SILENT GENOMES- Precision Diagnosis Study Eligibility criteria:

Families meeting ALL 3 POINTS below may be eligible to join this study

1) At least ONE of the proband's parents identifies as First Nations, Inuit or Métis.

2) The proband's condition must meet ONE of the following criteria:

- multiple congenital abnormalities affecting unrelated organ systems
- intellectual disability or global developmental delay or neurodegeneration
- disorder is limited to a single system, is most likely due to a single genomic cause in the patient, but an appropriate targeted test is not available, or available tests were non- diagnostic

3) The proband's condition must meet ALL of the following criteria:

- The condition is medically serious enough to affect quality of life.
- Features of the condition can potentially present in childhood.
- Alternate etiologies have been considered (e.g. environmental exposure, injury, autoimmunity, malignancy, infection).
- The likelihood of identifying an underlying genetic cause is significant. An acceptable probability threshold may vary according to the clinical scenario.
- WGS is more efficient and economical than the separate single-gene tests or panels that would be recommended and readily available, based on the differential diagnosis.
- Identifying the genetic cause through WGS is predicted to have a positive impact on health outcomes, which may include:
    - informing prognosis
    - application of specific treatments as well as withholding of contraindicated treatments
    - surveillance and earlier treatment for later-onset comorbidities
    - changes to goals of care
    - reducing the economic & psychological impact of diagnostic uncertainty
    - informing genetic counselling related to recurrence risk and prenatal diagnosis options
    - avoidance of further invasive diagnostic investigations, follow-up, or screening that would be recommended in the absence of testing