The Canadian Inherited Metabolic Diseases Research Network: Initial Findings from a Pan-Canadian Longitudinal Study of Affected Children

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 diseases (priority diseases, shown in bold, have been selected for more in-depth longitudinal data collection)

Amino acid / urea cycle disorders
- Phosphoarginine hydroxylase deficiency
- Arginase deficiency, Argininosuccinic aciduria, 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
- Carnitine uptake defect, Long chain 3-hydroxy-CoA dehydrogenase deficiency, Trifunctional protein deficiency

Organic acid disorders
- Methylmalonic aciduria, 3-ketoisovaleric aciduria, Glutaric acidemia type I, HMG-CoA lyase Deficiency, Taururic acidemia, 3-Methylcrotonyl-CoA carboxylase deficiency, Propionic acidemia

Other disorders
- Malonyl-CoA dehydrogenase deficiency, Glycogen storage disease type I, Pyruvate-dehydrogenase deficiency

Database:
- Hosted on: REDCap
- 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: Participant 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

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: www.cimdr.ca Administered & supported by: uOttawa

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