wai, Jane Alcorn, Stephanie Vuong, Bryan Acton, Scott Corley, Robert Laprairie, Andrew W. Lyon, Simona Meier, Darrell D. Mousseau, Doris Newmeyer, Erin Prosser-Loose, Blair Seifert, Jose Tellez-Zenteno, Linda Huh, Edward Leung and Philippe Major

*Frontiers in Neurology, 2019*

Purpose: There is uncertainty regarding the appropriate dose of Cannabidiol (CBD) for childhood epilepsy. We present the preliminary data of seven participants from the Cannabidiol in Children with Refractory Epileptic Encephalopathy (CARE-E) study. Methods: The study is an open-label, prospective, dose-escalation trial. Participants received escalating doses of a Cannabis Herbal Extract (CHE) preparation of 1:20  $\Delta^9$ -tetrahydrocannabinol (THC): CBD up to 10–12 mg CBD/kg/day. Seizure frequency was monitored in daily logs, participants underwent regular electroencephalograms, and parents filled out modified Quality of Life in Childhood Epilepsy (QOLCE) and Side Effect rating scale questionnaires. Steady-state trough levels (C<sub>ss</sub>, Min) of selected cannabinoids were quantified. Results: All seven participants tolerated the CHE up to 10–12 mg CBD/kg/day and had improvements in seizure frequency and QOLCE scores. C<sub>ss</sub>, Min plasma levels for CBD, THC, and cannabichromene (CBC) showed dose-independent pharmacokinetics in all but one participant. C<sub>ss</sub>, Min CBD levels associated with a >50% reduction in seizures and seizure freedom were lower than those reported previously with purified CBD. In most patients, C<sub>ss</sub>, Min levels of THC remained lower than what would be expected to cause intoxication. Conclusion: The preliminary data suggest an initial CBD target dose of 5–6 mg/kg/day when a 1:20 THC:CBD CHE is used. Possible non-linear pharmacokinetics of CBD and CBC needs investigation. The reduction in seizure frequency seen suggests improved seizure control when a whole plant CHE is used. Plasma THC levels suggest a low risk of THC intoxication when a 1:20 THC:CBD CHE is used in doses up to 12 mg/kg CBD/kg/day.