The Canadian Inherited Metabolic Diseases Research Network:

Initial Findings from a Pan-Canadian Longitudinal Study of Affected Children

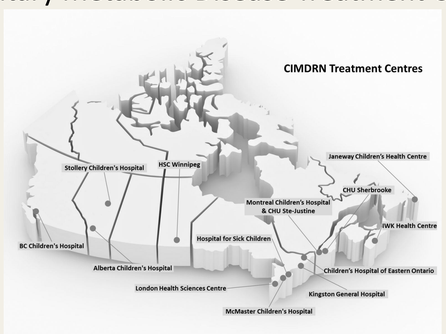
Chakraborty P[1,2], Wilson B[2], Kronick JB[3], Potter BK[2], Lamoureux M[1], Tingley K[2], Coyle D[2], Wilson K[2], Austin V[3], Brunel C[4], Buhas D[5], Chapman M[6], Chan AKJ[7], Dyack S[6], Feigenbaum A[3], Geraghty M[1,2], Giezen A[8], Gillis J[6], Jain S[7], Khan A[9], Langley E[1], Little J[2], MacKenzie J[10], Maranda B[11], Mhanni A[12], Mitchell G[4], Mitchell JJ[5], Nagy L[3], Pender A[13], Potter M[13], Prasad C[14], Siriwardena K[3], Sparkes R[9], Stockler S[8], Trakadis Y[5], Turner L[15], Van Karnebeek C[8], Vallance H[8], Walia J[10], on behalf of the Canadian Inherited Metabolic Diseases Research Network (CIMDRN)

1 Children's Hospital of Eastern Ontario, Ottawa, Ontario 2 University of Ottawa, Ottawa, Ontario 3 Hospital for Sick Children/University of Toronto, Toronto, Ontario 4 CHU Ste-Justine, Montreal, Quebec 5 McGill University/Montreal Children's Hospital, Montreal, Quebec
6 Dalhousie University/IWK Health Centre, Halifax, Nova Scotia 7 University of Alberta, Edmonton, Alberta 8 University of British Columbia/BC Children's Hospital, Vancouver, British Columbia 9 University of Calgary/Alberta Children's Hospital, Calgary, Alberta
10 Queen's University/Kingston General Hospital, Kingston, Ontario 11 University of Sherbrooke/CHU Sherbrooke, Sherbrooke, Quebec 12 University of Manitoba/HSC Winnipeg, Winnipeg, Manitoba 13 McMaster University, Hamilton, Ontario 14 Western University/LHSC London, London, Ontario
15 Memorial University/Janeway Children's Health Centre, St. John's, Newfoundland

The Research Network

Canadian Inherited Metabolic Diseases Research Network

- A national, multidisciplinary practice-based network, established in 2012 with funding from a Canadian Institutes of Health Research Emerging Team grant
- Over 40 investigators in the fields of pediatric care for inherited metabolic disease patients, epidemiology, and health services and policy research
- 14 Hereditary Metabolic Disease Treatment Centres



Objectives: Clinical Research Stream

- CIMDRN's overall goal is to generate observational, practice-based, evidence to improve care and outcomes for children with inherited metabolic diseases (IMD)
- Our research program has 3 streams: (i) clinical research; (ii) patient/family-reported outcomes and experiences; and (iii) health system impacts
- Our **clinical research stream** aims to:
  - provide the patient and family enrollment platform for CIMDRN's entire research program/network
  - describe the longitudinal experience of a population-based cohort of Canadian children with IMD
  - investigate associations between patterns of interventions and clinical outcomes in this cohort
  - support the integration of clinical data with patient-reported and health system data

Methods

Participants:

- Eligible children are born from 2006 to 2015 and receiving care from one of 14 Treatment Centres (consent-based)
- Diagnosed with an IMD from CIMDRN's 30 target disease list (priority diseases, shown in bold, have been selected for more in-depth longitudinal data collection)

Amino acid / urea cycle disorders
Phenylalanine hydroxylase deficiency, Arginase deficiency, Argininosuccinic acidemia, Carbamyl phosphate synthetase deficiency, Citrin deficiency, Citrullinemia, N-acetylglutamate synthetase deficiency, Ornithine transcarbamylase deficiency, Homocystinuria, Maple syrup urine disease, Tyrosinemia type I

Fatty acid oxidation disorders
Medium chain acyl-CoA dehydrogenase deficiency, Very long-chain acyl-CoA dehydrogenase deficiency, Carnitine uptake defect, Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency, Trifunctional protein deficiency

Organic acid disorders
Methylmalonic acidemias, ß-Ketothiolase deficiency, Glutaric acidemia type I, HMG-CoA lyase Deficiency, Isovaleric acidemia , 3-Methylcrotonyl-CoA carboxylase deficiency, Propionic acidemia

Other disorders
Mucopolysaccharidosis I, Guanidinoacetate methyltransferase deficiency, Multiple carboxylase deficiency, Galactosemia, Glycogen storage disease type 1, Pyridoxine-dependent epilepsy

Database:

- Hosted on: REDCap Research Electronic Data Capture
- Used to securely collect retrospective and prospective information from participants' medical charts from all Centres

Data:

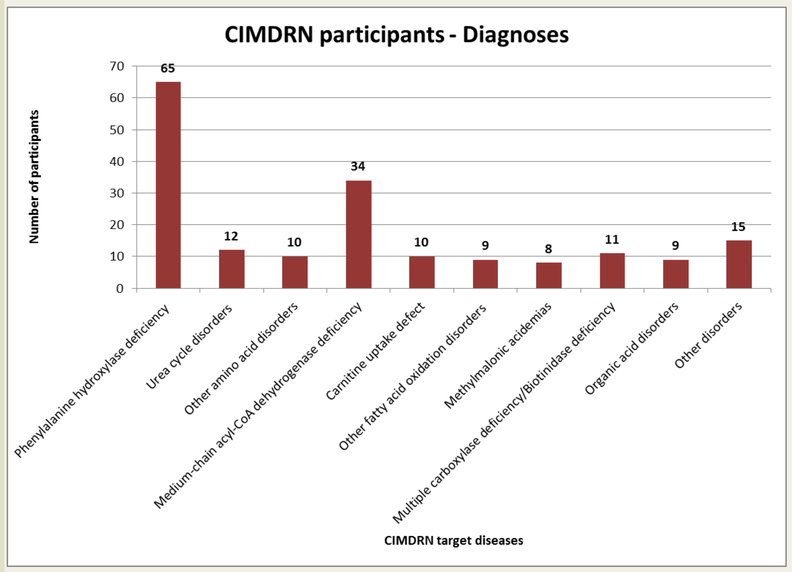
- General and disease-specific data elements, and baseline and longitudinal measures
- Data to support practice-based evidence include: clinical descriptors and indicators of prognosis; interventions received and potential modifiers of intervention effectiveness; clinical outcomes; intermediate indicators of disease management

Results to Date: Participant Enrollment

- In 2014-2015, patient recruitment and data collection began at 8 of the 14 participating Treatment Centres, within the provinces of British Columbia, Alberta, Manitoba, Ontario, Quebec, and Nova Scotia
- To date (March 2015), **185** children have been enrolled (data entered for 183 so far), 11 patients have declined
- The remaining 6 Centres plan to initiate enrollment in 2015; enrollment and data entry ongoing at all Centres

Results to Date: Patient Characteristics

- CIMDRN participants' diagnoses include **24** of CIMDRN's 30 target diseases, the majority with phenylalanine hydroxylase deficiency or medium-chain acyl-CoA dehydrogenase deficiency



- CIMDRN's cohort is **55%** male
- Participating children's current ages are distributed across the eligible range
- Of those participants for whom case ascertainment data have been entered to date (n=105), **76%** have been ascertained by newborn screening
- **14%** of participants are reported to be involved in other research studies

Next Steps

- Analysis plan: appraisal of the database and data collected, description of the participant characteristics and their clinical data, variation between participants' clinical data, and comparison of the clinical outcomes
- Integration of clinical data with patient/family-reported outcomes data (ex. quality of life measures)
- Linkage of clinical data with health administration data (ex. costs of care)

Summary

- **In the first year of patient recruitment, CIMDRN Treatment Centres have enrolled approximately 20% of the eventual planned target of 1000 participants (based on estimated birth prevalence of the included IMD).**
- **We have established a rich and sustainable dataset and have begun analyses to generate the practice-based evidence needed to overcome critical challenges of clinical longitudinal research toward improved care and outcomes for pediatric IMD.**

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Database hosted at: CHEO RESEARCH INSTITUTE

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Administered & supported by: uOttawa Faculté de médecine Faculty of Medicine

Principal Investigators: Beth Potter bpotter@uottawa.ca & **Pranesh Chakraborty** pchakraborty@cheo.on.ca