Diagnostic Yield of Exome Sequencing in Adults with Rare Disease: An Eight-Year Retrospective Study

Brooklynn Gasser, MS; Robert Pilarski, MS, CGC; John Ranola, PhD; Meghan C. Towne, MS, CGC; Grace E. VanNoy, MS, CGC

Ambry Genetics®

gvannoy@ambrygen.com Ambry Genetics, Aliso Viejo, CA

BACKGROUND

- Exome sequencing (ES) in pediatric patients has been well-studied and shown to positively impact diagnostic yield and medical management for many indications.
- Access to ES in adults can be limited due to the relative novelty of this test and age restrictions set by some insurance companies.
- The utility of ES in adults remains poorly defined due to limitations of prior studies, including small study populations, narrow phenotypic scope, and/or specialized inclusion criteria or analysis methods.

AIM: Characterize a cohort of adults with rare disease to identify factors that impact diagnostic yield and predict the benefit of ES.

METHODS

Retrospective Review: patients ages ≥18y with ES from 2016 - 2024

FACTORS: Age | Sex at Birth | Race/ Ancestry | Indication for testing | Family Structure

Family Structure: Parental trio | Non-parent trio | Duo | Proband-only

A logistic regression was used to assess the impact of demographic factors and family structure on the likelihood of receiving a diagnosis

RESULTS

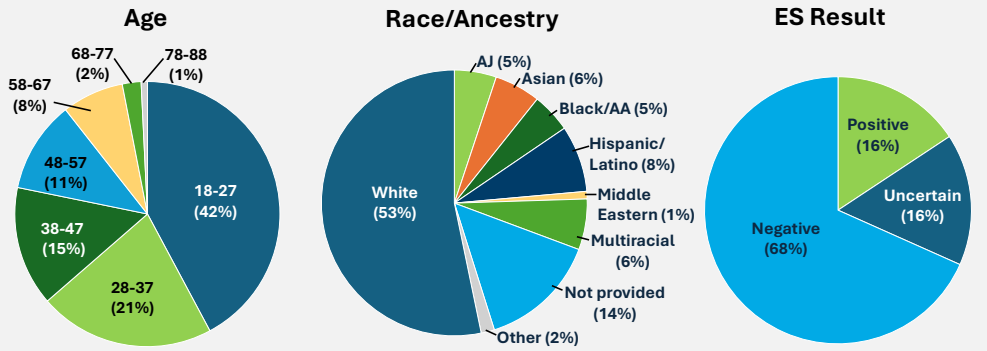

Figure 1. Summary of overall cohort characteristics.

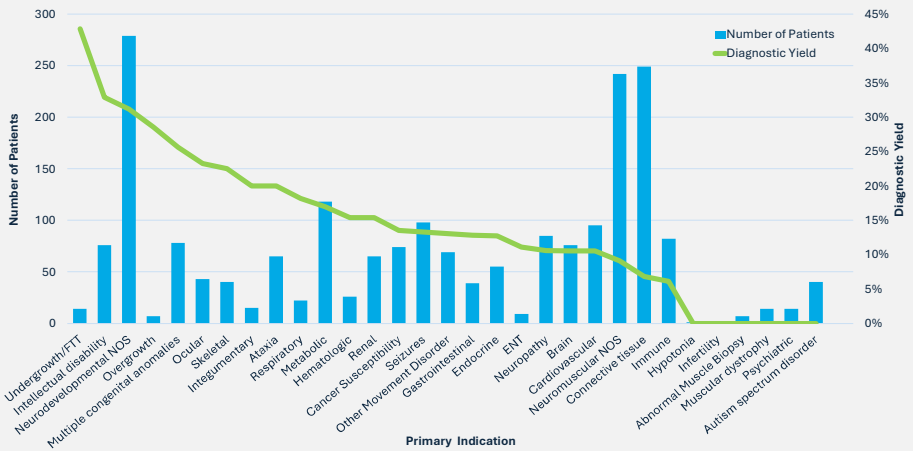

Figure 2. Number of patients and diagnostic yield by primary indication.

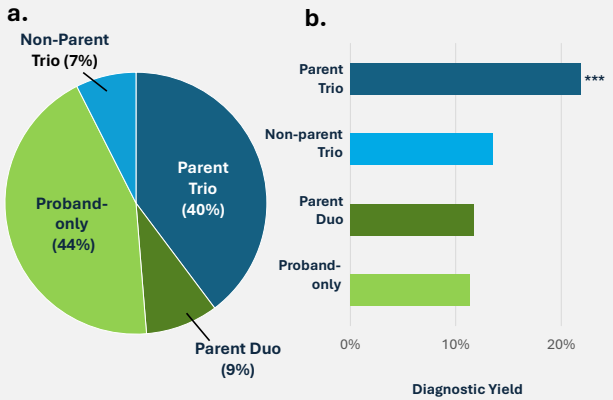

Figure 3. Impact of family structure. **a).** Overall cohort by family structure. **b).** Parent trio analysis significantly increased diagnostic yield to 21.8% (p=7.65E-5)

TAKE HOME POINTS

- The **overall diagnostic yield of 15.7%** in this adult cohort is likely negatively impacted by reduced parental availability and low-yield indications.
- **Parental trio family structure** significantly increases the likelihood of a diagnosis.
- **ES as a first-tier test in adults** with high-yield indications should be explored to improve access for adults who could benefit from testing.