CHRD 2022: Abstract & Poster Submission Form

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Presenter Status

○ Undergraduate Students

○ Masters Student

○ PhD Student

○ Post-Doctoral Fellows

○ Residents

◉ Non-Trainee

Research Category

○ Basic Science

◉ Clinical

○ Community Health / Policy

Role in the project

☐ Design

☐ Perform Experiments

☑ Analyze Data

☑ Write Abstract

☑ Research nurse (recruit & consent participants)

Title

Diagnostic yield of whole exome sequencing for suspected inherited metabolic disorders stratified by clinical features

Background

Advances in genomic technology have revolutionized our ability to make genetic diagnoses. Integrating this technology early in the genetic work-up (the “OMICS First” approach) of patients with possible Inherited Metabolic Disorders (IMDs) has the potential to make a diagnosis quickly and promote earlier access to therapies. However, it is unclear for which phenotypes this approach offers the greatest benefit.

Objective

To evaluate the diagnostic yields for clinical features suggestive of an IMD using data from year 1 of the Canadian Prairie Metabolic Network (CPMN) study.

Methods

The CPMN accepts referrals on undiagnosed patients with possible IMDs. Eligible participants provide an oral sponge sample for whole exome sequencing (WES). To explore diagnostic yields, participants were assigned to groups based on their major clinical features. Participants could be included in >1 group. The proportion of participants with a likely pathogenic/pathogenic variant that explained their phenotype (diagnostic yield) was calculated for each group with a sample size >1.

Results

WES is complete for 55 participants, 53% of whom had no previous genomic studies. The overall diagnostic yield was 24%; Table 1 provides diagnostic yields by clinical feature. Additionally, 40% of participants had at least one variant of uncertain significance, which ultimately may be the diagnosis.

Conclusion

As health care providers continue to consider the “OMICS First” approach for their patients with suspected IMDs, we will further evaluate the diagnostic yields for specific clinical features. We anticipate that the CPMN results will help inform which phenotypes should be prioritized for this approach.

Do you have a table/figure to upload?
◉ Yes ○ No

Diagnostic yield of WES for IMDs stratified by phenotype - Table.pdf

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Title: Diagnostic yield of whole exome sequencing for suspected inherited metabolic disorders stratified by clinical features

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Table 1. Diagnostic yield of WES by clinical feature

Clinical feature	Diagnostic yield of WES
Brain anomaly (n=2)	100%
Seizures (n=11)	55%
Ophthalmologic features (n=11)	46%
Rhabdomyolysis (n=3)	33%
Encephalopathy/neurodegenerative (n=7)	29%
Muscular/neuromuscular (n=24)	21%
Episodic (n=5)	20%
Movement disorder (n=10)	20%
Neuropathy (n=2)	0%
Hypoglycemia (n=4)	0%